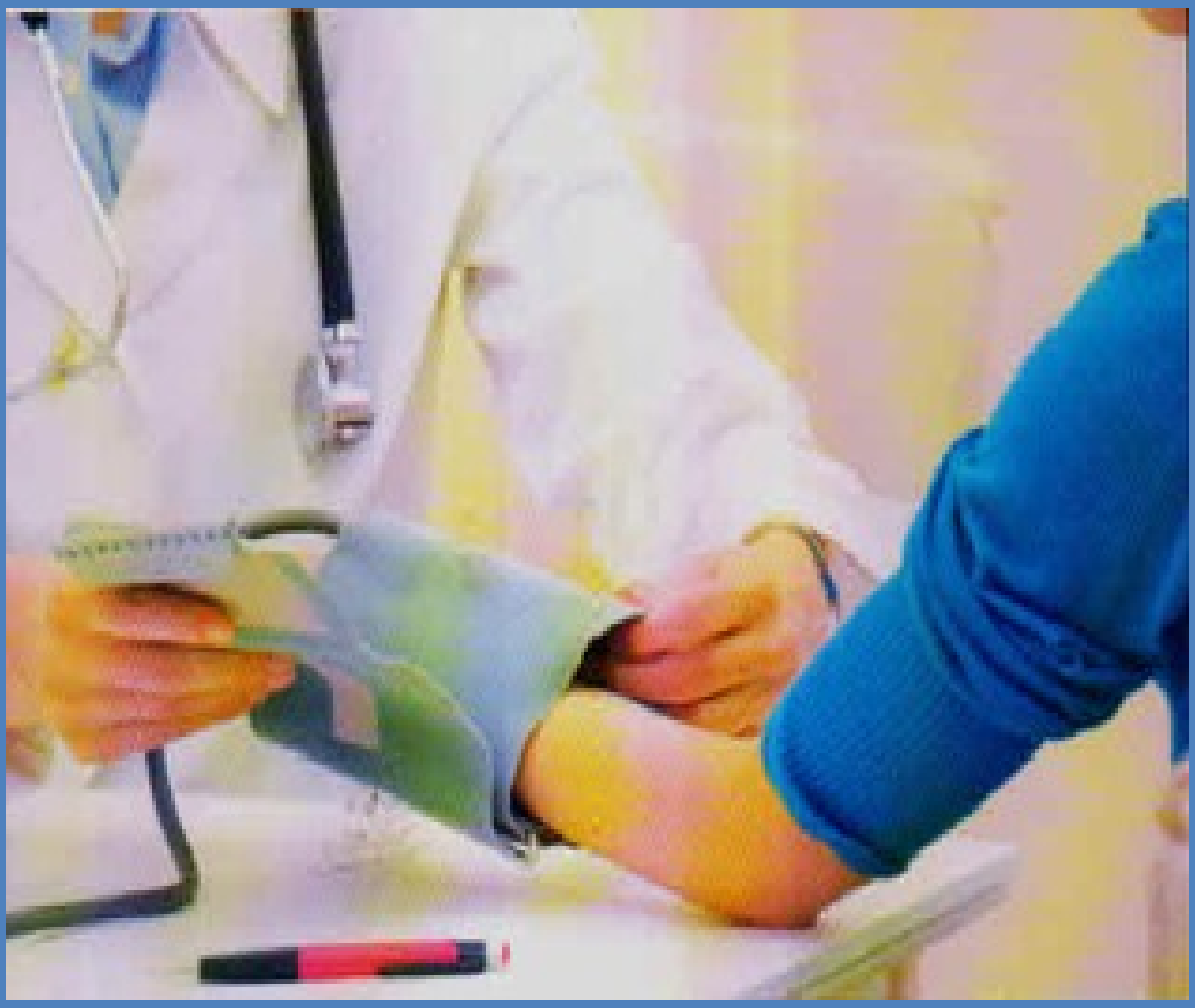
GENERAL PRACTICE

Part 1



Dr Osama Alagamawy

وَقُلِ اعْمَلُواْ فَسَيَرَى اللّهُ عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ وَسَتُرَدُّونَ إِلَى عَالِمِ الْغَيْبِ وَالشَّهَادَةِ

فَيُنَبِّئُكُم بِمَا كُنتُمْ تَعْمَلُون ۝ (التوبة-105)

Say, Work righteousness; GOD will see your work, and so will His messenger and the believers. Ultimately, you will be returned to the Knower of all secrets and declarations, then He will inform you of everything you had done.

Al-Tawba Verse No: 105

Dedication

To the soul of my mother

Letter to the Student

Dear Student,

Welcome to the exciting , fascinating world of general practice! Up to now in your studies, you have been learning the normal features of human beings (i.e. anatomy, physiology, etc). Now it is time to introduce you to the abnormalities that can occur in humans -i.e. to diseases. General practice is a vast & complicated field that is based on strong scientific & clinical foundations. Moreover it is rapidly evolving & one needs periodic updating & catching up ē the state of the art knowledge. Providing a comprehensive review of General practice is not only difficult but almost impossible, as the field is vast & extensive. Despite this limitation, i have tried to provide a basic framework for working knowledge of General practice. Essential topics are included as much as possible & some chapters & topics are dealt extensively, such as Infectious diseases in general & acute febrile illnesses, Hepatitis, Tuberculosis & HIV/AIDS in particular, as these are known to be the commonest causes of morbidity & mortality in developing countries, like ours, also parasite infestations ẃ is common in many African countries. This Book has been written primarily for medical students & all other health science students who deal é pts, who have medical illnesses. In this book, you will find the practical skills in diagnosis; how to read an ECG, how to do LP, measuring BP, jugular venous pulse, how to do thoracentesis, how to examine cranial nerves, etc. Also management of diseases, é emphasise on drug doses, side effects of drugs. The book is divided into 14 chapters on; Infectious Diseases, Hematologic Diseases, Disease of Respiratory System, Diseases of Cardiovascular System, Diseases of Kidneys, Diseases of Gastrointestinal System, Disease of Metabolism & Endocrine System, Diseases of Nervous System, Connective Tissue & Joints Diseases, Dermatology, Ophthalmology, Surge-

ry, Gynaecology, Psychology & followed by Multiple choice questions & their answers, in a simple, illustrative way to make it easy to understand, also it contains illustrative diagrams, photos and tables. Most of the topics represent the major categories of diseases. Therefore, after reading this book, you are encouraged to read books on different medical fields, because the book conceived when the previous curriculum was being implemented. In writing this book, I have tried to make it as clear & as brief as possible. Since too much brevity may compromise understanding, i have been a bit "liberal" in some areas including some details ẃ are necessary for the general practitioner's understanding. This is done to encourage understanding rather than memorization. This "book-part 1" will be followed by "part 2" ẃ will cover Perinatology & Paediatrics, - it is intended to be a textbook of general practice for medical students & those preparing for post graduate studies, even those beyond can use this book for review.

Dr. Osama Alagamawy

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ALPHABETICAL INDEX

ABBREVIATIONS & ACRONYMS

&	And
ē	With
éout	Without
2HPPBS	2 Hours Post Prandial Blood Sugar
5-HT	5 Hydroxy Treptophan
a.m.	At Morning
A1C	Glycosylated haemoglobin
ABC	Airway, Breathing, Circulation
ABG	Arterial Blood Gas
ABs	Antibodies
ACEIs	Angiotensin Converting Enzyme Inhibitors
ACTH	Adrenocorticotrophic Hormone
AD	Autosomal Dominant
ADH	Antidiuretic Hormone
AEDs	Anti-Epileptic Drugs
AF	Atrial Fibrillation
AFB	Acid Fast Bacilli
AFP	Alpha Feto Protein.
AIDS	Acquired Immunodeficiency Syndrome
ALT/SGPT	Alanine Aminotransferase
AMI	Acute Myocardial Infarction
Amp	Ampule
ANA	Antinuclear Antibodies
ANC	Antenatal Care
APOC	African Programme for Onchocerciasis Control
APTT	Activated Partial Thromboplastine Time
AR	Autosomal Recessive/ Aortic Regurgitation
ARDS	Adult Respiratory Distress Syndrome
ARF	Acute Rheumatic Fever/Acute Renal Failure
ARTs	Antiretroviral Therapies / Assisted Reproductive Technology
AS	Aortic Stenosis
ASA	Acetyl Salicylic Acid
ASD	Atrial Septal Defect
ASIS	Anterior Superior Iliac Spine
ASOT	Antistreptolysin O Titre
AST/SGOT	Aspartate Amino Transferase
ATN	Acute Tubular Necrosis
AV	Aortic Valve
AV Block	Atrioventricular Block
Bact	Bacteria
BCC	Basal Cell Carcinoma
BCG	Bacilli Calmette Guerin
BF	Blood Film

BG Blood Glucose
BID Twice A Day
BLCM Below Left Costal Margin
BM Bone Marrow
BMI Body Mass Index
BMR Basal Metabolic Rate
BMT Bone Marrow Transplant
BP Blood Pressure
BPH Benign Prostatic Hypertrophy
bpm Beat Per Minute
BS Blood Sugar
BT Bleeding Time
BUN Blood Urea Nitrogen
BW Body Weight
CA Carbohydrate Antigen
Ca. Ch. Bl. Calcium Channel Blockers
CA`s Coronary arteries
Ca^{++} Calcium
CAD Coronary Artery Disease
CAH Congenital Adrenal Hyperplasia
CAP Community Acquired Pneumonia
CBC Complete Blood Count
CEA Carcino Embryonic Antigen
Ch Chronic
CHD Congenital Hip Dislocation
CHD Coronary Heart Diseases/Congenital Heart Disease
CHF Congestive Heart Failure
CHO Carbohydrates
CIDP Chronic Inflammatory Demyelinating Polyneuropathy
CLL Chronic Lymphocytic Leukaemia
Clost Clostridium
CMV Cytomegalovirus
CNS Central Nervous System
COMTI Catechol O-Methytransferase Inhibitors
COP Cardiac Out Put
COPD Chronic Obstructive Pulmonary Disease
CPK Creatine Phosphokinase
CPPDC Calcium Pyrophosphate Dihydrate Crystals
CPT Chemoprophylaxis Therapy
Cr Creatinine
CRA Chronic Rheumatoid Arthritis
CRC Colo Rectal Cancer
CRD Chronic Renal Disease

CRF Chronic Renal Failure
CRH Corticotrophic Hormone
CRS Congenital Rubella Syndrome
CSF Cerebrospinal Fluid
CT Computerized Tomogram / Chemo Therapy/ Connective Tissues
CTD Connective Tissue Disease
CTLS Cytotoxic T Lymphocytes
CVD Cerebrovascular Diseases
CVP Carotid Venous Pulse / Central Venous Pressure
CVS Cardiovascular System
CXR Chest X-Ray
D/C Discontinue
D4T Stavudin
DA Dopamine
DAT Direct Agglutination Test
DBP Diastolic blood pressure
DDI Didanosine
DECT Dual Energy Computerized Tomography
Def Deficiency
DHF Dengue Haemorrhagic fever
DIC Disseminated Intravascular Coagulopathy
DIPJ Distal Intererphalangeal Joint
Direct IF Direct Immunofluorescent
DKA Diabetic Ketoacidosis
DM Diabetes Mellitus
DMARDs Disease Modifying Antirheumatic Drugs
DNA Deoxyribonucleic Acid
DOTS Directly Observed TB Treatment Short Course
DW Dextrose In Water
EB Epidermolysis Bullosa
EBV Epstein-Barr Virus
ECFV Extracellular Fluid Volume
ECG Electrocardiogram
EF Ejection Fraction
EFV Efavirenz
eGFR Estimated Glomerular Filtration Rate
ELISA Enzyme Linked Immunosorbent Assay
EN Erythema Nodosum
EP TB Eextra Pulmonary Tuberculosis
EPP Erythrocyte Protoporphyrin
ESR Erythrocyte Sedimentation Rate
ESRD End Stage Renal Disease
ETB Ethambutol
ETT Endotracheal Tubes

F/H Family History
FAB French-American-British
FBC Full Blood Count
FBG Fasting Blood Glucose
FEV Forced Expiratory Volume
FSH Follicle Stimulating Hormone
FT AB Florescent Treponima Pallidum Absorption Test
G6PDD Glucose 6 Phosphate Dehydrogenase Deficiency
GABA Gama Aminobutyric Acid
GAS Group A Streptococci
GBS Guillain-Barre Syndrome
GCS Glasgow Coma Scale
GDM Gestational Onset Diabetes Mellitus
GF Glomerular Filtration
GFR Glomerular Filtration Rate
GH Growth Hormone
GHIH Growth Hormone Inhibitory Hormone
GHRH Growth Hormone Releasing Hormone
GI Gastrointestinal
GIT Gastrointestinal Tract
GN Glomerulonephritis
GP General Practice
GTC Generalized Tonic Colonic
GTT - Glucose Tolerance Test
HAART Highly Active Antiretroviral Treatment
HAV Hepatitis A Virus
Hb Haemoglobin
HBcAg Hepatitis B Core Antigen
HBe Ag Hepatitis B Envelope Antigen
HBIG Hepatitis B Immunoglobulin
HBsAg Hepatitis B Surface Antigen
HBV Hepatitis B Virus
HCG Human Chorionic Gonadotrophine
HCM Hypertrophic Cardiomyopathy
HCV Hepatitis C Virus
HD Hodgkin`s Disease
HDL High-Density Lipoprotein
Hge Haemorrhage
HHV-8 Human Herpes Virus-8
HIV Human Immunodeficiency Virus
HOCM Hypertrophic Obstructive Cardio Myopathy
HPV Human Papilloma Virus
HTLV-I Human T-Cell Leukaemia-Lymphoma Virus-I

Hx History
IADHS Inappropriate Anti Diuretic Hormone Secretion
IC Hge Intra Cranial / Intracerebral Haemorrhage
ICF Intracellular Fluid
ICS Intercostal Space
ICU Intensive Care Unit
IDA Iron Deficiency Anaemia
IE Infective Endocarditis
IEM Inborn Error Metabolism
IGT Impaired Glucose Tolerance
IHD Ischemic Heart Disease
IM Intramuscular
INH Isoniazid
IP Incubation Period
ITP Idiopathic Thrombocytopenic Purpura
IUDS Intra Uterine Devices
IV Intravenous
IVDU Intravenous Drug Use
IVIG Intra Venous Immuno Globulin
JHR Jarisch Herxheimer Reaction
JVP Jugular Venous Pressure
K^+ Potassium
KS Kaposi Sarcoma
KUB Kidney Ureter Bladder
LAH Left atrial hypertrophy
LBBB Left Bundle Branch Block
LBRF Louse Borne Relapsing Fever
LBW Low-Birth-Weight
LDH Lactate Dehydrogenase
LDL Low-Density Lipoprotein
LFT Liver Function Tests
LGA Large For Gestational Age
LGV Lymphogranuloma Venereum
LH Luetenizing Hormone
LL Lower Limbs
LLSB Lower Left Sternal Border
LMWH Low Molecular Weight Heparin
LNs Lymph Nodes
LP Lumbar Puncture
LV Left Ventricle
LVF Left Ventricular Failure
LVH Left Ventricular Hypertrophy
m.m. Mucous Membrane
MAC Mycobacterium Avium Complex

MALT Mucosa-Associated Lymphatic Tissue
MCH Mean Corpuscular Hb
MCHC Mean Corpuscular Hb Concentration
MM Multiple Myeloma
MCL Mid Clavicular Line
MCV Mean Corpuscular Volume
MDR Multidrug Resistance
MGUS Monoclonal Gammopathy of Undetermined Significance
MI Myocardial Infarction
Min Minute
MODY 1, 2, 3 Maturity Onset Diabetes of the Young 1,2,3
MON Month
MPJ Metacarpophalangal Joints
MR Mitral Regurgitation / Mental Retardation
MRI Magnetic Resonant Imaging
MS Mitral Stenosis
MTCT Mother To Child Transmission
MV Mitral Valve
MVP Mitral Valve Prolapse
N/S Normal Saline
Na^+ Sodium
NCTs Nerve Conduction Test
NE Nor Epinephrine
NG Naso Gastric
NHD Non-Hodgkin`s Disease
NHP Non-Dihydropyridine
NK Cells Natural Killer Cells
NN Neonate
NPO Nothing Per Oral
NS Norma Saline
NSAIDs Non-Steroidal Anti-Inflammatory Drugs
NTD Neural Tube Defect.
NVE Native Valve Endocarditis
OCD Obsessive Compulsive Disorder
OCP Oral Contraceptive Pills
OEPA Onchocerciasis Elimination Program for Americas
OIs Opportunistic Infections
OLD Obstructive Lung Disease
OMs Opportunistic Malignancies
OPD Out Patient Department
ORS Oral Rehydration Solution
P TB Pulmonary Tuberculosis
P/E Physical Examination
PAD Pelvic Inflammatory Disease

PaO_2 Partial Pressure of Arterial Oxygen
PCP Pneumocystis Carinii Pneumonia
PCOS Poly Cystic Ovarian Syndrome
PCR Polymerase Chain Reaction
PD Parkinson's Diseases
PDA Patent Ductal Arteriosus
PFT Pulmonary Function Test
PGH Prostatic Growth Hormone
PGL Persistent Generalized Lymphadenopathy
Ph^{++} Phosphate
PIC Hge Primary Intracerebral Haemorrhage
PIPJ Proximal Interphalangeal Joint
PLWHA People Living With HIV/AIDS
PML Progressive Multifocal Leukoencephalopathy
PMTCT Prevention of Mother To Child Transmission
PND Paroxysmal Nocturnal Dyspnoea
PO Per Oral
PPD Purified Protein Derivative
PPMS Primary-Progressive Multiple Sclerosis
ppt Precipitate
PRM Premature Rupture Membrane / Prolonged Rupture Membrane
PRMS Progressive-Relapsing Multiple Sclerosis
PSVT Paroxysmal Supraventricular Tachycardia.
Pt Patient
PT Prothrombin Time
PTT Partial Thromboplastine Time
PTU Propylthiouracil
PUD Peptic Ulcer Diseases
PVCs Premature Ventricular Contractions
PUVA Psoralen & long-wave Ultra Violet radiation
PVS Permanent vegetative state
PZA Pyrazinamide
QD Once A Day
QID Four Times A Day
R/O Rule Out
RA Rheumatoid Arthritis
RAD Right Axis Deviation
RAH Right Atrial Hypertrophy
RAS Reticular Activating System
RBBB Right Bundle Branch Block
RBCs Red Blood Cells
RBS Random Blood Sugar
RD Respiratory Distress

Resp Respiratory
RF Relapsing Fever/Rheumatic Fever
RFT Renal Function Tests
RHD Rheumatic Heart Disease
RIF Rifampicin
RNA Ribonucleic Acid
RPR Rapid Plasma Reagin
RRMS Relapse-Remitting Multiple Sclerosis
RSV Respiratory Syncytial Virus
RT Radio Therapy
Rt-PA Recumbent Tissue Plasminogen Activator
RVH Right Ventricular Hypertrophy
Rx Treatment
S1 First Heart Sound
S2 Second Heart Sound
S3 Third Heart Sound
S4 Fourth Heart Sound
SA Hge Sub Arachnoid Haemorrhage
SBP Systolic Blood Pressure
SC Subcutaneous
SCC Squamous Cell Carcinoma
SCT Sub Cutaneous Tissue / Stem Cell Transplants
Sec Second
Seiz Seizures.
Ser Serum
SGA Small for Gestational Age
SGOT Serum Glutamic Oxaloacetic Transaminase
SIE Subacute Infective Endocarditis
SLE Systemic Lupus Erythrematosis
SNRIs Serotonin-Norepinephrine Reuptake Inhibitors
Sol Solution
SPMS Secondary-Progressive Multiple Sclerosis
SSRI's Serotonin Specific Reuptake Inhibitors
STDs Sexually Transmitted Diseases
Sy Syndrome / Syrup
tab Tablet
TB Tuberculosis
TBRF Tick Borne Relapsing Fever
TCAs Tri Cyclic Antidepressants
TEE Trans Esophageal ECHO
Temp Temperature
TFT Thyroid Function Tests
TIA Transient Ischemic Attack

tid Three times daily
TLCP TB Leprosy Control Programme
TM Trimester
TMJD Temporo Mandibular Joint Disorders
TMP-SMX Trimethoprim-Sulfamethoxazole
Tn I Troponin I
TOF Tracheo Oesophageal Fistula
TR Tricuspid Regurgitation
TRH Thyroid Releasing Hormone
TSH Thyroid Stimulating Hormone
TSIBC Total Serum Iron Binding Capacity
TST Tuberculin Skin Test
TTE Transthoracic ECHO
TTP Thrombotic Thrombocytopenic Purpura
u Unit
U/S Ultrasound
UL Upper Limb
UMNL Upper Motor Neurone Lesion
URTI Upper Respiratory Tract Infection
UT Urinary Tract
UTI Urinary Tract Infection
UVA Ultraviolet A
VDR Venereal Disease Research Laboratory
Vs Versus
VSD Ventricular Septal Defect
VWF Von Will brand Factor
VZV Varicella Zoster Virus
ẃ Which
WBC White Blood Cells
WHO World Health Organization
Wt Weight

CHAPTER 1

INFECTIOUS DISEASES

- *Introduction*
- *Human Immunodeficiency Virus &AIDS*
- *Tuberculosis*
- *Meningitis*
- *Viral Encephalitis*
- *Tetanus*
- *Rabies*
- *Sexually Transmitted Diseases*
- *Typhoid*
- *Brucellosis*
- *Anthrax*
- *Impetigo*
- *Typhus*
- *Relapsing Fever*
- *Helmenthiasis & Parasitic Diseases*
- *Yellow Fever*
- Kawasaki Disease
- Ebola Haemorrhagic fever
- Dengue Fever
- Avian Influenza

INTRODUCTION

Generally infectious diseases result from bacteria, viruses, fungi or parasites. Despite decades of dramatic progress in their treatment & prevention, infectious diseases remain a major cause of death & are responsible for worsening the living conditions of many millions people around the world. Infections frequently challenge the clinician's diagnostic skill. Many factors affect the likelihood of acquiring infection ẃ include, host, environmental & microbial factors, host & environmental factors. For any infectious process to occur, the parasite & the host must first encounter each other. Factors such as geography, environment disease vectors & host behaviour thus influence the likelihood of infection. Many host factors as age, immunization, prior illness, nutritional status, pregnancy, coexisting illnesses & emotional status all have some impact on the risk of infection after exposure to particular pathogen. Medical care itself can ⇧ the pt's risk of acquiring an infection ẃ can occur in several ways; either through contact é the pathogen during hospitalization or through injections, surgical incisions, via mucosal surfaces by ETT or bladder catheters, or through introduction of foreign bodies, or through alteration of the natural flora é antibiotics, or through Rx é suppressive drugs as steroids. Infection involves complicated interaction between parasites & host. In most cases a pathogenic process consisting of several steps is required for the development of infection. Since the competent host has a complex series of defence mechanisms to prevent infection, the successful parasite must utilize specific strategies at each of these steps. The specific strategies used by bacteria, viruses & parasites have some similarities, but the details are unique not only for each class of organism but also for individual species in each class.

Microbial virulence strategies

Microbes have developed variety of strategies for escaping immunity e.g. some organisms elaborate toxins/enzymes that facilitate the invasion of the host & often responsible for the disease state & many bacteria are encapsulated é polysaccharides that allow them to invade & deposit in the absence of specific antibodies.

Immune response

Is a defensive mechanism developed by the host for recognizing & responding to microorganisms. Is divided into 2 major classes:-

(1) Natural immunity: is the first line of defence, serves to protect the host éout prior exposure to the infectious agent. This immune response is nonspecific & has no memory. Examples of natural immunity include; intact skin & mm, ciliary function, phagocytosis by macrophages & neutrophils & complement system.

(2) Acquired immunity: specific immune mechanism developed against particular organism. It takes time to develop & it has long standing memory & has 2 arms:-

a) Cellular immunity: comprising T-lymphocytes, & natural killer cells.

b) Humeral: comprises of B-Lymphocytes & antibodies produced by plasma cells.

Laboratory diagnosis

Diagnosis of infections requires the demonstration of organism either;

1. Direct microscopic visualization of pathogens in clinical material or the growth of microorganisms in culture.

2. Indirect e.g. antibody/serology test, of viral, bacterial, mycotic, or parasitic agents in fluids, tissues, or excreta of the host.

Treatment

Optimal Rx for infectious diseases requires broad knowledge of medicine & careful clinical judgment. Life threatening infections as bacterial meningitis/sepsis require urge-

nt initiation of Rx often before a specific infective organism identified. Antimicrobial must be chosen empirically & must be against the range of potential infectious agents consistent é the clinical condition.

HUMAN IMMUNE DEFICIENCY VIRUS

Chronic infectious disease caused by HIV, characterized by spectrum starting from 1ry infection é or éout acute syndrome, followed by relatively long period of asymptomatic stage after ẃ in most pts progress to advanced &life threatening disease. The disease was 1st recognized in 1981, in USA among homosexual males. HIV was clearly demonstrated in 1984 to be a causative agent for AIDS.

Epidemiology

The number of people living é HIV rose from around 8 million in 1990 to 34 million by the end of 2011, out of ẃ 2.3 million were children & 17.7 million were women. According to WHO, an estimated 2.1 million individuals worldwide became newly infected é HIV in 2013. Sub-Saharan Africa is the worst affected region é 25.7 million living é HIV, out of ẃ 2.1 million are children <15 yrs. The overall adult prevalence in this region is 5.9% & about 2.1 million deaths yearly. The incidence in many African countries varies from 5-30% of population. The IP is 1-3 yrs.

Aetiology

HIV is retrovirus belongs to the subfamily of lente virus. There are 2 main types of the virus & many subtypes including:-

HIV-type 1: is the most common cause of HIV disease throughout the world & it has several groups & subtypes include the following:-

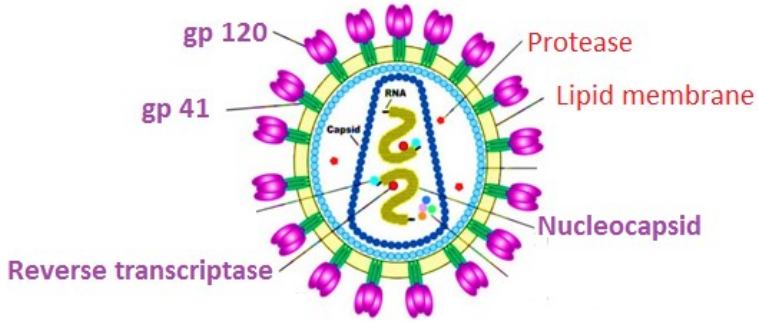
M group ẃ comprises 9 subtypes (A, B, C, D, F, G, H, J, K) as well as growing number of major circulating recombinant forms (e.g. AE, AG).

O group is relatively rare seen in Cameron & Gambia.

N group reported only in Cameron. In Africa: >75% of strains recovered to date have been subtypes A, C & DC. In Europe & Americas the subtype B is the predominant strain. In Asia the recombinant forms such AE account of infections in South East Asia while subtype C is prevalent in India.

HIV-type 2 mostly confined to West Africa.

Morphology & characters



HIV is spherical shaped, the viral envelop is the most important part of the virus, has many small spikes consists of 2 important glycoproteins (gp), the gp 41 & gp 120, play an important role when the virus attaches to its host cells. The other important part of the virus is the viral capsid (core) ẃ contains 2 single stranded viral RNA & an important enzyme for the virus called reverse transcriptase enzyme ẃ plays important step in the life cycle of the virus, it converts the single stranded viral RNA into double stranded DNA (this process is called reverse transcription). HIV infect cells that express CD4 receptor molecules ẃ are present on various types of blood cells including lymphocytes, macrophages, monocytes, tissue cells (e.g. dendritic cells in genital tract & anorectic region) & glial cells of brain.

Pathogenesis

CD4 +ve T-Lymphocytes (T helper cells) play central role in body defence mechanism against infection, they mainly coordinate the cell mediated immune system & also assist the antibody mediated immune system. HIV has special affinity to CD4 T-cells &

infects them. HIV infection characterized by profound immunodeficiency from progressive decline of T-helper cells.

Mode of transmission of HIV

Sexual transmission

Is major mode of transmission worldwide (90%). The virus was found in high quantities in the sexual fluids (seminal & vaginal fluid) of people é HIV infection, within the infected monocytes & in cell-free state. Anal sex appears to be the sexual practice carrying the highest risk of transmitting HIV. The reasons being rectal mucosa is thin, fragile & there are susceptible cells (Langerhans cells) in rectal mucosa. Vaginal sex also carry effective risk for transmission. The presence of other STDs as syphilis, gonorrhoea ⇧ the risk of acquiring or tran-smitting HIV infection by several fold, as the quantity of virus in seminal or vaginal fluid significantly ⇧ & the number of infected monocyte is high around the genital area in pts é STDs.

Transmission through blood & blood products

IV drug abusers who share needles & syringes have high risk. Blood or blood products transfusion from infected donors (risk of infection is 90-100%). Transmission through sharp instruments, needles. There may be a risk of transmission from one pt to another or from an infected pt to health care provider.

Mother to child transmission

The risk of mother to child transmission is 30-45%. HIV may be transmitted from infected mothers to foetus during pregnancy (10% before the 3rd TM & 70% in late pregnancy or during labour), or through breast feeding in 10-15% of cases. Mother to child transmission is by far the largest source of HIV infection in children <15yrs.

Clinical picture

The clinical consequences of HIV infection encompass a spectrum ranging from acute

syndrome associated é primary infection to a prolonged asymptomatic state to advanced disease. Pt may present é recurrent bacterial, fungal or viral infection, failure to thrive, delayed milestones &wasting. In particular the pt is very susceptible to pneumocystis carinii, CMV, toxoplasma, infectious mononucleosis, Kaposi's sarcoma, chronic diarrhoea & STDs.

Primary HIV Infection

Some pts are asymptomatic but 50% of infected individuals experience an acute clinical syndrome 3-6 wks after the primary infection. A flue like syndrome in ẃ symptoms persist from one to several wks & gradually subside. The typical presentation incl udes: •Fever. •Pharyngitis. •Lymphadenopathy. •Headache. •Arthralgia. •Myalgia. •Malaise. •GIT symptoms; anorexia, nausea, vomiting, diarrhoea. •Erythematous maculopapular rash & mucocutaneous ulceration. •Neurological symptoms; aseptic meningoencephalitis, HIV in CSF & peripheral neuropathy. Most pts (90%) recover spontaneously & 10% manifest a fulminate course of immunologic & clinical deterioration.

Asymptomatic stage-clinical latency

In most (90%) of pts, 1ry infection é or éout the acute syndrome is followed by prolonged period of clinical latency. The length of time from initial infection to the development of clinical disease varies greatly (median is 7-10 yrs). Viral replication continues during this period. So there is no virologic latency. Rate of disease progression is directly correlated é HIV RNA levels. Pt é high levels of HIV RNA progress to symptomatic disease faster than do pt é low levels of HIV RNA. The CD4 cell count fall progressively during this stage at an average rate of 50 cells/µl/year.

Early symptomatic diseases: pt begin to develop signs & symptoms when CD4 cell count is <500/µl. The clinical findings include:-

①Generalized lymphadenopathy: enlarged LNs (>1 cm) in 2 or more extra inguinal sit-

es for >3 months éout obvious cause. Is often the earliest symptom of HIV infection after the 1ry infection.

②Oral lesions: usually indicative of fairly advanced immunologic decline, occurring in pt é CD4 count ˂300/µl. include:-

Oral thrush; ẃ appears as a white, cheesy exudates, often on an erythematous mucosa (most commonly seen on the soft palate) ẃ gives an erythematous or bleeding surface on scraping. When it involves the oesophagus, pt complain of pain on swallowing. Is due to candidiasis.

Oral hairy leucoplakia; appears as filamentous white lesion, generally along the lateral borders of the tongue. Is presumed due to EBV.

Apthous ulcer; ulcer on oral cavity or pharynx of unknown aetiology, usually are painful & may interfere é swallowing.

Herpes zoster (shingles) seen in 20% of pts. It is a reactivation syndrome of VZV. Indicates a modest decline in immune function & is often the 1st clinical indication of immunodeficiency. Lesions usually localized to a single dermatome & may extend over several dermatomes. A Frank cutaneous dissemination may be seen. It has a relapse rate of 20%.

③Thrombocytopenia: has immunologic base (due to autoimmune destruction of platelets). Very similar to ITP. Since most pts have platelet count ˃50.000/µl, serious clinical problem are seen rarely. In some pts, when platelet count falls <10.000 clinical symptoms as bleeding of gums or extremity petechiae & easy bruisability are common presenting features. The bone marrow examination is normal or may show ⇧ in the megakaryocytes.

④Other clinical conditions: Molluscum contagiosum. Recurrent bouts of oral or genital herpes simplex & condylomata accuminata.

Staging of HIV/AIDS

There are different types of staging systems. The most common are:-

WHO Clinical Staging System for HIV/AIDS: designed for estimating the degree of immunosuppression on clinical criteria. Intended for use in pts. known to have HIV (i.e. HIV +ve antibody test). It is widely used in resource limited settings to make decisions as to when to start pt. on ART. According to this there are 4 clinical stages as shown in the following table:

stage 1	Asymptomatic
stage 2	Minor symptoms
stage 3	Moderate symptoms
stage 4	AIDS defining illnesses

Stage 1: •Asymptomatic. •PGL: defined as the presence of L.N. >1 cm size, in 2 extrainguinal sites & persisting for > 3 months.

Stage 2: •Unexplained moderate Wt loss (<10% of BW). •Recurrent URTI (sinusitis, tonsillitis, otitis media, pharyngitis). •Minor mucocutaneous manifestations (seborrheic dermatitis, fungal nail infections, recurrent oral ulcerations, angular chelitis).•Herpes zoster within the past 5 yrs (single dermatome).

Stage3: •Unexplained severe Wt loss (>10% of BW). •Unexplained chronic diarrhoea >1 month. •Unexplained prolonged fever >1 month. •Persistent oral candidiasis. •Oral hairy leucoplakia. •Pulmonary TB. •Severe bacterial infection (pneumonia, pyomyositis, meningitis, bacteraemia), acute necrotizing ulcerative stomatitis, gingivitis or periodontitis. •Unexplained anaemia (<8 gm/dl), neutropenia 500 /mm^3 &/or chronic thrombocytopenia (platelets <50,000/mm).

Stage 4: •HIV wasting syndrome. •Pneumocystis carinii pneumonia. •CNS toxoplasmosis. •Cryptosporidiosis or Isosporosis related watery diarrhoea >1month. •Extrapu-

lmonary cryptococcosis. •CMV disease of organ other than liver, spleen, or LNs (e.g. retinitis). •Chronic herpes simplex infection as labial, genital or anorectal lasting for ›1 month. •Disseminated mycosis (as histoplasmosis, coccidiodomycosis). •Oesophageal candidiasis (or involving trachea, or lungs). •Recurrent bacterial pneumonia. •Recurrent septicaemia. •Disseminated atypical mycobacterium. •Extrapulmonary TB. •Lymphoma (cerebral or B-cell non-Hodgkin). •Invasive cervical carcinoma. •Kaposi's sarcoma. •HIV encephalopathy. •HIV associated neuropathy.

The CDC staging system

Stage	CD4 count	CD4 %	Clinical Evidence
Stage 0	Early HIV infection		
Stage 1	> 500 cells/mm^3	> 26	No AIDS-defining condition
Stage 2	200-499 cells/mm^3	14-26	No AIDS-defining condition
Stage 3	< 200 cells/mm^3	< 14	or Documentation of AIDS-defining condition
Unknown	No data	No data	No information on presence of AIDS defining Condition

Comparison: WHO vs. CDC classification

•**WHO** classification does not require CD4 count & more appropriate to use in resource limited settings é high HIV prevalence.

•**CDC** clinical categories more dependent on expensive laboratories & is not adapted to resource poor settings.

Diagnosis of HIV

As mentioned before, the number of people living é HIV rose from around 8 million in 1990 to 34 million by the end of 2011, out of ẃ 2.3 million were children &17.7 million were women. So for all babies of infected mother you expect that all the babies will have antibodies (IgG) for HIV, this lasts for 12-18 months & 50% of those babies will have the disease. For diagnosis of neonatal AIDS we must isolate the virus, do PCR, qualitative & quantitative for viral load & to be repeated for confirmation.

① Serologic tests

a) HIV antibody tests: detect ABs formed by the immune system against HIV:-

ELISA used to be standard screening test for HIV, tests for number of ABs protein in combination. It is very sensitive test (99.5%) but not very specific. The test needs skilled personnel, takes several hrs & the +ve result needs to be confirmed by Western blot.

Western blot is excellent confirmatory test, has high specificity but relatively poor sensitivity, it should not be used for screening purpose.

Rapid HIV antibody tests have reasonably good sensitivity/specificity (>99%), easy logistically, does not need continuous water or electric supply in remote areas. Can be done by less skilled personnel & the interpretation of results is easy, the test result can be made available in <30 minutes.

b) HIV antigen assays

Is P24 antigen capture assay, detects P-24 viral protein in the blood of HIV infected individuals. This viral protein can be detected during early infection, before seroconversion. This test is used to detect blood donors during the window period.

②DNA-PCR "Viral replication"

Extremely sensitive test, can detect 1-10 copies of HIV proviral DNA/ml of blood. It uses PCR technology to amplify proviral DNA. It is costly & needs sophisticated instruments & highly skilled professional. The chance of false +ve is high. Hence it should not be used for making initial diagnosis of HIV infection. It is often used to make early diagnosis of HIV in HIV exposed infants as serology tests are unable to diagnose HIV till the infant is 18 months old, or to diagnose or confirm virologic failure in pt who is not responding to ARTs.

③CD4 T cell count

Measuring CD4 cell count, is important indicator of the level of immune suppression that pt infected é HIV has. Average CD4 count of normal person is 1000-1200 /mm^3. Pt é HIV. The CD4 count drops by an average of 50-100 cells/yr. It tells you the level of immune damage. It should never be used to make diagnosis of HIV. The CD4 cell count may be variable depending on circumstances for example if there is diurnal variation (higher level at evening & lower at midnight), or é intercurrent infection, or é use of steroids, or in case of stress. In fact any of them can affect the CD4 count. Following the trend in CD4 count is useful in clinical decision making; for example; to decide eligibility of pt for ART, or to follow the progress or failure of respond of the pt to ART.

④Additional tests

Should be done, include:- hepatitis markers, LFTs, kidney functions, FBS, ESR, CXR, AFB for TB, RPR for syphilis, blood film for malaria (in endemic areas), stool for parasites & pregnancy test for women in child bearing age.

Management

HIV infection progress to AIDS over 8-10 yrs, there Is no cure, but drugs help controlling the virus, enabling person to live healthy life.

Management of pregnant mother: if CD4 count <500, ARTs after the 14th wk gestation ,to be used &continued throughout pregnancy. Including; Zidovudine tab, 250mg 1X2 daily or Azidothymdine +ZDV, given IV 4 hrs before CS, amp 200 mg in 20 ml solution, dose is 2 mg/kg over 1 hr then 1 mg/kg/hr until umbilical cord clamped. For resistant cases: HAART should be used, it include; Efavirenz + Tenofaver+ Emtricitabine, according to certain protocol & follow up schedule for CD4 & PCR as will be discussed later

Management of Newborn: ZDV syrup 50 mg/tsp, 8 mg/Kg/day÷4 for 6 wks. If baby is

preterm or unable to tolerate feed, IV infusion given, monitoring PCR/CD4 monthly for the first 4 months, then every 3-4 months up to the age of 1.5 year. Septrin (40 mg TMS + 200 mg SMZ/5 ml), dose TMS 4-8 mg /Kg ÷2, used as prophylactic for pneumocystis carini, from age 6 wks, continued for 6 months. Repeated blo-od & plasma transfusion ẃ must be irradiated to avoid graft versus host disease. No breast feeding & No BCG vaccine or other living vaccines for such baby.

Classes of Antiretroviral Therapies

①Nucleoside Reverse Transcriptase Inhibitors: structurally these drugs resemble naturally occurring nucleosides, break the formation of viral DNA by breaking the chain (chain breakers), they include;

Zidovudine (AZT) 300 mg PO BID, side effects; anaemia, myalgia, bone marrow suppression.

Lamivudine (3TC) 150 mg BID or 300 QD, side effects; headache, occasional nausea.

Stavudine (d4T) 40 mg BID for pt weight 〉60 kg &30 mg BID, for pt 〈60 kg, side effects; peripheral neuropathy ac-idosis & pancreatitis.

Abacavir (ABC) 1X300 mg tab. BID. Toxicity; hypersensitivity reaction occurs within the first 6 wks of initiation of Rx. Never rechallenge such pt. again é ABC.

Tenofevir (TDF) is actually, a nucleotide 1X300 mg tab, QD. Toxicity; headache, nausea, diarrhoea, Lactic acidosis.

Didanosine (ddI) 1X400 mg enteric coated cap QD (if pt BW is > 60 kg, give 250 mg QD or 2X100 mg buffered tab BID. If pt BW is 〈60 kg, give 125 mg BID or 250mg QD. In case of using buffered tab, 2 or more tab must be used at each dose to provide adequate buffer, or 250 mg of reconstituted buffered powder BID. To be taken on empty stomach to avoid food interactions. Toxicity include; peripheral neuropathy, nausea, abdominal pain, pancreatitis & lactic acidosis.

②Non-Nucleoside Reverse Transcriptase Inhibitors: act by inhibiting the active site of reverse transcriptase enzyme. Include:-

Nevirapine (NVP, Nevipan®) 200 mg QD X2 wks, then 200 mg BID. Toxicity; skin rash (17%) ẃ may be in a milder form (dry rash) as erythematous or maculopapular, in such case continue Rx é close observation & antihistaminic may be given. The skin rash may be severe (wet rash) é mm involvement, Steven's Johnson sy & toxic epidermal necrolysis, such case need discontinuation of the drug & never rechallenge. Hepatitis is another side effect.

Efavirenz (EFV, Stocrin®) 3X200 mg capsules or 600 mg/day PO to be taken é low -fat meal because high-fat ⇧ its absorption by 50% leading to ⇧ of its side effects. Toxicity of EFV include; CNS changes in 52% of cases; insomnia, nightmares, poor concentration, mood change, dizziness, disequilibrium, depression, psychosis. Skin rash in 15-27% of cases usually does not require discontinuation. This drug is contraindicated during pregnancy.

③Protease Inhibitors: act by inhibiting viral assembly. Include:-

- **Ritonavir (Norvir).**
- **Lopinavir + Ritonavir (Kaletra).**
- **Nelfinavir (Viracept).**
- **Saquinavir-HGC (Invirase).**

The side effects of this group include; glucose intolerance (DM in some pts), hypertriglyceridemia, lipodystrophy; morphologic changes, at accumulation in the lower part of the body é atrophy of facial fat.

Goals of HAART (Highly Active Antiretroviral Treatment)

①To improve the length & quality of the pt`s life.

②To ⇧ the total lymphocytic & CD4 cell counts, allowing preservation or improveme-

nt of the immune function.

③To Keep HIV RNA < 400 copies/ml within 4-6 months of ART initiation.

④To reduce HIV-related morbidity & mortality. HAART is not a cure for HIV. If Rx stopped, the virus will continue to replicate, it cannot eliminate HIV completely.

What does HAART require to be effective?

•Strict adherence to the Rx regimen & proper monitoring of side effects & disease progression. Recognition & Rx of comorbidities & recognition of drug interactions •Baseline assessment before initiation of HAART. •Baseline medical history. •Physical examination & clinical staging. •Laboratory testing….

All together lead to development of the pt care plan.

WHO criteria to initiate ART in adults & adolescents

Stage	CD4 testing not available	CD4 testing available
1	Don't treat	Start ART if CD4 count is < 200
2	ART may be started if the TLC is <1200	
3	If symptomatic initiate ART irrespective of TLC	Start ART if CD4 is <350
4	Start ART irrespective of TLC	Start ART irrespective of CD4 count

HIV/AIDS associated illnesses

Opportunistic infections & Opportunistic malignancies: develop as a result of HIV- inflicted damage to the immune system & are leading causes of morbidity & mortality in HIV-infected persons. Most of the common OIs are preventable as well as treatable. In resource-limited settings, it may be difficult to diagnose & treat OIs.

The **OIs** develop when the CD4 count is <200 cells/ml & include:-

Bacterial: Streptococcal, Staph, H. Influenza & G -ve bacteria. Mycobacterial: M. TB, M. kansasi & M. Aveum.

Fungal: PCP, Cryptococcus Neofrmans, Histoplasmosis, Coccidiodeocomycosis & Aspergillosis.

Viral: CMV, HSV infection.

Parasitic: Toxoplasmosis & Strongyloidosis.

The **OMs** are neoplastic conditions, tend to occur more frequently in pt é underlying immunodeficiency, including; pulm. Kaposi's sarcoma or Non-Hodgkin lympho- ma. The type of OIs or OMs that pt develops depend on the degree of immunosuppression i.e. each of the OIs & OMs typically develop at or below characteristic CD4 cell count range. So CD4 is an excellent indicator of the risk of developing specific OIs or OMs. Knowing the disease stage will be useful in limiting the different- ial diagnosis. In advanced stages, a person may be infected by > one pathogen.

Opportunistic infections

Respiratory system

Is the most common site of HIV-associated complications/illnesses & are the leading cause of morbidity & mortality. Many of the respiratory problems are both preventable & treatable. Therefore, prevention, evaluation & treatment of pulmonary disease is essential part of managing AIDS. There is wide spectrum of pulmonary manifestations including the following:-Respiratory manifestations at any level of CD4 count: URTI: sinusitis, pharyngitis, acute bronchitis, bacterial Pneumonia, TB & non-Hodgkin's lymphoma. Respiratory manifestations at CD4 count $<500/mm^3$ include; bacterial pneumonia. pulmonary TB. Respiratory manifestaions at CD4 count $<200/mm^3$ include: pneumocystis carinii or cryptococcus neoformans pneumonias. Respiratory manifestations at CD4 count $<100/mm^3$ include: pulmonary Kaposi's sarcoma, bacterial pneumonia (G-ve bacilli & staph aureus) &Toxoplasma pneum. Respiratory manifestations at CD4 count $<50/mm^3$ include: disseminated histoplasma capsulatum or cocci-

dioides immitis, CMV pneumonitis, disseminated mycobacterium avium complex, disseminated mycobacterium (non-TB) & aspergillus species pneumonia.

Bacterial pneumonia

Common agents: streptococcal pneumonia, as the degree of immunosuppression worsens, pneumonia may be recurrent & associated é sepsis.

Clinical presentation: Abrupt onset é fever, cough, production of purulent sputum, dyspnoea & pleuritic chest pain.

Investigations: CXR, CBC, blood culture, gram stain & sputum culture. The comm- on findings in x ray are; pneumonic consolidation, infiltrates, or pleural effusion.

Treatment: Antibiotics: Penicillin (Procaine or Crystalline), Amoxicillin or Fluoroquinolones.

Pneumocystis carinii pneumonia

Etiologic agent: P. jiroveci is fungus.

Epidemiology: one of the commonest OIs, however the incidence has declined over the yrs due to HAART & use of CPT. 50% of pts experience at least 1 bout of PCP during their Lifetime. Infection transmitted from human or environment.

Clinical presentation: indolent course characterized by wks of vague symptoms prior to presentation or diagnosis. The median duration of symptom is 28 days. Dyspnoea & fever are the cardinal symptom. Cough é scanty sputum seen in ›2/3 of cases. The physical findings are minimal, the usual findings for pneumonia may not be noted; RD ±cyanosis, little abnormality on chest examination, rhonchi/wheeze may be heard, especially in pt é some other underlying pulm disease, findings of consolidation are usually absent. P carini appears to be capable of haematogen- ous spread & seeding a variety of organ systems as well as causing ear infection.

Diagnostic work-up

CXR: could be normal or shows diffuse bilateral alveolar/interstitial infiltrates is the usual findings.

LDH: ⇧ in ›90% of cases & has a very high -ve predictive value i.e. if LDH level is low in a pt, the diagnosis of PCP is less likely.

Definitive diagnosis

By demonstration of Trophozoites/cyst from the organisms in samples obtained from induced sputum in ẃ the yield is 60% or bronchoalveolar lavage in ẃ the yie-ld is 95%. Staining; wright- Giemsa, Methenamine silver, Direct IF, nPCR. Other tests: Gallium 67 scan, PFT, & ABG.

Treatment

Antibiotics: the gold standard for Rx is Cotrimoxazole IV or PO. It is effective in **>** 90% of pts, dose 15 mg/kg/day (Trimethoprim) in 3-4 divided doses, for 21 days. The major disadvantage is the relatively high incidence of side effects; rash, fever, leucopenia 10% (HIV-ve) Vs 50% (HIV +ve). The response to Rx may not occur until the end of 1st wk & the pt may get worse during the first few days owing to the inflammatory re-sponse resulting from the death of large number of organisms in the lungs. Alterna-tive regimens is Clindamycin 600 mg IV q 8 hrs, or 300-400 mg PO q 6 hrs + Prima-quine 15-30 mg base/day X 21 days, or Pentamidine 4 mg/kg/day IV X 21 days, or Atovaquone 750 mg PO bid é meal X 21 days.

Adjuvant Rx: O_2 supplementation may needed, the use of steroids ⇩ mortality by 50 % & ⇩ the need for mechanical ventilation & is indicated if pt is; moderately distress-ed or cyanotic or PaO_2 **<**70 mmHg. Prednisone 40 mg PO bid for 5 days or 20 mg/day for 11 days followed by gradual weaning.

Primary Prophylaxis: strongly recommended for HIV infected person é evidence of

significant immune deficiency: CD4 count <200/µl (CD4 cell % of < 15% in children) or é associated thrush or PUO.

Secondary prophylaxis: indicated for pt é prior episode of PCP. TMP-SMX 2 tab /day (single strength), or TMP-SMX 2 tab 3 times/wk. An alternative regimens is Dapsone 100mg PO daily, or Dapsone 50mg PO daily + Pyrimethamine 50mg PO weekly + Leucovirin 25 mg PO weekly. Aerosolized Pentamidine 300mg/month via nebulizer. Atovaqoune 1500mg daily. N.B. the prevention of PCP may also be beneficial in ⇩ the risk of having other HIV associated infections such as CNS toxoplasmosis & other bacterial infections.

Tuberculosis

Is the leading OIs in developing countries. There ⇧ incidence & prevalence of TB in HIV infected pt. The lifetime risk of developing TB is 50% among HIV +ve compared to to 5-10% in HIV-ve pts. HIV is the most potent factor known to ⇧ the risk of progression from M. TB infection to active disease. The seroprevalence of HIV among TB pts range from 30-60%. The next table differentiate the early & late manifestations of TB, according to the CD4 count.

Challenges/Problems

⇧ Morbidity, mortality & high case fatality rate. ⇧ Drug toxicity &interaction between anti-TB drugs & ARTs. Also the ⇩ of drug absorption & high pill burden may ⇩ adherence to Rx.

Impact of TB on HIV: TB hastens the rate of HIV progression & it is the leading cause of illness & death among HIV/AIDS pts.

Tuberculosis	Early stage, CD4 >200	Late stage, CD4 count < 200/mm^3
Clinical Picture	Similar to non HIV infectedé productive cough. Pulm. manifestations are dominate	Atypical presentation: extrapulm. TB more common. TB tends to disseminate (involving different organs like meninges, pleura, LNs)
Sputum Smear PPD	Often +ve Reactive é >10 mm.	Often -ve Often -ve or anergetic.
CXR	Typical findings of TB upper lobe & or bilateral infiltrates. Cavitations. Pulm. fibrosis	Atypical: interstitial infiltrates especially in lower zones é no features of cavitation/fibrosis. A -ve CXR may associated é sputum+ve AFB (12%). In the setting of HIV epidemic, it is no longer possible to look at CXR & say that it is TB or not TB!

Treatment

When TB & HIV are coexisting, TB is more life threatening & should be treated first & pt should be stabilized. The same combination anti-TB drugs are given based on the Rx category. Close follow up of pt on DOTS is required. Complete cure from TB may be achieved in 6-8 months. Most pts who have TB-HIV coinfection are eligible for ART. When to start ART in pt on anti-TB drugs depends on CD4 & the clinical condition. If CD4 <50/mm^3, start ART as soon as the pt tolerates the anti-TB drugs. If CD4 count 50-200 mm^3, start ART after completion of intensive phase of DOTs. If CD4 >200 mm^3, ART can initiated after compilation of anti-TB treatment.

INH preventive therapy

Rationale: life time risk of having active TB in pt é HIV is 50% é annual risk of 7-9% (compared to only 5-10% life time risk in non HIV infected). It is advisable to give INH prophylaxis & the pt should screened for active TB before giving preventive

treatment INH 300 mg/day for 6-9 months. Alternatively, Rifampicin for 4 months.

Neurological manifestations

The nervous system is the 2nd commonly affected system next to respiratory system in HIV infected person & is common cause of morbidity & mortality. Seen in 7-20% of pts é initial AIDS diagnosis & > 90% in post mortem studies. Neurological manifestations occur at any stage of HIV infection. All levels of neuroaxis can be involved & the clinical manifestations are variable.

Pathogenetic mechanisms

- *Directly related to HIV:* include; Aseptic meningitis, Dementia complex, Myelopathy, Peripheral Neuropathy (acute demyelinating distal polyneuropathy), Mononuritis Multiplex, Distal Sensory Polyneuropathy, Myopathy, or Vasculitis.
- Secondary to Immunodeficiency: including; CNS Toxoplasmosis, Cryptococcal meningitis, TB Meningitis/Tuberculoma, Progressive Multifocal Leukoencephalopthy,Neurosyphilis, CMV or Polyradiculopathy/Encephaliis. Primary CNS Lymphoma.
- Related to ARTs: drugs causing peripheral neuropathy as d4T & DDI. Drugs causing myopathy as ē ZDV, or causing psychiatric manifestations as é EFV.

Aseptic meningitis

May occur at any time in the course of HIV infection, most commonly at time of acute HIV infection. However it becomes increasingly rare. Pts experience head ache, photophobia, sometimes frank encephalitis & cranial nerve involvement (commonly the VII nerve). Diagnosis: the CSF will show lymphocyte pleocytosis 10-100 cells/µl + ⇧ protein & normal BG level. The symptoms usually resolves within 2-4 wks. The HIV serology may be negative if it occurs during the 1ry HIV infection. To confirm diagnosis of HIV, p24 antigen or DNA PCR may be done or repeat HIV serology after few weeks.

CNS Toxoplasmosis

Toxoplasmosis is caused by protozoa "Toxoplasma Gondi". It is a zoonotic infection, cats are definite hosts & excrete the oocysts in their faeces & can be transmitted from animals to humans. Toxoplasma Gondi cysts also found in undercooked meat .Is the most common cause of secondary CNS infection in pt. é AIDS. It is generally late complication of HIV infection, usually occurs when CD4 cell count <100/ mm^3. It is thought to represent a reactivation of prior infection.

Clinical features

Onset is subacute é fever, headache, hemiparesis, seizures & altered mentation. Over 90% of pts present é focal neurologic deficits & 10% of pts present é encephalitis picture; confusion or coma & become more toxic. The commonly affected areas are the basal ganglia, brain stem & cerebellum. The extracranial manifestation of toxoplasmosis include; retinitis, myocarditis & pneumonitis

Diagnosis

CT/MRI; multiple ring enhancing lesions are the findings in 90% of cases é mass effect & oedema. Preferential location are basal ganglia, grey-white junction & white matter. The serologic assays are of limited value. A -ve toxoplasma AB test makes the diagnosis less likely.

Treatment

Regimen 1: loading dose of Pyrimethamine 50-75mg/day for 2-3 days followed by 50mg/day +Sulfadiazine 2-4 gm/day in divided doses, PO + Folinic acid 10 mg/ day.

Regimen2: Pyrimethamine & Leucovorin **+** Clindamycin 450 mg q8 hrs for 6 wks, or 3 wks after complete resolution of lesions on CT scan. Continue suppressive Rx for life (Pyrimethamine 25mg/day **+** Sulfadiazine 2 gm/day & Folinic acid 10 mg/day). This regimen is associated é high rate of adverse reactions.

Regimen3: Fansidar (is combination of Pyrimethamine 25 mg + Sulfadoxin 500 mg) 2 tab PO BID for 2 days, then 1 tab/day + Folinic acid. If pt is very critical, add Doxycycline 100 mg PO BID. Side effects of Fansidar include; leukopenia is the main side effect. Higher dose of Fansidar (2 tab/day) has been found to be associated é frequent incidence of fatal Hge. Check for bleeding tendency; gum bleeding, epist- axis, haematuria. Do Hb, WBC & platelet count once/wk, to prevent these side effects & give Folinic 10 mg PO/day or advice to take cream cake daily. If there is bleeding tendency, stop Fansidar & start Doxycycline 100 mg PO BID. Alternatives: Cotrimoxazole or Clindamycin + Pyrimethamine/ Azithromycin, Clarithromycin.

Indications for steroids: evidence of marked ⇧ of ICP & altered mentation. Dexamethasone 8 mg IV stat, then 4 mg IV QID, for 2 days.

Suppressive Rx: Fansidar 1 tab/day should be continued. Can be stopped when the CD4 count is > 200 for 6 months.

Preventive Rx: indicated if CD4 cell count ˂100 cells. TMP-SMX 2 tab/day or 2 tab 3 times/wk. Alternative regimens: Dapsone + Pyrimethamine + Leucovorin. The preventive Rx can be stopped if CD4 count ˃200 cells/ml for ˃3 months following HAART.

Cryptococcal Meningitis

Aetiology: is yeast-like fungus. Pigeon droppings commonly contains serotypes A or D. The infection acquired through inhalation.

Epidemiology

Is the leading cause of meningitis in pt é AIDS & is the initial AIDS defining illness in 2% of pts. Particularly common in pts é AIDS in Africa.

Clinical features

Occurs late in the course of the disease when CD4 **<**100/mm^3. CNS & meningeal involvement seen in 67-85% of pts. Papilledema seen in 30 % of pts. Neck stiffeness, phot-

ophobia, meningeal signs seen in 30% of pts. Low grade fever, nausea, vomiting & headache. Both fever & nuchal rigidity are often mild or lacking. The late manifestations include; confusion, altered consciousness, coma, extrracranial manifestations: include pulmonary disease, disseminated disease (10% of cases), fungemia, lymphadenopathy, cutaneous cryptococcosis (centrally umblicated multiple lesions on the face (looks like molluscum contagiosum).

Diagnosis

- CSF analysis: opening pressure of CSF is high. The WBC differential, protein & glucose are normal in 1/3 of pts. The Indian ink is +ve in 60-80% CSF.
- Cryptococcal Ag is +ve in 95-99 %.
- Cryptococcal culture is gold standard.

Treatment

Induction; Amphotericin B (é or é/out Flucytosine) 0.7mg/kg for 2-3 wks, followed by consolidation: Fluconazole 400mg, PO, daily for 8-10 wks or until CSF is sterile. Maintenance Rx using Fluconazole, 200mg, PO, daily life long. If CSF opening pressure raised, do drainage until CSF pressure is **<** 200mmH_2O & repeat LP daily until stable or CSF pressure normalizes. There is no place for Dexamethasone & discontinue the maintenance prophylaxis when the CD4 count **>**200/mm3 for **>**6 months.

Progressive Multifocal Leukoencephalopathy

Epidemiology: reactivation of JC virus seen in 2-4% of AIDS pts.

Clinical presentation

Occurs late in the course of HIV when CD4 count is **<**100. Subacute onset, pt is afebrile, alert, no headache, multifocal neurologic deficit. Classic triad include;

Dementia, Hemiparesis & Hemianopia.

Diagnosis

- CSF often non-diagnostic.
- JCV PCR may help to make diagnosis.
- Serology: 90% adults are sero positive for JC virus.

Treatment: no effective Rx, but initiation of HAART ⇧ survival.

Primary CNS Lymphoma

Clinical presentation

- Occurs late in the course of HIV when CD4 count is <100. Seen in 4% of AIDS pts.
- Confusion, lethargy, memory loss- seen in 57% of cases.
- Hemiparesis or Aphasia- seen in 40% of cases.
- Seizures- seen in 14% of cases.
- Cranial nerve palsy- seen in 9% of cases.
- Headaches- seen in 3% of cases. No fever unless concomitant infection.

Diagnosis

- CT/MRI: multiple lesions as frequent as single lesion, irregular & solid enhancement, subependymal enhancement are more specific, variable mass effect. Localization mainly periventricular.
- CSF: EBV DNA PCR (sensitivity 85% & specificity 98%).
- Histology: diffusely infiltrating, multicentric tumour of B cell lineage é the presence of EBV genome in ~100%.

Treatment

- Cytotoxic drugs is not effective. Radiotherapy can help some pts.
- Response to steroids is variable.

Dementia Complex

Is the first AIDS defining illness in up to 5-10% of pts é AIDS & is the major cause of

dementia in young people. Its major feature is the development of dementia (decline in cognitive ability from a previous level). Characterized by triad of:-

•Cognitive. •Behavioural. & •Motor dysfunction.

Stages of ADIS Dementia Complex

	Cognition	Behaviour	Motor
Early	Inability to concentrate	Altered personality	
Mid	Mental slowing, Forgetfulness	Social withdrawal	Poor coordinate
Late	Global dementia	Apathy	Paraparesis

Diagnosis

Neuropsychological tests. Mini-mental test. Is often a diagnosis of exclusion.

Treatment

Most pts improve é HAART é possible benefit from ART agents that penetrate CNS.

Peripheral Neuropathies

Occurs in 30% of pts é AIDS. Include:-

•Mononeuropathy e.g. Bell's palsy.

•Mononuritis multiplex.

•Distal sensory peripheral polyneuropathy (the most common).

The peripheral neuropathies may be caused by HIV infection or ART mainly the d4T & DDI drugs. Presents é symmetric bilateral painful burning sensation, paraesthesia, tingling of the feet & LL.

Diagnosis: ■Nerve conduction study. ■ Exclusion of other causes.

Treatment

Symptomatic & discontinuation or changing the drug ẃ is causing it.

Seizure

Relatively frequent complication of HIV infection. May be a consequence of OIs or OMs. The seizure threshold is often < normal in pt é HIV infection owing to the frequ-

ent presence of electrolyte abnormalities & it may be the presenting clinical symptom of HIV disease.

Causes: CNS toxoplasmosis 25% of pts. Primary CNS lymphoma 20% of pts. Cryptococcal meningitis 8% of pts. HIV encephalopathy 7-50%.

Treatment: Anticonvulsant indicated to all pts é HIV inf. associated é seizures, unless a rapidly correctable cause is found. Phenytoin (100mg PO TID) remains the Rx of choice, Phenobarb (100mg PO daily)or Valproic acid are alternatives.

GIT manifestations

Candidiasis: caused by Candida Albicans, include the following:-

Oral Candidiasis

Appears as white, cheesy exudates, often on an erythematous mucosa (most commonly on soft palate) ẃ gives an erythematous or bleeding surface on scraping.

Treatment: Nystatin suspension 2.5-5 ml gargled 5 X daily. 2% Miconazole oral gel applied 2-3 X daily. Amphotericin B lozenges. Fluconazole 100-200 mg PO/day for 7-14 days in severe cases. Oral hygiene, D/C steroids/antibiotics if pt is taking.

Oesophageal Candidiasis

Usually coincides é CD4 count of ˂50. Causes substantial pain or sense of obstruction on swallowing. Most lesions occur on distal 1/3 of the oesophagus & appear on endoscopy as redness, oedema & focal white patches or ulcers. If HIV infected person has oral thrush & substernal pain on swallowing presumed diagnosis of oesophageal candidiasis can be made. Endoscopy would prove the diagnosis, but is unnecessary if the pt responds to antifungal treatment. A linear ulcerations of oesophagus may be seen on barium X ray.

Treatment

The 1st line is Fluconazole 200 mg/day PO (maximum 400 mg/day) for 14-21 days.

Diarrhoea

Common clinical condition in HIV infected pts (> 50% of cases). May be acute or chronic, watery, mucoid or bloody. May be associated é fever. Pathogens may be bacterial, viral, protozoal, fungal, spirochaetal, mycobacterial, or others (malignan- cies). The mechanism of diarrhoea is through adhesion to mucosal surface, enterotoxin enteroinvasion & atrophy of mucosal surface.

Chronic diarrhoea

Diarrhoea lasting for ›2 wks é a single watery bowel motion &/or 3 or more loose stools/day. Diarrhoea occurs in 60% of HIV +ve cases. Frequency of diarrhoea ⇧ as the CD4 count falls. The incidence of chronic diarrhoea ⇩ é HAART. The protozoa causing chronic diarrhoea in HIV pts include; Cryptosporidium & Microsporidium.

Enteropathy

Chronic diarrhoea for ẃ no etiologic agent other than HIV can be identified. It is most likely a direct result of HIV infection.

Clinical features: in the early stage it is intermittent self-limiting diarrhoea, however in advanced stage it may be persistent life threatening diarrhoea presenting é copious amount of stool several times/day associated é abdominal cramp, nausea & vomiting may be also present. Significant weight loss (wasting) may occur due to the associated malabsorption. Fluid & electrolyte depletion.

Investigation: •Stool microscopy & culture •Intestinal biopsy •Special stains: modified AFB stain.

Treatment: 1. General Rx of chronic diarrhoea include: Hydration: oral or parenteral é electrolyte replacement. Symptomatic treatment include; antidiarrheal agents (Loperamide 2-4 mg QID- Lomotil 5 mg QID).

2. Specific Rx: for Cryptosporidium: Paromomycin 1 gm BID + Azithromycin 600 mg

QD For Isospora: Cotrimoxazole 2 tab QID for 10 days, then bid for 3 wks, or Pyrimethamine 75 mg + Folinic acid. For secondary prevention we use Cotrimoxazole 2 tab/day or Pyrimethamine 25 mg + Folinic acid 5 mg QD.

Problem: malabsorption of drugs.

Strongyloidosis

Parasitic infection caused by strongyliod stercolaris. Acquired thr-ough skin penetration of its larva form. Usually mild disease in immunocompetent individuals, but disseminated infection common in immunocompromised hosts & systemic manifestation may mimic sepsis.

Manifestation: asymptomatic or mild symptoms in immunocompetent individuals é occasional severe pruritus. May manifest é mild diarrhoea & epigastric pain. In immunocompromised pt a large amount of filariform larva are released & may invade the GIT causing enteritis é severe diarrhoea & malabsorption, or the filariform larva invade the lungs causing cough, shortness of breath (Loffler pneumonia). The CNS, peritoneum or liver may invaded. Severe systemic symptoms are commonly seen in disseminated infection & may be complicated by G -ve sepsis.

Treatment: Ivermectine 200 µg 1-2 days, or Thiabendazole 75 mg/kg bid for 3 days. Or Albendazole 400 mg/day for 5 days.

Skin Manifestations

80-90% of HIV pts have skin manifestation. Skin problems could be the first organ system affected. Various type of skin disease occur.

Classification

•Infections: bacterial. staph aureus is common pathogen. The common manifestations of it are:- Bullous impetigo, Folliculitits, Furuncle, Carbuncle & Cellulitis.

•Infestations; parasites.

•Inflammatory conditions.

•Malignancy.

Treatment: topical or systemic antibiotics depending on the severity.

Syphilis

Has atypical presentations in HIV pts, the 1ry chancre is usually painless, can be tender. The latent period before development of meningovascular syphilis is shorter & rapidly progresses to tertiary syphilis. Relapses éout reexposure.

Investigations: •Screening tests (VDRL/RPR). •Specific test(FT-AB absorption test).

Treatment: Benzathin Penicillin 2.4 mega unit IM weekly for 3 doses. Penicillin IV/ 2-4 mega unit every 4 hrs for 10-14 days, in case of CNS involvement. Follow up at intervals of 1, 2, 3, 6, 9 & 12 months.

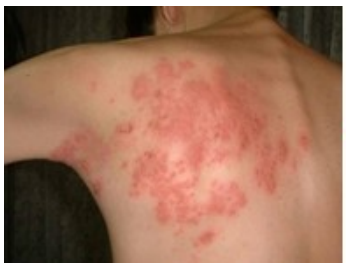
Herpes Simplex Virus

Is due to reactivation of latent virus. The usual manifestations are grouped vesicle é erythematous base. In HIV infected pts however may presented é atypical presentation as chronic non healing deep ulcer, verrucous erosion, or mixed infection are common. High frequency of reactivation. Widespread local extension. Higher incidence of dissemination, viremic spread to visceral organs, ẃ is life threatening.

Treatment

Systemic Acyclovir tab 200 mg, amp 250 mg, 15 mg/kg/day ÷3 for 5-10 days. Acyclovir 50 mg/kg/8 hrs where absorption is poor. Acyclovir 400 mg 2 X day in frequuent relapse. Famcyclovir 125 mg 2X daily for 5 days.

Herpes Zoster Virus



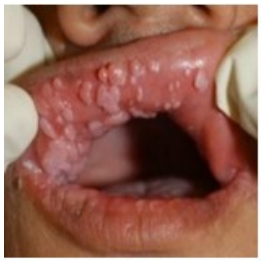
Varicella Zoster Virus

There is ⇧ incidence of HZV infection in pt é HIV infection & it is one of the earliest OIs to occur.

Clinical picture: are atypical presentation, may present é haemorrhagic necrotic or chronic verrucous lesions or multiple dermatomal involvement. Tendency to be generalized. May occur recurrently.

Treatment: Primary varicella: Acyclovir IV 10 mg/kg/8 hrs for 7-10 days. Herpes zoster: Acyclovir 800 mg 5 X a day for 7-10 days.

Human Papilloma Virus

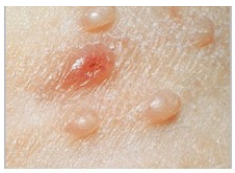


Human Papilloma Virus

Wart is common infection in HIV. Refractory to Rx & its complications include; neoplastic changes & ⇧ risk of cervical carcinoma.

Treatment: Podophyllin 20% or 5-Fluorouracil. or Cryotherapy or excision if big.

Molluscum Contagiosum



Molluscum Contagiosum

Caused by pox virus. Occurs in HIV pt é low CD4 count. Atypical presentations are common. Commonly seen in children. Tends to be generalized, giant molluscum contagiosum & secondary infection.

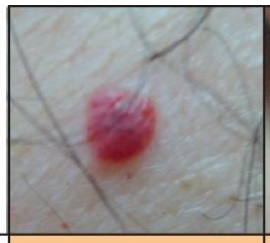
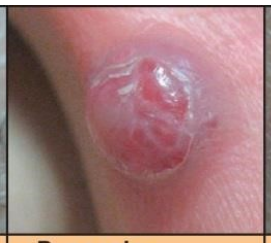
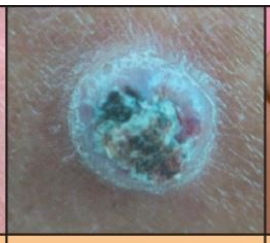
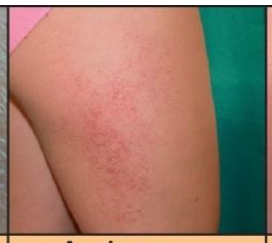
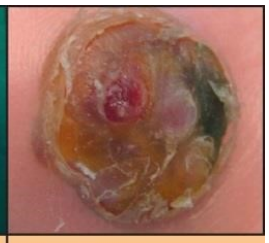
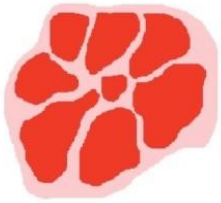
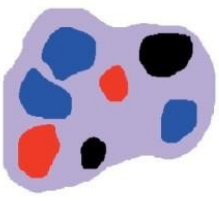
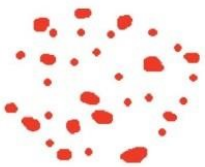
Treatment: cryosurgery or Curettage or Electrosurgery. Podophyllin or Cantaridine or 5-Fluorouracil.

Pruritic Papular Eruption

Chronic itchy condition commonly seen in HIV infected pts. Prevalence 46% in HIV infected persons. Symmetrical non-follicular papules in the trunk & extensors of extremities.

Diagnosis: biopsy.

Treatment: Topical antipruritic lotion, Corticosteroid, Oatmeal bath, Systemic antihistaminic. or Phototherapy, UV-B,UVA+ Psoralen.

					
Lesion	**Angioma**	**Pyogenic Granuloma**	**Angiokeratoma**	**Angioma Serpiginosum**	**Kaposi Sarcoma**
Type of vessels	Red lacunae	Wide variety: dotted, hairpin, linear irregular, and polymorphous	Dark lacunae and red lacunae	Small red lacunae	Rainbow pattern (areas with different colors in the same lesion)
Distribution	Regular and well-demarcated	Nonspecific	Nonspecific	Regular, scattered throughout the lesion	Nonspecific
Additional criteria	- Absence of blood vessels or other structures inside	- Homogeneous reddish area - Peripheral whitish collarette - White lines that cross the lesion	- Whitish veil - Erythema - Hemorrhagic crusts	- Absence of other dermatoscopically visible structures	- Homogeneous bluish-red pigmentation - Lacunae - Scaling surface
Diagram					

Cytomegalovirus

High incidence, 30-40% of the general population are +ve for AB of CMV & >90% of IV drug abusers are +ve. 20-30% of pts. é AIDS had CMV reactivation prior to the era of HAART.

Clinical Picture

*CMV retinitis: visual disturbances, floaters, flashes of light, photophobia, blurring of vision, painless &gradual loss of vision, usually bilateral. Diagnosis confirmed by retinal examination.

*CMV esophageal ulcers: pain& difficulty in swallowing. Diagnosis by tissue biopsy.

*CMV colitis: abdominal pain, watery diarrhoea, sometimes bloody, rarely perforation, fever. Diagnosis by tissue biopsy.

Treatment

Valganciclovir (PO). Ganciclovir (IV). Ganciclovir Intraocular implant. Foscarnet (IV).

Visceral Leishmaniasis

VL is caused by *L. Donovanii* (protozoa). Has become an important OIs among persons infected é HIV-1. Most coinfected pts have CD4 cell count <200. The infections affect the same cell lines, causing cumulative deficiency of the immuneresponse. Pts present é fever, organomegaly, anemia/pancytopenia. Presentation could be atypical, but VL should be suspected in those é travel history to endemic areas.

Diagnosis

- Serological tests are less sensitive in immunocompromised pt.
- Parasite could be detected in peripheral blood in immunocomprmised pts.
- Bone marrow aspirate.
- Splenic aspirate (most sensitive).

Treatment

First line: Pentavalent antimonials. Alternatives: Pentamidine, Amphotericin B. The relapse & toxicity are common in pts coinfected é HIV.

Opportunistic Malignancies

Kaposi's sarcoma

Etiology/Pathogenesis

Multifactorial. Vascular neoplasm affecting the skin & mucosa. Immunosuppressi- on ⇧ the risk of KS 500 times >general population. Presence of HHV-8 found in all types of KS. The HIV Tat protein potentiates the milieu conducive to KS growth.

Transmission

Studies have shown that HHV-8 ẃ is the etiologic agent for KS is believed to be sexually transmitted. The risk factors are multiple partners, history of STDs & being HIV +ve. More common in homosexual men. Multiple heterosexual contacts is a risk factor for HHV-8 in Africa. IV drug users, or via saliva as the HHV-8 titre 2-3 times higher in saliva than in semen, anorectal or prostate fluid samples.

Epidemiology: KS is the most common OMs among HIV +ve pts. The incidence of KS has declined by 66% é the use of HAART.

Clinical Picture

Can affect almost any organ system. Most common sites include:-

Skin: flat/ nodular lesions; can progress to significant infiltration of skin & necrosis. Oral cavity: flat to invasive lesions.

GIT: can have KS anywhere in GIT, ẃ can cause intestinal blockage & bleeding. Pulmonary: can spread along bronchi & vessels.

Diagnosis

Skin & oral lesions can be diagnosed by visual examination even though skin biopsy is most accurate to make diagnosis. Resolution of skin lesions é HAART can give pre-sumptive diagnosis. Testing for HV-8 is more research than clinically applicable. Lung & GIT lesion would need endoscopy & biopsy.

Treatment

Primary Rx: lesions significantly regress é HAART. Local Rx for skin lesions:-

- Alitretinoin gel (35-50% response).
- Local radiation (20-70% response).
- Intralesional Vinblastine/Vincristine (70-90% response).
- Cryotherapy (85% response).
- Photodynamic Rx or surgical.

Systemic Rx: immunotherapy; Interferon-α: immunomodulatory antiviral & antiangio-genic. This Rx may have superior efficacy if combined é HAART. Indicated for rapidly progresssive oral or visceral disease. Liposomal Doxorubicin/Daunorubicin is superior to conventional chemotherapy é less toxicity.

Lymphomas

There are 120 X ⇧ incidence of lymphoma among HIV pts. 6% of all AIDS pts develop lymphoma at some time in the course of their illness. As HIV disease progress the risk of lymphoma ⇧. The incidence of lymphoma hasn't shown dramatic ⇩ even after HAART is being widely used by HIV pts worldwide. Lymphoma is a late manifestation & often occurs when CD4 count is <200.

Categories

❍ Grade III or IV immunoblastic lymphoma (60%).

❍ Burkett's (20%) associated to EBV. ❍ Primary CNS lymphoma.

Treatment

✶In pt é high CD4 count -intensive chemotherapy

✶In pt é low CD4 count - a low dose chemotherapy.

✶Palliative measures to ⇩ the size of lesion & associated oedema: RT + steroid.

Cervical cancer

There is 5 fold risk of developing cervical cancer in women é AIDS. Is associated é human papilloma virus infection. Invasive cancer of the cervix is an AIDS defining illness. Abnormal PAP smear is seen in 60% of HIV infected women.

Logo World AIDS Day
December 1

TUBERCULOSIS

Chronic necrotizing disease caused by mycobacterium TB complex. Usually affects the lungs but almost all organs may be affected. Classified into:-

Pulmonary TB accounts for 80 % of all TB cases. Smear +ve accounts 75-80% of all pulmonary TB cases while smear -ve accounts 20-25%.

Extrapulmonary TB accounts for 20% of all TB cases.

Aetiology

Mycobacterium belongs to the mycobacteriaceae family. The species commonly involved are M. Tuberculosis, M. Bovis, M. Africanum & M. Microti. But of all, M. Tuberculosis is by far the commonest. M. tuberculosis is a rod-shaped, non-spore forming, thin aerobic bacterium measuring about 0.5 X 3µm. The bacterium is demonstrated by acid fast staining technique.

Epidemiology

TB is one of the most prevalent diseases in the world. About ***1/3*** of the world's population is infected é TB & thus at risk of developing active disease. It is estimated that 8.4 million people develop active TB every year & 2.3 million die. **>**90% of TB cases & deaths occur in developing countries & 75% of those are in the most economically productive age group. Not everyone exposed becomes infected, the probability of transmission depends on many factors as:-

*Infectiousness.

*Type of environment.

*Length of exposure.

Most people who are exposed to TB never develop symptoms because the bacteria can live in inactive form in the body. But if the immune system weakens, such as people é HIV or elderly adults, TB bacteria can become active. In their active state, TB bacteria cause death of tissue in the organs they infect. The active TB dis-

ease can be fatal if left untreated. 10% of infected persons will develop TB disease at some point in their lives. Coinfection é HIV significantly ⇧ the risk of developing active TB. HIV has become the most important risk for developing active TB. In HIV-infected persons, the risk of developing TB ⇧ by >10 times compared to those who are HIV -ve. The incidence & prevalence of TB, in recent years has doubled or tripled because of the HIV pandemic, especially in developing countries. It is also shown that active TB can result in rapid progression of HIV infection in a pt. Multi-drug resistant TB, ẃ often results from poor management is becoming a serious concern in many countries.

Transmission

Adults é smear +ve TB (cavitory & laryngeal) are sources of infection. Pts who are culture -ve pulmonary TB or é extrapulmonary TB are not infectious. M. tuberculosis is commonly transmitted from a pt é infectious TB to a healthy individual through:- inhalation of droplets excreted via coughing, sneezing. Unboiled milk could also transmit M. bovis but the incidence seems to ⇩ because of health education on boiling or pasteurizing milk.

Factors facilitate transmission

- Infectivity of the contact (pt é heavy bacterial load).
- Overcrowding.
- Prolonged exposure.
- Intimacy (how close the subject are). Pts who acquire the infection may not develop the disease. The rate of clinical disease is highest during late adolescence & early adulthood, but the reasons are not clear, especially young women > men.

Diseases ⇧ the risk of TB

- The commonest is HIV, ẃ suppresses cellular immunity
- Hematologic & other

malignancies as lymphoma & leukaemia •DM, CRF, immunosuppressive drugs like long term steroids •Old age because of ⇩ immunity & malnutrition.

Pathogenesis

M. tuberculosis enters the body mostly via resp. tract through coughed out droplets from an infectious pt. Interacts é host immune system immediately after entry. The activated alveolar macrophages ingest the bacilli; after ẃ they release chemicals to activate other immune system components & try to control the infection or multiplication of bacilli. This process will bring about cell-mediated immune response. These activated cells (macrophages) aggregate around the lesion & the centre becomes necrotic, soft cheese like material called caseous necrosis. The centre, however, may still contain live bacteria that become dormant. These bacteria will flare up & multiply when the person's immunity is depressed. But if bacteria inside the macrophage multiply rapidly, they will kill the macrophage & are released but to be taken up by other macrophages again. If this process is not arrested, pt. may develop disseminated infection.

Clinical manifestations

Primary pulmonary TB

Clinical illness directly after infection is called primary TB; this is common in children **<** 4 yrs of age. Thus, it results from an initial infection. Frequently it involves the middle & lower lung zones. In the majority it heals spontaneously leaving a healed scar on the lung called Ghon lesion. It may be contained by immunity into dormant stage only to flare up in immunocompromised state. In children or immunocompromised individuals the disease is usually rapid involving the lungs, pleura & mediastinal LNs. It may disseminate into the blood stream causing milliary TB or TB meningitis that may be rapidly fatal.

Secondary pulmonary TB

If no clinical disease developed after the 1ry TB infection, dormant bacilli may persist for yrs/decades before being reactivated, when this happens, it is called 2ry TB. Therefore this is from endogenous reactivation of latent infection, is more common in adults & typically involves the apical lobes. But any portion of lungs may be involved. The disease extend from small infiltrates to large cavitory lesions. Pt é cavitory lesion expectorate the TB bacilli é sputum. Early in the course, the pt. may have intermittent fever, night sweats, wt loss, anorexia & weakness. Most pts have cough, ẃ may be dry at first & later becomes productive, it is frequently blood streaked & pt may have exercise dyspnoea.

Physical examination

May reveal a chronically sick pt. é pallor & clubbing. Inspiratory crepitations seen in some cases.

Laboratory findings

May include ⇧ ESR, anaemia or leucocytosis. Sputum examination may be +ve for AFB. The CXR findings are non-specific; infiltrations, consolidation or cavitory lesions may be present.

Extra-Pulmonary TB

Commonly affected organs are: LNs, pleura, meninges, genitourinary tract, bones, joints & peritoneum, each will be discussed separately:-

Tuberculous Lymphadenitis

Seen more in HIV pt, commonest sites are cervical & supraclavicular. LNs typically matted, firm & sometimes discharging pus. Diagnosis is made by fine needle aspiration or biopsy.

Pleural Tuberculosis

May be asymptomatic or pt. could have fever, pleuritic chest pain & dyspnoea. On physical examination, typically there will be ⇩ tactile fremitus, dullness & ⇩ breath sounds on the affected side. Fluid should be aspirated from pleural space & analysed. CXR is helpful, it may show homogenous opacity é meniscus sign. Empyema (pus in the pleural space) may complicate pleural TB.

Genitourinary Tuberculosis

Affects more females & may present as infertility or pelvic pain. Can involve any part of genitourinary system. Dysuria, intermittent haematuria & flank pain are common presentations. But it may be asymptomatic for a long period of time. Urine analysis shows pyuria & haematuria éout bacteria in majority of cases (commonly called sterile pyuria). Diagnosed by culturing urine repeatedly.

Skeletal Tuberculosis

It is usually reactivation of haematogenous site or extension from a nearby LNs. Most common sites are spine, hips & knees.

Spinal Tuberculosis

“Pott's disease” or “TB spondylitis”. In adults, lower thoracic or lumbar vertebrae commonly affected. Pt present é swelling & pain on the back é/éout paraparesis or paraplegia due to cord compression. TB in other bones usually present é pain & swelling. Any joint can be affected but weight bearing joints; particularly hip & knee are commonly involved. Pt present é progressive joint swelling usually é pain & limitation of movement & if left untreated, joint may be destroyed.

Tuberculous Meningitis

Commonly seen in children & immunocompromised people. 50% of cases have evidence of disease in the lungs. AFB can be seen in CSF sediment in only 20% of cases;

this % ⇧ if the examined CSF volume is increased. The culture may be +ve in 80% of cases, but it takes 4-6 wks to grow.

Gastrointestinal Tuberculosis

Can affect anywhere from the mouth to the anus. Bacteria could reach GIT by swallowing sputum, or through blood, or ingesting raw milk. The commonest sites to be involved are terminal ileum & cecum. Abdominal pain, diarrhoea, symptoms of intestinal obstruction & hematochezia (frank blood on stool) may be the presenting symptoms. There could be associated fever, night sweats, wt loss & anorexia. There could be a palpable mass in abdomen. Pt could have involvement of peritoneum, liver & spleen. TB peritonitis arises from ruptured abdominal LNs, or through blood. Pt usually presents é abdominal swelling & pain, wt loss, fever & night sweating. Aspiration of peritoneal fluid (paracentesis) reveals exudative fluid é many WBC, predominantly lymphocytes. AFB is rarely +ve & culture positivity is very low. Involvement of the liver & spleen are parts of disseminated TB & the pt will present é hepatomegaly &/or splenomegaly. There may be evidence of other organs involvement.

Tuberculous Pericarditis

Frequently seen in pt é HIV. Pt usually present é fever, retrosternal pain, cough, dyspnoea & generalized oedema. Cardiac tamponade may appear later. Constrictive pericarditis may develop as complication even after Rx & pt can present é symptoms & signs of RHF. Diagnosis usually reached by analysing the pericardial effusion. It may show lymphocytosis, but yield for AFB is low. The CXR may show cardiomegaly (pericardial effusion). ECHO (detect effusion).

Milliary Tuberculosis

This is secondary to haematogenous dissemination of the bacilli. More common in-children & immunocompromised pt. The manifestations of military TB are nonspecific

é fever, night sweat, anorexia, weakness & Wt loss ± respiratory symptoms. Physical examination findings includes; seriously sick pt é hepatosplenomegaly & lymphadenopathy. Since symptoms & signs are not specific, high index of suspicious is required for the diagnosis. CXR usually shows milliary infiltration bilaterally.

Diagnosis of Tuberculosis

Clinical suspicion very important, pt who have suggestive symptoms & signs for TB should undergo further tests including the following:-

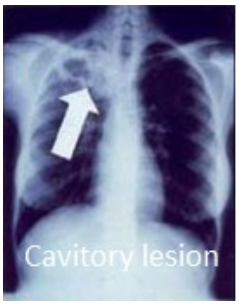
AFB Microscopy: AFB is found on microscopy from specimens like sputum, pleural, peritoneal, CSF & body discharges, but the yield is different. However, definitive diagnosis depends on detection of M. tuberculosis from a culture of specimen.

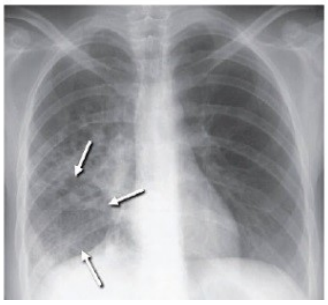
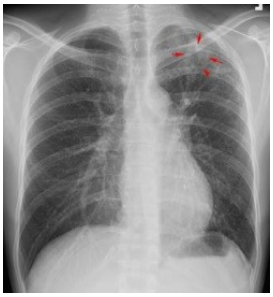
Sputum examination: is extremely important in pt who have sputum production . AFB stain should be done 3 times in 2 consecutive days (spot-early morning). Sputum smear is said to be +ve when at least 3 AFB are seen. Or smear +ve TB is diagnosed when 1-2 smears are +ve plus suggestive CXR finding. If all 3 sputum smears are -ve & the pt has suggestive clinical & CXR findings, first the pt should treated é broad spectrum antibiotics to R/O other bacterial causes. If the pt does not respo- nd, smear -ve pulmonary TB can be strongly considered.

Mycobacterial culture: gold standard for diagnosis. However the bacillus is slowly multiplying, it takes several wks. to grow the bacilli in a culture media. May be used for drug sensitivity tests.

Chest X Ray

Presentations are varied. Although any CXR finding is possible, typically there will be nodular infiltrates & cavities in the upper lobe; pleural effusion is also common. But CXR findings alone do not confirm diagnosis.



Raised ESR: very important clue for diagnosis even though this is nonspecific.

PPD skin test: widely used to screen TB in developed countries where the prevalence of TB is low. Positive reaction obtained when pt have the infection but do not have active disease or they have received BCG for immunization.

Mantoux tuberculin skin test: 0.1 mL/5u of purified protein derivative solution is injected ID, use a 27 gauge needle. Read within 48-72 hrs, measure induration, not erythema. A +ve reaction can be measured accurately for up to 7 days. A -ve reaction can be read accurately for only 72 hours.

Interpretation of TST is as follow:-

5 mm of induration is +ve in:- HIV-infected persons, or close contacts to an infectious TB case, or in persons who have CXR findings consistent é prior untreated TB, or organ transplant recipients, or persons who are immunosuppressed (e.g. those taking the equivalent of >15 mg/day of prednisone for 1 month).

False +ve reaction: non-tuberculous mycobacteria: induration are usually ≤ 0 mm. BCG vaccination: generally wanes over time.

No reaction: anergy, or inability to react to TST due to weak immune system, or recent TB infection (2-10 wks after exposure), or very young age (newborns), or recent live-virus vaccination (temporarily suppress TST), or poor TST administration technique (too shallow or deep).

Standardized case definition of TB

After making diagnosis of TB proper case definition should be made to decide on ap

propriate Rx. Definition of TB case depend on the following points:-

①Site of TB (Pulmonary Vs Extrapulmonary).

Pulmonary TB: refers to disease involving lung parenchyma. Therefore tuberculous intrathoracic lymphadenopathy (mediastinal or hilar) or tuberculous pleural effusion, éout radiographic abnormalities in the lungs, constitutes a case of extrapulmonar TB. Pt. é both pulmonary & extra pulmonary TB should be classified as a case of pulmonary TB. Milliary TB is classified as pulmonary TB because there are lesions in the lungs.

Extrapulmonary TB: refers to TB of organs other than the lungs, e.g. pleura, LNs ,abdomen, genitourinary tract, skin, joints, bones, meninges. Diagnosis based on one culture +ve specimen, or histological or strong clinical evidence consistent é active extra-pulmonary TB, followed by decision by a clinician to treat é a full cou-rse of TB chemotherapy. The case definition of extra-pulmonary TB case é several sites affected depends on the site of the most severe form of disease.

②Bacteriology (sputum smear)

Identification of smear +ve cases is important, because they are the most infectious cases & usually have higher mortality.

Pulmonary TB +ve sputum smear: ≥ 2 initial sputum smear examinations are +ve for AFB or 1 sputum smear +ve + CXR abnormalities consistent é active pulmonary TB as determined by a clinician, or one sputum smear +ve & sputum culture +ve.

Pulmonary TB -ve sputum smear: case of pulmonary TB that don`t meet the above definition for smear +ve TB. This group includes cases éout smear result, ẃ should be exceptional in adults but relatively more frequent in children.

Note: in keeping é good clinical & public health practice, diagnostic criteria for pul monary TB should include:- at least 3 sputum specimens -ve for AFB & CXR abnormal ities consistent é active pulmonary TB & no response to a course of broad

spectrum TB antibiotics & decision by Dr to treat é a full course of anti TB chemotherapy. In health facilities where microscopy laboratory services available & diagnostic criteria are properly applied. Pulmonary TB smear +ve cases represent at least 65% of the total of pulmonary TB cases in adults.

Note: these proportions may be lower in high HIV-incidence populations. It is apparent from the above definitions that in the absence of culture positivity, the standard CXR is necessary to document cases of smear -ve pulm. TB.

③History of previous Rx of TB

In order to identify those pts at ⇧ risk of acquired drug resistance & to prescribe appropriate Rx, a case should be defined according to whether or not the pt has previously received TB Rx. Pt may be new case, or relapse after cure, or failure of present Rx, or é interruption of Rx for >2 months, or pt transferred from another TB register to continue Rx, or sputum +ve pt at the end of Rx regime, or chronic case.

④Severity of the diseases

Bacillary load, extent of disease & anatomical site are considerations in determining TB disease severity & therefore the appropriate Rx. Involvement of an anatomical site results in classification as severe disease if there is a significant acute threat to life (e.g. pericardial TB), a risk of subsequent severe handicap (e.g. spinal TB).

Case definitions

TB suspect: any person who presents é symptoms/signs suggestive of TB, in particular cough of long duration (>2 wks).

TB Case: TB has been bacteriologically confirmed or diagnosed by a clinician.

Definite case of TB: +ve culture for the M.TB complex.

Management

Initial phase			Continuation phase		
Reg	Drug	Duration	Reg	Drug	Duration
1	INH RIF PZA EMB	7 days/week for 8 wks or 5 days/wk for 40 doses	1a 1b 1c	INH/RIF INH/RIF INH/RPT	7 days/wk for18 wks or 5 days/wk for 18 wks twice weekly for 18 wks Once weekly for 18 wks
2	INH RIF PZA EMB	7 days/wk for 2 wks then twice weekly for 12 doses. or 5 days/wk for 2 wks then twice weekly for 6 wks	2a 2b	INH/RIF INH/RPT	Twice weekly for 18 wks Once weekly for 18 wks
3	INH RIF EMB	Three times weekly for 8 wks	3a	INH/RIF	3 Times weekly for 18 wks
4	INH RIF EMB	7 days/week for 8 wks or 5 days/ week for 8 wks	4a 4b	INH/RIF INH/RIF	7 days/wk for 31 wks or 5 days/week for 31 wks Twice weekly for 31wks

*The aim of treatment

To cure pt, prevent death & complications. To ⇩ transmission of TB.

The intensive phase

Combination of ≥ 3 or more drugs is given for 2 months using the (DOTS). In the re-treatment regimen DOTS is continued for 3 months, to ⇩ the bacterial load & make the pt non-infectious rapidly.

Continuation phase

2-3 drugs used for 4-5 months . This phase follows the intensive phase & the aim is to achieve complete cure.

•Streptomycin should not be given to pregnant woman & pt é RF, or ear problems. It should be replaced by Ethambutol. The dose of streptomycin should not be >750 mg if the pt's age >50 yrs.

Important points

•Children ≤ 6 yrs old should not be given Ethambutol because of damage to the eyes & children may not complain of it.

•Pts should be strictly followed after initiation of the drugs.

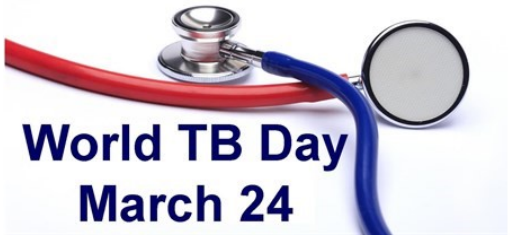
•All sputum +ve pts. on DOTS must have one sputum specimen examined at the end of the 2nd, 5th & 7th month.

•Steroids are added in case of TB meningitis, pericarditis & spinal TB.

•If sputum is -ve at the end of 8 wks, the continuation phase can be started.

Side effects of Anti TB drugs

Drug	Common side effects
Isoniazide	Peripheral neuropathy, Hepatitis, Histamine release after ingestion of red fish e.g. Bala, Kelawalla
Rifampicin	Nausea, Vomiting, Hepatitis, reduced effect of contraceptives, anti- epilep-tics, oral hypoglycaemic drugs & Theophillines
Pyrazinamide	Joint pain, Hepatitis
Streptomycin	Audio & Vestibular damage, (also to the foetus), renal damage
Ethambutol	Optic neuritis



MENINGITIS

Inflammation of the arachnoid layer of the meninges & the fluid that circulates in the ventricles & subarachnoid space (CSF).

Etiologic agents

The causes of bacterial meningitis vary é age:-

Infants (<1 yr): E. coli, B strept & Listeria monocytegenous are the commonest.

Young children/toddlers (age 1-6 yrs): Haemophilus influenza & Meningococcus account for > 50% of cases.

Adolescents/Adults: Meningococcus & Pneumococcus are the commonest.

Immunocompromised & cancer pts: Listeria, Staphylococcus & Pseudomonas.

Rout of infection

- **Droplet infection through the upper airways:** e.g. in meningoccus meningitis, é possibly epidemic spread.
- **Haematogenous spread:** e.g. in pneumococcus pneumonia.
- **Contagious spread from adjacent sites:** e.g. otitis media, or sinusitis.
- **Direct:** e.g. in open head injury.

Epidemiology

In the west due to the availability of vaccines for N. meningitides & H. influenza, the S. pneumonia has become the leading cause of bacterial meningitis. However, in African & most developing countries, Neisseria meningitidis is still the leading cause of bacterial meningitis in adolescents & adults. An outbreak of meningitis epidemic has been documented to occur every 7-10 yrs in the meningitis belt in Africa. Neisseria meningitidis, often referred to as meningococcus, is a gram -ve bacterium that can cause meningitis & other forms of meningococcal disease such as meningococcemia, a life-threatening sepsis. The bacterium is referred to as a coccus because it is round & more specifically, diplococcus because of its tendency

to form pairs. About 10% of adults are carrier of the bacteria in their nasopharynx. As an exclusively human pathogen it is the main cause of bacterial meningitis in children & young adults, causing developmental impairment & death in about 10% of cases. It causes the only form of bacterial meningitis known to occur epidemically, mainly in Africa & Asia. N. meningitidis is spread through saliva & respiratory secretions during coughing, sneezing, kissing & chewing on toys.

Clinical presentation

The IP for meningococcal meningitis range from 1-10 days, but mostly the clinical manifestations occur within 2-4 days. Meningitis may manifest as an acute fulminant illness that progress rapidly in few hrs or as a subacute infection that progressively worsens over several days. The classic clinical triad of Fever, Headache, Nuchal rigidity (neck stiffness) is seen in >90% of pts. Alteration in mental status can occur in >75% of pts & can vary from lethargy to coma. Nausea &vomiting are common symptoms. Avoiding light (photophobia) seen in some pts. Seizures occur as part of the initial presentation of bacterial meningitis, or during the course of the illness in 20-40% of pts. In Meningococcal meningitis of sudden onset é severe course, pt. develop diffuse erythematous maculpapular rash ẃ rapidly becomes petechial, purpural or bullous lesions. The petechiae are found on the trunk, lower extremities, in m.m., conjunctiva & occasionally on the palms & soles. In older/debilitated pt meningitis symptoms may be subtle.

Meningococcal rashes

Meningeal signs

Are clinical signs often sound in pt é meningitis, include:-

Neck stiffness: when head is flexed passively.

Brzezinski's sign: upon passively flexing the head, one notices flexion of both legs at the knees.

Kerning's sign: severe stiffness of hamstrings muscles causes an inability to straighten the leg when the hip is flexed to 90^0.

Note: these classic meningeal signs may not be seen in infants, or old persons & in case of the pt is in coma.

Complications

•Brain oedema.

•Hydrocephalus.

•Brain abscess.

•Septic vein thrombosis.

•Hearing impairment.

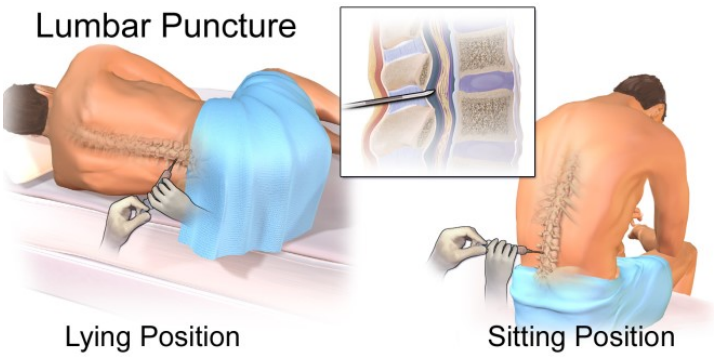
•Fulminant meningococcal sepsis: Water-house-Friedrichsen syndrome (a clinical condition resulting from haemorrhagic necrosis of the adrenal gland é multiorgan fail-ure. Pts are hypotensive or in shock, DIC é skin & mucosal purpura & bleeding are com-monly seen associated features.

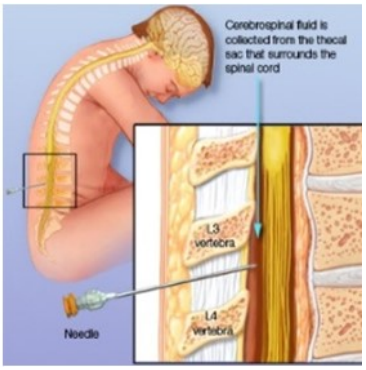
Diagnostic approach

- History, physical examination.
- Search for possible source of infection (pneumonia, otitis media, sinusitis).
- Blood culture; meningococcus are seen as gram -ve intracellular diplococcic.
- PCR, serologic antibody test: latex agglutination test.
- Lumbar puncture.

Technique of lumbar puncture

Feel the upper border of iliac crest it's at the level of L5 vertebrae, go up to touch spine of L4 vertebrae & under complete aseptic conditions introduce needle (size FG 21, 22, for infants &children) into the disc space between L4-L3 vertebrae, dire- cting the needle towards the umbilicus, if CSF was found to come out under high pressure stop the procedure to avoid conning of cerebellum. Collect CSF in 3 tub-es, 10 drops in each for cells, biochemistry & culture. Take blood sample for BS aft- er you finish to compare é CSF sugar (normally the CSF sugar is ⟨2/3 of blood sugar), ⇩ CSF sugar seen in bacterial meningitis.





CSF analysis

Gross appearance & opening pressure: CSF looks turbid &the opening pressure is⇧ (due to ⇧ICP).

Cell count/µl & differential: polymorphonuclear leucocytosis (several thousands in bacterial & several hundred in viral or TB. meningitis).

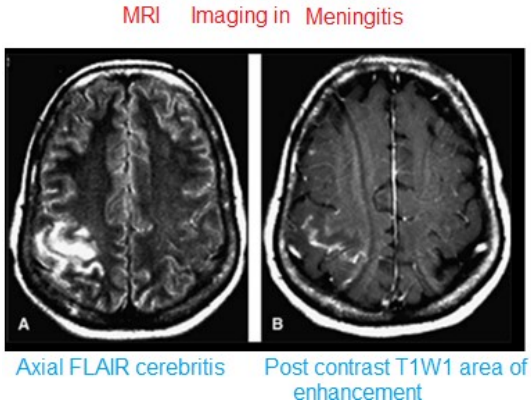
Cell type: granulocytes (PMNLs) in bacterial meningitis. Lymphocytes (viral meningitis). Lymphocytes + Monocytes (seen é TB. meningitis).

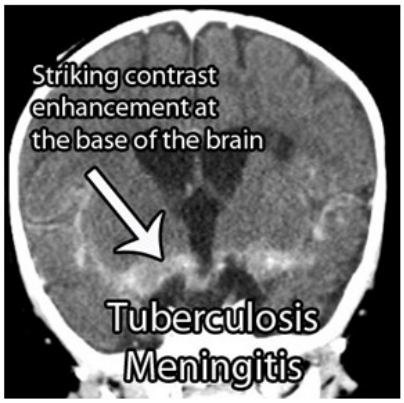
Protein& Glucose: ⇩ glucose & ⇧ protein (bacterial meningitis).

Gram stain culture/sensitivity: for identification of type of bacteria.

Parameter	Normal	Bact Meningitis	Viral Meningitis	Fungal Meningitis	Tuberculosis
Opening pres. (mm H_2O)	<180	200-500	NA	> 250	NA
WBC count (mm^3)	0-5	100-20.000 (mean 800)	5-500 (mean 80)	20-2000 (mean 100)	5-2000 (mean 200)
WBC Differen,	No predominance	> 80% PMN	> 50% L < 20% PMN	> 50% L	> 80% L
Protein (mg/dL)	15-50	100-500	30-150	40-150	> 50
Glucose (mg/dL)	45-100 (2/3 of serum)	<40 (<40% of serum)	30-70	30-70	< 40
Gram stain	NA	60-90% +ve	-	-	37-87% +ve (AFB smear)

Imaging in Bacterial Meningitis





Neuroimaging can identify conditions that may predispose to bacterial meningitis; thus, it is indicated in pts who have evidence of head trauma, sinus or mastoid infection, skull fracture & congenital anomalies. In addition, neuroimaging studies are typically used to identify & monitor complications of meningitis, such as hydrocephalus, subdural effusion, empyema, infarction & to exclude parenchymal abscess & ventriculitis. Identifying cerebral complications early is important as some complications, as symptomatic hydrocephalus, subdural empyema & cerebral abscess, require prompt

neurosurgical intervention. The diagnosis of acute bact meningitis is not made on the basis of imaging studies. Rather, it is established by the affected pt's history, physical examination findings & laboratory results. The CSF is the single most important diagnostic study. Imaging studies performed in pt. é acute meningitis may provide normal findings. The results of an imaging study do not exclude or prove acute meningitis.

Differential Diagnosis

•Virally caused Meningoencephalitis: Coxsackie, Mumps, Measles, HIV, CMV, VZV, HSV •Chronic meningitis: TB/Cryptococcal •SAHge.

Treatment:

1. Empirical antibiotic therapy: bacterial meningitis is a medical emergency & antibiotics should initiated immediately before results of CSF gram stain/culture. Antibiotics should be given IV at higher doses. In adults éout underlying disease; Ceftriaxone 2 gm IV BID **+** Ampicillin 2 gm IV QID for 2 wks. Crystalline penicillin 3-4 million u, IV/4 hrs **+** Chloramphenicol 1 gm IV QID are alternative for a resource limited setting. Pts é ENT infection or head injury: we use Ceftriaxone 2gm IV BID **+** Vancomycin 1 gm IV BID **+** Rx of the underlying cause. If suspected hospital-acquired infection; Ceftriaxone 2 gm IV BID **+** Vancomycin 1 gm IV BID + Gentamycin 80 mg TID. In case of immunodeficient pt we use: Ceftriaxone 2 gm IV BID **+** Vancomycin 1 gm IV BID **+** Ampicillin 2 gm IV QID (Ceftriaxone is 3rd gen. Cephalosporine & Vancomycin is Aminoglycoside).

2. Specific antibiotic therapy: when specific agent identified:- **N. meningitidis**: 3rd gen. Cephalosporin e.g. Cefotaxime provide adequate empirical coverage, Penicillin G remains the drug of choice for N. meningitides, 3-4 million U, IV/4 hrs for 7-10 days may be adequate. **Pneumococcal meningitis**: antibiotic Rx is initiated é Ceftriaxone 2 gm IV BID & Vancomycin 1 gm IV BID for 2 wks. **H. influenza**: Ceftriaxone 2 gm IV BID for 10-14 days may be enough. Chloramphenicol 1 gm IV QID may be an alternative,

antibiotic, for pts who may not afford Ceftriaxone.

Symptomatic & Adjunctive therapy

Steroids: Dexamethasone when initiated be- before antibiotic therapy ⇩ the num-ber of unfavourable outcomes, including death & neurologic complications. It is mainly advantageous in children, predominantly é meningitis due to H. influenza or St. pneumonias. 10 mg IV 15-20 min. before the first dose of antibiotics & 4 mg IV QID for 4 days.

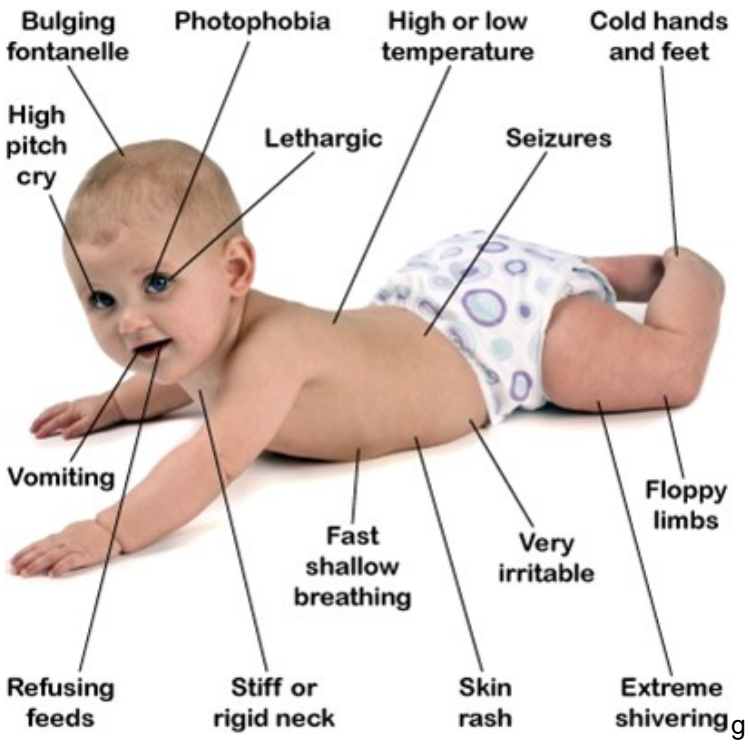
Treatment of ⇧ ICP: elevation of the pts head to 30-45^0. Intubation & hyperventila-tion (till P_aco_2 is 25-30 mmHg). Mannitol IV infusion.

Isolate the patient

Regulate water, electrolyte balance, thromboembolism prophylaxis.

Chemoprophylaxis

In case of *N. Meningitides,* all close contact to the pt should be given chemoprophy-laxis:- Rifampicin 600 mg PO BID for 2 days for adults & 10 mg/ kg PO BID for children ›1 yr. Ciprofloxacin 750 mg PO stat, may be given as alternative (adults).



VIRAL ENCEPHALITIS

Inflammation of the brain parenchyma, é/éout involvement of the meninges, caused by virus. The spinal cord &/or nerve roots may be involved rarely.

Causes

- Common: Arbovirus. Enterovirus, HSV-1, Mumps.
- Less common: CMV, EBV, HIV, Measles, VZV.
- Rare: Adeno V, CTFV, Influenza A, Parainfluenza, Rabies, Rubella.

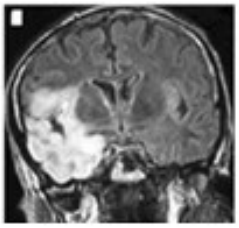
Signs & symptoms

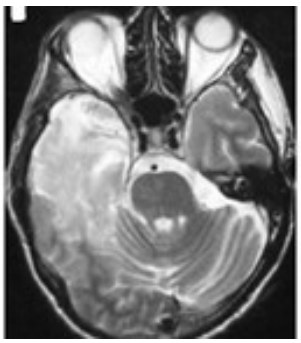
Acute febrile illness é evidence of meningeal involvement. Altered level of consciousness (ranging from lethargy to coma). Abnormal mental state (hallucinations, agitation, personality change, psychosis). Evidence of either focal or diffuse neurologic signs/symptoms. Focal or generalized seizures occur in >50% of cases. Most common focal findings: aphasia, ataxia, hemiparesis (é hyperactive tendon reflexes), involuntary movements & cranial nerves palsy.

Laboratory findings

CSF examination: check for ⇧ ICP first. The characteristic profile of CSF consists of lymphocytic pleocytosis,⇧ protein & normal glucose level. CSF PCR. CSF culture usually -ve (especially in HSV-1) .

Serologic studies & antigen detection. **MRI, CT & EEG:** done to exclude alternative diagnosis & assist in differentiation between focal & diffuse encephalitic process (90% of pts é HSV-1 infection have abnormalities in the temporal lobe on MRI).





MRI brain(T2W image) right temporal lobe high signal in a pt with herpes encephalitis

Treatment

Supportive Rx (usually in ICU): check vital signs, restrict fluid & give antipyretics. Treat seizures/or give prophylactic therapy (high risk for seizures!).

Medication: Acyclovir 10 mg/kg TID for at least 14 days (for herpes). Gancyclovir (5 mg/kg BID) or Foscarnet (60 mg/kg TID) are especially recommended for CMV.

TETANUS

Neurologic disease characterized by ⇧ muscle tone & spasms caused by toxin released from the bacteria clostridium tetany. it is spore forming anaerobic, motile & rod shaped. Forms oval, colourless, terminal spores (tennis racket or drumstick shape), spores are very resistant to heat, chemicals, radiation, drying & can survive for long time in environment (months up to yrs, decades), it is found worldwide in soil, in inanimate environment, in animal, faeces, skin surfaces, contaminated substances including heroin. Disease occurs sporadically, affects unimmunized, or partially immunized, or fully immunized who fail to maintain adequate immunity é booster doses of vaccine. Tetanus Neonatorum is caused through an unvaccinated mother, or é home deliveries & unhygienic cutting of umbilical cord. It is common in the 3rd world countries as a result of the high % of home deliveries & lack of vaccination & poor sanitary conditions, causing several hundred thousand deaths/ yr. Tetanus caused by exotoxin produced by the G +ve bacteria Clostridium tetany ẃ produces 2 exotoxins; tetanolysin; its action not known & tetanospasmin ẃ is neurotoxin bind to CNS interfering é the neurotransmitter release to block inhibitor impulses causing the clinical manifestations of the disease.

Epidemiology

Tetanus is more common in rural areas where there is frequent contact é soil. Occurs more frequently in warmer climates, during summer months & in males.

Most cases follow injuries especially during farming, gardening or other outdoor activities. Tetanus may also be associated é surgery, otitis media, abortion, home deliveries, or canine tetanus (dogs, wild animals).

Pathogenesis

Although Cl. tetany frequently contaminates wounds. Germination & toxin production, however, takes place in wounds é necrotic tissue, foreign bodies or infection that is active. Often the wound is trivial or could seem to be healed from outside. Tetanospasmin: toxin produced by the bacteria in the wound binds to peripheral motor neuron terminals, enters the axon & is taken to spinal cord & brain stem by retrograde transport. Toxin then inhibits release of inhibitory neurotransmitter & GABA é diminished inhibition, there will be ⇧ excitation, spasm & rigidity. Tetanospasmin may also block neurotransmitter release at the neuromuscular junction producing weakness or paralysis. Generalized tetanus occurs when toxin enters into blood stream & lymphatic to affect distant nerve endings.

Clinical Manifestations

The IP (time between injury & 1st symptom) of tetanus is about 7-10 days but it may range from 1 day to 2 months. The period of onset (time between 1st symptom & spasm) ranges 1-7 days. The shorter the IP & period of onset, the more severe the disease becomes. There are different forms of tetanus:-

Generalized Tetanus

Is the most common form. The median time of onset after injury is 7 days; but could occur as early as within 3 days. Usually the first symptom is ⇧tone in masseter muscle

(trismus, or lock jaw) & pt. is unable to open his mouth. Immediately after this the pt. develops dysphagia, stiffness in the neck & back. Then the pt develops contraction of facial muscles to produce rhesus sardonicus (sneer or grimace). There may be arched back (opisthotonos). Generalized muscle spasm triggered by stimulus such as light, noise, or touch. The deep tendon reflexes may be exaggerated & there may be dysphagia or paralytic ileus.

Localized tetanus

Rare form of tetanus. Presents é rigidity & spasm around the portal of entry. While most localized tetanus have good prognosis, cephalic tetanus has high mortality, comes after head/or face injury or ear infection. Pt may come é wide ranges of wound severity, although most have trivial or healed wound. In fact 20% of pts may not give history of injury.

Neonatal tetanus

Occurs in NN of non-immunized mother & those delivered in unhygienic condition. It is a very severe form of tetanus é **>** 90% mortality. NN should referred urgently to a nearby hospital if there is suspicion of clinical tetanus. NN tetanus presents most often after the 7^{th} day of life (IP) é short history of failure to feed. Spasms are typical but the diagnosis can be mistaken for meningitis or sepsis. NN present é generalized rigidity, painful, paroxysmal convulsions, spasm of voluntary muscles involving; masseters (lock jaw), facial muscles (risus sardonicus), muscles of back & neck (opisthotonos position), difficult swallowing & fever in 40% of cases. The NN consciousness is retained. Tetanus may be graded according to severity into the

following grades:-

Grade I (mild): mild trismus, mild spasticity.

Grade II (moderate): moderate trismus, moderate & short lasting spasms, tachypnea (RR 30-35/min) & mild dysphagia.

Grade III (severe): severe trismus, generalized spasticity, resp. embarrassment (RR >40/min), apnoeic spells, tachycardia (>120/min) & severe dysphagia.

Grade IV (very severe): features of grade III + severe autonomic disturbance of CVS, including episodes of hypertension & tachycardia alternating é relative hypotension& bradycardia or sever persistent hypertension (DBP >110 mmHg) or hypotension (SBP <90 mmHg).

Poor prognostic factor

•Pts é higher grades. •Short IP. •Cephalic tetanus. •Pts é comorbidities.

Diagnosis

Based entirely on clinical grounds. •Spatula test; touching the oropharynx é spatula ,baby develop reflex spasm of masseters, bite the spatula. •Culture from woun-ds for clostridium tetany or superinfection. •The CSF analysis is normal.

Treatment

Goals of Rx include; Eliminate source of toxin, Neutralize unbound toxin, Preventi- on of muscle spasm.

General measures

Pt should be admitted to a quiet room in ICU, where frequent monitoring is possible. If there are wounds, they should be explored & cleaned. Respiratory care includes; Intubation & tracheostomy may be required &should be done as early as possible if indicated. These procedures are required for hypoventilation caused by laryngospasm or over sedation or to avoid aspiration. For the autonomic dysfunction; no definitive

treatment has so far been outlined. But hypotension requires fluid expansion& vasopressor drug. Other measures include; hydration, nasogastric tube for nutrition. Physiotherapy should be instituted as soon as possible to avoid contracture. Input & output should be monitored. Bed sores & other infections should be prevented. Recovering pt should start active immunization for tetanus.

Specific Rx

Antibiotic: this helps to eradicate the vegetative bacteria, not the toxin. Crystalline Penicillin/Penicillin G 200.000 u/Kg/day ÷ 4 IV for 10 days for infants & children or 3 million u, IV 4 hourly for 10 days. Erythromycin & Clindamycin are alternatives for allergic pt. Metronidazole active against various anaerobic bacteria & protozoa, 15 mg/Kg/day IV or 500 mg/6 hrs or 1 gm/12 hrs (for adults).

Antiitoxin: this neutralizes only circulating toxins ẃ are not bound. Use of human tetanus immunoglobulin is the choice & should be given early. But tetanus antitoxin ẃ is available in our setup, can be given in doses of 10,000 IU IV + 10,000 IU IM.

Control of muscle spasm*s: Diazepam (Valium) & Chlorpromazine (Neurazien) are given 6 hourly, alternatively. Valium amp 5, 10mg, dose 0.25mg/Kg/dose IV or IM stat ,suppository 5, 10 mg, then 0.1-0.2 mg/3-6 hrs IV. Fortecortine/Decadrone amp 8 mg/2ml, 0.1 mg/Kg/dose IV/IM repeated 6 hourly, then gradual weaning. If spasms are not controlled by the above medication, neuromuscular blockers & mechanical ventilation can be used. The spasms may continue for 3-4 wks & complete recovery may take months. The neonatal mortality even é Rx is 80%, clinical tetanus does not produce state of immunity, therefore survived infant will require active immunization.

Prevention

Immunization of pregnant women é tetanus toxoid, 2 doses of tetanus toxoid to all pregnant women between 16-36 wks of gestation é interval of 1-2 months between

the 2 doses, highly recommended in developing countries. If pregnant woman previously immunized, booster dose is sufficient. If pregnant woman not immunized, the NN should be protected against tetanus by giving tetanus human immunoglobulin 750 U within 6 hrs of birth.

RABIES

One of the so called “neglected zoonotic diseases”. High case fatality rate. Rabies is acute CNS disease that is caused by rabies virus.

Etiology

Rabies virus is single stranded RNA virus ẃ belongs to rhabdovirus family.

Epidemiology

Rabies is found in animals in most regions of the world. Source of infection could be domestic or wild animals. It is 100% preventable, about 55.000 humans die from it each yr around the world, mostly from exposure to dogs. Human infection occurs through contact é unimmunized domestic animals or exposure to wild animals like fox & bats. Domestic dogs are responsible for >90% of cases. The IP of rabies is very variable, ranges from 7 days to as late as ›1 yr, (mean 1-2 months).

Pathogenesis

Virus enters the body through skin or mucous membrane. There is initial replication of virus at the muscles around port of entry then virus ascends to the CNS through the neuromuscular junction. Once in the CNS, the virus replicates in the grey matters. The virus then passes to other organs like kidneys, salivary glands, heart & skin, following the autonomic nervous system. The passage of the virus into Salivary gland facilitates further transmission.-

Clinical manifestations

1. Prodromal stage: usually lasts ˂4 days; manifested by fever, headache, malaise, anorexia & vomiting.

2. *Encephalitis phase:* starts é excitation & agitation, later there will be confusion, hallucination, aggressive behaviour, muscle spasm, meningismus, opisthotonus, seizure & focal paralysis. Pt may have fever, irregular pupils, salivation, perspiration & postural hypotension.

***3. Brain stem dysfunction*:** begins soon after the encephalitis phase. Multiple cranial nerve deficits. Excessive salivation & inability to swallow the excessive saliva. Hydrophobia is seen in 50% of cases.

4. Death: pt rapidly develop coma, death due to respiratory failure.

Laboratory Findings

Early in the course, the routine investigations are normal. Later the WBCs usually moderately elevated, but it may as well be normal. However, diagnosis rests on identification of the virus or serologic tests, PCR of skin biopsy, serology (direct fluorescent antibody test).

Treatment

Once clinical disease appears, mortality is 100%. Therefore any one é history of domestic or wild animal bite should be taken seriously.

Post exposure prophylaxis

Should be considered in people who had physical contact é saliva or secretions of infected animals or bitten by unprovoked animal. This include;

rigorous cleansing & Rx of the wound. Administration of Rabies Vaccine + Anti-Rabies Immunoglobulin. As the IP of rabies is variable, post exposure prophylaxis should be initiated as long as there is no clinical evidence of rabies.

Category I: touching, feeding of animals or licks on intact skin. No exposure therefore no Rx if history reliable.

Category II: minor scratches/abrasions éout bleeding or licks on broken skin & nib-bling of uncovered skin ⇨ use vaccine alone.

Category III: single/multiple transdermal bites, scratches or contamination of mucous membrane é saliva (i.e. licks) ⇨ use Immunoglobulin **+** Vaccine. The administ- ration of RIG is by infiltrate into the depth of the wound & around the wound, the dose is 20 U/kg for Human RIG or 40 U/kg of Equine RIG. Two regimes are used; the classical 5 doses IM regime; one dose of the vaccine to be given on days 0, 3, 7 ,14, 28 in the deltoid region or in small children to be given into the anterolateral area of the thigh muscle. The other regime as an alternative, is the 2, 1, 1 regimen, 2 doses given on day 0 in the deltoid, right & left arm, then additional one dose in the day 7 & the last dose on day 21.

Pre-exposure prophylaxis

People who are at risk of contact é rabies like veterinarian, laboratory workers, ani-mal handlers, toddlers & children in highly endemic areas may be considered, should receive pre-exposure prophylaxis: as 3 doses of vaccine on days 0, 7 & 28. The dose is either 1 standard IM dose (0.5 or 1 ml) or 0.1 ml ID. If antimalarial chemoprophylaxis is applied concurrently, IM are preferable to ID injection. Site of injection (never use gluteal area for vaccination). Adults to be given in deltoid muscle while for children to be given in the anterolateral area of the thigh.

SEXUALLY TRANSMITTED INFECTIONS

Diverse group of infections caused by different types of microbial agents, that are frequently transmitted by sexual contact. At present there are >20 known causes of STDs. Most STDs are rarely if ever transmitted by fomites, food, flies, or casual contact. At least one sexual partner is always infected; the apparent exceptions usually can be attributed to prolonged subclinical infection in one/both partners. So, risk assessment & management of sexual partners are important.

Epidemiology

STDs are major public health problems in all countries, but are especially in developing countries where access to adequate diagnostic & management facilities is very limited or non-existent. There is limited information on the incidence & prevalence of STDs in Egypt. Large proportion of STDs are symptomatic & most symptomatic pts seek Rx from traditional healers, pharmacists….

URETHRAL DISCHARGE

Is the most common presenting compliant of men é STDs. In urethral discharge, exudate is present in the anterior urethra & discharge is often accompanied by dysuria or urethral discomfort. It may lead to epididymitis & complications such as infertility & urethral stricture.

Aetiology

For practical purposes, STDs-related urethritis is divided into the following:-

Gonococcal urethritis: caused by Neisseria Gonorrhoea, also known as Gonococci, or Gonococcus, is a species of Gram -ve coffee bean-shaped diplococci bacteria responsible for the sexually transmitted infection “gonorrhoea”. It has IP (2-3 days).

Vast majority of cases present é abundant, purulent discharge. Tend to produce more severe UTI symptoms like dysuria, urgency & frequency.

Nongonococcal urethritis: usually caused by Chlamydia Trachomatis or Ureaplasm Urealyticum ẃ is a bacterium belonging to the family Mycoplasmataceae. Ureaplasm noted for its lack of cell wall. It is found in about 70% of sexually active humans. Its type strain is T 960, has long IP (1-3 wks). Has scanty to moderate, white, mucoid / serous discharge & mild UTI symptoms. The quantity & appearance of the discharge can be used to distinguish accurately Gonococcal from Non-Gonococcal urethritis in 75-80% of pts who have not urinated recently. It can't of course, be used to diagnose dual infection é N. Gonorrhoea & C. Trachomatis. Milking of urethra may be necessary to get good amount of discharge sample.

Laboratory

Microscopy of urethral discharge stained é methylene blue or gram stain shows: pus cells é intracellular coffee bean shaped diplococcic é gonococcal urethritis, while it shows pus cells éout intracellular diplococcic in non-gnococcal urethritis.

Treatment

When the accurate etiologic diagnosis is made include:-

Gonococcal Urethritis

Treated é Ceftriaxone 250 mg IM stat, or Ciprofloxacin 500 mg PO stat. or Spectinomycin 2 mg IM stat.

Non Gonococcal Urethritis

Treated é Doxycycline 100 mg PO BID for 7 days or Tetracycline 500 mg PO QID for 7 days, or Erythromycin 500 mg PO QID for 7 days.

When there is no etiologic diagnosis: treatment should cover both Gonococcal & Chlamydial infections.

VAGINAL DISCHARGE

Aetiology

①Nisseriagonorrhea ②Chlamydia Trachomatis ③Trichomonas Vaginalis ④Gardnerella Vaginalis ⑤Candida Albicans ⑥Vaginal anaerobes ("bacterial vaginosis"). The first 3 are sexually acquired. The last 3 are endogenous infection. Also the first 2 cause cervicitis while the last 4 cause vaginitis. Bacterial vaginosis is the leading cause of vaginal discharge. As urethritis in males. Coinfection é Chlamydia Trachomatis is common in women é gonorrhoea (~50%).

Clinical picture

Many women have a small amount of vaginal discharge (Physiologic leucorrhoea), ẃ is clear & odourless. It becomes abnormal if the woman notes a change in the amount, colour or odour of the discharge. In general, most women é abnormal vaginal discharge will complain of excessive secretions, soiling of undergarments, changes in colour &/or odour of discharge, may be associated ē itching, dysuria, dyspareunia & redness of vulva. Sometimes accompanied by lower abdominal pain. The initial assessment of pt who has vaginal discharge include:-

-Risk assessment.

-Clinical evaluation é speculum examination to determine site of infection.

Vaginitis

Bacterial vaginosis & vaginal trichomoniasis are more frequent among sexually active women while vaginal candidiasis occurs when there is impairment of local or systemic defensive mechanism. The discharge in bacterial vaginosis is homogenous é typical fishy odour due to the presence of volatile amines & this may be apparent during examination or when the discharge is mixed é 10% KOH. The discharge in trichomoniasis is profuse, runny, mal odorous, while that of vaginal candidiasis is often white, curd-like é pruritus. On speculum examination of isolated vaginitis, the cervix looks healthy

& discharge is not coming from the cervix.

Cervicitis

Is frequently asymptomatic. It may be detected on routine pelvic examination or during evaluation of pt é vaginal discharge. Presence of purulent exudates from the cervical os indicates infection é Neisseria Gonorrhoea or Chlamydia.

Risk factors for vaginal discharge

- Multiple sexual partners in the last 3 months.
- New sexual partner in last 3 months.
- Age ˂25 yrs.
- Having ever traded sex.

Complications of vaginal discharge

- Infertility. - Chronic pelvic pain. - PRM during pregnancy. - Preterm labour.

Laboratory investigations

Specimen of vaginal discharge used mainly for the diagnosis of trichomoniasis, bacterial vaginosis & candidiasis. In trichomonos vaginalis; characteristic jerky motility of the parasite é many WBCs. In bacterial vaginosis; typical fishy odour ẃ enha- nced by the addition of 1-2 drops of potassium hydroxide to the specimen of vaginal discharge (sniff test); number of epithelial cells per microscopic field exceeds the number of leukocytes (cornified squamous epithelial cells covered by coccobacilli “Clue cells”). In candidiasis; look for yeast, the addition of 10% KOH may improve diagnostic sensitivity. **N.B.** in general, Gram stain not helpful in diagnosing gonorrhoea in females (low sensitivity).

Treatment

Trichomonos Vaginalis: Metronidazole 2 gm PO stat.

Bacterial Vaginosis; only symptomatic women need Rx, Metronidazole 500 mg PO

BID for 7 days or 2 gm (single dose), repeat after 2 days.

Vulvovaginal Candidiasis; topical antifungal; Nystatin 100,000-1,000,000u/day intravaginally for 14 days, or Clotrimazole 200 mg intravaginally/day for 3 days.

Mucopurulent discharge; Rx for gonorrhoea & chlamydia.

Recommended treatment for Vaginal Discharge syndrome	
Risk Assessment +ve	Risk Assessment -ve
Ciprofloxacin 500mg PO stat or Spectinomycin 2gm IM stat + Doxycycline 100 mg PO BID for 7 days + Metronidazole 500 mg Po ID for 7 days	Metronidazole 500mg Po ID for 7 days + Clotrimazole vaginal tabs 200 mg at bed time for 3 days

GENITAL ULCER

Is loss of continuity of the skin of the genitalia, is either painful or painless & frequently accompanied by inguinal lymphadenopathy.

Causes

Syphilis

Caused by Treponema Pallidum. The genital ulcer occurs in the 1ry stage of the diseases. Starts as small papular lesion that rapidly ulcerates to produce a non-te-nder indurated lesion é clean base & raised margins known as chancre. The chancre may appear at any point of contact: genitals, anus, mouth. The ulcer heal éout treatment in 1-6 wks. Swollen LNs may appear.

Complications

- Secondary Syphilis.
- Aortitis é valvulitis.
- Neurosyphilis.

Management

Benzanthine Penicillin 2.4 million U IM stat or Procaine Penicillin 1.2 million U daily IM for 10 days. In Penicillin allergic pts, Idoxycycline 100 mg PO BID for 15 days.

Genital Herpes

HSV has 2 types; HSV-1 causes dominantly oral disease & HSV-2 causes dominantly genital disease. Worldwide, herpes is the most common cause of genital ulcer. Latency & frequent recurrence characterizes genital herpes, producing a lifelong infection. Herpetic ulcers usually painful & multiple. Starts as clear vesicle & becomes pustule ẃ later erodes to an ulcer & then crusts. Heals spontaneously after 2-3 wks. Recurrence possible but milder (the number of vesicles are fewer). It tends to be aggressive in HIV pt é extensive tissue involvement & chronic ulceration. May also disseminated to CNS, or skin.

Complications: ⅄Recurrence ⅄Aseptic meningitis ⅄Encephalitis.

Management: Acyclovir (200 mg tab) 15 mg/ kg/day ÷ 3 for 10 days.

Chancroid

Caused by Haemophilus Ducreyi, is one of the commonest causes of genital ulcers. IP: 3-15 days. Ulcer on the penile shaft or prepuce. It is painful progressing from small papule to pustule, then ulcer é soft margins described as soft chancre é yellow grey exudative covering & erythema. Inguinal lymphadenopathy that becomes necrotic & fluctuant (bubo) follows the ulcer within 1-2 wks.

Complication: penile auto amputation.

Management: Ceftriaxone 250mg 1M stat or Erythromycin 500mg TID for 7 days.

Lymphogranuloma Venereum

Caused by L1, L2 & L3 serovars of Chlamydia Trachomatis. Major pathology occurs in the lymphatic system. The primary stage is marked by a painless vesiculopapular ulceration at the site of inoculation, located in the penis in men & on the labia & posterior vagina in women. The primary lesion usually not noticed. The secondary stage is described as the inguinal syndrome; a painful inguinal lymphadenitis ē co-

nstitutional symptoms. In men infection usually spreads through the lymphatics causing inguinal & femoral lymphadenitis. In women upper vaginal & cervical infection results in enlargement of the obturator & iliac LNs (sometimes pelvic LNs). Inguinal lymphadenopathy is usually unilateral (2/3 of cases). The LNs initially discreet & later becomes fluctuant & suppurative developing multiple draining fistulas. Bubo may grooved by the inguinal ligament "groove sign". External genitalia may be oedematous & swollen. May cause anatomical distortion, particularly of penis. Spontaneous healing after several months possible.

Complications: genital elephantiasis, adhesion, stricture & fistula of penis, or urethra or rectum.

Management: Doxycycline 100 mg PO BID for 14 days or Tetracycline 500 mg PO QID for 14 days

Granuloma Inguinal

Chronic & progressively destructive bacterial infection of the genital region éout systemic symptoms.

Aetiology: Calymmato bacterium Granuloma is G-ve intracellular bacteria, transmitted through sexual & nonsexual contact. Distribution mainly in Australia, Caribbean, India, Southern Africa.

Clinical manifestation: IP usually 1-4 wks, may be as long as a year. Pt usually presents é non suppurative genital lesion ẃ develops from small firm papule to painless ulcer é beefy red appearance &non purulent base. Lesion bleeds easily & expand gradually. 50% of women have lesion on cervix & 6% have extra inguinal.

Complications:•Elephantiasis of labia •Adhesion •Urethral/vaginal/rectal stenosis.

Management: Cotrimoxazole 2 tab PO BID for 14 days.

NB: tetracycline is contraindicated during pregnancy.

INGUINAL BUBO

Inguinal bubo is enlargement of the lymph glands in the groin area.

Aetiology

The common sexually transmitted pathogen associated é Inguinal bubo include:- Chlamydia Trachomatis server L1-L3 (Lymphogranuloma Venereum). Haemophilus Ducreyi (Chancroid). Calymmatobacterium Granulomatis (Granuloma Inguinal). Trep-onema Pallidum (Syphilis) may sometimes cause it. Except in case of LGV, bubo is rarely a sole manifestation of STDs & usually found together é the aetiologically relat-ed genital ulcer. Non-sexually transmitted local or systemic infections can also cause inguinal lymphadenopathy.

Clinical feature

Usually pt complains of unilateral or bilateral painful swelling in the groin, but bubos can be painless.

Treatment

Fluctuant buboes require aspiration through adjacent healthy skin & don't incise for drainage. If genital ulcers are present, treat é the aetiologically related cause.

Recommended Rx Inguinal Bubo Ciprofloxacin 500 mg PO BID for 3 days + Doxy-cycline 100 mg PO BID for 14 days or Erythromycin 500 mg PO BID for 14 days.

SCROTAL SWELLING

The cause of scrotal swelling depend on the age of the pt: for those ‹35 yrs: Nisse-ria Gonorrhoea & Chlamydia Tracomatis. For those›35 yrs: Gram -ve organisms, TB & other causes including Brucellosis, Mumps, Onchocerciasis, Wuchereria Buncrof- ti. It is important to exclude other causes of scrotal swelling ẃ may require urgent surgical evaluation & management as; testicular torsion, trauma, or incarcerated inguinal hernia.

Complications: •Epididymitis •Infertility •Impotence •Prostatitis.

Management

- Supportive Rx; analgesia & scrotal support may be indicated é severe pain.
- Antibiotics; Ciprofloxacin 500 mg PO or Spectinomycin 2 gm IM stat + Doxycycline 100 mg PO BID, or Tetracycline 500 mg PO QID for 7 days.

LOWER ABDOMINAL PAIN

Lower abdominal pain in women is associated é PID e.g. salpingitis, endometritis, parametritis, oopheritis, caused by microorganisms ẃ generally ascend from lower genital tract to invade the endometrium, fallopian tubes, ovaries, other adjacent tissues & peritoneum.

Aetiology

Commonly Neisseria Gonorrhoea & Chlamydia Trachomatis. PID often polymicrobial & may be associated é mycoplasma, bacteroids, strept, E. coli, H. influenza, ẃ may not be sexually transmitted.

Risk factors

The occurrence of vaginal discharge may be an antecedent event. The risk factors include; STDs, IUDs, postpartum & postabortal ascending infections.

Clinical features

Mild to severe bilateral lower abdominal pain is the most common complaint, ẃ may first to be noticed during or shortly after menses & ẃ is sometimes associated é fever. Presence of vaginal discharge support the diagnosis of PID, pain during intercourse or urination may also be present.

Physical examination

Lower abdominal & adnexal tenderness together é cervical excitation may be indicative of PID. Tender pelvic mass together é fever, nausea/vomiting can also be

detected. Vaginal discharge, genital ulcer, presence of IUD, open cervix (abortion tissue seen or felt) support the diagnosis of PID.

Diagnosis

Is often difficult. Over diagnosis & Rx may be justified in order to prevent complications. R/O other cause of lower abdominal pain in women as appendicitis, ectopic pregnancy & cholecystitis. Direct wet mount microscopy of a vaginal specimen is necessary. The presence of pus cells in numbers exceeding those of epithelial cells suggests infection of the lower genital tract.

Complications

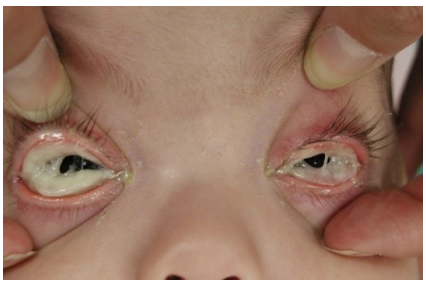
Peritonitis -Intra-abdominal abscess -Adhesion -Intestinal obstruction -Ectopic pregnancy -Infertility.

Treatment

Most pts. é mild/moderate PID can treated as out pt. Some pts need hospital admission. Indications for admission include; uncertain diagnosis, pelvic abscess, pre- gnancy, coinfection é HIV. As the infection is polymicrobial in nature instead of sin- gle, combination of antibiotics should be prescribed. The spectrum of antimicrobial should cover the following organisms; N. Gonorrhoea, C. Trachomatous, Aerobic & Anaerobic Bacteria. Antibiotics should be initiated empirically even before the microbiological report is available.

Recommended Rx for lower abdominal pain as Out patient	Recommended Rx for lower abdominal pain as In patient
Ciprofloxacin 500 mg PO stat or Spectinomycin 2 gm IM stat + Doxycycline 100 mg PO BID for 14 days + Metronidazole 500mg mg PO/day for 14 days. Admit the pt if there is no improvement within 72 hrs.	Metronidazole 500 mg PO/day for 7 days + Clotrimazole vaginal tab. 200 mg at bed time for 3 day.

NEONATAL CONJUNCTIVITIS



Defined as mucoid, mucopurulent or purulent discharge from one or both eyes in the first month of life. Any discharge, even a watery secretion from baby`s eyes during the first week should be viewed é suspicion, since tears are not secreted so early in life. Neisseria gonococcal cause mucopurulent/purulent discharge, marked chemosis & retractor may be required to examine the eyes, the eye lids are tense & swollen, a false membrane may be form. Corneal ulceration may occur. It is preventable disease occurring in newborn baby due to maternal infection acquired at the time of birth & used to be responsible for 50% of blindness among children. Recently -NN conjunctivitis almost eliminated except in communities é poor hygiene & limited health care.

Differential diagnosis

Gonococcal infection, Chlamydial, other bacteria, viral, or congenitally blocked nasolacrimal duct, or dacrocystitis.

Bacteriological examination

Examination of discharge, or conjunctival scrapings, should be done in every case, gram stain, culture/sensitivity.

Complications

- Perforation.
- Cataract.
- Panophthalmia.
- Corneal opacities.

Management

According to the time of onset, classified as follow:-

- Seen within the first 48 hrs of life: Neisseria Gonorrhoea-treated é Ceftriaxone IM, Gentamicin drops, Bacitracin ointment. Chemical conjunctivitis needs washing of eyes, Erythromycin ointment, observe, usually improves in 24 hrs.
- Seen within the 48-72 hrs of life: Staph, Strept, G-ve Coliforms, treated é Neomycin/Bacitracin ointment. Gentamicin or Tobramycin drops.
- Seen within the 5^{th}-7^{th} day of life: HSV-II, treated é Acyclovir 3% eye ointment, systemic Acyclovir for systemic involvement.
- Seen after the 1^{st} wk of life: Chlamydia Trachomties, treated é Erythromycin/Chlortetracycline eye ointment. Oral Erythromycin for systemic infection & parents to be treated.

Differential Diagnosis of Bacterial, Viral & Allergic Conjunctivitis

Clinical Finding	Bacterial	Viral	Allergic
Bilateral eyes	50% to 74%	35%	Mostly
Discharge	Mucopurulent in younger children	Mild, watery, or "sleepers" only	Rare
Redness	Common in older children, uncommon in infants and toddlers	Usually	Usually
Acute otitis media	32% to 39%	10%	No
Pruritic	No (but many rub eyes)	No	Major

TYPHOID FEVER

Definition

Systemic infection characterized by fever& abdominal pain, caused by dissemination of salmonella typhi & occasionally salmonella paratyphi A, B & salmonella typhimarium. All of them are non-capsulated, G -ve motile bacteria.

Epidemiology

Human beings are the only hosts for salmonella typhi & paratyphi, thus enteric fever is transmitted only through close contact é acutely infected individual or chronic carrier through ingestion of contaminated food or water. Chronic carriers are the source of infection harbouring the organisms in their gall bladder (especially in presence of gall stones) & rarely at other sites. It affects people of all ages & both sexes. Typhoid is endemic in most developing countries. The disease observed at great frequency in AIDS pts than general population.

Pathogenesis

Following ingestion of the organism in contaminated food/drink, salmonella typhi passes the gastric barrier & reach the upper small intestine where the bacilli invade the intestinal epithelium &they are engulfed by phagosoms ẃ reside in the payer's patches. The bacilli multiply & enter the blood stream causing transient bacteraemia. At this stage salmonellae disseminate throughout the body in the macrophages via lymphatic & colonize RES (liver, spleen, LNs & bone marrow). Pts have relatively fewer or no signs & symptoms during this initial IP. The signs & symptoms, including fever & abdominal pain result when a critical number of bacteria have replicated during wks after initial colonization, further inflammation of Payer's patches may result enlargement & necrosis ẃ may result in intestinal Hge & perforation. Infection may become persistent & invade gall bladder. The clinical phase of typhoid fever depends on host defence & bacteria multiplication.

Clinical manifestation

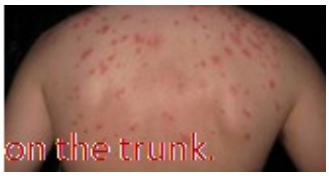
IP varies from 3-60 days & manifestation is dependent on inoculum size, state of host defence & duration of the disease. Severity of the illness range from mild, brief illness or acute severe disease or CNS involvement & death.

1st wk: fever is high grade é daily ⇧ in a stepladder pattern for the 1st wk then be- comes persistent. Headache, malaise & abdominal pain. Initially diarrhoea follow- ed by constipation in adults, while diarrhoea is dominate feature in children. Relative bradycardia. Splenomegaly & hepatomegaly. Rose spots not commonly seen in black pts. In whites it appears as small, pale red, blanching macules commonly over chest, abdomen & back lasting for 2-3 days. Epistaxis may be seen.

2nd wk: fever becomes continuous. Pt becomes very ill, withdrawn, confused, deliri- ous & sometimes may be even comatose.

3rd wk: pt goes to a pattern of “typhoidal state" characterized by extreme toxaemia, disorientation, “pea-soup” diarrhoea & sometimes may be complicated by intestinal perforation & Hge.

4th wk: fever star- ts to decline**,** pt may defervesce é resolution of symptoms. At this point pt may lose weight. Relapse may occur in 10% of cases.



Rose spots on 5th day on the trunk.

Complications

GIT perforation & Hge are late complications that may occur in the 3rd - 4th wk. May develop despite clinical improvement. These complications are life threatening & need immediate medical & surgical interventions. Other less common complications include; hepatitis, meningitis, arthritis, osteomyelitis, parotitis, orchitis, nephritis, myocarditis, bronchitis & pneumonia. These complications can be prevented by pro-

mpt diagnosis & Rx of typhoid from the start.

Chronic carriers

1-5% of pts become asymptomatic chronic carriers. They shed salmonella typhi in either urine or stool for >1 yr. The incidence is higher in women & among pts é biliary abnormality (stone or carcinoma of gall bladder) & other GIT malignancies.

Diagnosis

Suggested by the presence of:-

- Persistent fever.
- Relative bradycardia found to occur in 80% of cases.
- Rose spots seen in 70% of whites & 20% of others.
- Leukopenia.

But definitive diagnosis of the disease requires laboratory tests including:-

o**Blood culture:** up to 90% of pts have +ve culture in the first week & only 50% by the third week. The yield is much lower if pt has taken antibiotics prior to the test o**Stool culture:** is -ve in the first wk, becomes +ve in 75% of pts in the third wk. Urine culture parallels stool culture.

o**Widal test for O & H antigens:** the O (somatic) antigen indicate active infection, whereas the H (flagellar) antigen could be indicative of past infection or immunization of typhoid. Widal test is a test involving agglutination of typhoid bacilli when they are mixed é serum containing typhoid antibodies from an individual having typhoid fever; used to detect the presence of salmonella typhi & paratyphi. The widal test has certain limitations & to make a diagnosis of current infection a 4 X (fold) ⇧ in titre on paired sera taken during the acute & convalescence phases is necessary (in normal individual widal test value is < 160).

Limitations of Widal test: include the following; it is non specific & +ve test could be

due to; •Infection by other salmonellae (as the antigen used for the test is also shared by other salmonellae). •Recent vaccination for typhoid, or •Past typhoid infection (already treated). The demonstration of 4 -fold ⇧ in titre on paired sera is not useful for Rx of acute cases, as this requires waiting for the convalescence phase & at this stage if the pt is lucky recovery will occur.

o**PCR for typhoid.** in general the PCR is the most sensitive of the existing rapid methods to detect microbial pathogens in clinical specimens.

Treatment

Antibiotic Rx is curative. These drugs can be given either PO or IV, depending on pt condition & the severity of the disease. One should note that fever may persist for 4-6 days despite effective antibiotic Rx. First line nowadays for Rx is 4-Amino Quinolones ẃ are the drugs of choice because of their effectiveness on multidrug resistant typhoid & low relapse & carrier rates. Ciprofloxacin, Norfloxacin, Ofloxacin are all equally effective. Other antibiotics as ampicillin, chloramphenicol, trimethoprim-sulfamethoxazole, amoxicillin are also effective

Claforan (cefotaxime) 500 mg amp, 50 mg/kg/D÷3 IV OR Oral 4th gen. cephalo: Orelox sy 40mg, 8 mg/Kg/D ÷2 X 5D, or Zinnat susp, 125 mg, 8 mg/Kg/D ÷2 X 5D.

IV Drugs recommended for critical pts or for pt unable to take orally:-

- Prompt administration of high-dose dexamethasone reduces mortality in pts ē
- severe typhoid fever without increasing incidence of complications, carrier
- states, or relapse among survivors.
- Initial dose of 3 mg/kg by slow IV over 30 min, 1mg/kg 6 hourly for 2days.

Chronic carrier eradication

-Ciprofloxacin for 4 wks is effective, much better than other drugs. or

-Ampicillin or Amoxicillin 100 mg/kg/D taken é Probenecid 30mg/kg/day for 6 wks. –

-Cotrimexazole (160/800 mg twice a day) + Rifampicin 600 mg PO/ day for 6 weeks.

N.B. drug treatment does not eradicate infection in 40% of cases of chronic carriers. Hence surgical resection of gall bladder may sometimes be necessary.

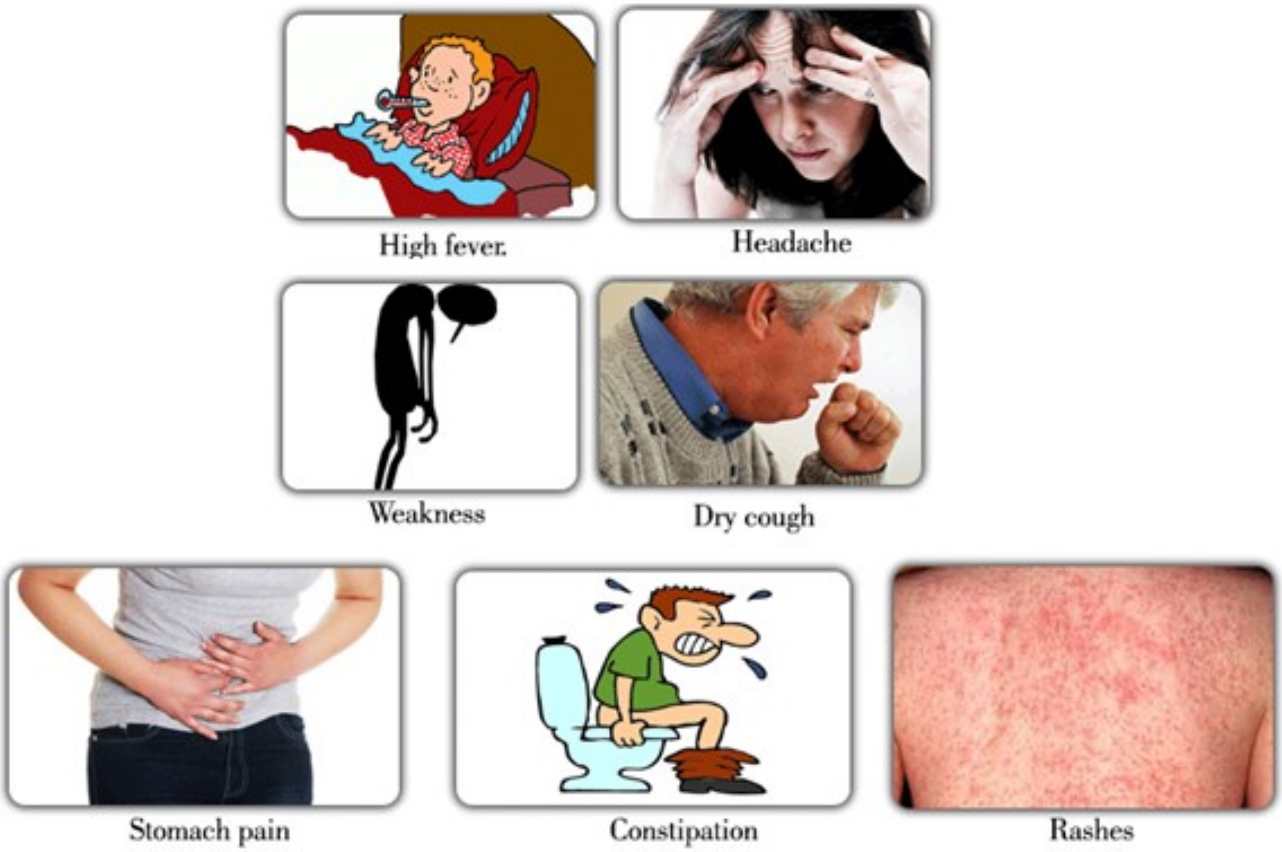
Prevention & control of typhoid

✶Improve environmental sanitation.

✶Identification& Rx of chronic carriers.

✶Avoid food handling by chronic carriers.

✶Vaccination for food dealers, those working in restaurants, vaccination of travellers to endemic areas: - live oral vaccine 3 dosses can be given to those **>** 6 yrs, is protective for several yrs. The purified Vi polysaccharide vaccine given in a single dose to those **>**2 yrs age & HIV +ve individuals, is as effective as live vaccine.



BRUCELLOSIS

Zoonotic disease caused by *Brucella species* characterized by remittent type of fever & multiorgan involvement. It is transmitted to humans from infected animals.

Aetiology

It is caused by 4 different types of Brucella. They are small aerobic Gram -ve bacilli; are non-motile & facultative intracellular, include:-

Brucella melitensis (the most common & most virulent type) acquired from goats, sheep & camels.

Brucella abortus from cattle.

Brucella suis from hogs.

Brucela canis from dogs.

Epidemiology

It is found worldwide, but the true incidence is not known. In communities where brucellosis is endemic, it occurs in children & family members of infected persons are at risk. Commonly affected are farmers, meat-processing workers, veterinarians & lab workers. Brucella is transmitted commonly through the ingestion of untreated milk/or milk products, raw meat & bone marrow have been implicated. But also can be transmitted by inhalation from close contact é animals.

Pathogenesis

In blood, brucella ingested by PMNLs & macrophages but they resist intracellular-phagocytosis. Severity of the disease is largely determined by the outcome of pathog-

en-phagocyte interaction. The organisms multiply, reach blood stream via lymphatics & then reside in different organs; liver, spleen, bone, kidneys, LNs, heart valves, nervous system & testes. In the infected organs there will be inflammatory responses or non-caseating granulomas. Serum IgM will appear within a wk & later on IgG & IgA.

Clinical manifestations & complications

Brucellosis is a systemic illness & its manifestations mimic other febrile illnesses. The IP is about 1-3 wks. The illness may begin suddenly or it could be gradual. The most common symptoms are fever, chills, sweating especially by night, headache, myalgia, fatigue, anorexia, joint or low back pain, Wt loss, generalised lymphadenopathy, constipation, sore throat & dry cough. Pt may look well é no findings or may exhibit physical findings related to the organ affected. Fever has no distinctive features but it occurs in late afternoons or evenings. Pts may have reactive asymmetric polyarthritis involving the large joints & lumbar vertebral osteomyelitis. CVS complications of brucellosis include endocarditis, myocarditis, pericarditis, thrombophlebitis & pulmonary embolism. Respiratory manifestations like sore throat, tonsillitis, dry cough, even pneumonia &lung abscess. The GIT manifestations are generally mild include; nausea, vomiting, abdominal pain & diarrhoea; there is tender hepatosplenomegaly (Morphy sign) in about 15-20% of pts. Pts may have genitourinary infection &present é epididymoorchitis, prostatitis, amenorrhea, tub ovarian abscess, salpingitis, acute pyelonephritis & glomerulonephritis. The Nervous system involvement is uncommon but if involved, pt may have meningitis, brain abscess, hemiplegia & cranial nerve deficit. Other manifestations are conjunctivitis, retinopathy, abortion, anaemia, leukopenia & thrombocytopenia.

Diagnosis:

- History of exposure & Clinical features.

•Significantly ⇧ levels of Brucella agglutinin >1/160 confirms the active infection.

•CBC: leukopenia é lymphocytosis.

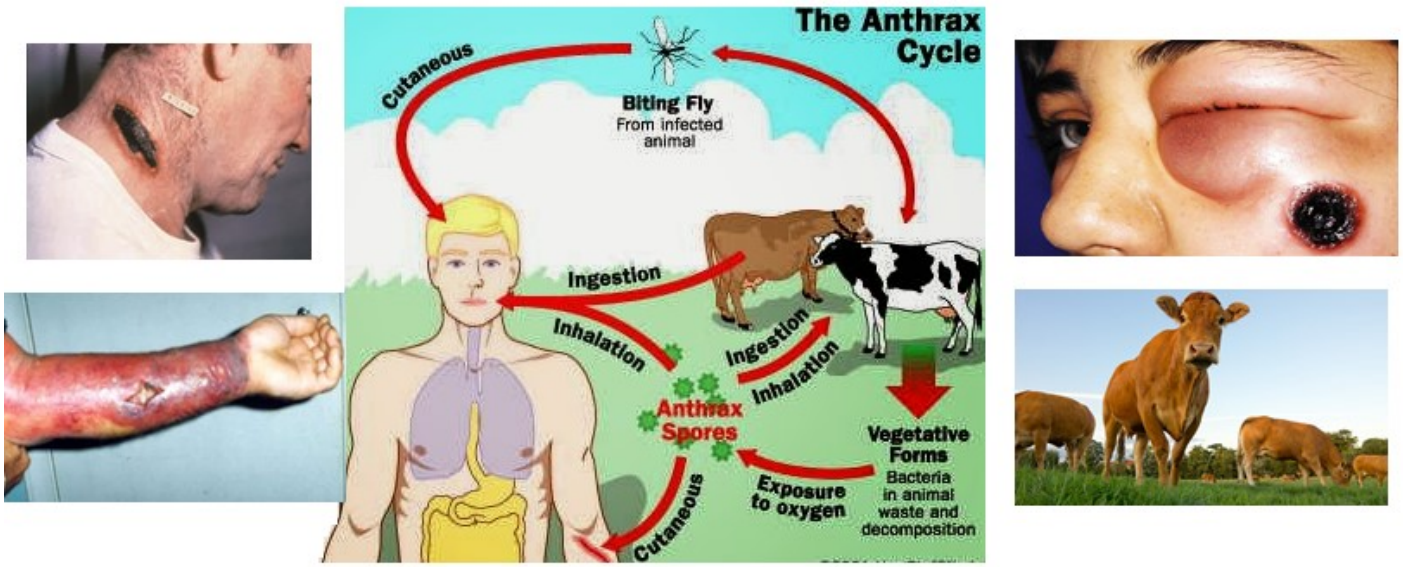
•Blood C/S. •Antibodies for brucella (IgM) •ELISA •PCR.

Treatment

The combination of Doxycycline & Aminoglycoside for 4 wks followed by the combination of Doxycycline & Rifampin for 4-8 wks is the most effective Rx. Pt é serious illness & complication need admission for Rx é IV medications & possible surgical intervention.

Prevention: immunization of animals, boiling or pasteurizing milk.

ANTHRAX



Is occupational disease, affect workers in farms & dealer é animals. The disease transmitted from infected animals to man through skin to skin contact, causing an ugly ulcer, or through inhalation of spores from dead animal tissue causing respiratory symptoms, pneumonia, or through ingestion of spores in undercooked meat causing GIT symptoms & may lead to meningitis.

Aetiology

Bacillus anthracis is a large, aerobic, spore-forming, G +ve rod, ẃ is encapsulated & non-motile.

Epidemiology

Is more common in herbivorous animals like cattle, sheep& goats. They are infected while grazing on contaminated grass. Humans may acquire anthrax from agricultural sites through contact é animal like butchering & feeding or from industrial sites thr-ough exposure to contaminated hides, wool or bones.

Pathogenesis

Cutaneous anthrax is initiated when spores of *B.* Anthracis are introduced through ab-rasions of the skin or insect bite. Inhalation anthrax is acquired by directly inhaling the agent. The GIT form is acquired through ingestion of contaminated raw or partially cooked meat. Bacillus Anthracis goes to the blood stream & replicates rapidly. It is re-sistant to phagocytosis & produces anthrax toxin, ẃ cause oedema & inhibition of polymorph nuclear leucocyte function. Moreover it causes release of cytokines, shock & death.

Clinical Manifestations

IP is 1-5 days. About 95% of anthrax is cutaneous form, 5% is through inhalation. The GIT form is very rare & is more common in areas where raw meat is ingested. ***Cuta-neous Anthrax***

Lesions more common on exposed areas as extremities, face & neck. Lesion start as a small red macule develops within days, this will become pustule, then forms a central necrotic ulcer (black eshcar) é surrounding oedema; its painless. Usually there is asso-ciated painful regional lymphadenopathy. Most pts recover spontaneously but about 10% develop progressive infection, bacteraemia, high grade fever & rapid death.

Inhalational Anthrax (wool sorter's disease)

Resembles severe viral respiratory disease & thus the diagnosis is difficult. This form

may be used as biological warfare. Within 3 days of infection pt will develop fever, dyspnoea, stridor, hypoxemia, hypotension & may die within 24 hrs once pt become symptomatic.

GIT Anthrax

Pt may have nausea, vomiting, abdominal pain, bloody diarrhoea, fever & they may develop ascites.

Investigations

- CBC.
- Blood culture.
- Chest X ray.
- Sputum culture.

Treatment

Cutaneous Anthrax: treated é Crystalline Penicillin 2 million units 6 hourly until oedema subsides then oral Penicillin for 7-10 days.

For allergic pt Ciprofloxacin, Erythromycin, or Chloramphenicol may be given. The wound should be cleaned, debrided & dressed.

Inhalation & GIT form: should treated é high dose Penicillin 8-12 million units/day ÷ 4-6 doses for 2 wks.

Mortality rate

Cutaneous anthrax is 10-20%, inhalational anthrax 100% & GIT anthrax is 50%.

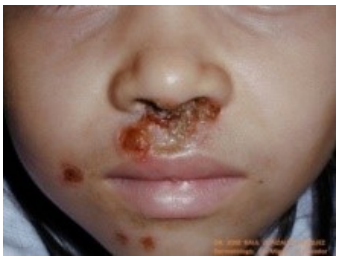
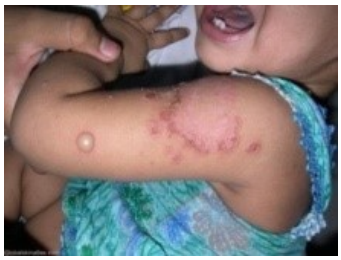
Prevention

☑ Mass vaccination of animals.

☑ Avoiding feeding of infected cattle.

☑ Proper disposal of dead animals & Keeping personal hygiene.

IMPETIGO

Impetigo is a superficial disease. This means that it is on skin surface. Most comm- on in children & can affect skin é no visible breaks in it. It is contagious & can be spread through pus from touching an infected person. Commonly occurs around the nose, mouth, hands, forearms & in diaper areas on infants.

Causes

•Staphylococcus or streptococcus bacteria. •Methicillin-resistant staph aureus is a common cause. •The breaking of the barrier of skin, some of these occurrences are animal or human bites, injury or trauma, or insect bites. •Any blister or rash that is scratched a lot can be turned to impetigo.

Symptoms

Pus filled blisters, red base when popped, easy to pop blisters, it is itchy & yellow pus filled é crusty outsides. Skin lesions. Rashes that can spread é scratching. Swollen LNs. Can be diagnosed é sample of the pus from the lesion for bacteriological examination.

Complications

•Spread to other parts of the body (common) •Rashes in kids •Can cause kidney fail- ure (rare) •Permanent damage to the skin (rare)

Treatment

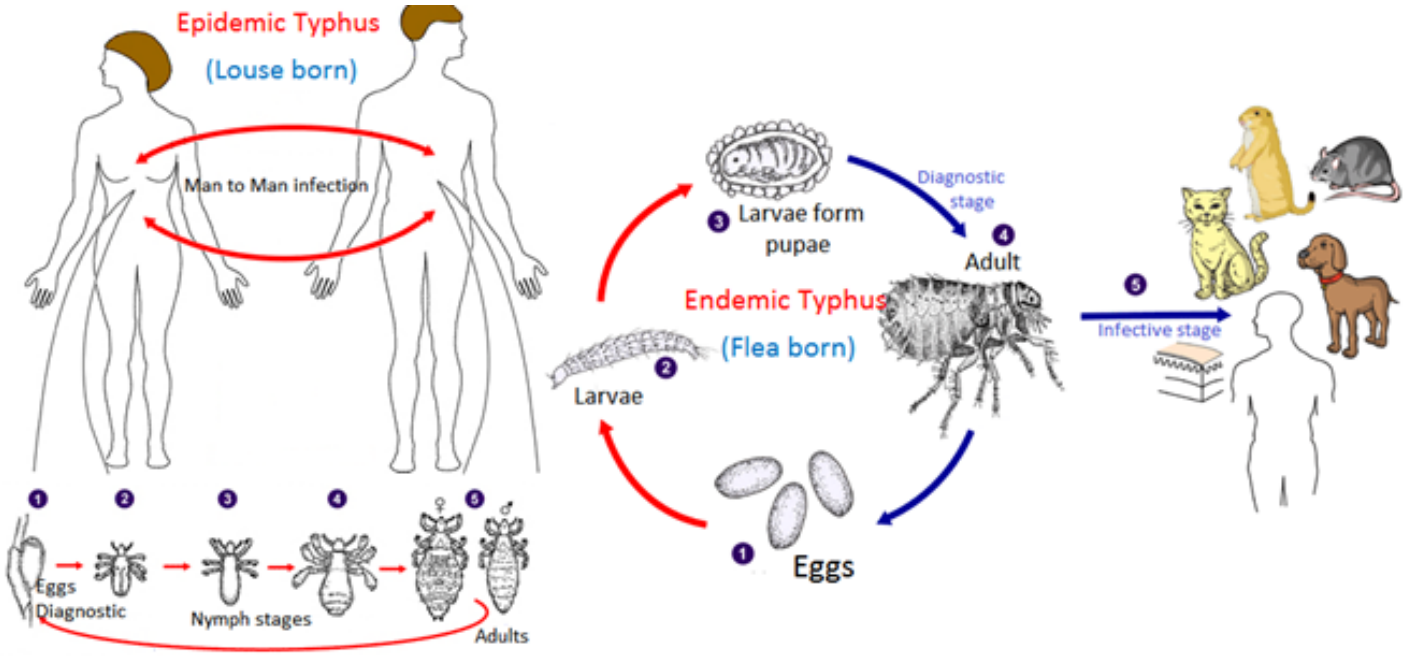
☑ Prescription antibiotic cream for mild rashes.

☑ Systemic antibiotics for more severe cases.

☑ Washing several times a day é antibacterial soap & warm water to remove the cru- st & pus from the lesions.

TYPHUS

Rickettsial disease. Rickettsia are small intracellular bacteria that are spread to man by arthropod vectors, namely human body lice, fleas, ticks & larval mites by the direct bite of the vector or inoculation of the organism contained in the faeces of the vector by bite induced body itching. These infections are characterized by persistence in the body, widespread vasculitis (invading endothelial cells of small blood vessels) & multi-system involvement.



Epidemic Typhus

Louse born, caused by R. Prowazekii, transmitted by human body louse (pediculus humanus corporis). Lice acquire the rickettsia while ingesting a blood mealfrom an in-fected pt, the rickettsia multiply in the midgut epithelial cells of the louse & excr-eted via louse faeces. The infected louse defecates during a blood meal, the pt autoinocu-lates the organisms by scratching. The disease commonly associated é pov-erty, cold weather, natural disasters & wars.

Pathophysiology

In human rickettsia multiply in the endothelial cells of capillaries causing lesions in the skin, brain, lung, heart, kidneys & skeletal muscles. Endothelial proliferation coupled é

perivascular reaction causes thrombosis & small haemorrhages. However, tissue & organ injury is commonly due to ⇧ vascular permeability é resulting oedema, hypovolemia & organ ischemia. This leads to multisystem involvement é complications as non-cardiogenic pulmonary oedema, cardiac arrhythmia, encephalitis, renal or hepatic failure & bleeding.

Clinical Features

•IP of epidemic typhus is one wk. •Abrupt onset of illness é prostration •Severe headache. •Rapidly rising fever of 39-40°C. •Cough seen in 70% of pts. •Myalgia may also occur ẃ may be severe. •Rash, begins on upper trunk around 5th day & then becomes generalized, involving entire body except face, palms & soles; at first, rash is macular, becoming maculopapular, petechial & confluent éout Rx, although in black people, rash may be absent (*spotless epidemic typhus*) •Photophobia é conjunctival injetion & eye pain. •Tongue may be dry, brown, furred. •Signs of CNS involvement, commonly as meningoencephalitis, appear towards the end of first wk progressing to seizure & coma.

Brill-Zinsser disease

This is a mild form of epidemic typhus caused by reactivation of dormant R. prowazekii in the body (in LNs) as a result of immuosuppression or old age. Occurs after several yrs of acute infection. The manifestation are similar to acute epidemic typhus but milder. Organisms may infect other people in the presence of the vectors.

Endemic Typhus

Flea born, caused by R. typhi. Fleas acquire R. typhi from rikettsemic rats, carry the organism throughout the rest of their life. Humans & Rats are infected when rickettsia laden fleas are scratched into pruritic bite lesions. Endemic typhus is relatively milder, its IP is 1-3 wks, followed by sudden onset of fever, rigors, frontal headache, pain

in in the back & limbs, constipation & cough (bronchitis). Fever becomes constant after the 3rd day, associated é conjunctivitis & orbital pain. Rash appears on the 5th day initially as blanching macules at the anterior axillary folds, ẃ subsequently spread to involve other parts of the body (sparing face & neck) & become purpuric. During the 2nd wk symptoms worsen & additional manifestations ns, as sore lips, dry brown tremulous tongue, feeble pulse, enlarged spleen & delirium.

Complications

•Skin necrosis, gangrene of digits •Venous thrombosis •Interstitial pneumonia in severe cases •Myocarditis •Renal failure •Parotitis.

Diagnosis

•Based on history, clinical course & epidemiologic of the disease.

•Indirect fluorescent antibody test.

•Weil-Felix agglutination test: not specific or sensitive.

•Isolation of the organism by inoculation into laboratory animals is possible, it is time consuming & technically demanding.

Treatment

Epidemic typhus

Doxycycline 200 mg as single dose PO until the pt is afebrile for 24 hour + Delousi-ng louse borne typhus, improving hygienic condition, health education & environ- mental sanitation.

Endemic Typhus

Doxycycline 1500 mg bid PO for 7-15 days or Chloramphenicol 1500 mg QID PO for 7-15 days + fleas control & the prophylactic measures.

Supportive therapy: attention to fluid balance, prevention of bed sores. Treat agitation é Diazepam. Steroid (Prednisolone 20 mg/day for adults) in severe cases.

Prognosis

Untreated disease is fatal in 7-40% of cases, depending on condition of host. In untreated survivors, renal insufficiency, multiorgan involvement & neurologic manifestations (12%). in endemic typhus the prognosis is better é mortality of 1-2%.

Prevention

Epidemic typhus

Eradicate all lice on clothing & bedding using insecticides (1% malathion powder), including all family contacts. DDT is not useful as the lice are often resistant to it. Wash the pt é soap & water & apply insecticides all over & disinfect clothing é insecticides in a bag or autoclaving. Protective wearing smeared é insect repellents is recommended for nurses & other attendants.

Endemic typhus

Elimination of fleas on clothing & bedding using insecticides like 1% Malathion powder. Apply residual insecticide powder on the floor & bedding to kill hatching fleas, in addition to rodent control using chemicals.

Chemoprophylaxis

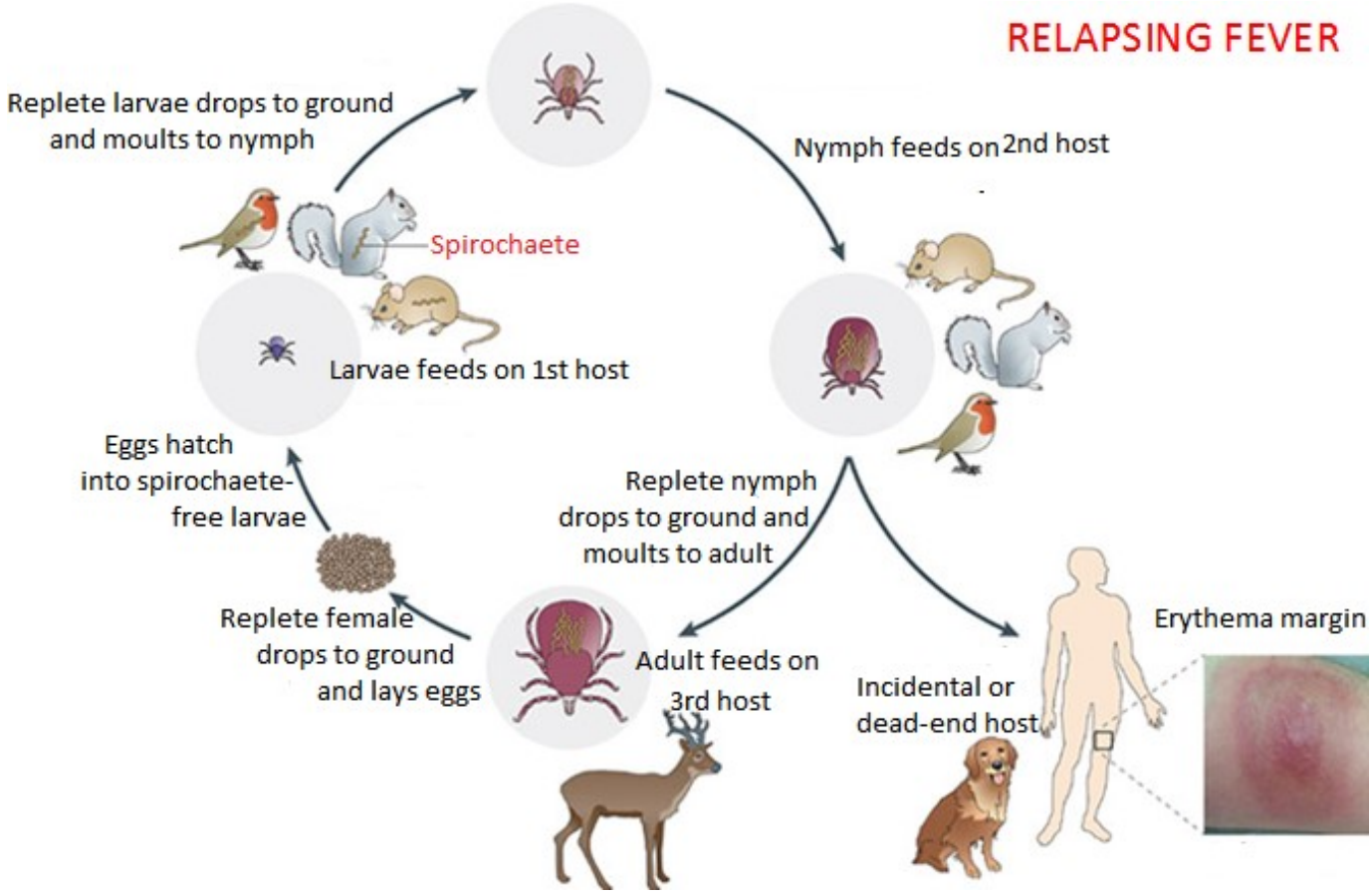
Doxycycline 100mg weekly will protect those at risk.

RELAPSING FEVER

Acute febrile illness caused by Borrelia species, presenting é recurrence of characteristic febrile periods lasting for days alternating é afebrile periods. Relapsing fever describes 2 distinct diseases:-

- Louse borne (endemic): transmitted by body louse pediculus humanis by spirochetal G -ve Borrelia Recurrentis.
- Tick borne (epidemic): transmitted by tick by spirochete Borrelia Duttoni.

Transmission



LBRF: body lice become infected by B. recurrentis while feeding on spirochetemic human blood (the only reservoir of infection). Humans acquire infection when infected body lice are crushed & their fluids contaminate mucous membrane or breaks in the skin (such as abrasions caused by scratching of pruritic louse bites). Disease affects mostly homeless men living crowded together in very unhygienic circumstances especially during rainy seasons. Some of the risk factors are overcrowding like in military camps, civilian population disrupted by war & other disasters.

TBRF: rodents are the primary hosts, the vector ticks become infected when they feeds spirochetemic rodents. Ticks transmit borrelia vertically over several generations. Is most highly endemic in subsaharan Africa but also is found in Mediterranean & Eastern countries.

Pathophysiology

In humans, borrelia after entering the body multiply in the blood & circulate in great

number during febrile periods. They are also found in the spleen, liver, CNS, bone marrow & may be sequestered in these organs during periods of remission. Severity is related to spirochaetal density in blood but systemic manifestations are related to release of various cytokines. The disease characterized by sub capsular & parenchymal Hge é infarcts of spleen, liver, heart & brain is seen. Thus, pts will have enlarged spleen & liver é variable oedema & swelling of brain, lung & kidneys. Relapsing fever in pregnancy can result abortion, or still birth & fatal NN infection. Death from TBRF is rare. In contrast fatality rate of LBRF may reach up to 20% during outbreaks, mainly among malnourished & stressed population

Clinical Features

The manifestation of both LBRF & TBRF are similar. The IP is 7 days (ranging 2-18 days). The onset is sudden é high grade irregular fever, headache, chills, myalgias, arthralgias & insomnia. Pt will be withdrawn, disinterested to food & other stimuli & thirsty. Delirium associated é high fever, tachycardia & dry tongue, injected conjunctiva & photophobia. Gallop, occasionally resulting from myocardial involvement. Upper abdominal tenderness é hepatosplenomegaly. Scattered petechiae over the trunk, extremities & mucous membrane in 1/3 of cases of LBRF & fewer TBRF. Symptoms & Signs of meningeal irritation may seen in some pts. Icteric sclera may be found in late stage of the disease. Without Rx, symptoms intensify over 2-7 days period & subside é spontaneous crisis during ẃ borrelia disappear from circulation. Such cycles of febrile periods alternating é afebrile periods may recur.

Diagnosis

- Giemsa or wright stained peripheral blood smear is the most commonly done laboratory test & the ideal test in resource limited setting. Spiral organisms can be demonstrated on peripheral blood taken during febrile period preceding the crisis,

is +ve in > 70% of cases of LBRF & in lower % of pts é TBRF.

•Dark field microscopy of unstained blood/CSF •Serologic tests for Borrelia.

Complications

Life threatening complications are unusual in otherwise healthy persons if the disease is diagnosed & treated early. Complications are common in late disease in untreated pts. Complications include:-

•Epistaxis of blood streaked sputum, other bleeding tendencies.

•Neurologic manifestations like meningitis, coma, isolated cranial nerve palsies.

•Pneumonitis. •Myocarditis. •Splenic rupture.

Treatment

Antibiotics. In LBRF single dose of either Erythromycin, Tetracycline, Doxycycline or Chloramphenicol, produces rapid clearance of borrelia from the blood & remission of symptoms. TBRF is less sensitive to these antibiotics & requires a 7 days course. Doses as follow; Erythromycin 500mg/6 hrs or Tetracycline 500mg/6 hrs or Doxycycline 100 mg/12 hrs. Chloramphenicol 500mg/6 hrs. Parenteral: Penicillin (Procaine) 600,000 I.M stat & 600,000 IM daily.

Delousing of pts: important to prevent transmission/recurrence.

Jarisch- Herxheimer reaction: rapidly acting antibiotics ppt JHR within 1-4 hrs of the first dose. It is more sever in pts é LBRF than TBRF. More sever when high numbers of spirochetes circulating in blood. JHR has 3 phases:-

Chill phase: lasts for 10-30 min, rigor, hyperventilation, ⇧ COP, high fever (40^0C) accompanied by, agitation, confusion.

Flush phase: ⇩ in body temp, sweating, potential dangerous fall in BP (as peripheral vascular resistance falls), clinical & ECG evidence of myocarditis may be seen, S3 gallop & prolonged QT interval. Vitals signs must monitored closely during this time ẃ

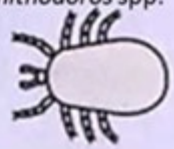
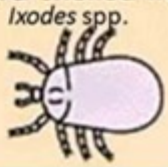
usually lasts for < 8 hrs.

Recovery phase: vital signs slowly improve & pt is exhausted.

Treatment of JHR: close monitoring of vital signs. Careful fluid management. Control of high body temperature. Short term Digoxin IV in pts é evidence of myocardial dys-function.

Prevention & Control

- Avoiding overcrowding.
- Applying hygienic practices & health education.
- Elimination of ticks.
- Early detection & Rx of infected persons & close contacts.
- In outbreaks of LBRF, empirical single dose Rx (Doxycycline).
- Eradication of rodents to control TBRF (Rodenticides).

	Infection	Reservoir	Vector
1. Borrelia recurrentis	Relapsing fever Epidemic (louse-borne)	Humans	Body louse *Pediculus humanus* 
2. Borrelia spp.	Relapsing fever Endemic (tick-borne)	Rodents, soft-shelled ticks	Soft-shelled tick *Ornithodoros spp.* 
3. Borrelia burgdorferi	Lyme disease	Rodents, deer, domestic pets, hard-shelled ticks	Hard-shelled tick *Ixodes spp.* 

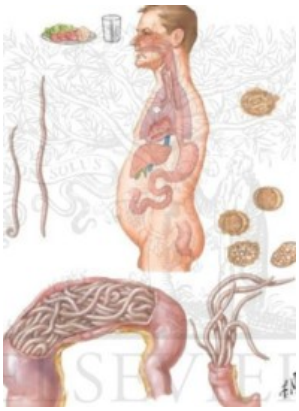
HELMENTHIASIS & PARASITIC DISEASES

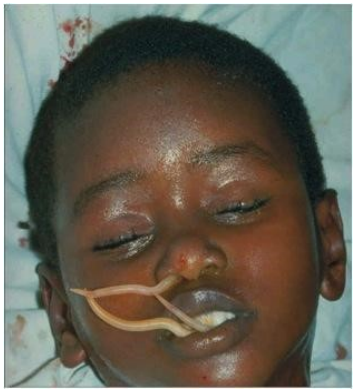
INTESTINAL NEMATODES

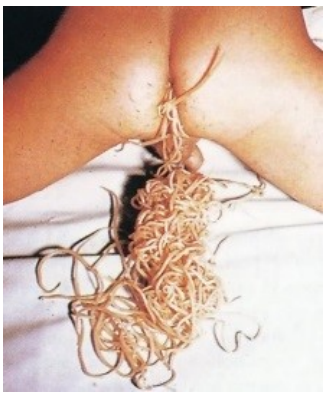
Nematodes

Are elongated, symmetric round worms. These can be classified as intestinal & tissue nematodes. Some of the intestinal nematode species are*, Ascaris lumbricoides, Necator Americanos & Ancylostoma duodenale, Strongyloides stercoralis, Enterobius vermicular is, Trichuris trichuira*more. More than a billion people world-wide are infected é one or more species of intestinal nematodes. They are most common in regions é poor sanitation, especially in developing countries. The tissue nematodes include Trichinosis, Visceral/Ocular/Cutaneous larva migrans, Cerebral angiostrogliasis & Gnathostomiasis.

ASCARIASIS







Ascaris Lumbricoides is the largest of the intestinal nematodes parasitizing humans & is the most common worm found in human. It is worldwide in distribution & most prevalent throughout the tropics, subtropics & more prevalent in the cou-ntryside than in the city.

Morphology

Adult warm It is elongated, cylindrical & tapering at both ends. Sexes are separate. The female is 20-35 cm long, 4-6mm in diameter. Male is smaller being 15-30cm long, 2-4 mm in diameter. The posterior end of male is curved having penial setae near end

As many as 500-5000 adult worms may inhabit a single host.

Life cycle

The infective stage is the embryonated eggs &the route of infection is through ingestion of embryonated eggs in contaminated food or drink or from contaminated fingers. No intermediate & reservoir hosts. The life span of the adult is about 1 yr. Warm lives in small intestine, feeding on its contents, the fertilized female can produce approximately 240,000 eggs/day, ẃ are passed in feces (unsegmented eggs & non infective stage), they require about 3 wks in the outside environment to develop into the embryonated eggs (infective stage), after ingestion of embryonated eggs in contaminated food or drink or from contaminated fingers, host digestive juices acts on the egg shell & liberate the larva into the small intestine. These larvae penetrate the intestinal mucosa & enter lymphatics & mesenteric vessels, carried by circulation to the liver, right heart & finally to the lungs where they penetrate the capillaries into the alveoli in ẃ they molt twice & stay for 10-14 days & then carried or migrate, up the bronchioles, bronchi & trachea to the epiglottis. When swallowed, the larvae pass down into small intestine where they develop into adults. The time from the ingestion of embryonated eggs to oviposition by the females is about 60-75 days.

Pathogenesis

There are two phase in ascariasis:-

The blood-lung migration phase of the larvae: during ẃ the larvae may cause a pneumonia (low fever, cough, blood-tinged sputum, asthma) & large numbers of worms may give rise to allergic sympt- oms. Eosinophilia is generally present. These clinical manifestation is also called “Loffler’s syndrome”.

The intestinal phase of the adults warm: the presence of a few adult worms in the lumen of the small intestine usually produces no symptoms, but may give rise to vague

abdominal pain or intermittent colic especially in children. A heavy worm burden can result in malnutrition. More serious manifestations have been observed. Wandering adult warms may block the appendicular lumen or common bile duct & even perforate the intestinal wall. Thus complications of ascariasis, as intestinal obstruction, appendicitis, biliary ascariasis, perforation of the intestine, cholecystitis, pancreatitis & peritonitis may occur, of ẃ biliary ascariasis is the most common complication.

Clinical Features

During the lung phase pt may develop an irritating non-productive cough & burning substantial discomfort. Fever is usual during this phase & CXR may show evidence of pneumonitis (Leoffler's sy). In established infections, pts are often asymptomatic, or may have abdominal discomfort & nausea in mild cases. In heavy infections, particularly in children, large bolus of worms may cause pain & small-bowel obstruction, or they could have chronic abdominal discomfort & growth retardantion. Large worm can enter & occlude the biliary tree, causing biliary colic, cholecystitis & pancreatitis. Fatality may occur when mass of warms blocks the intestine.

Diagnosis

The symptoms & signs are for reference only. The confirmative diagnosis depends on the recovery & identification of worm or the characteristic ascaris eggs in faeces. Ascaris pneumonitis confirmed through examination of sputum for ascaris larvae is sometimes successful. For intestinal ascariasis, feces are examined for the ascaris eggs. Direct fecal film is simple & effective. Eggs are easily found using this way due to a large number of the female oviposition, 240,000 eggs per worm/day, or recovery of adult worms: in feces or vomit.

Treatment

•Mebendazole 100 mg twice daily for 3 days or •Albendazole in a single dose of 400

mg is also effective.

NB: Mebendazole & Albendazole are contraindicated in pregnancy; but Piperazine & Pyrantel pamoate & are safe.

- Piperazine 75 mg/kg (maxim 3.5 gm) single dose daily for 2 days or
- Pyrantel Pamoate in a single dose of 10 mg/kg.

Prevention

- Keeping good sanitation conditions is the only way for prevention of ascaris.
- Sanitary disposal of feces & health education.
- Pollution of soil é human feces should be avoided.
- Vegetable should be thoroughly washed in mild solution of potassium permanganate &properly cooked before use.
- Finger nails should be regularly cut to avoid the collection of dirt & eggs below them, hands should be properly washed before touching edibles or eating.

ANKYLOSTOMIASIS

2 *Hookworm* species; *Ankylostoma Duodenale & Necator Americanos.*

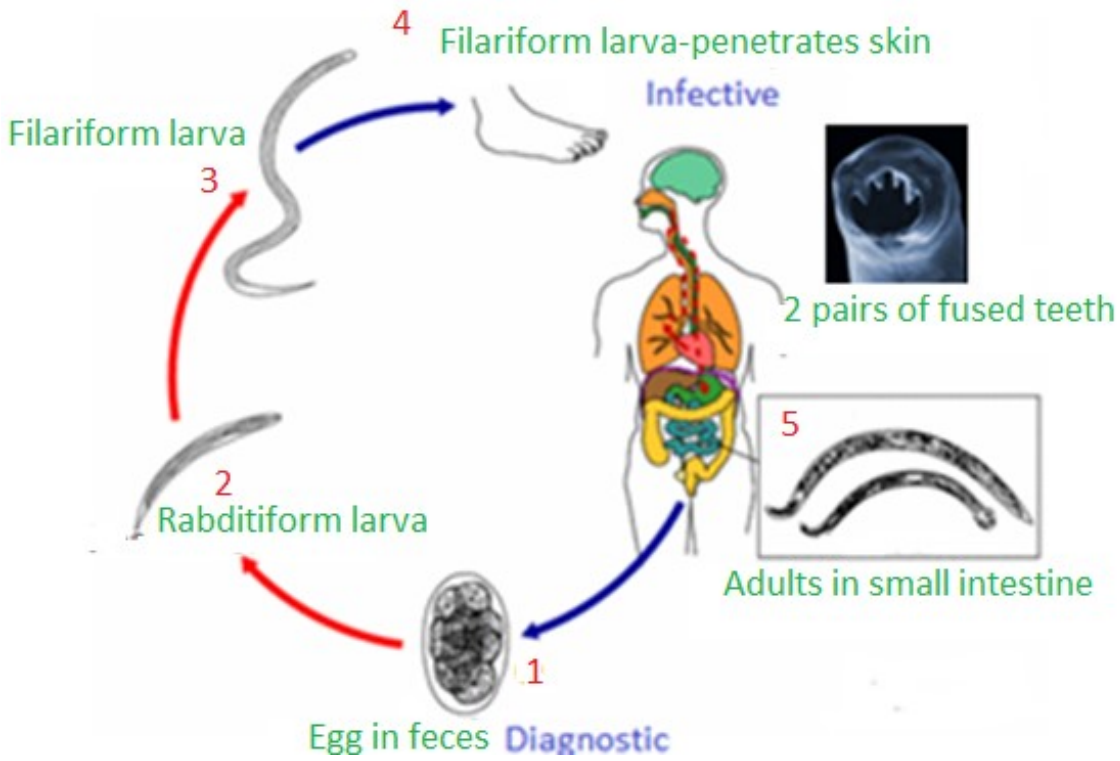
Epidemiology

Worldwide prevalent. But older children have the greatest incidence & intensity of hookworm infection. Prevalent in areas é poor sanitary conditions, particularly in relation to human waste disposal. Adults usually infected when walking bare-footed. Hookworm is one of the most common contributing factors for the development of iron deficiency anaemia in developing countries.

Life cycle

Adult warms are pink or creamy white. The oval buccal capsule contains 2 pairs of fused teeth. Male 8-11 mm long & female 10-13 mm. The adult hookworms live attached

to the mucosa of the small intestine. Females liberate eggs into the lumen, ẃ are eliminated é the faeces. Under optimum conditions of moisture & temperature they hatch within 24-48 hrs & then develop to become infective (filariform) larvae ẃ when come into contact é unprotected human skin (usually bare foot), they penetrate the skin layers, enter the blood stream & are transported to the lungs. Then migrate up to the bronchi, trachea & down to the oesophagus to reach small intestine where maturity is attained.



Clinical features

Most hookworm infections are asymptomatic. Infective larvae may provoke pruritic skin lesion at the site of penetration, as well as at subcutaneous migration. Infe-cted people may rarely present é mild transient pneumonitis. In the early intestinal phase, there may be epigastric pain, inflammatory diarrhoea or other GI symptoms. The major consequence of chronic hookworm infection is iron deficiency because worms suck blood from intestine. Anaemia usually develops if there is pre-existing iron deficiency states like malnutrition & pregnancy.

Diagnosis: the detection of the characteristic oval hookworm eggs in **faeces**. Eggs of the 2 species are not distinguishable. Anaemia of blood loss é hypochromic microcytic picture may be seen in **CBC.**

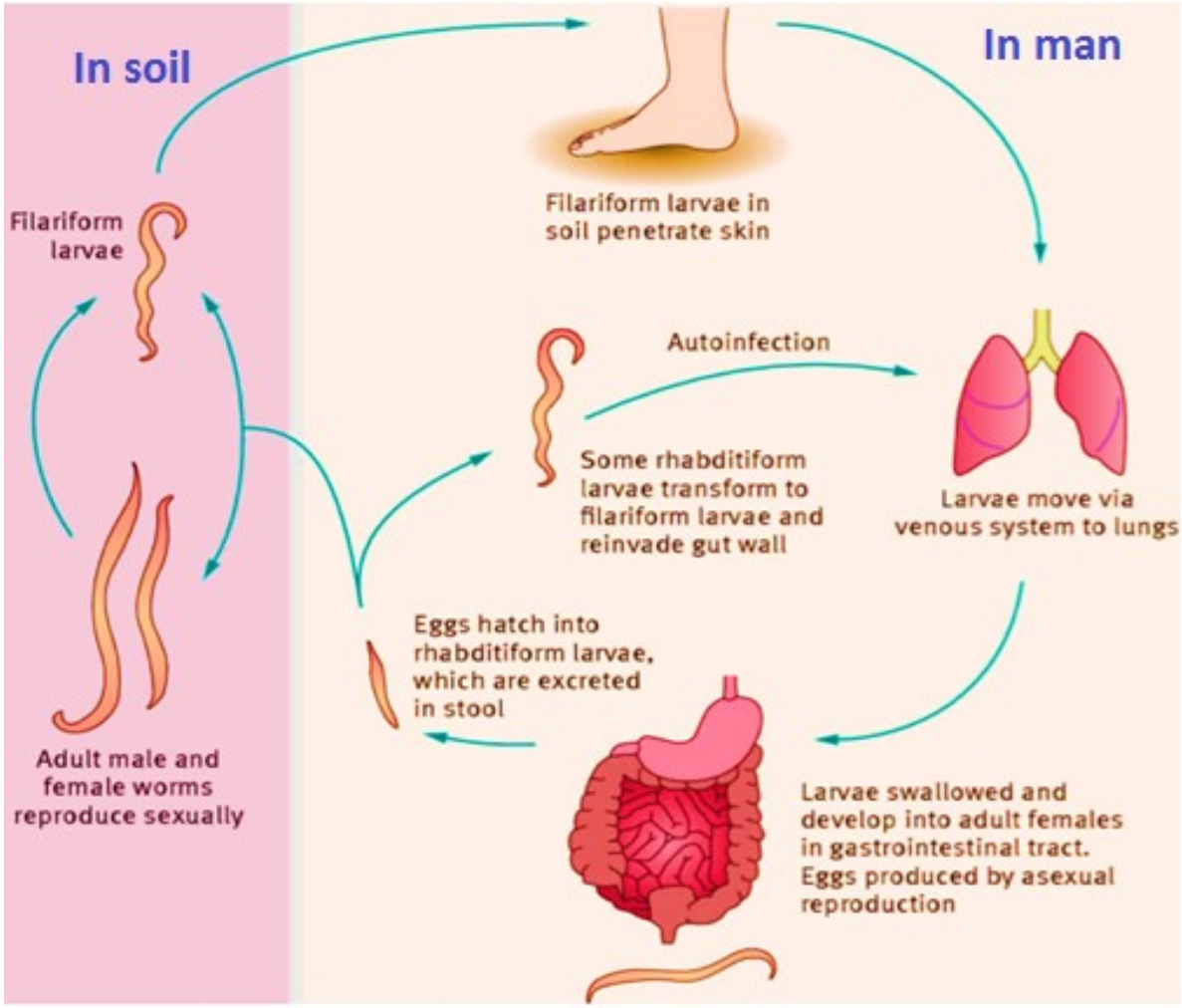
Treatment

Mebendazole 100 mg twice daily for 3 days. or Albendazole 400 mg (single dose).

STRONGYLOIDOSIS

Infection by the nematode Strongyloides Stercoralis, the female of ẃ usually is embedded in the mucosa of the small intestine of humans. Mainly distributed in tropical areas.

Life cycle



Female worm 2.5 mm long, move through the lining of the small intestine (duodenum & jejunum), produce eggs ẃ laid in the mucosa of intestines, hatch within ho-

urs into rhabditiform larva that penetrate the glandular epithelium & pass into the lumen of the intestine & out the feces. Rhabditiform larvae can survive for some time as free-living nematodes, even reproducing through several generations. Sooner or later, however infective parasitic larvae develop filariform larvae pass in stool, it is about ½ mm long, penetrate bare skin of human (the definitive host are human, dogs & cats), move via venous system to lungs, swallowed & arriving to the intestine within a couple of days to continue their parasitic life cycle. All parasitic larva mature to female worms & reproduce éout the contribution of a male (there are males 0.7 mm in length in the free-living soil stages), the adult female worm reproduce by themselves autoinfection cycle.

Clinical features

Mild infections are usually asymptomatic. Recurrent urticaria, often involving the buttocks & wrists, is the most common cutaneous manifestation. Adult parasites burrow into the duodenojejunal mucosa & can cause abdominal pain (usually mid epigastric) ẃ resembles peptic ulcer pain, nausea, diarrhoea, GI bleeding, mild colitis & wt. loss can occur. The autoinfection cycle of strongyloidosis is normally contained by unknown factors of the host's immune system. In immunocompromi- sed hosts, strongyloidosis result in hyper infection é colitis, enteritis or malabsorption. In disseminated disease larvae invade not only the GIT & lung, but also the CNS, peritoneum, liver &kidneys. Bacteraemia may develop from enteric bacteria entering through the disrupted intestinal mucosa.

Diagnosis

In uncomplicated strongyloidosis, the finding of Rhabditiform larvae in faeces is diagnostic & serial stool examinations may be needed. Eggs are almost never seen in stool because they hatch in intestines.

Treatment

Even asymptomatic pts should treated.

•Thiabendazole, is still the drug of choice, 25 mg/kg BID (maximum 3 gm/day) for 3 days. There are however common side effects like nausea, vomiting, diarrhoea, dizziness & neuropsychiatric disturbances.

•Ivermectin 200 µg/kg as a single daily dose for 1-2 days is better tolerated. The disseminated cases treated for 5-7 days.

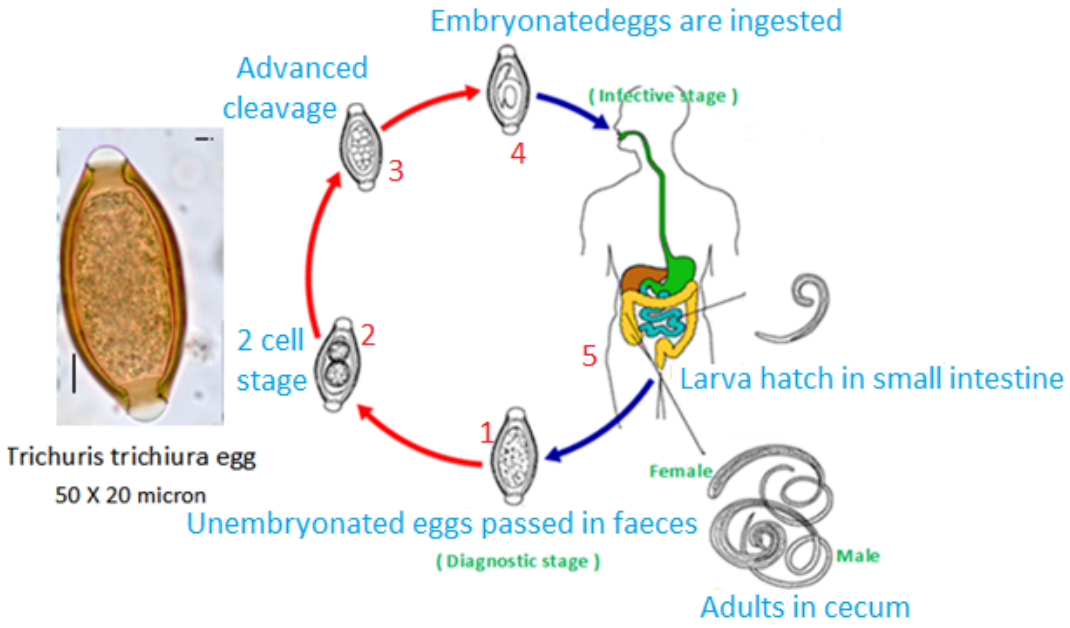
•Albendazole 200 mg/day PO for 3 days gives 100% cure rate.

TRICHURIASIS

Definition

Trichuriasis (whip-worm infection) is an infection of the human intestinal tract caused by the nematode Trichuris Trichiura. It is distributed worldwide, but is most abundant in the warm, moist regions of the world, the tropics & subtropics.

Life cycle



The parasites have a characteristic whip like shape. The anterior portion is long & thread like, the posterior portion is broader & comprises about 2/5 of the worm. Females are slightly longer than males (3-5cm long). The adult worms reside in the

colon & caecum. The anterior portions threaded into the superficial mucosa. Thousands of eggs are laid daily & pass é faeces. They mature in the soil. After ingestion, the eggs hatch in the duodenum, releasing larvae that mature before migrating to large bowel. Adult worms may live for several yrs.

Clinical picture

Most infections are asymptomatic. Large worm burden may be associated especially in children é diarrhoea of long duration, dysentery, mucoid stools, abdominal pain &tenderness, dehydration, anaemia, wt loss &weakness. Rectal prolapse may occur, particularly in children.

Diagnosis

Demonstration of characteristic lemon-shaped eggs, or adult worms, ẃ are about 3-5 cm long, can be seen on proctoscopy.

Treatment: Mebendazole 100 mg 1 X 2 X 3 days or Albendazol 4 mg/kg.

ENTEROBIASIS

Infection of the human intestinal tract by the pinworm Enterobius Verfmicularis.

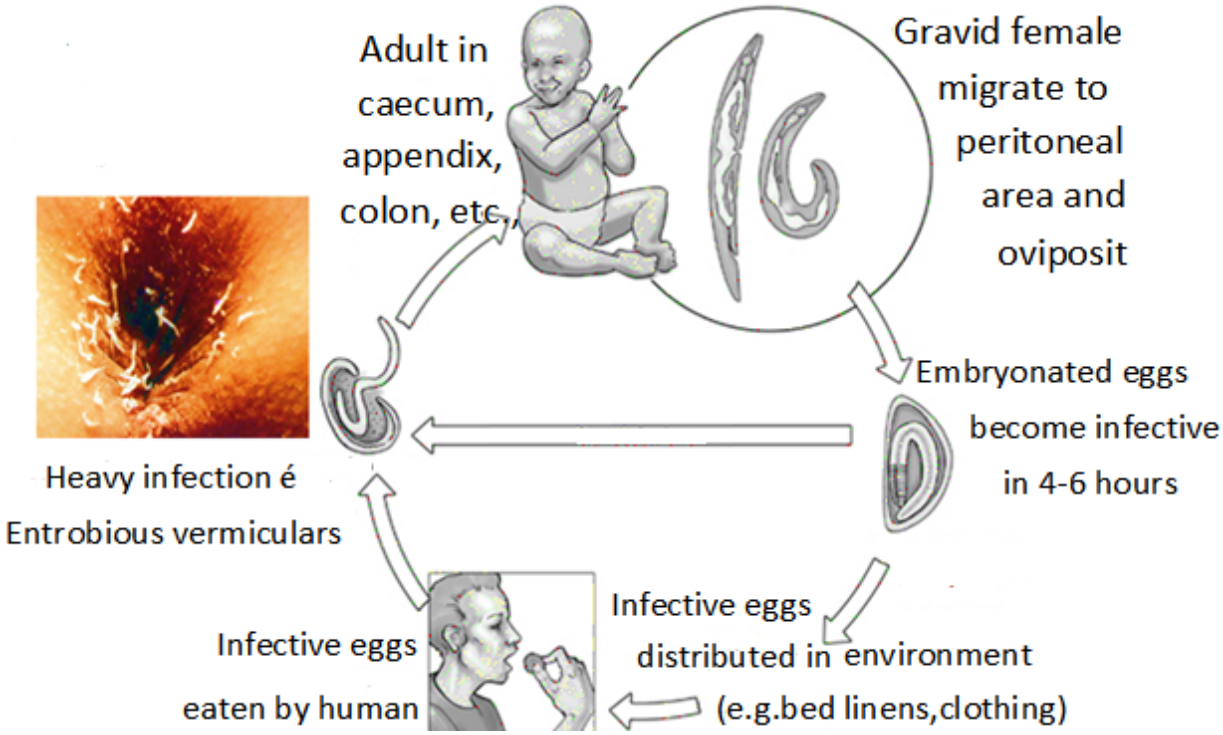
Epidemiology

Pinworms are one of the most common intestinal nematodes, cosmopolitan, more in temperate zones é about 30-50% of the population infected, more common in white than colored people, more prevalent in children than adults. Enterobiasis is most common where people live under crowded conditions as orphanages, kindergartens, primary school students & large families.

Life cycle

Adult worms inhabit the cecum & colon. Right after mating, the male dies. Therefore, the male worms are rarely seen. The gravid female worm migrates nocturnally out into the perianal region & releases up to 10.000 immature eggs. The eggs are rapidly in-

fective & are transmitted by hand-to-mouth passage. The larvae hatch, mature entirely within the intestine. Self-infection results from perianal scratching & transport of eggs to the hands or nails & then to mouth (autoinfection). Pinworm infections are very common among family members. The female worm measures 8-13 mm in size & is fusiform in shape. The male adult is 2-5 mm & the tail is curved. The egg is 50-60 X 25 µm, persimmon seed-like, colorless & transparent, thick & asymmetric shell, content is a larva. The embryonated egg is the infective stage & the life span of the worm is 1-2 months.



Clinical picture

About one-third of pinworm-infected persons are asymptomatic. The adult worms may cause slight irritation of the intestinal mucosa. Major symptom is anal pruritus, ẃ associates é the nocturnal migration of the gravid fem ales from the anus & deposition of eggs in the perianal folds of the skin. Restlessness, nervousness & irritability, probably resulting from poor sleep associated é anal pruritus. In young girls, migration of the worms may produce vaginitis, salpingitis or granuloma of the peritoneal cavity.

Diagnosis

•Microscopic identification of eggs collected in the perianal area by cellophane (Graham Scotch) tape method or anal swabs. The tape is then transferred to slide to be seen under microscope. This must be done in the morning, before defecation.

•Detection of adult warm on anal skin.

•The diagnosis often made clinically by observing female worm/worms in the perianal region.

Treatment

Since the life span of the pinworm is < 2 months, the major problem is reinfection. Albendazole & Mebendazol are 95% effective but do not kill eggs, 2 or more courses of treatment needed for radical cure. Also treatment of all the members of the family even adults is recommended. Bendax/Vermizole/Alzental 100 mg suspension, 200mg tab., single dose 2 tsp for children < 2 yrs & 4 tsp for children >2 yrs & 2 tab for adults & to be repeated for all after 2 wks.

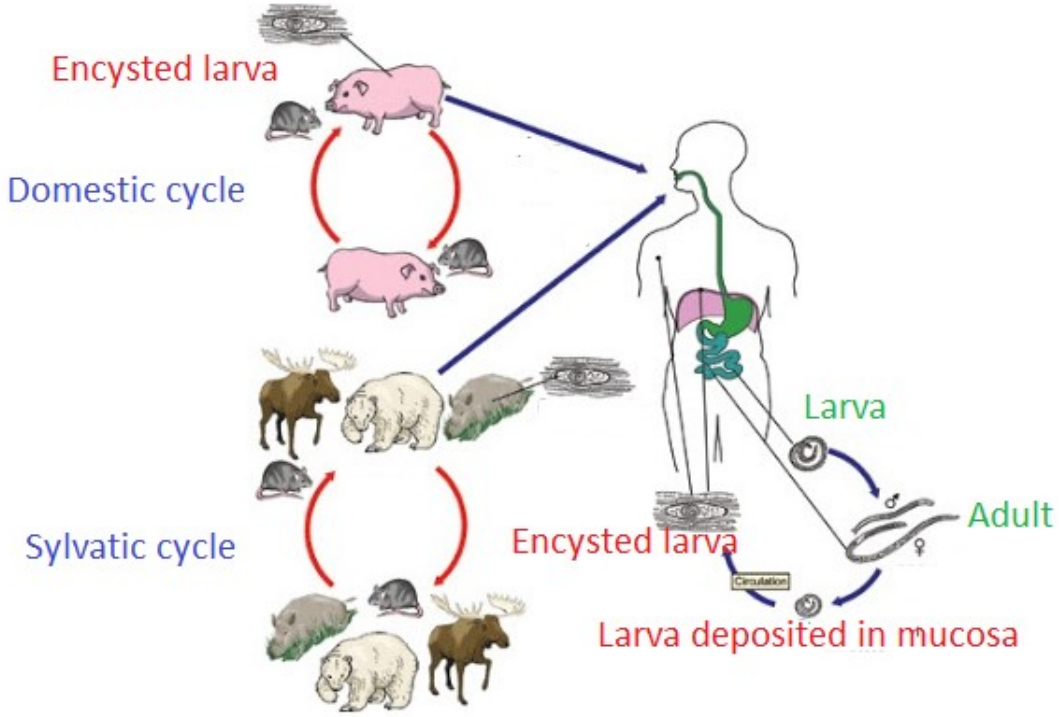
Prevention

Treatment of pts & carriers, health education & hygienic habits, sanitation of clothing , beading & environment.

TISSUE NEMATODES

The tissue nematodes include Trichinosis, Visceral or Ocular or Cutaneous larva migrans, Cerebral angiostrogliasis & Gnathostomiasis.

TRICHINOSIS



Disease caused by the parasite Trichinella Spiralis, characterized by acute & rapid course é fever, GIT symptoms, myalgia & eosinophilia.

Epidemiology

Widely spread throughout the temperate regions of the world wherever pork or pork products are eaten. It is enzootic in wildlife in Africa & man is involved sporadically by eating fresh or inadequately cooked pork.

Life cycle

The trichina worm is white round worm just visible to the naked eye. Adult male 1.4-1.6 mm in length by 40-60 µm in diameter; the female is longer, 3-4 mm in length & about 1½ times as broad as the male. The worm gains entrance to the digestive tract as larva encysted in muscle tissue. By the time they reach small intestine, freed from their cysts, penetrate the duodenal epithelium, mature within a few days. The female

is fertilized & produce between 1000-1500 larva during the 3-16 wks period they parasitizes man. The larva circulates in blood, then invade different tissues mainly the muscles.

Clinical features

24 hrs following ingestion of encysted larva in undercooked meat, signs of GIT disturbances like nausea, vomiting, diarrhoea & abdominal pain may occur. With the muscular infiltration there may be periorbital oedema, myalgia & persistent fever up to 40 ^{o}C, the last stage is characterized by neurologic symptoms & sometimes myocarditis.

Diagnosis

Blood eosinophilia develops in >90% of cases, 2-4 wks after infection serum levels of IgE & muscle enzymes including CPK, LDL, & AST are ⇧ in most symptomatic pts, a presumptive diagnosis can be made based on fever, eosinophilia, periorbital oedema & myalgia after a suspected meal. Diagnosis is confirmed by ⇧ titres of parasite specific antibody or muscle biopsy demonstrating the larva.

Treatment

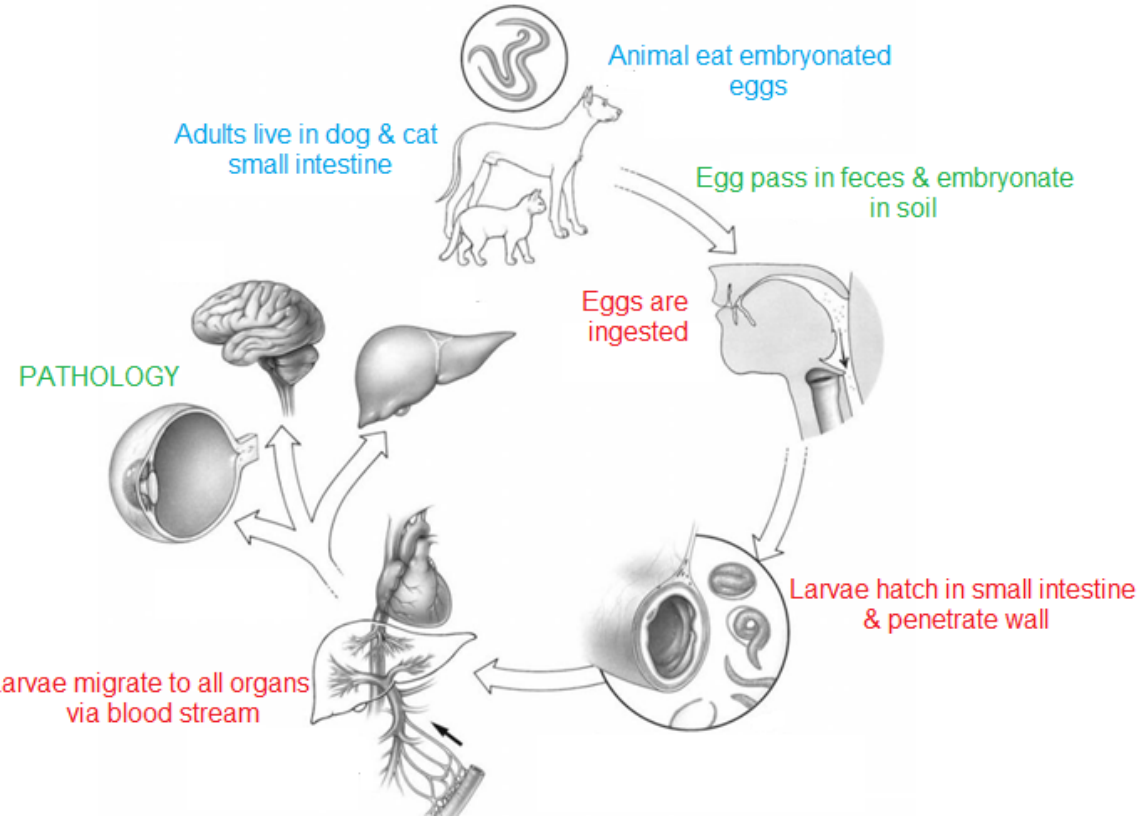
As is desirable é most diseases, early Rx is better & ⇩ the risk of developing disease. If larvae do encyst in skeletal muscle cells, they can remain infectious for months to yrs. Early administration of antihelminthics, as Mebendazole or Albendazole, ⇩ the likelihood of larval encystation, particularly if given within 3 days of infection. However most cases diagnosed after this time. Mebendazole 200-400 mg X 3 X 3 days or Albendazole 400 mg X2 for 8-14 days. These drugs prevent newly hatched larvae from developing, but should not be given to pregnant women or children < 2 yrs of age. Glucocorticoids (e.g. Prednisolone 1 mg/kg/day) are helpful for severe myositis & myocarditis.

TOXOCARIASIS

Zoonotic infection caused by the parasitic round worms commonly found in the intestine of dogs & cats (Toxocara).

Life cycle

Toxocariasis include 2 types according to the normal habitant; Toxocara canis (in dogs), Toxocara catis (in cats). The mature worm is about 6-10 cm in length. Man infected through ingestion of contaminated food or soil é feces of dogs or cats which contain eggs, the egg hatches in human intestine forming larva ẃ penetrate mucosa of intestine & pass to blood to settle in different body organs.



Clinical picture

Most people infected é *Toxocara* do not have any symptoms. There are 2 major forms; Visceral Toxocariasis (VT), also called Visceral Larva Migrans (VLM), Ocular Toxocariasis (OT), also called Ocular Larva Migrans (OLM). The syndromes VLM & OLM can be caused by infection é the migrating larvae of other kinds of parasites ẃ cause symptoms similar to those caused by migrating T*oxocara larvae.* In few people

who are infected é high numbers of *toxocara larvae* or have repeated infections, the larva can travel through parts of the body as the liver, lungs or CNS causing symptoms as fever, cough, pneumonia, enlarged liver. The larva can also travel to the eye & cause OT, ẃ occurs when microscopic toxocara larva enters the eye, causing inflammation & scarring on retina resulting in visual deterioration, chorioretinitis, red eye, typically occur in one eye.

Investigations

- Detection antibodies to toxocariasis: ELISA test, sensitive up to 90%.
- CBC: shows marked ⇧ of eosinophilic count, leukocytesis.
- Immunoglobulins: hypergammaglobinaemia (IgG, IgM, IgE).
- Sonar/C-T/MRI: visualize granuloma anywhere.

Management

- Albendazole suspension 100 mg, 2-4 tsp daily for 3-5 days for children. 2 tab (200 mg/tab), daily for 3-5 days for adults.
- Steroids used to reduce inflammation & granulomatous reaction.

FILARIASIS

Filariasis is caused by Wuchereria Bancrofti, Brugia Malayi or Brugia Timori. While the later 2 are found in Asia, the former is prevalent in the tropics & subtropics. Therefore, W. Bancrofti is discussed below.

LYMPHATIC FILARIASIS

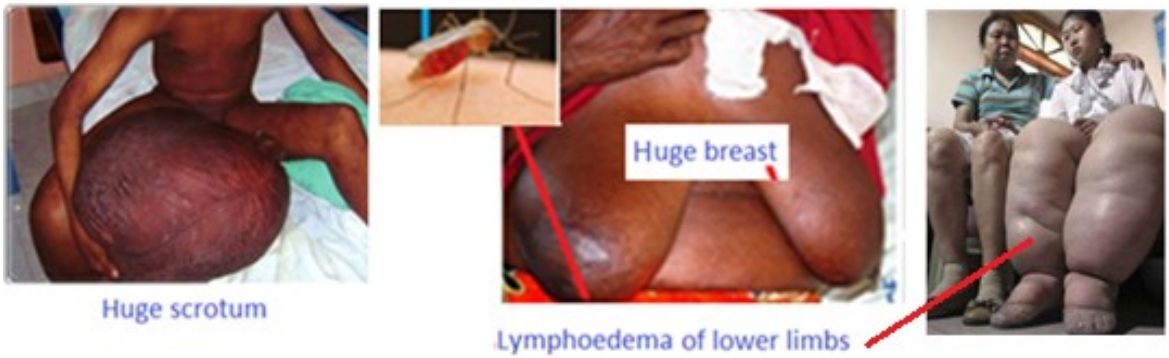
Lymphatic filariasis is due to the presence of adult W. Bancrofti in the lymphatic system or connective tissues of man. Many species of anopheles; culex, mansonia & aedes are acting as a vectors.

Epidemiology

It is widespread throughout most of the tropics & subtropics. Also found in some fare-

ast countries. The mosquito, inoculate microfilaria into human skin, it pass to lymphatics or SC tissue where it proliferate to adult warms & in turn gives microfilaria. The adult warm length 4-10 micron & microfilaria 150-300 micron.

Clinical picture



Most of infected individuals have few symptoms despite large numbers of circulating microfilaria in the peripheral blood. But subclinical disease is common é microscopic haematuria &/or proteinuria & in men scrotal lymphangiectasia. Only few pts progress to the acute & chronic stages of infection. Pt may present acutely é high-grade fever, lymphangitis & transient local oedema. Later on pt may have lymphedema (upper & lower extremities) & scrotal swelling. Lymphatic filariasis may affect breast, vulva & may associated é 2ry bacterial infection due to impairment of blood circulation.

Diagnosis

- Demonstration of microfilaria from blood, or hydrocele fluid or other body fluids at night (because periodicity of microfilaria).
- CBC: marked eosinophilia.
- ⇧ of IgE
- ELISA for detection of antibodies against Filariasis.
- Blood film for Wucheraria bancrofti using Giemsa stain.
- Isolation of warm from fluid collection (in scrotum, legs, or breast).
- U/S of scrotum, breast for detection of the warms.

Treatment

Diethyl Carbamazepine 6 mg/kg daily for 12 days is the Rx of choice. Albendazol 400 mg twice daily for 21 days has been shown to have microfilaricidal activity.

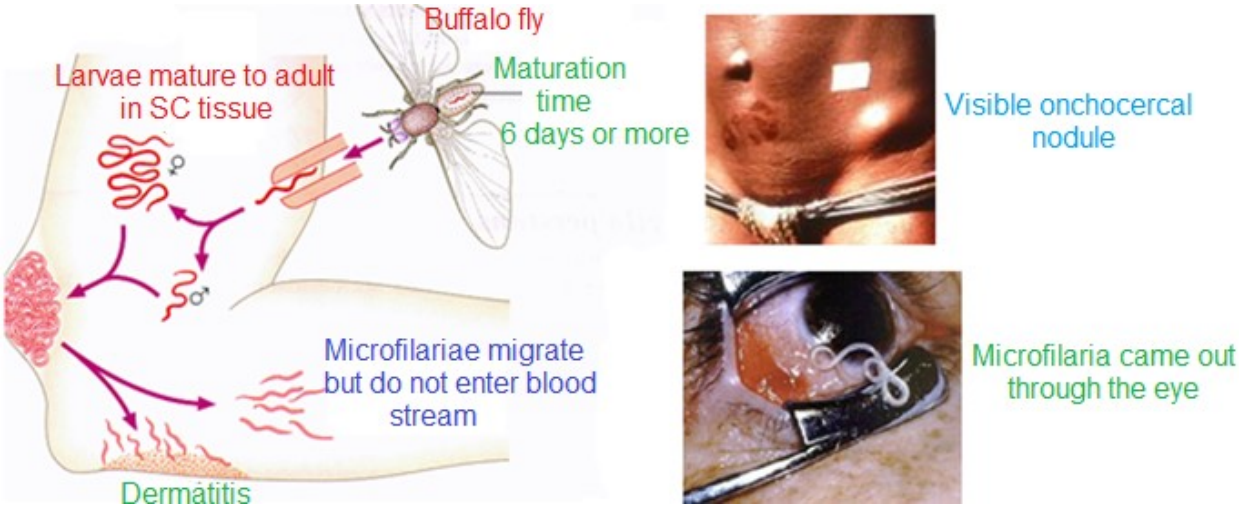
ONCHOCERCIASIS

Onchocerciasis is caused by the filarial nematode Onchocerca volvulus & is spread by the bite of an infected Black Fly, is also called river blindness because infections are most intense in remote African rural agricultural villages, located near rapidly flowing streams.

Aetiology/Epidemiology

Global onchocerciasis prevalence is 17.7 million. 99% of infected persons are in Africa. It is the world's 2nd leading infectious cause of blindness. The living parasites are white or cream coloured & transparent. The males are 19-42 mm long & the females 33-50 cm long.

Life cycle



Vector is the Black Fly ẃ breed on the sides of running river for many kilometers arou-nd the river, the fly inoculate larva into skin of man, the severity of the disease depe-nds on the intensity of bites. The larvae maturate to adult warm male & female in the SC tissue forming a nodule. About 7 months -3 yrs after infection, the gravid female

releases microfilariae that migrate out of the nodule & throughout the tissues, infection is transmitted to other person when female Black Fly ingests microfilaria from the host's skin, these microfilaria then develop into infective larvae. It takes about 1-3 wks for microfilaria to develop into infective larva inside the fly & to be inoculated into another persons, the warm does not penetrate the blood stream, but migrate through SC tissue & lymphatics to different body parts.

Clinical features

Following the bite of an infected fly, there is an IP of several months before nodules appear. The SC nodules "onchocercomata" are the most characteristic lesions. Usually appear on legs, coccyx, sacrum, thigh or in bony prominences. This granuloma may be seen anywhere in the body, may be single or multiple up to over 100 nodules, may form huge mass in the skin, associated é loss of elasticity, wrinkling of skin & epidermal atrophy that can be more often lead to hypopigmentation than hyperpigmentation & eczematous dermatitis é sever itching. Visual impairment is the most serious complication. Early lesions in the eye are conjunctivitis é photophobia, iridocyclitis, sclerosing keratitis leading to blindness. The microfilariae can be seen by naked eye coming out through the eye. Pt could have enlarged inguinal LN (hanging groin). Heavily infected pt could have severe wasting.

Diagnosis

- Demonstration of microfilariae in the skin snip or nodules. Microfilaria are rarely found in blood smear, but may be seen in urine.
- CBC: marked eosinophilia.
- PCR.
- Marked ⇧ in IgE. .

Treatment

Once a victim infected, there is no cure from the disease, but its progress can be delayed é oral medication.

Ivermectin: is the Rx of choice, PO as a single dose of 60 mg tab, ½ -2 tab, or 150 mcg/Kg (max. 120 mg), repeat every 6 months or every yr. It inhibits the production of microfilariae by adult female worms for some months, killing off almost 95% of the tiny worms. Be sure there is no Loa Loa infection as the drug may cause severe reaction. The drug has many advantages as; no severe ocular reaction & prevents blindness due to optic nerve disease by 50%, but it is contraindicated if there is coinfection é Loa Loa or pregnant or lactating women or children **<** 5 yrs.

Antihistamines: should be given for the pruritus.

Surgical excision of the nodules.

Prevention

The disease is highly preventable, control based on strategies:-

•Vector control by spraying insecticides, controlling insect breeding sites in rivers is one of the pillars of prevention by spraying the aerial spaces & rivers.

•Personal exposure in endemic areas can reduced by avoiding black fly localities & by protective clothing.

•Repellents are of value only for short periods as they are washed off by sweat. •Free distribution of the highly effective medicine-Mectizan (Iverectin), this medication provides a yearly protection from a single dose (Levine, 2007). Diethyl carbamazine is contraindicated because it is associated é severe & fatal post treatment reaction.

TREMATODES

Trematodes or flatworms are a group of morphologically & biologically heterogeneous parasitic helminths that belong to the phylum platy helminthes. Human trematode infections are classified according to the site they involve; the adult flukes may involve blood, biliary tree, intestines or lungs. Blood flukes are Schistosoma Mansoni, Hematobium, Japonicum, Intercalatum & Mekongi. Biliary flukes are Opisthorchis Viverini, Clonorchs Sinensis & Fasciola Hepatica. Intestinal flukes are Fasciolopsis Buski, Heterophyes. Finally, lung flukes are Paragonimus Westermani. Because of its public health importance, only Schistosomiasis is discussed here.

SCHISTOSOMIASIS

Schistosomiasis (Biliharziasis) is a group of diseases caused by the genus schistosoma affecting mainly the GIT & genitourinary organs.

Geographical distribution

- Sch. Haematobium: in Middle East & Africa.
- Sch. Mansoni: is found in Middle East, Africa, South America.
- Sch. Japonicum: in Japan & Far East.
- Sch. Mekongi & Sch. Intercalatum: are found focally in South East Asia & Central West Africa.

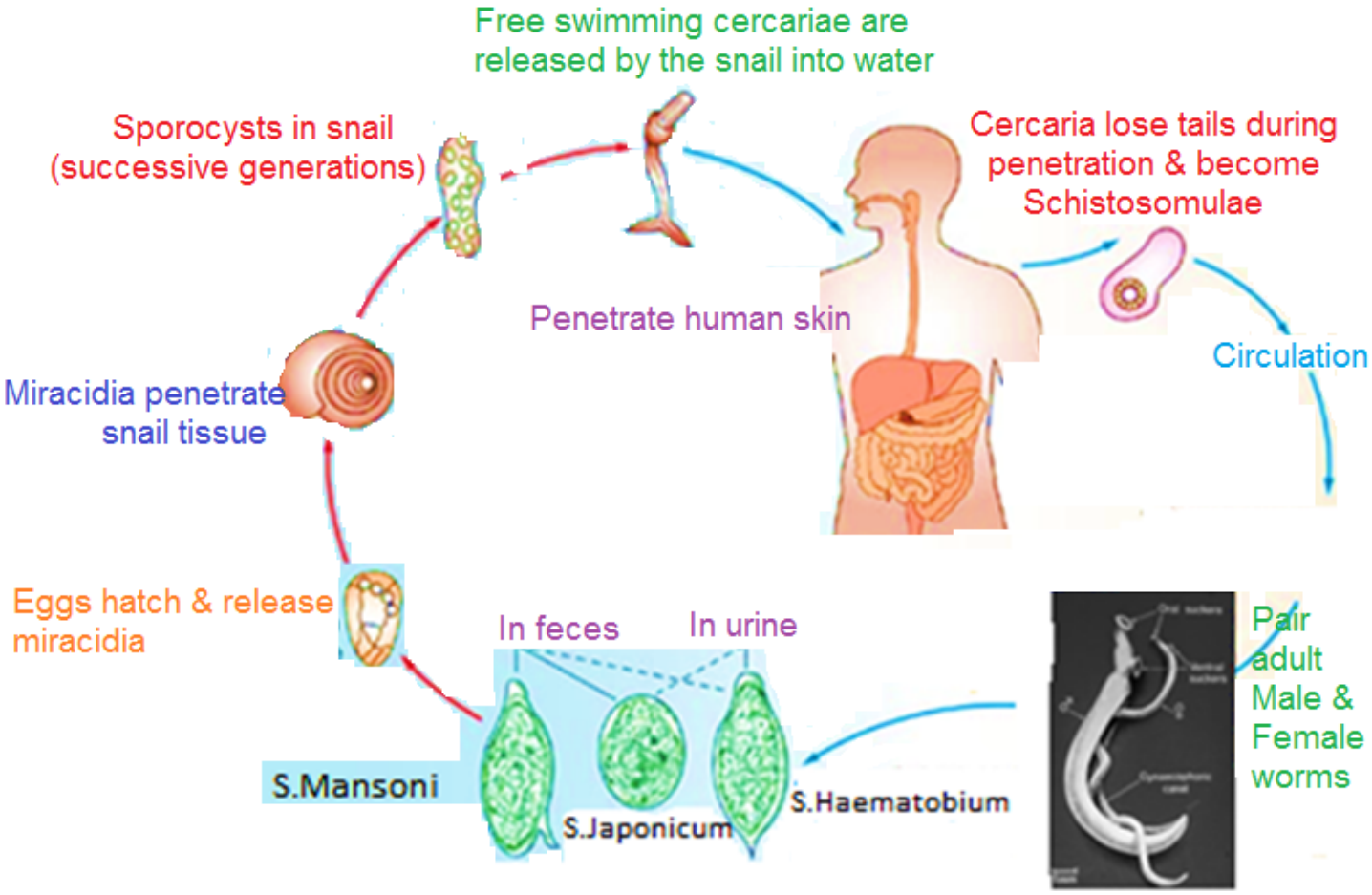
Sch.Haematobium is the cause of urinary Schistosomaiasis while all the rest cause intestinal Schistosomiasis.

Life cycle

Man is the definitive host where sexual reproduction takes place after cercarial entry by skin penetration. Snails are the intermediate hosts in ẃ asexual regeneration continues. Each species of Schistosoma has a specific snail host. The parasite eggs released into fresh water (from human urine or feces according to species).

Eggs hatch giving rise to the ciliated miracidia (free swimming). Miracidia find & infect snail host (different species prefer different snail species), each miracidia transforms into many fork-tailed, free swimming forms (Cercariae) within 4-6 wks of entering snail. The cercariae leave snail &move into water for up to 18 days. When cercariae find a human host, it the penetrate skin & differentiate into larval forms called-Schistosomulae. Schistosomulae migrate through the host's skin, gain access to the lymphatic system, travel to the lungs (stay 3-8 days), then migrate to liver portal system where they mature into adult worms. Male & Female adult worms in liver pair up, female inserts herself into the gynecophoral canal of male, they are now 'paired', migrate to favoured sites according to species:-

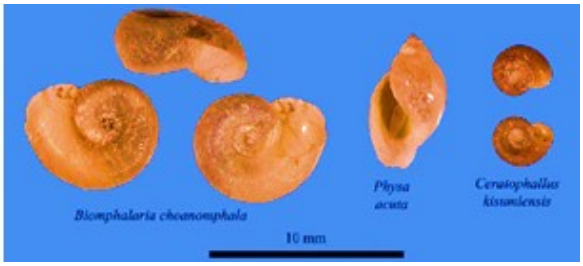
- Sch. Haematobium migrate to perivesical venous plexus surrounding the bladder
- Sch. Mansoni migrate to mesenteric venules of large bowel & rectum.
- Sch. Japonicum migrate to mesenteric veins of the small intestine.



S. mansoni - Biomphalaria species.

S. haematobium - Bulinus species.

S. japonicum - Onchomelania species.



Clinical picture

Intestinal schistosomiasis is caused by all human Schistosoma except Sch. Haematobium, ẃ is the only cause for urinary Schistosomiasis. It affects the large bowel, the liver (intestinal form), manifestations are dependent on the stage of infection. The following first 2 stages are the same for all species & the 3rd stage is different:-

First stage: swimmer's itch (invasion): is the first clinical sign of acute infection appearing soon after exposure, usually within 24-48 hrs & characterized by itching at sites of cercarial entry. Seen in new comers & not common in indigenous people.

Second stage: acute stage (toxaemia). It is an early allergic manifestation to egg deposition in response to massive antigenic stimulus of eggs. Include fever, headache, chills, myalgias, profuse diarrhoea, nausea & vomiting. Pt may have generalized lymphadenopathy, heapatosplenomegaly, urticaria & leucocytosis é marked eosinophilia. Severity depends on intensity of infection & tends to be mild in indigenous population. Such clinical manifestations come out after 4-8 wks of infection, similar to the time from egg to adult worm (40 days).

Third stage: is the chronic stage, occurs 3 months to several years later, coincides é deposition of eggs in the tissues. The clinical picture represents the effect of the pathologic lesions caused by the eggs on the urinary & GIT systems. Differ in their manifestations, as follow:-

i) Intestinal Schistosomiasis: the disease is very light & symptomless for months, then presenting é recurrent bloody diarrhoea & lethargy. They may have intestinal polyps &progressive fibrosis of the intestinal wall leading to formation of strictures but intes-

tinal obstruction is rare. Moreover, granulomatous hepatitis followed by progressive periportal fibrosis (also called pipe stem fibrosis) may develop resulting in portal hypertension é splenomegaly, ascites & oesophageal varices.

ii) Urinary Schistosomiasis: eggs deposition in the wall of urinary bladder induces the formation of pseudo tubercles & epithelial hyperplasia é subsequent fibrosis & calcification causing dribbling, incontinence, frequency, dysuria & haematuria. Chronic infection leads to obstructive uropathy, hydronephrosis, chronic pyelonephritis, renal failure & contraction of the bladder. Rarely the gonads, CNS "brain, spinal cord", lungs & endocrine organs may involved by egg deposition.

Diagnosis:

- Identification of the characteristic ova in stool or urine by direct smear method; easy but light infection can be missed.
- Rectal snip/bladder biopsy if it cannot be detected in stool or urine.
- Antibody detection; the most frequently used technique is ELISA, but antibody levels do not differentiate between past & present infection & do not give any information about intensity of infection, therefore, can`t be used as cure monitor.
- Circulating antigen assays: acts as a reliable cure monitor.

Clinical diagnosis

Intestinal schistosomiasis

- Sigmoidoscopy & rectal snip: identifies lesions & ova of the parasite.
- U/S of liver & spleen: demonstrate periportal fibrosis & spleen enlargement.
- Liver biopsy

Urinary schistosomiasis

- Cystoscopy: demonstrates fibrosis & calcification of the bladder, bladder biopsy & histology demonstrates ova.

- Plain abdominal X ray may detect bladder calcification.
- IV pyelogram to see for the presence of obstructive uropathy.
- Renal U/S .

Treatment

Drug treatment is both safe &effective. Praziquantel: has wide spectrum, effective against all species, single dose, has high cure rate. The dose for Sch. Mansoni & Haematobium is 40 mg/kg & for Sch. Japonicum is 60 mg/kg.

Prevention

Prevention & control requires multidisciplinary approach:

- ***Environmental sanitation***: avoidance of pollution of surface water; provision of latrine & sanitary waste disposal, prevention of human contact é infected water, provision of safe & adequate water, protective clothing when contact is unavoidable, health education.
- **Elimination of the disease**: in the reservoir by chemotherapy. Case finding & Rx & mass Rx in selected population.
- ***Snail control***: eliminating the water-born snails ẃ are natural reservoirs for the disease, usually done by identifying bodies of water, as lakes, ponds, ẃ are infested. Snail control include;

-Physical control: removal of vegetation, drainage of swamps.

-Chemical control (molluscicides) to the water in order to kill snails.

-Biological control by using fish or other snails that feed on vector snails.

CESTODES

Cestodes (tapeworms) are segmented worms. Tapeworms can divided into two. In one group the definitive hosts are humans, these include: Taenia saginata, Diphylobthrium, Hymenolepsis & Dipylidium Canium. In the other group, humans are intermediate hosts, these include: Echinococcosis, Sparganosis & Coenurosis. Humans can be a definitive or intermediate host to T.solium.

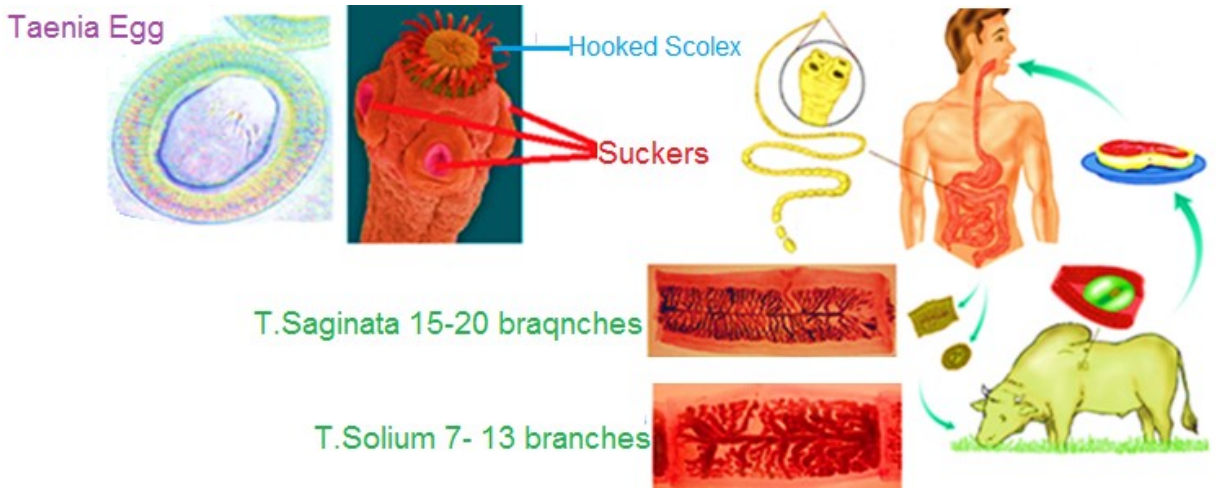
TAENIASIS SAGINATA

Taeniasis Saginata (beef tapeworm) infection is caused by the presence of the adult beef tapeworm, in the intestine of humans.

Distribution

It is found all over the world. Occurs in all countries where raw-meat is ingested. Prevalent in sub-saharan Africa & Middle East.

Life cycle



T. Saginata is a large tapeworm usually 5-10 meters in length. The scolex carries 4 round suckers. Behind the scolex there is a short neck from ẃ proglottids (segments) form. Each proglottid matures, it is displaced further back from the neck by the formation of new, less mature segments. Humans are the only definitive host. Eggs deposited on vegetation can persist for months or yrs, until ingested by cattle. Embryo from cattle intestine migrates to the muscle &transform into cysticercus. When eaten

raw/undercooked meat, this cysticercus infects human.

Clinical picture

Usually pt is asymptomatic & often infection is detected when pt pass proglottids é stool or alone. Abdominal pain, nausea & wt. loss can occur.

Diagnosis

- Demonstrating the eggs or proglottids in pt`s stool.
- Each gravid proglottids of T. Saginata passed in stool (approximately 6 proglottid/day) may produce up to 100.000 eggs.

Treatment

Prazequantel 5-10 mg/kg in a single dose or

Niclosamide 2 gm as single morning dose before breakfast as alternative.

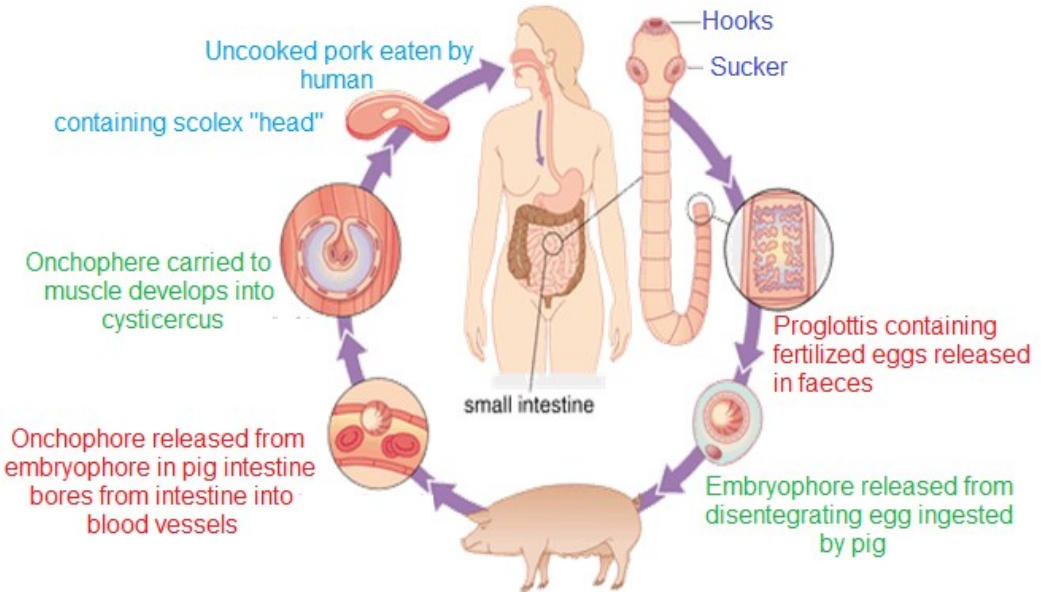
TAENIASIS SOLIUM

It is caused by T. Solium from eating raw or undercooked pork.

Etiology

The adult tapeworm resides in the upper jejunum, similar to T. Saginata. Its scolex attaches to intestinal wall by both sucking disk & 2 rows of hooklets.

Life cycle



T. Solium has a very similar transmission pattern to T. Saginata. Humans are the only

known definitive host. Infection begins é the ingestion of infected raw or undercooked pork. The T. Solium larvae gets digested out of the meat & attaches itself to the upper small intestine. In the small intestine it will mature & ⇧ its number of proglottids. Terminal gravid proglottids will break off from the main body & will either pass out é stool or worm its way out of the anus. In certain cases, 3-4 attached proglottids will pass out together. The eggs housed in the proglottids will be released & remain viable in the soil for wks, single proglottid may produce 50,000 eggs. However, unlike T. Saginata, both pigs & humans can become intermediate hosts to the T. Solium. When pigs & humans ingest the eggs, the oncospheres will pierce through the intestinal walls, travel through the circulatory system, plant itself in SC tissue & muscles such as the brain & eyes. Cysticercosis will develop in these areas &become infective in 9-10 wks. Pigs will die in several months. In humans, cysticercosis has a variety of damaging effects on the CNS, vision & brain. In humans, autoinfection of T. Solium eggs can occur by reverse peristalsis of the intestine. Similar to beef tapeworm. However, both the adult tapeworm & the larvae (cysticerca) infect people.

Clinical features

Mostly the pts are asymptomatic; but they could have epigastric discomfort, nausea & wt. loss. Pt may note passage of proglottids in stool. When infected é cysticerica (cysticercosis), they are distributed all over the body. The major manifestations come from the CNS é seizures, headache, ⇧ ICP & mental changes etc….

Diagnosis

Detection of eggs or proglottides in stool.

Diagnosis is difficult in cysticercosis ẃ is done by different clinical & laboratory criteria

Treatment

Prazequantel, single dose 5-10 mg/kg.

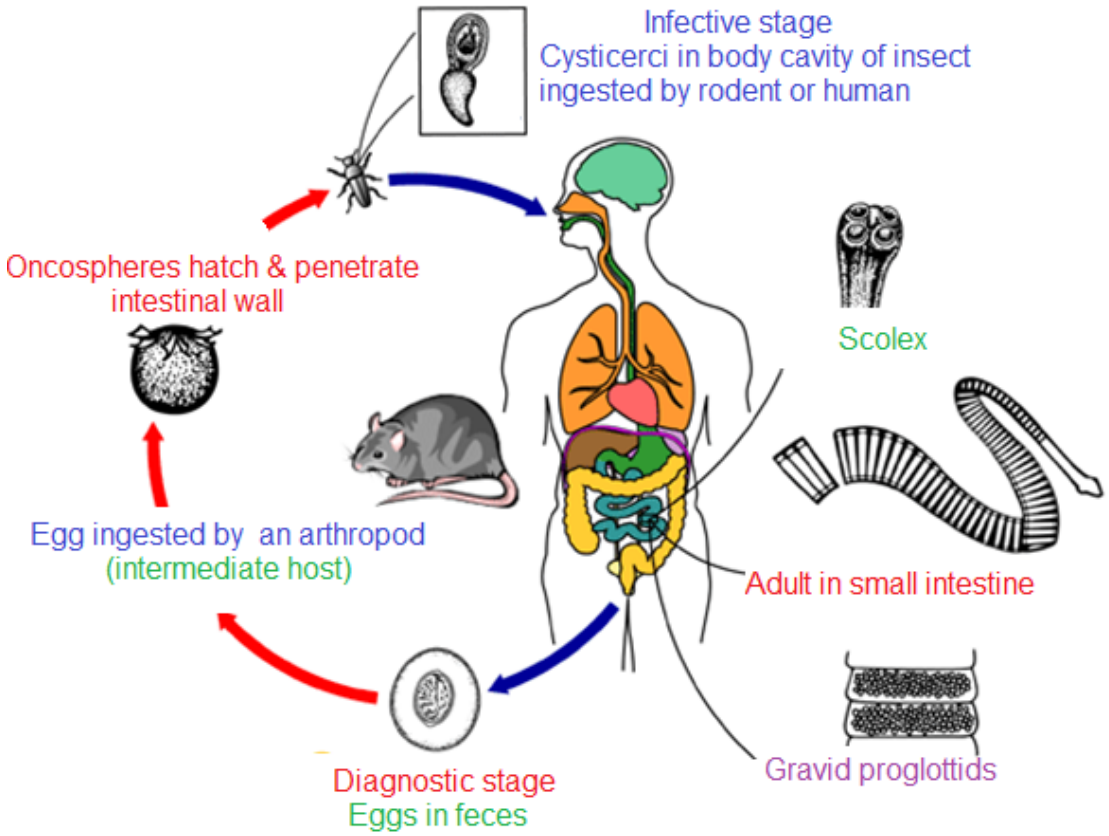
HYMENOLEPIS NANA

Commonly called the dwarf tapeworm “Nanos=dwarf”.

Epidemiology

One of the most common cestodes, infecting human, especially children.

Life cycle



Dwarf tapeworm is 25-40 mm in length X 1 mm in breadth. The scolex bears 4 sm-all suckers. Eggs measure 30-47 microns in diameter, they are round to oval & sho-uld contain a 6-hooked oncosphere (useful in diagnosis under the microscope & differen-tiation of parasite eggs), also they have polar filaments that lie between the egg shell & the oncosphere. Definitive hosts are human, mice, rats. Intermediate host (option-al): fleas & beetles. H. Nana is the only cestode that parasitizes humans éout requiring an intermediate host. Eggs of H. Nana are immediately infective when passed é stool & can`t survive > 10 days in the external environment. Human infection occur as a re-sult of:- accidental ingestion of tapeworm eggs, or ingestion of fecally contaminated foods & water or by touching mouth é contaminated fingers or by ingestion of conta-

minated soil & also when eggs ingested by an arthropod intermediate host where they develop into cysticercoids, ẃ can infect human or rodent upon ingestion. When eggs are ingested (food, water, hands, arthropod intermediate host) the oncospheres contained in the eggs are released. The oncospheres penetrate the intestinal villus & develop into cysticercoid larvae. Upon rupture of the villus, the cysticercoids return to the intestinal lumen, evaginate their scoleces & attach to the intestinal mucosa where they develop into adults that reside in the ileal portion of the small intestine producing gravid proglottids. Eggs are passed in the feces when released from proglottids after the proglottids disintegrate in the small intestine. An alternate mode of infection consists of internal autoinfection, where the eggs release their oncospheres, ẃ pentrates the villus continuing the infective cycle éout passage through the external environment. The life span of adult worms is 4-6 wks, but internal autoinfection allows the infection to persist for yrs.

Clinical features

Most infections are asymptomatic. Severe infections may manifest é abdominal pain, anorexia & diarrhoea.

Diagnosis: based upon demonstration of the eggs in the stool.

Treatment

Praziquantel 25 mg/kg as single dose is the Rx of choice. A course of Niclosamide for 7 days is also effective.

Prevention

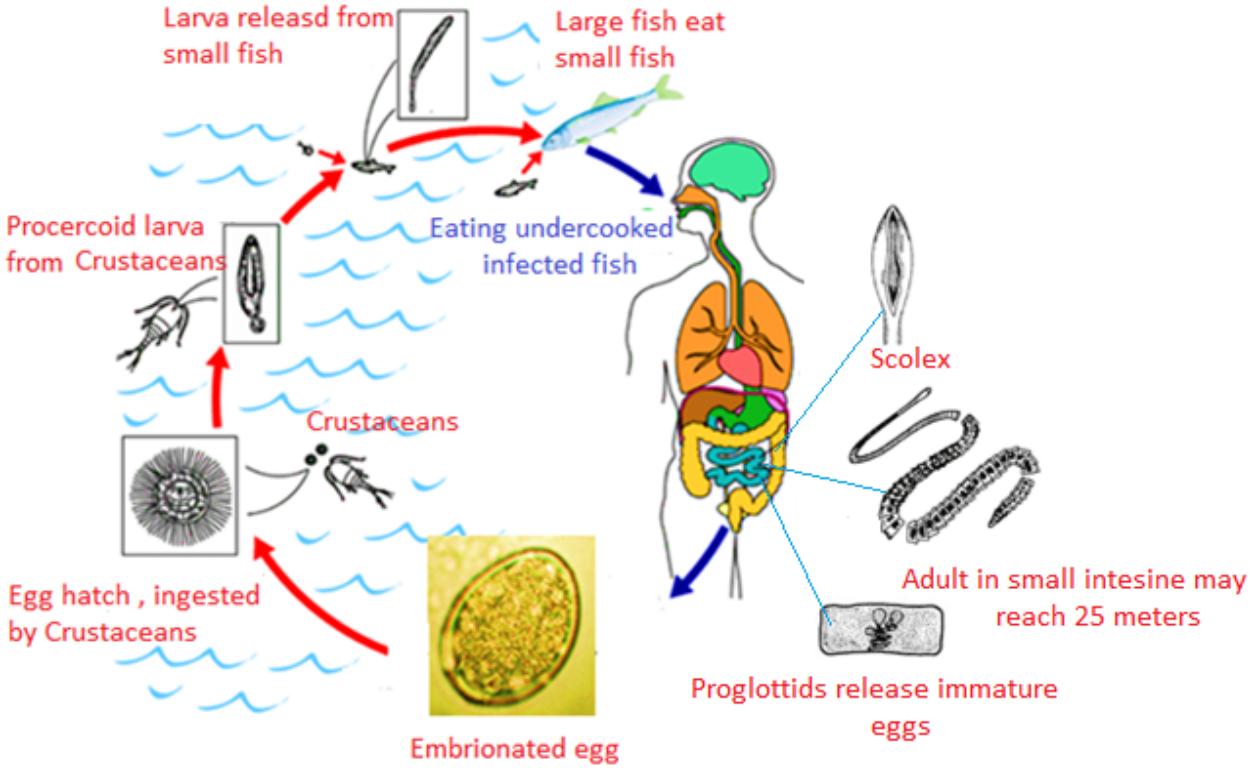
Good hygiene, elimination of rats & mice, a well-balanced diet to promote resistance to infection, public health & sanitation programs.

DIPHYLLOBOTHRIASIS

Etiology/Epidemiology

Diphyllobothriasis is infection caused by adult diphyllobothrium latum. It is acquir-ired from eating raw fish. Diphyllobothriasis occurs in the Northern Hemisphere (Eu-rope, North America & Asia) & in South America (Uruguay & Chile).

Life cycle



Immature eggs are passed in feces. Under appropriate conditions, the eggs mature (approximately 18-20 days) & yield oncospheres ẃ develop into a coracidia. Aft er in-gestion by suitable freshwater crustacean (copepod first intermediate host) the cora-cidia develop into procercoid larvae. Following ingestion of the copepod by a suitable second intermediate host, typically minnows &other small freshwater fish ,the pro-cercoid larvae are released from the crustacean & migrate into the fish flesh where they develop into a plerocercoid larvae (sparganum). The plerocercoid larvae are the infective stage for humans. Because humans do not generally eat undercooked min-nows & similar small freshwater fish, these do not represent an important source of infection. Nevertheless,these small second intermediate hosts can be eaten by larger

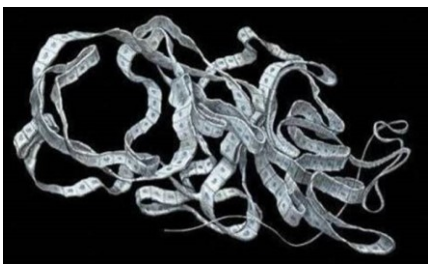
predator species, e.g. trout, perch, walleyed pike. In this case, the sparganum can migrate to the musculature of the larger predator fish & humans can acquire the disease by eating these later intermediate infected host fish raw or undercooked. After ingestion of the infected fish, the plerocercoid develop into immature adults & then into mature adult tapeworms ẃ will reside in the small intestine. The adults of D. latum attach to the intestinal mucosa by mea-ns of the 2 bilateral groves (bothria) of their scolex . The adults can reach >10 m in length, ē > 3,000 proglottids. Immature eggs are discharged from the proglottids (up to 1,000,000 eggs per day per worm) & are passed in the feces. Eggs appear in the feces 5-6 wks after infection. In addition to humans, many other mammals can also serve as definitive hosts for D. latum.

Clinical Picture

Many people are asymptomatic. But pt could have abdominal pain, loss of appeti- te, anorexia, nausea, diarrhoea or loss of weight. Since this tap worm consumes a lot of Vit. B_{12} & interferes é its absorption, it can cause Vit. B_{12} deficiency (megaloblastic anaemia).

Treatment

Praziquantel 5-10 mg/kg once is very effective. Vit. B_{12} deficiency should be treated if present.

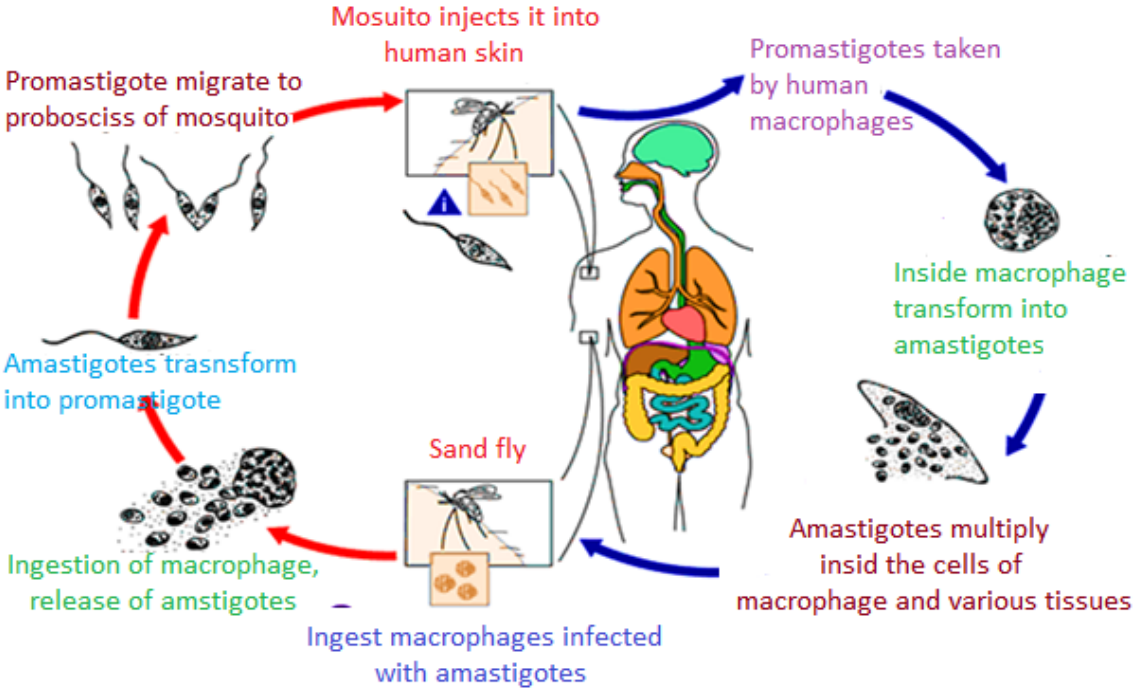


LEISHMANIASIS

Infectious disease caused by the protozoa called *Leishmania.* Leishmaniasis transmitted to man from animals through *Sand Fly.* There are 3 major clinical forms **:-**

Visceral, Cutaneous & Mucocutaneous leishmaniasis.

Life cycle



Life cycle starts when parasitized female sand fly takes a blood meal from a human host (sand fly is very small, may be hard to see, they are 1/3 size of typical mosquitoes, fly éout making any noise). As the sand fly feeds, **promastigote** forms of the leish- manial parasite (the flagellated forms) enter the human host via the proboscis. Within the human host, the promastgote forms are ingested by macrophage where they metamorphose into **amastigote** forms (non flagellate form), reproduce by binary fission & ⇧ in number until the cell eventually bursts, then infect other phagocytic cells & continue the cycle. The IP of leishmaniasis varies from wks to yrs. If infected host is bitten by another female sand fly, the parasites are up by the fly during the blood meal, transformed inside the fly & delivered**to** newhost & lifecycle continues.

VISCERAL LEISHMANIASIS

Epidemiology

Visceral leishmaniasis (Kala Azar).affects many countries in Africa, mainly Ethiopia, Sudan, Middle East, southern Soviet Union, India & south America. The disease is becoming a common opportunistic infection in AIDS.

Transmission

The commonest way of transmission is by inoculation of promastigotes into hum- ans by the bite of the Sand Fly ẃ breed in termite hills & forests. The source of the aflagellate forms may be either humans or extra human vertebrate reservoirs & the disease may have life cycles that involve humans & sand flies only, or humans, sand flies & extra human vertebrate reservoirs together. Rarely transmission may occur via blood transfusion or injections.

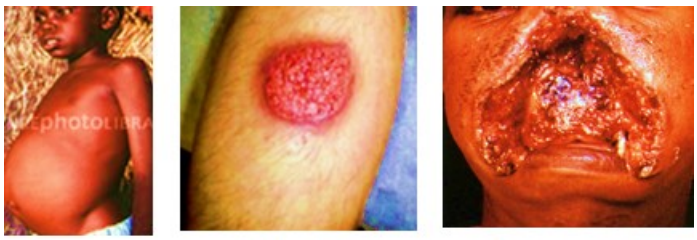
Pathogenesis

The common site of entrance is the skin where primary cutaneous lesion appears at the sites of sand fly bite. The lesion is tiny, may pass unnoticed. This is also called primary leishmanioma. Here a cellular reaction by lymphocytes & plasma cells develop around the amastigote- filled histiocytes in the dermis. As the immune response develops epitheloid & giant cells appear, followed in some pts by healing & in some others -usually 4-6 months later- the amastigotes escape to the blood in macrophages, leading to haematogenous spread & colonization of the cells of RES , where they multiply further, released after rupture of the cells &transported to new cells. The cells affected include that of spleen, liver, bone marrow & lymphatic glands, where the parasite multiplies & cause overcrowding of cells & as a result these organs are enlarged. Spleen is grossly enlarged é smooth capsule initially, ẃ become thickened & nodular as the disease progresses. The involvement of bone marrow leads to the development of pancytopenia. The liver é its Kuppfer cells packed é amastigotes is enlar-

ged é resultant progressive cirrhosis. The LNs are enlarged & congested especially the mesenteric LNs.

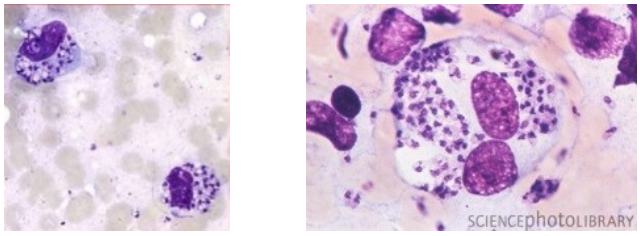
Clinical features

Visceral infections remain subclinical or become symptomatic é acute, subacute or chronic course. The onset is often gradual but can be sudden é high grade fever (intermittent or remittent) lasting for 2-6 wks. In those é gradual onset in endemic areas discomfort below left costal margin is common due to enlarged spleen & have cough, epistaxis & diarrhoea. The pt will be markedly emaciated é hepatosplenomegaly, generalized peripheral lymphadenopathy & marked pallor in the late stage of the disease. Oedema of the legs, brittle dry hair, Hge from any site (gum, skin etc.) é purpura & petechiae of the skin may occur. Some pts develop post-kala -Azar dermal leishmaniasis after months or years of Rx for visceral leishmaniasis.



Visceral Cutaneous Mucocutaneous

Diagnosis



L. Donovani amastigotes (3 um) inside WBCs in blood (left) & in tissues (right).

Definitive diagnosis is based on demonstration of the parasite by:-

- Giemsa stained smear of peripheral blood.
- Culture of tissue aspirates taken from the spleen, BM, liver or LNs.
- Serologic diagnosis – ELISA or DAT, both 100% sensitive & specific.
- Montenegro skin test is -ve in visceral leishmaniasis, becomes +ve 6-8 wks after rec-

overy •CBC- pancytopenia.

Management

Is difficult to treat. Rx include; Pentavalent antimony compounds, 20 mg/Kg/day IV or IM for 28 days or Miltefosine 50 mg capsule 1 X 2 X 28 days (approved by FDA 2014). The supportive Rx include; Blood transfusion to correct anaemia, Rx of any additional infection, & correction of malnutrition.

Prevention

•Reduction of human contact é sand flies; using insecticide impregnated bed nets.

•Wearing protective clothing, covering as much skin as possible.

•Chemical repellents applied on exposed skin before hours of sand fly activity (dusk & night) are effective.

•Combustion of Permethrin containing mosquito coils & Screening doors.

•Reduction of sand fly population, through using insecticides.

•Control of reservoir- dogs, rodents.

•Construct huts/camps away from breeding sites (hills & forests) & destroying of sand fly breeding sites.

CUTANEOUS LEISHMANIASIS

Oriental sore, the skin is one of the organs commonly affected by leishmania. Following the bite of sand flies, leishmania multiply in the macrophages of skin. Single or multiple painless nodules occur on exposed areas of the body, within 1 wk-3 months of the bite. The nodules may enlarge & ulcerate é erythematous raised border & overlying rust ẃ may spontaneously heal over months to yrs.

Investigation

•Giemsa staining of smear from a split skin: Leishmania in 80% of cases.

•Culture followed by smear.

•Leishmanin skin test +ve in >90% & -ve in case of diffuse cutaneous leishmaniasis.

Clinical patterns according to etiology

In the old world			
Species	**Distribution**	**Reservoir**	**Clinical Pattern**
L.Major L.Tropica	Russia, Eastern Europe, Middle east, Meditrra-nean,subSahara & west Africa	Desert rodent for L. major. Dog &humans for L. tropica.	Spontaneous healing é scaring
L. Ethiopia	Highlands Ethiopia	Hyrax	Spontaneous healing within 6 month
In the new world			
L. Amazon			Diffuse cutaneous leishmaniasis ,resembling lepromatous leprosy(spares nasal septum)
L. Peruvia	Cooler climates		Single/multiple ulcers, heal spontaneously
L. Mexican	Mexico, Guatemala Brazil, Venezuela & Panama.		Infection of Pinna (chiclero`s ear),causes de-struction of Pinna, lesion persisting>20 yrs.

Treatment

Small lesions don't require Rx. However large lesions or those on cosmetically im-portant sites require Rx either:-

•Locally-by surgery, curettage, cryotherapy or hyperthermia. or

•Systemic Rx: drugs like Pentostam. Rx is less successful than visceral leishmaniasis as the antimonials are poorly concentrated in skin.

MUCOCUTANEOUS LEISHMANIASIS

Caused by L. Braziliensis, commonly seen in Latin America. In the early stage it affects the skin, but in the secondary stage of the disease it involves the upper respiratory mucosa. Present initially é painful, itchy nodules appear on the lower lim-bs then ul-cerate é lymphangitis.The lesion may heal spontaneously in 6 months.

In about 40% of pts the secondary lesions appear several yrs later at the mucocutane-

ous junctions of nasopharynx. This leads to nasal obstruction, ulceration, septal perforations & destruction of the nasal cartilage called “Espundia”.

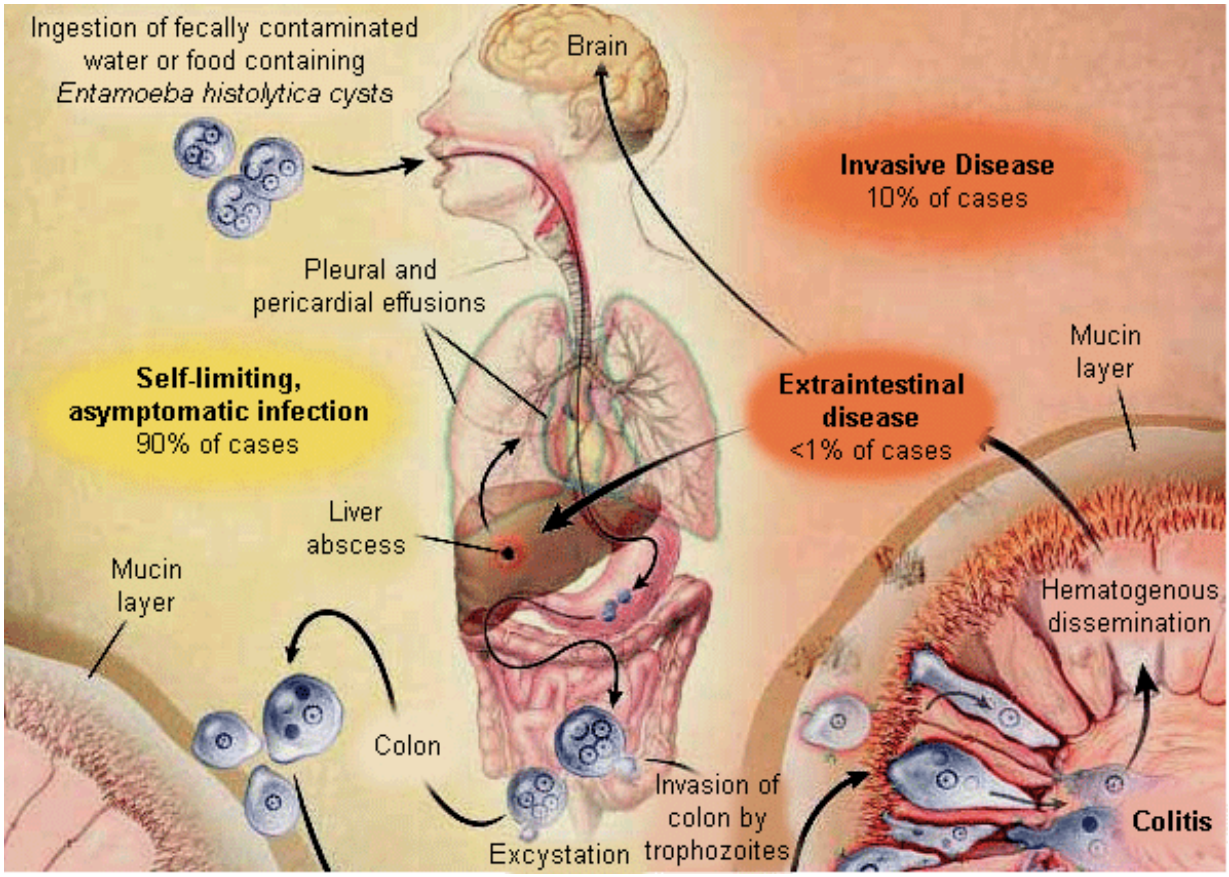
Diagnosis: •Leishmanin skin test is often +ve. •Antibody tests (ELISA) often +ve.

Treatment: Requires systemic antimonials (Pentostam) but relapses common.

AMOEBIASIS

Is a major health problem. Infection é protozoa Entamoeba histolytica. 90% of infection are asymptomatic & 10% have clinical symptoms ranging from dysentery to abscess of liver/other organs. Amoebiasis is the second leading cause of death among parasitic diseases. The parasite exist in 2 forms; cyst (infective form) & tro-phozoite stage (invasive disease).

Life cycle



A person may carry the pathogen éout evidence of clinical disease (asymptomatic cyst passers)

Infection occurs following ingestion of amoebic cyst (infective form); this is usually via contaminated food or water. Cysts can remain viable in the environment for wks

to months & ingestion of a single cyst is sufficient to cause disease. The cysts pass through the stomach to the small intestine where they excyst to form trophozoites (form that causes invasive disease). Trophozoites graw & reproduce in intestinal tract, invade & penetrate mucosa barrier of the colon causing tissue destruction & ⇧ intestinal secretions & can lead to bloody diarrhoea.

Clinical presentation

- Asymptomatic intestinal infection (carriers, passing cysts).
- Mild to moderate disease (non-dysenteric colitis).
- Severe intestinal infection (dysentery).
- Hepatic abscess.
- Ameboma (localized granulomatous lesion of colon).

Diagnosis

- ***Stool analysis:*** demonstration of cysts or trophozoites suggest amebiasis of colon
- ***Antibody detection:*** ELISA test detects antibody specific for E. Histolytica in approximately 95% of pts é extra-intestinal amebiasis & 70% of pts é active intestinal infection & 10% of asymptomatic person who are passing cysts of E. Histolytica.
- ***Indirect Hemagglutination test:*** +ve in 90% of pts.

Management

Amoebiasis: sometimes is a difficult disease to treat because of its tendency to chronicity & the inability of various drugs to eradicate the cystic forms of the parasite completely.

Amoebic dysentery: Metronidazole (Flagyl) tab 500 mg tds & syrup for children, 125 mg/tsp, 15 mg/Kg/Day for 5-7 days, is the drug of choice, very effective in killing amoebas in the wall of intestine & blood & liver abscesses. Almost 90% of pts é moderate amoebic dysentery responds clinically to oral Metronidazole. Severe cases may

need IV injections of Metronidazole (500 mg /100 ml bottle).

Asymptomatic cyst passers & chronic amoebiasis: Diloxanide furoate tab (Amoebyl) 500 mg 3 times daily for 10 days kills trophozoites & cysts in the lumen of the intestine. A combination of Diiodohydroxyquinoline 1.8 gm daily &Tetracycline 1 gm daily in divided doses for 10 days. or Furazole + Colimex suspension 1 tsp each X 3/day for 10 days. Chronic amoebic colitis is sometimes difficult to treat & usually more than one drug given in rotation.

Hepatic Amoebiasis: Metronidazole is the drug of choice. Emetine Hydrochloride & Chloroquine Diphosphate also effective. Surgery may be necessary in amoebic liver abscess & should be followed by luminal amoebicide course.

GIARDIASIS

Giardia Lamblia is a flagellated protozoan that infects the duodenum, small intestine, bile ducts & gall bladder, causing Giardiasis.

Cosmopolitan in distribution é prevalence ranges from 2-70% in populations.

The infective stage is the cyst.

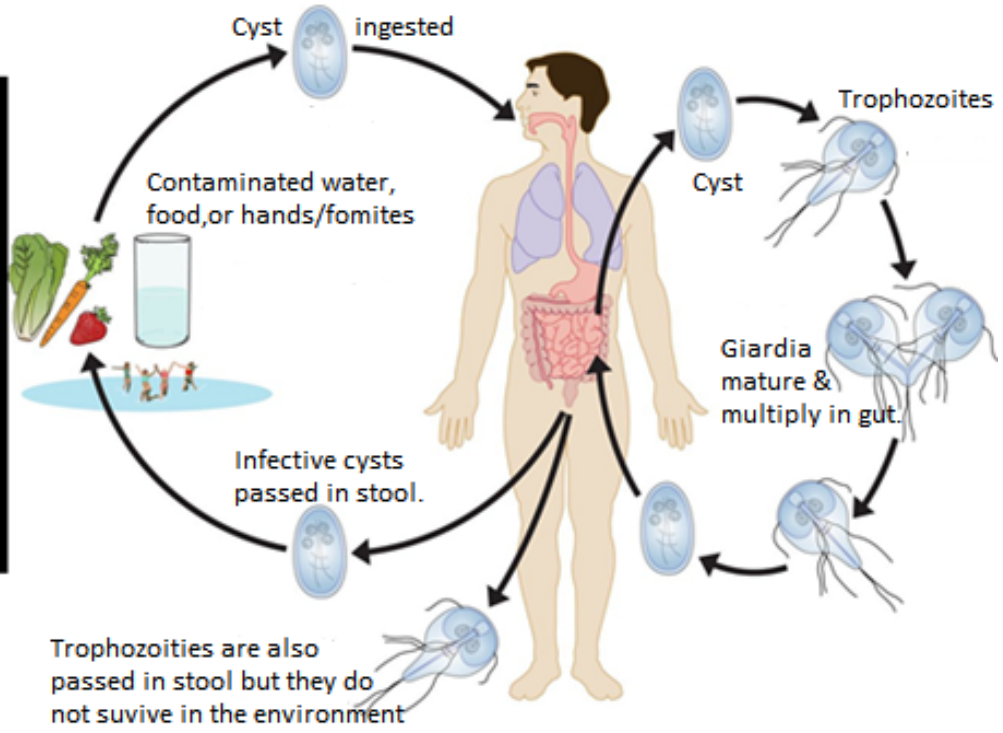
The mode of infection is through contaminated food or water, flies, food handlers (faecooral route) & hands/vomite.

Life cycle

Trophozoite stage: trophozoites attach to epithelial cells, not penetrating mucosa, feeds on mucous that forms in response to irritation, also absorbs vitamin & amino acids, interferes é lipids, vitamins & nutrient absorption:- Vit. A deficiency affect vision. Vitamin D deficiency may lead to rickets.

Cyst stage: cysts may remain viable in external environment (usually water) for many months, as few as 10 cysts can cause disease & up to 900 million cysts can be released by an infected person in one day.

Giardia-Trophozoite-Electron ic Microscope.



Clinical features

IP is 1-2 wks, is of gradual onset, & may present é nausea, vomiting, watery diarrhea, dehydration, malaise, flatulence, low-grade fever & steatorrhoea. Its sequely include; malabsorption, lactase deficiency, wt loss, fatigue & rarely arthritis.

Diagnosis

•Fecal examination: water like feces (associated é trophozoites), formed feces (associated é cysts), at least 3 exams -one every other day - before judge -ve.

•Duodenal fluid or bile examination.

•ELISA tests: detect soluble antigen (trophozoites).

•PCR analysis: detect giardia DNA from both trophozoites & cysts.

Treatment

Metronidazole tab 500 mg tds (infusion 500mg/100ml solution) & for children syrup 125 mg/tsp, 15mg/ Kg/day for 5-7 days is the drug of choice, or

Furazoldine 2 mg/Kg X 6 hrs X 7-10 days, or

Quinacrine HcL 2 mg/Kg X 8 hrs X 5-10 days.

MALARIA

Aetiology

Protozoal disease transmitted to man by the bite of the female anopheles mosquitoes. Malaria is caused by the protozoan genus plasmodium. 4 species are known to cause disease in man:-

P. Falciparum: also called malignant malaria.

P. Vivax: tertian malaria.

P. Ovale: tertian malaria.

P. Malariae: quartan malaria.

Almost all deaths are caused by P. falciparum.

Epidemiology

Malaria is one of the commonest infectious diseases of man, one of the oldest known diseases, King Tut died of Malaria? 40% of the world's population lives in endemic areas. 300-500 million clinical cases per year. 1.5-2.7 million deaths per year (of them 90% in Africa). The prevalence of malaria is increasing because of the emergence of DDT resistant anopheles mosquitoes, drug resistant plasmodia & the global weather changes. Transmission is common in low-lands during rainy season, especially é migration of non-immune individuals to these areas. Rare cases of congenital transmission are known. Endemicity of malaria is defined based on ***splenic rates*** (palpable spleen) in children between 2-9 yrs. Depending on this, regions are classified into 4 endemicity areas:-

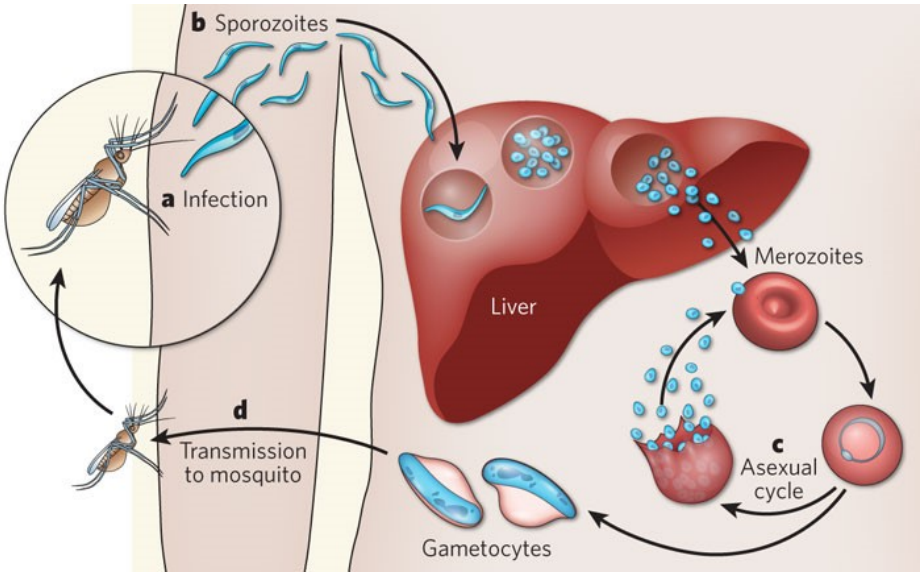
- Hypo endemic- where < 10% of children has enlarged spleen.
- Meso endemic- where 10-50% of children have enlarged spleen.
- Hyper endemic-where 51-75% of children have enlarged spleen.
- Holo endemic- where >75% of children have enlarged spleen.

In Holoendemic & Hyperendemic areas there is an intense transmission of P. falciparum & people can sustain >one infectious mosquito bit/day. In such places, morbidity & mortality are considerable during childhood. Immunity against disease is hard one & during adulthood most infections are asymptomatic. This frequent round-year transmission termed stable transmission. In Hypoendemic & Mesoendemic areas the transmission is low, or focal, full protective immunity is not acquired & symptomatic disease may occur at all ages termed unstable transmission.

Characteristics of stable & unstable transmission of malaria.

	Stable	Unstable
Mosquito life	Long	Short
Mosquito bites	Frequent	Rare
Human immunity	High	Low
Epidemics	No (only é rainy Season &migration of non-immunes to the area	Yes
Eradication/contr.	Difficult	Possible

Life cycle



The life cycle of plasmodium is divided into 2, namely:-

1- Asexual cycle: occurs in human, include 2 phases (Liver & Erythrocytic)

2- Sexual cycle: occurs inside anopheles mosquitoes.

Asexual cycle

Liver phase: human infection initiated when sporozoites are injected é saliva during mosquito feeding. The sporozoites enter the circulatory system & within 30-60 minutes will invade a liver cell, undergoes asexual replication. A single sporozoite produces thousands of merozoites (10.000-30.000). This replicative stage called exoerythrocytic (or pre-erythrocytic) schizogony. In P. vivax & ovale some of the sporozoites do not immediately undergo asexual replication, but enter dormant phase known as hypnozoite. This hypnozoite can reactivate & undergo schizogony at a later time resulting in a relapse. The second phase of the asexual cycle is the Erythrocytic phase: in ẃ the swollen liver cells rupture, discharge merozoites into blood stream ẃ then invade RBCs & multiply 6-20 fold every 48-72 hrs. Merozoites recognize specific proteins on the surface of the RBC & actively invade the cell, after entering the RBC the parasite undergoes a trophic period followed by an asexual replication. The erythrocyte form Ring form due to its morphology in geimsa stained blood smears & as the parasite ⇧ in size this ”ring” morphology disappears & is called trophozoite. During the trophic period the parasite ingests the RBC cytoplasm & breaks down the Hb into amino acids. A by-product of the Hb digestion is the malaria pigment called hemozoin. These golden-brown to black granules of malaria pigment have been long recognized as distinctive feature of blood-stage parasites. The nuclear division marks the end of the trophozoite stage & the beginning of the schizont stage. Erythrocytic schizogony consists of 3-5 rounds of nuclear replication (depending on species), followed by budding process. Late stage schizont in ẃ the individual merozoites become discernable are called segmente- rs. The host RBC ruptures & releases the merozoites. These merozoites invade ne-w RBCs & initiate another round of schizogony. Same cycle repeated invading another RBCs. This explains the anaemia in malaria ẃ is largely due to the

destrucion of RBCs. When parasites reach certain density in blood, the symptomatic stage begins. During this process the infected RBCs & sometimes uninfected ones are removed from the circulation by the spleen clearance function & contribute its share to anaemia. This immunologic function of spleen causes its enlargement. In P. falciparum: the infected RBC containing mature forms adhere to small blood vessels (called cytoadherence) & also é uninfected RBCs forming rosettes (called Rosetting) both of ẃ result in sequesteration of RBCs in vital organs like the brain & heart, interfering é the microcirculation & metabolism & contribute to its severity. This makes detection of mature forms difficult, only ring forms & gametocytes can be found on peripheral blood films. Sequestration is not a feature of other species of malaria & all stages of the parasite can be seen in the peripheral blood film.

Sexual cycle

After serial of asexual cycles some of the parasites develop into morphologically distinct long lived sexual forms -*microgametocytes*- include male & female, the gametocytes do not cause pathology in the human host & will disappear from the circulation if not taken up by a mosquito that can transmit malaria. After ingestion by the mosquito, the microgametocyte undergoes 3 rounds of nuclear replication, the male & female gametocytes form zygotes, in insect's midgut, this zygotes mature into ookinetes ẃ then develop to oocystes. The oocysts undergo asexual replication (sporogony), ẃ culminates in the production of several thousand of sporozoites. This generally takes 10-28 days depending on species & temperature. Upon maturation the oocyst ruptures & releases the sporozoites ẃ cross the basal lamina into the hemocoel (body cavity of the mosquito). Now it is ready for inoculation to new host.

Clinical picture

The IP is 10-14 days for P. Vivax, Ovale & Falciparum, while it is 18 days - 6 weeks, in

case of P. Malaria. The symptoms & signs of malaria resemble many types of febrile illnesses. Early symptoms are nonspecific- malaise, fatigue, headache, muscle pain & abdominal discomfort followed by fever, nausea & vomiting is common. Classically, malaria manifests in regular paroxysms of high grade fever, chills & rigor, occurring every two days in P. Vivax or ovale & every three days in P. Malaria, but it is irregular in P. Falciparum. The malarial febrile paroxysms (ẃ are due to rupture of schizonts & release of pyrogens) typically have 3 stages; The "cold stage" in ẃ the pt feels intensely cold & has shivering, lasts for 30-60 minutes & characterized by; vasoconstriction of vessels & the temperature ⇧ rapidly. The "hot stage" pt feels hot, uncomfortable, become delirious, this stage lasts for 2-6 hours. The third & last stage is the "sweating stage" in ẃ the pt will have profuse sweating & exhausted.

Physical findings

Uncomplicated infection: has few physical findings fever, malaise, mild anaemia, palpable spleen & liver é mild jaundice (especially children). Suspect in every child é fever **>** 38.5 ^{0}C in endemic areas.

Severe/complicated malaria: defined as life threatening malaria caused by P. Falciparum & the asexual form of the parasite demonstrated in blood film.

Severe/complicated P. Falciparum malaria in adults include:-

- Cerebral malaria: state of unarousable coma lasting for>30 minutes & other causes of coma ruled out. The change of level of consciousness is less marked than unarousable coma.
- Generalized tonic clonic seizure (>2/day).
- Severe normocytic anaemia (Hb <5 gm/dl).
- ARF (oliguria <400 ml/24hr &/or creatinine >3 mg/dl).
- Pulm oedema or ARDS. •Hypoglycaemia (BG <40mg/dl) is multifactorial (the parasite

consumes glucose, the catabolic state ⇧ the glucose demand of the host, anorexia associated é the illness & drugs like Quinine can cause hypoglycaemia).

•Metabolic acidosis (pH<7.25; plasma bicarbonate <15 mmol/l).

•Circulatory collapse, shock, septicaemia: SBP<80 mmHg.

•Spontaneous bleeding/DIC.

•Haemoglobinuria. •Jaundice, S.B.>3mg/dl.

•Hyperparasitemia: >5% of RBCs affected by plasmodium or >100.000 plasmodium/µl of blood.

•P. Falciparum malaria in pregnant women is also considered as severe because it is associated é adverse outcomes to mother & foetus. The severe complications may occur singly, or more commonly, in combination in the same pt.

People at risk of developing severe malaria in high transmission are:-

- Young Children.
- Pregnant women.
- Visitors to endemic areas.

Types of plasmodium & clinical feature

	Malaria type	I. P.	Fever pattern	Recurrence
Benign	P. Malaria P. Vivax/Ovale	21-42 days 10-21 days	No fever for 2 ay No fever for 1 day	No relapses Relapses possible up to 5 yrs
Malignant	P. Falciparum	10-21 days	Irregular fever	No relapses

Differential Diagnosis

•Trypansomiasis •Relapsing fever •Filariasis •Meningitis •TB •Yellow fever •Typh-oid fever •Brucellosis.

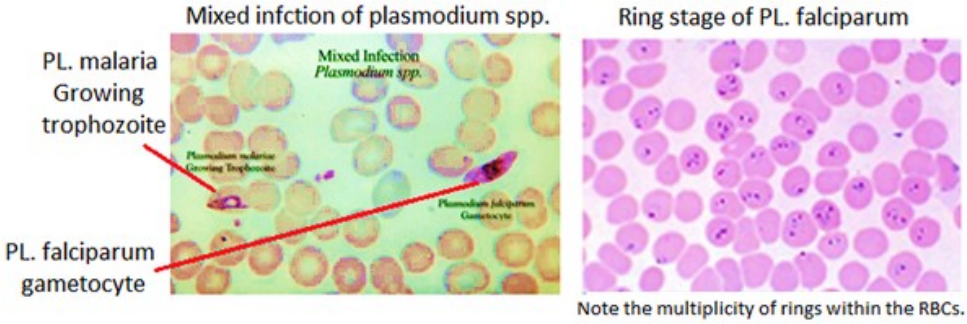
Complications

• Tropical splenomegaly (hyper-reactive malarial splenomegaly) is syndrome resulting

from abnormal immunologic response to repeated infection, seen in some residents of malaria endemic area in tropical Africa & Asia, characterized by huge spleen >10 cm BLCM é/éout hepatomegaly. Hypersplenism (anaemia, pancytopenia), marked ⇧of serum IgM & antimalarial antibody, hepatic sinusoidal lymphocytes, peripheral blood cell lymphocytosis. Splenectomy only indicated for those é failure of antimalarial prophylaxis at least given for 6 months.

•Agranulocytosis • Rupture spleen • Hepatitis • Pigment gall stones • Black water fever • Retinal He • Delirium • Coma.

Investigations



• ***Demonstration of parasite:*** thin & thick blood film (Giemsa stain):-

Thin blood film is methanol fixed; you can see intact RBC é parasites inside it. Advantage: species identification is simple; % of RBC parasiteized can be estimated.

Thick blood film, not methanol fixed, RBCs are lysed during staining, parasites are seen free from RBC. Its advantage include; concentrates parasite 30 times & this helps to determine parasite conc. N.B. a single blood film examination does not R/O malaria & it should be repeatedly done possibly during febrile episodes. However, studies have shown that blood film can be -ve in small % of pts é malaria.

• ***The % of parasite count***: is of prognostic value é Rx, repeat/12 hrs.

• ***Test for sickle cell disease & G6PD deficiency.:*** if proven, ⇩ the dose & prolong the duration of Rx for such proven cases.

• ***Serological studies;*** for detection of antigen: immunochromatography. Detection of

antibodies; indirect florescent antibody assays.

• ***Other tests:*** CBC: anaemia can be detected, RBC appearance, WBCs. CSF when indicated to R/O meningitis. BUN/creatinine, SGOT, SGPT, electrolytes, BG levels.

Treatment

Benign forms of malaria (P. Malariae/Vivax/Ovale)

Chloroquine is effective: the initial dose is 600 mg PO followed by 300 mg after 6, 24 & 48 hrs subsequently, (Chloroquine has no effect on exoerythrocytic liver form &to protect from later recurrences, Chloroquine should be followed by Primaquine 15 mg/day over 2 wks, ẃ is effective against liver forms & gametocytes).

Treatment of P. Falciparum Malaria

a) Aritemisinin & its derivatives: have proved to be highly effective in adults & children. There are different preparations like; Artemether (PO or IM) & Artesunate (PO or IV), Artemether-Lumefantrine: (Coartem or Atmal 20/120): is the most widely used drug, tab containing 20mg Artemether + 120mg Lumefantrine in a fixed dose combination. Adult é < 35 kg BW to be given 3 tab. PO BID for 3 days & for those >35 Kg: 4 tab. PO BID for 3 days. Side effects; dizziness, fatigue, anorexia, nausea, vomiting, abdominal pain, palpitations, myalgia, sleep disorders, arthralgia, headache & rash. These drugs are contraindicated as malaria prophylaxis either alone or in combination, or in case of person é previous history of reaction after using the drug, also contraindicated é pregnant women & mothers é infants <3 months of age & or <5 kg body weight.

b) Quinine: adult dose: 600 mg PO TID for 5-7 days alone or in combination é Tetracycline 500 mg PO QID or Doxycycline 100 mg PO/day for 5-7 days. Side effects: cinchonism: tinnitus, hearing loss, dizziness, tremors, nausea, restlessness, blurring of vision. Hypoglycaemia: is the commonest adverse effect.

c) Mefloquine: dose is 15mg/kg followed by 2nd dose of 10 mg/kg after 8-12 hrs. Stru-

cturally resembles Quinine. The drug is effective against all species of malarial including multidrug resistant P. Falciparum. However some resistance strains of P. Falciparum are reported in some tropical countries. Side Effects include; nausea, abdominal cramp, vertigo, insomnia, sometimes acute psychosis & convulsion.

d) Sulfadoxine-pyrimethamine (Fansidar): dose is 3 tab. stat as a single dose. (1 tab 500 mg Sulfadoxine + 25 mg Pyrimethamine). Due to high prevalence of resistance to this combination, Fansidar is not recommended for Rx of P. Falciparum in most tropical countries & it is contraindicated for children < one year age.

Treatment of severe & complicated Falciparum Malaria

Pts should be admitted & treated in a hospital setting.

A) Drug treatment

i) Quinine: is the drug of choice for severe & complicated malaria, 20 mg salt/kg by IV infusion over 4 hrs, in 5% Dextrose saline (5-10 ml/kg depending on the pt's overall fluid balance). Maintenance dose: 12 hrs after the start of the loading dose, give 10 mg/kg in Dextrose saline over 4/hrs. Repeat/8 hrs until the pt can take oral medication. Wherever IV administration of Quinine is not possible, give Quinine Dihydrochloride 20 mg salt/Kg loading dose IM divided into 2 sites, in the anterior thigh, then 10 mg salt/kg IM every 8 hrs until pt can swallow.

ii) Artesunate injection: 2.4 mg/kg IV or IM stat followed by 1.2 mg/kg at 12 & 24 hrs & then daily.

B) Supportive treatment

- Bring down fever (cold sponges, paracetamol).
- Administer glucose IV or PO to prevent hypoglycaemia & encourage early PO intake of food.
- Insure adequate fluid intake, check input, output & control water/electrolyte, bewa-

re of pulmonary oedema due to fluid overload.

- Consider blood transfusion in severe Falciparum malaria é high parasitemia (**>** 20% of erythrocytes affected by plasmodium).
- Check renal function tests.
- For comatose or unconscious pt proper nursing is mandatory; position pt on his/her sides; turn every 2 hrs to avoid bed sores.
- Catheterize the bladder, monitor input & output, avoid fluid overload.
- Monitor BG regularly & adequate nutrition.

Treatment of Cerebral Malaria/Coma

- Artemether 80 mg amp, starting dose 3.2 mg/Kg IM, then 1.6 mg/Kg daily or Atmal 20/120, 80/240 amp (Artemether + Lumefantrene).
- Dexamethasone, 8 mg /2 ml, 0.5 mg mg /Kg IV/12-24 hrs for 2 days.
- IVF & fluid chart: alternatively use NS, Ringer`s sol & Glucose 5%. Urine catheter.
- Heparin 5000 u/ml/6 hrs
- Dextran 500 ml over 24 hrs
- Monitor CBC, Malaria indices (% of parasite level 6 hourly).

Prevention

A. General measures

Mechanical barriers: •Draining water collections & swampy areas. •Use of chemi-cal impregnated mosquito nets around beds. •Wire mesh across windows. •Stayi-ng in-doors at night. •Use of long sleeved shirts/trousers.

Insecticides: •Use insecticide spray aerosols (Permethrin, & Chlorinated Hydrocar-bons). •Insect repellents to exposed skin (e.g. Diethyltoluamide). •DDT sprayed in the interior of houses is effective in killing the adult mosquito for many months.

B. Drug prophylaxis

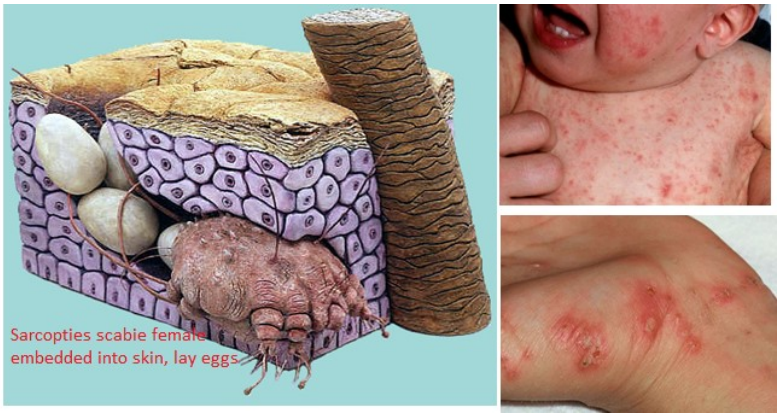
In areas where there is Chloroquine resistant P. Falciparum:-

- Mefloquine (resemble Quinin) 250 mg/wk PO, safe during pregnancy.
- Doxycycline 100mg daily orally, not used for children <8 yrs or during pregnancy
- Maloprim (Pyrimethamine + Dapson) 1 tab PO/wk.
- Chloroquine + Proguanil combination.

SCABIES

Scabies is an itchy rash caused by little mite that burrows in the skin surface. The human scabies mite's scientific name is Sarcoptes Scabiei Var. Hominis, is a common world-wide public health problem é an estimated global prevalence of 300 million. The infestation causes considerable discomfort & can lead to secondary infection & complications such as post-strept glomerulonephritis. The Mites are tiny, just 1/3 mm long, have 8 legs (in contrast to insects, ẃ have 6 legs), not visible é naked eye but can be seen é a magnifying glass or microscope they burrow into the skin to produce intense itching, ẃ tends to be worse at night. A female mite lays eggs under the skin of a human & stays inside until she dies. Mite cannot live> 3 days éout a human host but it can survive up to a month when living on a human. The Mite also lays eggs in human skin that hatch & grow into adult mites.

This means that symptoms can last for months or even yrs.



Transmission

Scabies affects everyone regardless of age, race, gender, social class or personal hygiene habits. Transmission of the mites involves close person-to-person contact of the

skin-to-skin variety. It can be transmitted sexually as well as by nonsexual close skin to skin contact especially within family & at school. Almost impossible to get from shaking hands or sitting next to someone. The sexual contact is the most common form of transmission.

Clinical picture

When **>** one member of household is affected é an intensely pruritic eruption, scabies infestation must be considered. Scabies only affects the skin, causing extreme itching, ẃ is usually worse at night. For the first wks, itching is subtle but gradually becomes more intense until, after a month or two, sleep is almost impossible. Itching may be associated é rashes, blisters, or bumps. Rashes & itching may last for 2-3 wks, even after being treated, mainly found in In between the fingers, around the head & neck, wrist, nipple, elbow, waist, armpit, buttocks, penis & shoulder. In children it is especially seen in hands & feet. Text book descriptions of scabies always mention "burrows" or "tunnels“, these are tiny thread-like projections, ranging from 2-15 mm long, ẃ appear as thin gray, brown, or red lines in the affected areas, the burrows can be very difficult to see.

Management

Permethrin 5% cream left on for 8-10 hrs, or 2 applications one wk apart of an aqueous solution to the whole body excluding the head, is usually successful, contraindicated in infants **<** 2 months of age & in pregnancy or lactating mothers. Or 0.5% Aqueous Malathion lotion, left on for 24 hrs. Or Gamma Benzen Hexachlorid 1% lotion. Or Benzyl Benzoate 25% lotion. Sulphur 6% cream daily night application for 3 nights is safe for infants, pregnant & lactating mothers. In some clinical situations such as poor compliance, immunocompromised pt or é heavy infestations (Norwegian scabies), systemic Rx é Ivermectin (200 µg/kg) as a single oral do-

se would be appropriate. The combination Rx é various topical gent + systemic agent in AIDS & immunocompromised pt ensure eradication.

YELLOW FEVER

Viral haemorrhagic fever, transmitted to man form monkeys through female mosquito Aedes Egypti, This female Aedes egypti mosquito is a known transmitter of dengue fever & yellow fever & lastly Zeka virus (in South America) ẃ cause microcephaly & incomplete brain development. The Zika virus was first discovered in the 1940s, though most people had never heard of it until this year. That's because for decades, Zika outbreaks were sporadic and tiny & the disease seemed to do little harm. The Yellow fever was diagnosed in 1648. The disease occurs now only in Africa, Central & South America. A Egypti is sometimes referred to as the yellow fever mosquito. The viruses are transferred to the host when man has been bitten by a female mosquito. IP 3 -6 days, Hge result from affection of liver & ⇩ of all clotting factors, progress to DIC & death rate is 3%.

Clinical Picture

- Mild cases: high fever, ⇩ HR, Headache, back pain, chills & muscle aches.
- Second phase: jaundice, hepatosplenomegaly, hepatic necrosis, bleeding from nose, epistaxis & hematemesis (black vomit).

Investigations

- CBC: leucopenia, thrombocytopenia.
- ELISA test, PCR: for detection of antibodies to virus, & for follow up.
- Liver function tests.

Management

Supportive treatment: including:- ❄ IVF & Plasma. ❄ Peritoneal dialysis may be needed. ❄Prophylactic vaccination.

KAWASAKI DISEASE

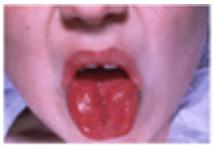
A self-limited, diopathic multisystem disease characterized by vasculitis of small & medium blood vessels, including coronary arteries of unknown etiology ? viral, that predominantly affects children < 5 yrs age. The peak age onset is 9-11 months. It is now the most common cause of children acquired heart disease.

Epidemiology

Incidence in the UK is 8.1/100 000 children < 5 yrs old. In Japan its 220/100.000 children < 5 yrs old. It is over-represented in Asian & African-Americans. Seasonal variation- more cases in winter & spring but it can occurs throughout the year.

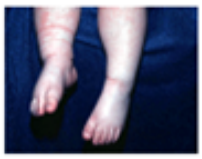
History of Kawasaki Disease

Original case observed by Kawasaki, January 1961, 4 yrs old boy, “diagnosis unknown”. Coronary artery thrombosis first recognized 1965 on autopsy of child previously diagnosed ē /MCOS. First Japanese report of 50 cases, 1967. First English language report from Dr. Kawasaki 1974, simultaneously recognized in Hawaii.

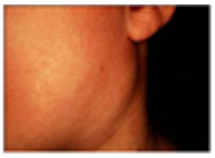


1- Oropharyngeal changes 90% of cases.

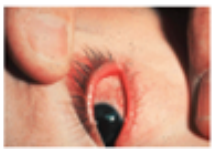
4-Polymorphous rash 95%+ of cases.



2- Changes in peripheral extremities 90%+of cases.



5-Cervical lymphadenopathy ~75% of cases.



3- Bilateral non-purulent conjunctival injection 90%+ of cases.

Diagnostic Criteria

✶Fever for at least 5 days & At least 4 of the following 5 features:-

①Changes in the extremities - oedema, erythema, desquamation.

②Polymorphous exanthema, usually truncal.

③Conjunctival injection.

④Erythema &/or fissuring of lips & oral cavity. ⑤Cervical lymphadenopathy.

✶Diffuse dilation of coronary arteries during the acute phase occurs in in 30-50% of pts. The aneurysms persist in 15%, while 50% regress to no observable lesion.

✶ECG changes; arrhythmias, abnormal Q waves, prolonged PR &/or QT intervals, low voltage, ST-T wave changes.

✶ECHO & CXR for CA`s aneurysm & cardiomegaly.

Management

✓ IVIG 2 gm/kg over 12 hrs.

✓ Aspirin 30-50 mg/kg/day ÷ 4, then 2-5 mg/kg/day for 48 hrs after fever settles.

✓ Corticosteroid: not recommended to use & only can prescribed when the therapeutic effect of IVIG is not satisfied, Prednisolone in a dose of 2 mg/kg, 2-4 wks, then gradual tapering.

EBOLA HEMORRHAGIC FEVER

Epidemiology

The deadly African virus, > 20 previous Ebola & Marburg virus outbreaks. 2014 West Africa Ebola outbreak caused by *Zaire Ebola virus* species (five known Ebola virus species). Early diagnosis is rare, condition mimic malaria, marburg disease, typhoid. IP 2 days -3 wks, transmitted from wild animals to man through monkeys, fruit bats, pigs. Spread as epidemic from man to man through direct contact é blood, body fluids, air born, droplet infection from cough. When WBCs attack the EBOLA virus, the WBCs dissolve liberating chemicals in blood ẃ in return stimulate the release of other chemicals in blood as cytokines, procoagulase, anticoagulants, causing permanent bleeding ẃ is characteristic feature.

Clinical picture

- Day 7-9: headache, fatigue, fever, muscle soreness.
- Day 10: sudden high fever, haematemesis, passive behaviour.
- Day 11: brusing, brain damage, epistaxis, bleeding from nose, mouth, eyes.
- Day 12: loss of consciousness, seizures, massive internal bleeding, & death. Ebola is associated é impairment of LFTs & RFTs, maculopapular rash, echymosis, purpura, hematoma, especially around needle injection site in about 50% of cases, DIC, bleeding represent very poor prognosis associated é focal tissue necrosis of kidney & liver.

Investigations

*__CBC:__ leukopenia followed by neutrophilia, platelets ⇩ (50,000-100,000/ml).

*__Coagulation profile:__ prolonged PT & PTT.

*__LFTs:__ ⇧ SGOT & SGPT.

*__RFTs:__ proteinuria, ⇧ creatinine.

*__Electrolyte__ abnormalities from fluid shifts.

*__RT-PCR:__ used for diagnose of acute infection.

*__Virus isolation:__ requires biosafety level 4 laboratory, can take several days

*__Serologic testing:__ for IgM & IgG antibodies (ELISA) for detection of viral antibodies in specimens, blood, serum, or tissue/

*__Monitoring:__ of the immune response in confirmed Ebola pts.

Management

- No specific Rx, no vaccination available & the mortality rate is 90%.
- IVFs. Some try to use blood transfusion?
- Complete precautions for medical staff, wearing several layers of protective clothes covering the entire body, masks, gloves.
- Proper disposal of excretions.

✶ Proper disposal of victims bodies after death.

✶Disinfectant of homes of dead or infected persons.

✶Stop contact é infected animals & consumption of their meat.

DENGUE FEVER

Epidemiology

Dengue in recent yrs has become major international public health concern. Dengue is found in tropical & subtropical regions around the world, predominantly in urban & semi-urban areas. Was 1st recognized in the 1950s during the dengue epidemics in the Philippines & Thailand, but today DHF affects most of Asian countries & has become a leading cause of hospitalization & death among children. The disease is now endemic in > 100 countries in Africa, Americas, Eastern Mediterranean, Southeast Asia & the Western Pacific. WHO currently estimates there may be 50 million cases of dengue infection worldwide every year.

Vector: Aedes aegypti & Aedes albopictus.

Clinical Picture

⅄Fever: continuous for 3 to 5 days. ⅄Severe headache. ⅄Painful limbs, joints, ba-ck muscles, pain behind eye ball. ⅄Rash appears on the 3rd - 4th day after onset ⅄Nau-sea, vomiting. ⅄Slight gum bleeding & nasal bleeding. ⅄Extreme fatigue & depres-sion may follow recovery. ⅄In very rare cases, the condition may worsen into DHF, leading to Hge, shock or even death. DHF include 4 grades:-

*Grade 1: Fever & nonspecific constitutional symptoms.

*Grade 2: grade 1 manifestations +spontaneous bleeding.

*Grade 3: signs of circulatory failure (rapid/weak pulse, narrow pulse pressure, hypo-tension, cold/clammy skin).

*Grade 4: profound shock (undetectable pulse & BP).

Investigations

⦿***Isolation of the virus.***

⦿ ⇧ ***IgG or IgM antibodies titres.***

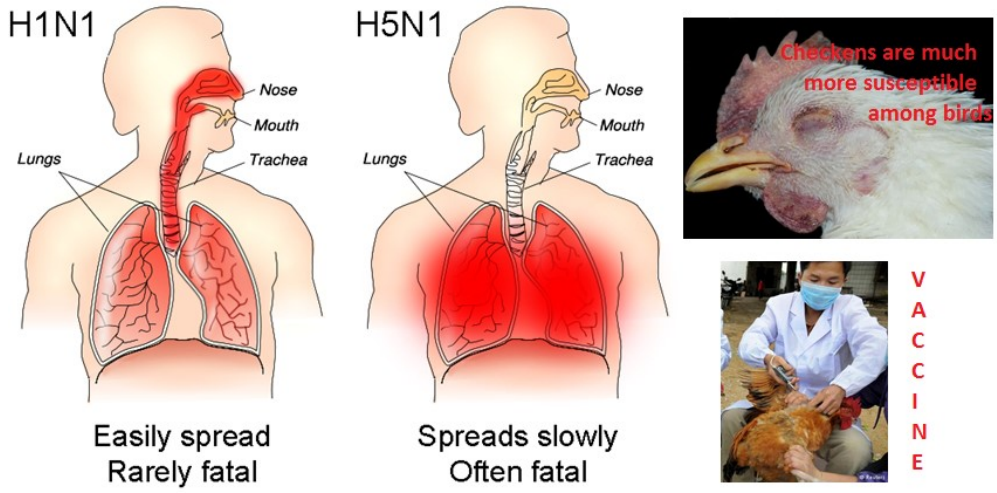
⦿ ***Antigen detection:*** immunohistochemistry, immunofluroscence, ELISA. PCR.

⦿***CBC:*** leucopenia & thrompocytopenia.

Management

At present, there is no specific Rx, pts é classical dengue usually rec- overs in 1 to 2 wks. For serious cases, supportive Rx is provided by hospitals. No aspirin because they worsen the Hge, no pain killers, no antibiotics are of proven value, no steroids. Plenty of water & salt are required. Paracetamol for fever.

AVIAN INFLUENZA



Avian influenza virus of the genus Influenza virus A, Family Orthomy-xoviridae. Classi-fied into many subtypes based on the surface antigens “Hemagglutinin” ẃ include 16 types & Neuraminidase 9 types. The high pathogenicity avian influenza (HPAI), causes severe disease in poultry. The low pathogenicity avian influenza (LPAI)

cause mild disease in poultry, The LPAI can mutate into HPAI.

Reservoirs: waterfowl & shorebirds

Incubation period: difficult to determine- 2-17 days possible

Clinical picture

H5N1 infections in humans cause; high fever, upper respiratory symptoms, mucosal bleeding, gastrointestinal symptoms & pt may deteriorate rapidly. The late symptoms include; organ failure, DIC.

Communicability

Rare cases of person-to-person transmission. No cases of sustained transmission.

Faecal shedding & transplacental transmission are ?

Diagnosis

RT-PCR, Primary test to identify H5N1, Antigen detection, Virus isolation

Management

Antiviral drugs; Amantadine, Rimantadine, Zanamivir, Oseltamivir. Currently circulating H5N1 viruses may be resistant to Amantadine & Rimantadine

Protection of humans

From H5N1 Avian Influenza include; avoidanance of contact é poultry, food safety inspection service, proper food handling & preparation & bird vaccination.

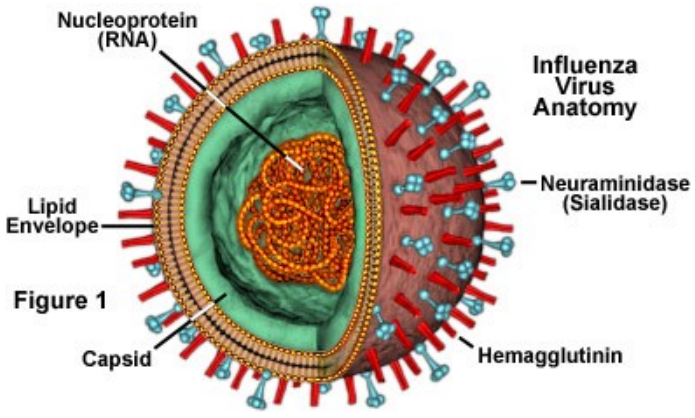


Figure 1

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CHAPTER II

HEMATOLOGIC DISEASES

- Anaemia
- Leukaemia
- Lymphoma
- Coagulation Disorders
- Platelet Disorders

ANAEMIA

Definition

Functional definition: significant reduction in red cell mass & a corresponding ⇩ in the O_2 carrying capacity of the blood.

Laboratory definition: ⇩ Hb, RBCs mass, or Hct to below the normal levels. In women of childbearing age, their blood values are 10% lower than men.

Criteria of anaemia in adults

Factor	Women	Men
RBCx 10^{12}/ L	< 4.0	< 4.5
Hb (gm/dl)	< 12	< 14
HCT (%)	< 37	< 40

The blood values may not accurately reflect alteration in red cell mass. For instan- ce:- Hb or Hct could be falsely elevated as a result of ⇩ plasma volume e.g. Hge, burns, vigorous diuresis, or dehydration due to hemoconcentration. The Hb or Hct may be falsely low as a result of ⇧ plasma volume leading to hemodilution e.g. splenomeg- aly, CHF, cirrhosis, pregnancy.

Clinical approach

Anaemia is a manifestation of an underlying pathological condition. Results from:-

① ⇩ Production.

② ⇧ Destruction/Haemolysis.

③ Blood loss/Bleeding.

④ Multifactorial: a combination of all the above.

Accurate history provides information crucial for diagnosis of underlying cause this in- clude; •Nutritional/Dietary history. •Underlying diseases. •History of Blood loss. •Family history of anaemia. •Exposure to drugs/toxins e.g. Methyldopa. •Geogra- phical location. & •Pregnancy.

Symptoms

Depend on the rapidity of development of anaemia, age of pt & presence of underlying disease. Symptoms are often non-specific including; fatigue, dizziness, dyspnoea, palpitation, syncope, exercise &cold intolerance, angina, tinnitus, vertigo, throbbing headache, anorexia, indigestion, nausea, bowel irregularity (due to shunting of blood from the splanchnic bed), irritability, difficulty in concentration, worsened dementia, impotence or⇩ libido & intermittent claudication.

Physical examination

Comprehensive examination é emphasis on the following findings:- •Skin & mucous membrane: look for pallor, icterus, bleeding sites, leg ulcer. •Spooning of finger nails in iron def anaemia. •Atrophy of tongue, sore tongue (glossitis), angular stomatitis ẃ may be seen in iron def. anaemia. •Splenomegaly, hepatomegaly, evidence of gall stone. •Pelvic & rectal examination to look for possible site of bleeding. •Bone tenderness & lymphadenopathy to R/o hematologic malignancies. •Neurological examination to look for gait, reflexes, vibration & position sense ẃ may help to look for neurologic changes associated é Vit. B_{12} deficiency. •Fundoscopy to look for retinal Hge. •CVS: for modest tachycardia, wide pulse pressure, hyperdynamic precordium, flow murmur & in severe chronic anaemia pt may develop CHF.

Laboratory studies

CBC: Hb, Hct, ESR, Platelet, WBC é differentia.

RBC indices: MCV=Hct/RBC (normally 80-95 fl). MCH=Hgb/RBC (normally 27-32 pg) MCHC = Hgb/Hct (normally 32-36%).

Peripheral blood smear: morphology, size, colour, cells abnormality.

•Hypochromic microcytic anaemia: seen in iron deficiency anaemia, chronic diseases, thalassemia & sideroblastic anaemia.

•Anisopoikilocytes: variation in size & shape may be seen in iron def. anaemia.

•Macrocytic RBCs: macroovalocytes é hypersegmented neutrophils indicate megaloblastic anaemia & Myelodysplasia.

•Schistocytes (fragmented RBC) seen in microangiopathies, DIC, vasculitis & é prosthetic heart valve.

•Retic count: >2-3% or 100,000/mm^3 total, are seen in blood loss & hemolytic processes, although up to 25% of hemolytic anemia will present é normal retic count due to immune destruction of RBC precursors. Retic count is most helpful if extremely low < 0.1%, or >3% .

Causes

Physiological anaemia

Common in the 1^{st} & 2^{nd} month of life. Give supplementary iron, no blood transfusion except if Hb level ⟨7 gm/dl & Hct ⟨20.

Impaired production

Disturbance of proliferation & differentiation of stem cells

•Pure red cell aplasia.

•Aplastic anaemia ẃ affect all kinds of blood cells (Fanconi anaemia is hereditary disorder é variable other abnormalities).

•Anaemia of renal failure as a result of ins-sufficient erythropoietin production

•Anaemia of endocrinal disorders as é hypothyroidism.

•Anaemia secondary to chemotherapy from bone marrow suppression.

Disturbance of proliferation &maturation of erythroblasts:

•Pernicious anaemia, a form of Megaloblastic anaemia due to Vit. B_{12} def.

•Folic acid def. anaemia •Iron def. anaemia.

•Thalassemia.

- Anaemia of renal failure (also causing stem cell dysfunction).
- Anaemia of chronic inflammation.
- Myelophthisic anaemia: is severe type of anaemia resulting from replacement of bone marrow by other materials as malignant tumours or granulomas.

Increased destruction

- Defects of RBC membrane as in case of hereditary spherocytosis or elliptocytosis
- Defects of Hb as in case of thalassemia, sickle cell anaemia, hypersplenism, sequestration of blood as é portal hypertension.
- Defects of RBC as in case of G6PD, Pyruvate kinase deficiency & paroxysmal nocturnal hemoglobinuria.
- Antibody mediated; in case of Rh incompatibility, or transfusion reaction, or autoimmune haemolytic anaemia in ẃ the immune system mistakes RBCs for foreign invaders & begins destroying them (SLE, CLL, Hodgkin lymphoma & Rh^{ed} arthritis).
- Drug induced anaemia.
- Mechanical trauma induced anaemia; Burns, Haemodialysis, Malaria, Microangiopathic haemolytic anaemia; DIC, TTP, Haemolytic uremic sy & Heart surgery.

Blood loss

Acute blood loss:- Trauma, Surgery (immediately after blood loss, Hb is normal, after fluid replacement Hb ⇩ but the cells look normal, then after 2-3 days you see reticulocytosis).

Chronic blood loss:- GIT He. Piles. Parasite infestation. Gynaecological disturbance-es. Repeated blood sampling from premature or critically ill pt.

Fluid overload

As a result of hypervolemia ẃ cause ⇩ in Hb concentration & apparent anaemia as a result of;- Anaemia of pregnancy. Over hydration or CHF.

IRON DEFICIENCY ANAEMIA

IDA occurs when body iron stores become inadequate for the needs of normal RBC production. Characterized by:-

oHypochromia & microcytosis of the circulating RBCs.

oLow plasma iron & ⇩ ferritin concentration.

oTransferrin saturation of 〈15% (normally~35%).

IDA is a manifestation of diseases, not by itself a complete diagnosis.

IDA is the commonest cause of anaemia worldwide.

Iron metabolism

Daily 10-30 mg iron are ingested, 5-10% of the ingested is absorbed to balance precisely the amount of the daily iron loss ẃ is equal to 1 mg, under physiologic condition. The amount absorbed can ⇧ up to five fold if body iron store are depleted or erythropoiesis accelerated. Iron absorption takes place in the duodenum & proximal jejunum, its absorption facilitated by stomach acidity, ascorbic acid & citrates, while is reduced by; phosphates, oxalates, tannates (tea) & pyrates (plant food). Transferrin is the transport protein that carries iron in the plasma & ECF.

Causes

•Malnutrition & poor diet.•⇧Demands: as é prematurity in newborn, rapid growth (adolescency).•Hiatal hernia.•Peptic ulcer.•Aspirin ingestion.•Carcinoma of the stomach or caecum/colon/rectum, hook worm infestation.•Colitis.•Piles.•Diverticulosis.•Intravascular haemolysis & disorders of haemostasis.•Malabsorption of iron: gastrectomy, celiac disease.•Rarely haematuria or hemoglobinuria or pulmonary hemosiderosis.•Pica: craving for unusual foods.

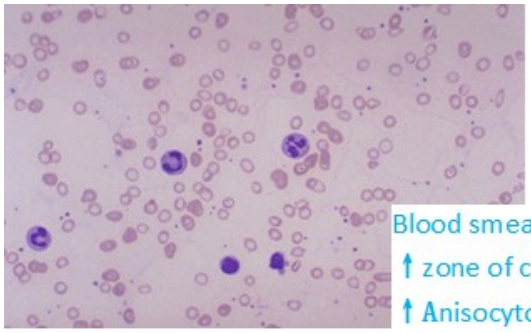
Clinical picture

Is insidious in onset & progressive in course, include; •Pallor of skin & conjunctiva.

•Weakness. •Shortness of breath. •Koilonychia: spoon shaped nails seen é iron or

B_{12} or folic A deficiency. •Angular cheilosis: as bilateral fissuring at corners of mouth, is sign of hypochromic anaemia seen especially in IDA. •Atrophic glossitis: as red large swollen tongue, seen in iron, B_{12}, or folic acid deficiency. •Plummer Vinson/Peterson-Kelly syndrome: characterized by IDA, (koilonychias & dysphagia due to post-cricoid oesophageal web).

Investigations



•***CBC:*** ⇩ Hb, ⇩ Hct.

•***Blood smear:*** microcytic hypochromic; ⇩ MCV , ⇩ MCH, ⇩ reticulocyte count, occa-sional target cells & poikilocyts.

•***Serum iron***: < 60 microgram/Dl.

•***TIBC:*** > 360 micrograms/dL.

•***Serum Ferritin:*** <20 nanograms/mL, can be“falsely” normal in inflammatory state

•***Other investigations:*** for identification of the cause include; ***Stool:*** for occult blo- od & hook worm infestation. ***Urine:*** for haematuria or hemosiderinuria ***CXR:*** to exclude pulmonary hemosiderosis. ***Upper/Lower GI radiologic & Endoscopy:*** to R/O oesophageal varices, hiatal hernia; peptic ulcer, cancer of stomach or caecum/col-on or rectum, colitis, piles & diverticulosis.

Differential Diagnosis

Hypochromic microcytic anaemia é normal or ⇧ body iron store:-

①Impaired iron metabolism: anaemia of chronic diseases.

②Disorder of globin synthesis: thalassemia.

③Disorders of hem synthesis: sideroblastic anaemia.

④ Both impaired iron metabolism & defective globin synthesis- as lead poisoning.

Management

Identify underlying cause, treat it & correct anaemia & replenish stores by oral iron:- Ferrous Sulphate 300 mg (60 mg elemental iron), dropper 15 mg, syrup 50 mg/tsp, dose 6 mg/Kg/day÷2 (therapeutic dose), for 4-6 months. Absorption ⇧ by giving be-tween meals, but side effects are less if given é meals. Common side effects include; GI upset, nausea, dyspepsia, constipation/diarrhoea, black stool, +ve hem occult test. If the side effects are not tolerable, reduced dose or change bra-nd e.g. to Ferrous Gluconate or Ferrous Lactate syrup.

Response to Rx: after 10 days from starting Rx serum iron start to ⇧ 0.1-0.2 gm /dl/day, repeat investigation after one month & continue Rx for 3-6 months.

Follow-up: reticulocytosis will start after 3-4 days & peak is on the 10^{th} day after initi-ation of Rx. An ⇧ in Hb conc. of at least 2 gm/dl after 3 wks of Rx is consider-ed a good response. Rx should be continued for 3-6 months after resolution of anaemia to replenish iron store.

Inadequate response: may imply: •Continuing He. •Non compliance to Rx. •Wrong diagnosis. •Mixed deficiencies as é associated Folate or Vit B_{12} •Presence of another cause for anaemia as malignancy, or inflammation. •Malabsorption. •Use of slow re-lease preparations.

Use of parenteral iron: indicated in case of oral iron intolerance, malabsorption or

inability or unwillingness to take orally. Iron-dextran complex or iron sorbitol citrate can be used IM/IV. Dose in ml = (0.0442 X (desired Hb - observed Hb) X BW (Kg) + (0.26 X B.Wt. (Kg)).

ANAEMIA OF CHRONIC DISEASES

Associated é variety of chronic inflammatory & malignant diseases.

Aetiologies

Chronic inflammatory diseases: include:-

Infections as pulm abscess, TB, osteomyelitis, pneumonia, bacterial endocarditis.

Non-infectious as Rh^{ed} arthritis, SLE , other connective tissue diseases, sarcoidosis, or crohn's disease.

Malignancy; as carcinoma, lymphoma & sarcoma.

Characteristic features

- Normocytic normochromic, or mildly hypochromic anaemia.
- Non progressive (Hb rarely <9.0 gm/dl), severity is related to the underlying dis.
- Associated é ⇩ of both SI & TSIBC + normal or ⇧ of serum ferritin.
- Normal bone marrow storage iron & ⇩ of erythroblast iron.

Pathogenesis

Related to release of cytokines ẃ mediate:-

- ⇩ Release of iron from macrophages to plasma.
- ⇩ RBC life span (~80 days).
- Ineffective erythropoiesis. &
- Inadequate erythropoietin response to anaemia.

Treatment

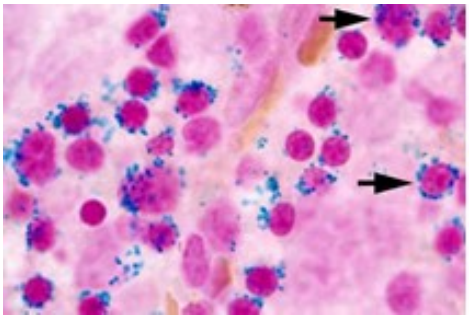
- ***Correction of underlying disease:*** Erythropoietin (give 40-80% success rate).
- ***Correction of reversible contributors*** (e.g. iron, folate).

SIDEROBLASTIC ANAEMIA

Refractory anaemia é hypochromia & ⇧ marrow iron. Caused by defect in hem synthesis. Many pathological ring "sideroblasts" found in bone marrow.

Classification

- ***Hereditary:*** sex linked recessive trait, related to gamma-mino-levulinic acid synthetize gene.
- ***Acquired***
  - Primary: myelodysplasia. or
  - Secondary: malignant diseases of the marrow, or drugs e.g. Cyclosrine, alcohol, Lead, or as a result of haemolytic or megaloblastic anaemia, or malabsorption. The disease characterized by ⇧ of SI, normal TIBC & ⇧ of Ferritin & the ring sideroblasts (é iron laden mitochondria).



B.film showing an erythroblast that contains one or more aggregates of non hem iron appears as Prussian blue-stainable granules, seen in Myelodysplasia, Myeloid leukaemia, Malignancy, Rheumatoid arthritis, and Alcoholics.

Management

Pyridoxine, folic acid: may bring some response.

Repeated transfusion is ultimate choice.

LEAD POISONING

Effect of lead: inhibits both hem & globulin synthesis. Interfere é the breakdown of RNA by inhibiting the enzyme pyrimidine 5 nucleotidase?, accumulation of denatured RNA in RBCs giving rise to basophilic stippling. Lead poisoning cause hypochromic/haemolytic anaemia é bone marrow ring sideroblast & ⇧ of the free erythrocyte protoporphyrin & blood lead level.

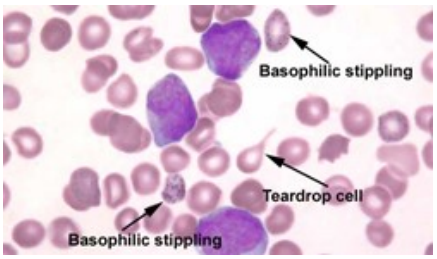
Causes

Lead is everywhere in the environment due to industrialization, environmental pollution through; leaded gasoline & the car exhaust ẃ contaminate air, agricultures, water surfaces, animals & even clothes through dust house, or lead taken by inhalation or ingestion or drinking of contaminated water through lead melting factories or polluted air or through using lead pipes in houses, also through traditional practices seen especially in Bedouin communities, Africa & Islamic countries, as using alkohl as cosmetic for eyes, putting it on the umbilical cord of babies, or as cosmetic for eyes of lactating women as lead was found to be excreted in breast milk or through toys containing lead, or kitchen utensils made from or its component contain lead as é ceramic glazes, or from herbal medicine, pesticides, wall paints or wall paper containing lead through Pica.

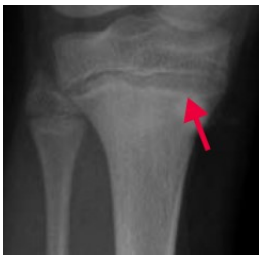
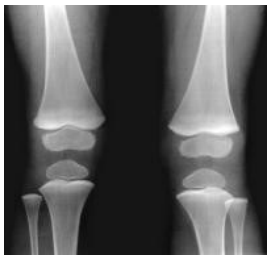
Clinical picture

Hypochromic/haemolytic anaemia, reduction in IQ & attention span, poor school performance, behavioral problems (e.g. Hyperactivity), impaired growth & hearing loss, lead encephalopathy, seizures, coma & even death. Abdominal or joint pain.

Investigations



Blood film



Lead lines on metaphysis of long bones on X ray

- **CBC:** Hypochromic anaemia.
- **Basophilic stippling.**
- **Blood lead level;** normal level is <10µg/dl.

⮝⇧ of lead level >10 µg/dl may cause im-paired cognitive development in children.

⮝⇧ of lead level >45 µg/dl cause gastointestinal symptoms.

➢ ⇧ of lead level >70 µg/dl carries high risk of acute CNS symptoms

➢ ⇧ of lead level >100 µg/dl may be life-threatening.

•**Erythrocyte protoporphyrin:** >200

•**X ray bones:** may show transverse line in tubular growing bones.

Management

Current British paediatric opinion generally accept that a conc. of 37ug/100 ml or above is evidence of excessive exposure. At least 2 tests are required before initiation of Rx including:- ①An indication of the internal accumulation of lead.

②An indication of adverse metabolic effects.

Blood lead 37-49 ug/100 ml & normal-moderate ⇧ of EPP

Adequate dietary intake particularly calcium, iron & zinc must be assured. Follow-up every 3 months for at least one year until blood lead steadily ⇩ & stabilises at or near the normal range.

Blood lead 37-49 ug/100 ml & EPP markedly elevated (〉500 ug/dl)

Do Ca-EDTA mobilization test: by giving a single IM injection of CaEDTA, if 〉1ug of lead for each mg of CaEDTA administered excreted in 24 hrs collection of urine, this provides evidence that there is excessive lead in the body & that the test is +ve. This test sho-uld not used in pt é symptoms of plumbism. In such case of +ve CaEDTA mo-bilization test, give pt D-Penicillamine 20 mg/kg/day for 2 doses, PO, for 2 days.

Blood Lead 50-69ug/100 ml & EPP 〈250 ug/dl & +ve Ca-EDTA mobilization test give Ca-EDTA 50 mg/kg/day, 3-5 day course of deep IM injections. Do urine analysis & se-rum creatinine every 48 hrs during the course of Rx to ensure no side effects. **N.B.:** Ca-EDTA is a non-metabolisable drug, excreted exclusively by kidneys.

Blood Lead 70 ug/100ml or more & EPP 〉250 ug/dl

Give Ca-EDTA 50 mg/kg/day, 3-5 day course of deep IM inj + BAL 500 mg/M^2/day cou-

rse, deeply IM. BAL is contraindicated in pt é acute hepatocellular injury or males é G6PDD. BAL often causes vomiting & pt. receiving it should placed on parenteral fluids or clear liquids orally. In general the chelating agents should not be given for more than a week at a time, but several courses may be given at short intervals over a period of 1-2 months.

Acute lead encephalopathy

In emergencies in ẃ lead tests are not immediately available & where acute lead encephalopathy is a diagnostic possibility, the find-ing of strongly +ve qualitative urinary coproporphyrin (CP-U test), of many stippled erythrocytes in bone marrow & of glycosuria & hypophosphatemia indicate presumptive plumbism. In such condition the following management should be instituted:-

- BAL 500 mg/M^2/day 4 hourly by deep IM for 2-3 days only. After the first dose of BAL use BAL & Ca-EDTA at a separate IM sites. The recommended dose of Ca-EDTA is 1500 mg/M^2/day, 4 hourly for 2 days then 1000 mg/M^2/day, 8 hourly for 3 days.
- Control of seizures - Diazepam to start é then long-term anticonvulsant therapy é Phenobarbital.
- Reducing cerebral oedema: careful calculation of the minimal fluid requirement. Mannitol may be needed to establish adequate urine flow.
- For young children é Pica, they should be followed at least until school age in order to prevent recurrences & to assess the degree of residual brain damage; ẃ may not become evident until several yrs after an acute episode.

SICKLE CELL ANAEMIA

SCA is related to chromosome 1, Gene HBB, Location 11p 15.4. Discovered by, cardiologist Dr. James B. Herik, USA, in 1904. The disease inherited as AR. It is abnormality in the shape of RBCs. Usually started by age 6 months é the replacement of HbF by either HbSS or HbSA. The abnormal HbSS is prone to crystallization when O_2 tension is low, the RBC's change shape into long, thin sickle forms that sludge in capillaries causing further ⇩ in blood flow & ⇩ of O_2 tension. Persons é sickle cell trait (Hb AS) are much less likely to have this happen. Normally at birth, about 80% of HB is HbF & 20% is HbA & by age of 3 months 10% of Hb is HbF & 90% is HbA, this picture will be different in stickler's, where Hb AS, or SS will be detected, in addition to the abnormality of shape of RBCs in blood film.

Incidence: 75% of cases occur in Africa, where carrier rate about 10-40%

Clinical picture

Commonest presentation is vasoocclusive crises affecting both hands & foot (dactylitis) represent as as painful, symmetric swelling of hands & feet. Recurrent painful episodes of abdominal pain from affection of any internal organ may be seen. The crises occur nearly on daily basis, may affect kidney, spleen, may cause priapism, or acute chest pain, may affect brain -stroke-or affect retina "Angioid Streaks" Sickler is very susceptible to infection, especially malaria in the endemic areas, so giving antimalarial drugs in daily basis to such pt. in such places is recommended.

Diagnosis

- ***CBC:*** severe normocytic normochromic anaemia (Hb 5-7 gm/dl).

- ***Hb- Electrophoresis:*** detect presence of Hb SS, or AS.
- ***Blood film:*** reticulocytosis, sickle shaped RBCs, Howell jolly bodies ẃ may indica-te hyposplinism, anisocytosis, poikelocytosis, neutrophilia & thrombocytosis.
- ⇩ ***ESR:*** as the sickle cells fail to form rouleaux.
- ***U/S Abdomen:*** may show evidence of internal organ damage.
- ***Liver/ Renal function tests:*** may show evidences of organ damage.
- ***CT scan Brain:*** may show multiple tinny infarcts.
- ***Fundus examination:*** may show angioid streaks.

Management

•Avoidance ppt factors as fever, dehydration, hypoxia, acidosis. •IVF: overhydrati- on using 150% of daily maintenance requirement.

•Analgesics: Morphia, Codeine. Aspirin to be given for those ›5yrs (to avoid Reye sy). Paracetamol can be given safely, drops 100 mg/dropper, syrup & suppository 125, 250 mg, maximum total daily dose is 1200 mg.

•Prophylactic antibiotics.

•Vit C & Folic acid (daily requirement).

•Vaccination: the routine vaccination + Pneumococcal vaccine.

•Blood transfusion: if Hb ‹5 gm, using whole blood the amount of blood to be given calculated according to the formula (normal Hct -pt Hct) ÷ donner Hct) X BL Vol of pt. (BL.Vol.= BW X 80 ml). •Haematopoietic cell transplant: is curative.

Reye`s syndrome clinical staging system

Stage 1:	vomiting, lab. evidenc of liver dysfunction, lethargic, sleepy
Stage 2:	deeply lethargic, confused, delirious, combative, hyperventilation, & Hyperreflexia
Stage 3:	obtunded or in a light coma, decorticate rigidity
Stage 4:	deepening coma, seizures, decorticate rigidity, fixed pupils
Stage 5:	seizures, deep coma, flaccid paralysis, loss reflexes, resp. arrest & fixed dilated pupils

BETA THALASSEMIA MAJOR

In Greek Thalassi (Sea) & Emia (Blood), the disease described in 1932. Inherited as AR, related to chromosome 11, Gene HBB, location 11P-15.5. It is defective production in B chain of Hb.

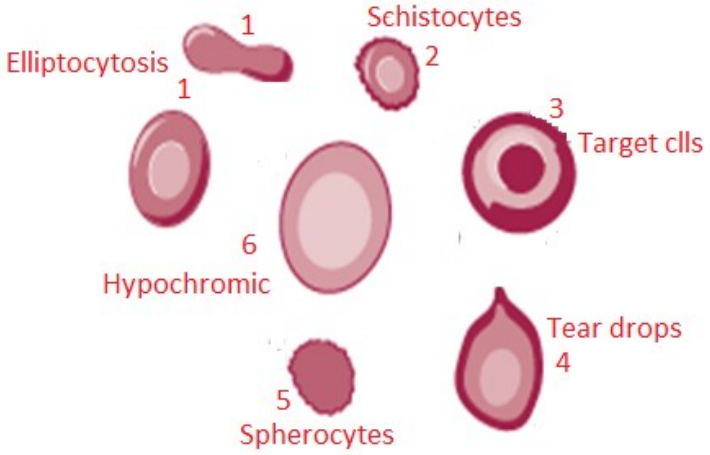
Incidence

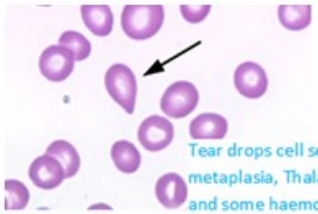
Prevalent in Mediterranean people é highest incidence in Cyprus & Maldives where the carrier rate is 18% of population.

Clinical picture

Symptoms started by age 6 months. Pallor, mongoloid features, prominent check bone (expansion of marrow cavity of bones of skull & face, protrusion upper jaw as a result of extramedullary erythropoiesis). Growth retardation. Deposition of ir-on an-ywhere in the body (sidrosis). Hepatosplenomegaly. Beta thalassemia carries poor prognosis & children die usually before adolescency.

Diagnosis





Poikilocytic RBCs usually present in Thalassemia Major

- ***CBC:*** severe microcytic hypochromic anaemia, target cells, reticulocytosis, leucopenia & thrombocytopenia.
- ***Hb electrophoresis:*** ⇧ HbF 80-90% by age 3 months + ⇩ HbA. (normally by age 3 months HbF < 10% & HbA about 90%).
- ⇧ ***Serum iron*** ***Carrier state:*** Hb A_2 > 3.5%, HbF is zero & HbA is normal.

Management

•***Packed red cells transfusion***, keep Hb ›10 gm/dL, nearly will need 2 units/month, amount of packed cells can calculated according to the formula (normal Hb – Pt. Hb) X BW X 3.5 (or 10-15 ml/Kg). One unit packed cells ⇧ Hb level 1 gm/dl.

•***Iron chelation:*** Desferoxamine amp 500 mg, 20 mg/kg IV over 5 hrs, diluted é glucose 5% 50 ml or IM daily for 5 days/wk .

•***Vit. C & Folic acid: 1*** tab/day.

•***Splenectomy:*** is only indicated for massive splenomegaly interfering é breathing & giving post-splenectomy immunization-Pneumovax (usually by age of 8 yrs).

•***Genetic induction of HbA:*** Erythropoietin amp. 4000 u, twice weekly for one yr.

•***Bone marrow transplantation:*** curative.

•***Premarriage counselling & public awareness.***

BETA THALASSEMIA MINOR

Prevalence as high as 10% in Mediterranean, African & Southeast Asian populatio- ns. Typically present ē mild anaemia & marked microcytosis, the Hb A2 is > 3.5 ass- ociated ē normal Hb A. Can coexist ē other Hb abnormalities, ē ⇧ severity of the anaemia & ⇧ mortality concern, but true beta-thalassemia minor (trait) has no excess mortality concerns.

ALPHA (α) THALASSEMIA

The disease is manifested immediately at birth. There are normally four (α) chains, so there is a great variety in the severity of the disease. At birth there are excess γ chains & later there are excess β chains. These form stable, nonfunctional tetramers that precipitate as the RBCs age leading to ⇩ RBC survival. The disease is usually due to deletions of the α gene & occasionally to a functionally abnormal α gene. Is inherited

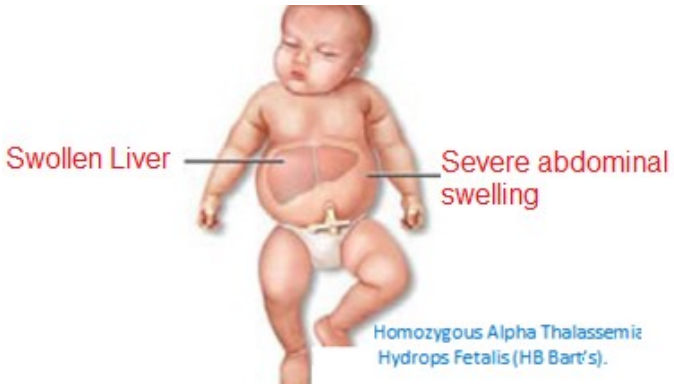
as AR, related to chromosome 16, genes HBA1 & HBA 2, Location 16 p13-3. It is a Defective production of ∝ chain of Hb. The Human cells contain 2 copies of Hb A_1 & 2 copies of Hb A_2, by means that the disease is under control of 4 genes:-

① Absence of the 4 genes (homozygous ∝ thalassemia) result in production of Hb Bart's (hydrops fetalis) ẃ is incompatible é live, it is common in Gulf area. S. Arabia.

②Absence of 3 genes (heterozygous ∝ thalassemia) results in production of HbH.

③Absence of 2 genes (∝ thalassa trait) presented é microcytic hypochromic anaemia.

④Absence of 1 gene (∝ thalassemia silent) is asymptomatic



Diagnosis

•Hbelectrophoresis (Hb Bart's, or HbH). •CBC.

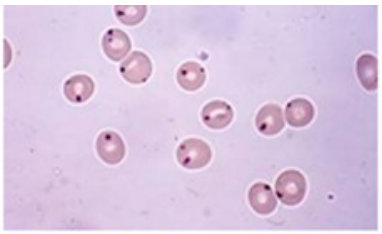
GLUCOSE 6 PHOSPHATE DEHYDROGENASE DEFICIENCY

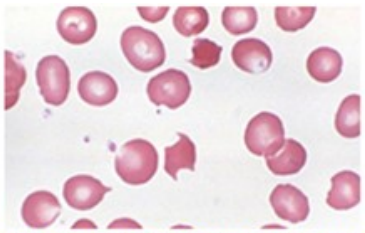
G6PDD is X Linked AR, related to X-chromosome, gene G6PD, Location Xq 28. Common in Negros & Middle East. Occur in 11-13% of African. Estimated 400 milli- on people worldwide carry the gene. Result in breakdown of RBCs, ẃ can be triggered by; infections, severe stress, certain foods, **Fava beans**, oxidant drugs (especially Primaquine, Sulpha, Amiodarone, Antimalarial, Nitrofurantoin, Antihistamini- cs, Antituberculous & Aspirin). G6PDD is significant cause of mild/severe jaundice in newborns (unconjugated hyperbilirubinaemia).

Clinical picture

•Anaemia. •NN jaundice. •Fatigue. •Tachycardia. •Shortness of breath. •Dark ur-ine. •Splenomegaly.

Diagnosis


B. Smear- G6PD, showing Heinz Bodies


B. Smear- G6PD, showing Bite cells

- ***CBC:*** anaemia.
- ***Blood Film:*** macrocytosis due to ⇩ Folic acid ẃ is required for erythropoiesis.
- ⇧ ***Reticulocyte Count:*** gives indication of the bone marrow activity.
- ***Heinz Bodies:*** acute haemolysis from G6PD can produce Heinz bodies ẃ are denatured Hb & bite cells (cells é Heinz bodies that pass through the spleen have part of the membrane removed)
- ⇩ ***Haptoglobin,*** ⇧ ***Bilirubin & Hemoglobinuria (in case of haemolysis).***
- ***Direct Antiglobulin test:*** for other causes of haemolysis. Should be -ve in G6PDD.
- ***Renal Function:*** to ensure no renal failure as a precipitant.
- ***LFTs:*** to R/O other causes of ⇧ bilirubin.
- ***G6PD Enzyme Activity:*** is the definitive test. Performing assays for G6PD during haemolysis & reticulocytosis may affect levels & not reflect baseline values.
- ***U/S Abdomen:*** may reveal splenomegaly & gall-stones.

Differential Diagnosis

Sickle cell disease (painful crisis). Pyruvate kinase deficiency (not precipitated by drugs or infection).

Management

- Infants are more susceptible to NN jaundice, especially if prematures & exchange transfusion may be required.
- Avoidance of ppt factors.
- Supplementation é Folic acid.
- Blood transfusions may be needed.
- Dialysis may be required in acute kidney injury.
- Splenectomy may help.

"G6PDD gradually improve by age".

MEGALOBLASTIC ANAEMIA

It's descriptive morphologic term in ẃ maturation of the nucleus is delayed relative to that of cytoplasm, the delay of nucleus maturation is attributed to defective DNA synthesis. This condition leads to megaloblastic marrow & ineffective erythropoiesis. The immature erythroblasts are destroyed within the bone marrow (intramedulary haemolysis) ẃ results megaloblastic anaemia**.**

Etiology

•Vit B_{12} deficiency or Abnormalities of Vit B_{12} or Folate metabolism.

•Folate deficiency or Transcobalamine deficiency or Anti-Folate drugs.

•Other defects of DNA synthesis (cong. enzyme def.), alcohol, treatment é hyroxyurea

Difference between Cobalamine & Folate

Feature	Cobalamine	Folate
Source	Animal (meat product).	Vegetable. fruits, animal product
Daily require.	2-5 µg	100 mg (50-200 mg)
Body store	3-5 mg	5-20 mg
Time to develop	3-4 years	4-6 months
Cooking	Little effect	Easily destroyed
Plasma transport	Specifically bound by transcobalamin I, II, III	2/3 easily bound to albumin, 1/3 is free
Treatment	Hydroxocobalamine	Folic acid

VIT B12 DEFICIENCY ANAEMIA

Vit B12 (Cobalamin) is a water-soluble vit é a key role in the normal functioning of the brain & nervous system & for the formation of blood. It is 1 of 8 B vitamins (Thiamin (B1). Riboflavin. Niacin. Pantothenic acid. Biotin. Vit B6 (pyridoxine). Folate (called folic acid when included in supplements). & Vit B12 (cyanocobalamin).

Causes

*__Nutritional__: especially in vegetarians.

*__Malabsorption:__ as a result of the following

*Gastric causes: ①Adult (Addisonian) pernicious anaemia. ②Congenital lack or abnormality of intrinsic factor. ③Total/partial gastrectomy.

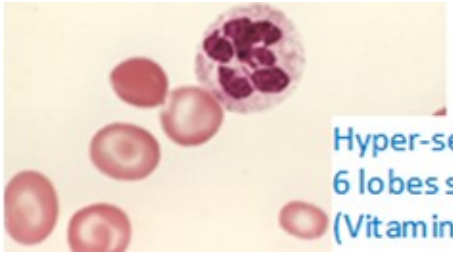
*Intestinal causes: ①Intestinal stagnant loop sy., jejunal diverticulosis, blind loop or stricture. ② Chronic tropical sprue. ③Ileal resection & crohn's disease. ④Congenital selective malabsorption é proteinuria. ⑤Fish tapeworm.

PERNICIOUS ANAEMIA

Failure of secretion of intrinsic factor from parietal cells of gastric mucosa as a result of atrophic gastritis in old age (pernicious anaemia is a disease of elderly 5^{th}- 8^{th} decade), or in younger age secondary to gastrectomy (total or partial), also may be associated é autoimmune diseases & the formation of antibodies to intrinsic factor in diseases like Hashimoto, Graves, Vitiligo, DM, Myasthenia Gravis. Another causes are parasite infestation (Fish Tape Warm-Diphyllobothrium Latum), malabsorption, crohn`s disease of small intestine, ileal resection (as Vit B12 after combination é intrinsic factor will be absorbed from the ileum) or from deficient dietary intake of Vit B12 (as in case of vegetarians), also it may be associated é genetic predisposition. The pt é pernicious anaemia has ⇧ risk of gastric cancer.

Clinical picture: deficiency can result in neuropsychiatric symptoms; spastic ataxia, psychosis, loss of vibratory sense, dementia, the manifestations are frequently not reversible é cobalamin replacement.

Investigations



Megaloblastic anaemia

Hyper-segmented polymorph nuclear cells, 6 lobes suggest Megaloblastic anaemia (Vitamin B 12, Folate deficiency).

•***CBC:*** insufficient conc of Hb, the RBCs are larger than the normalvolume, there is ⇧ of MCV -the normal erythrocyte volume in humans is about 80-100 fl (fl=10^{-15}).

•***Bone marrow:*** will show hyper cellularity & megaloblasts.

•***Peripheral blood film:*** neutrophilic hyper segmentation indicated by: 1 neutrophil é 7 segments, or 2-3 neutrophils é 6 segments, or 5 neutrophils é 5 segments.

•***Schilling test:*** helps to identify the underlying cause of Vit B12 def. Radioactive Cobalamin is given orally + unlabelled Cobalamin IM (to saturate body needs). Then the 24 hrs urine Cobalamin excretion should be determined. Normally >8% should be excreted. If the excretion rate is <8%, it indicate Vit B_{12} malabsorption.

Treatment

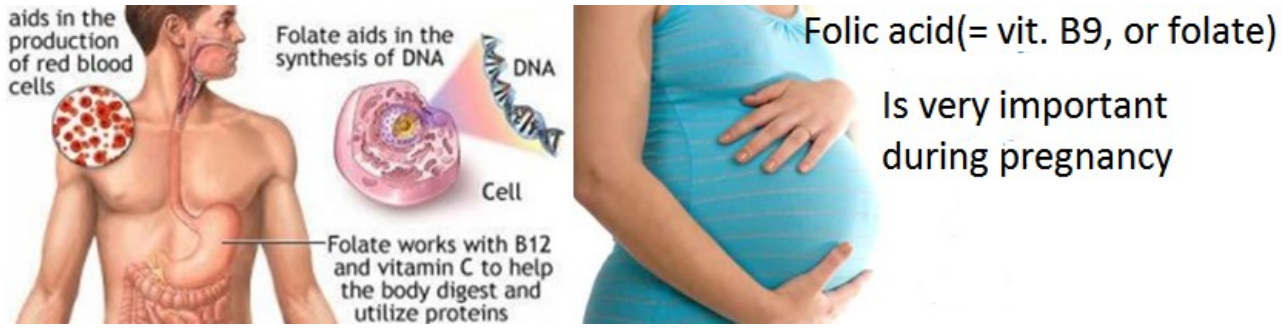
•***Vit B12 deficiency:*** Hydroxy Cobalamin is given parentally in initial dose of 1000 µg IM/day for 1 wk & maintenance 1000 µg IM/3 months. A prophylactic Rx is indicated for pts é total gastrectomy or Ileal resection.

•***Folate deficiency:*** Folic acid 5 mg PO daily. A prophylactic Rx is indicated for pregnant women, premature newborns & pt on dialysis.

•***Additional measures:*** correct underlying cause; antibiotics for bacterial overgrowth, Rx of fish tapeworm if present.

Response to Rx; reticulocytosis begins in 3-4 days & peaks in 7-10 days. If both Folate & Cobalamin are deficient give Cobalamin first.

FOLIC ACID DEFICIENCY ANAEMIA



Folic acid is B vitamin, involved in DNA synthesis, is necessary for RBC production & prevention of neural tube defects in embryo, repeated studies have shown that woman who get 400 mcg daily prior to conception & during early pregnancy in addition to

foods high in folate such as fruits & leafy green vegetables, dried beans, peas & nuts, enriched breads, cereals & other grain products, this will reduce the risk that their baby will be born é severe NTD (as spina bifida, anencephaly, encephalocele) all these defects occur during the first 28 days of pregnancy usually before a woman even know she`s is pregnant. in addition Folic acid supports growth of the placenta & foetus & is necessary for overall good health. Folic A. normally absorbed in duodenum & proximal jejunum. Deficiency often occur é ⇩ oral intake, ⇧ demands, ⇧ utilization or é impaired absorption. Folic A deficiency anaemia found in malabsorption, coeliac disease, regional enteritis, amyloidosis & seen also in alcoholics because the enzyme required for deglutamation of folate inhibited by alcohol. Folic A def anaemia often found in pregnant women & in case of desquamating skin disorders & sicklers. The daily requirements of folic acid is 400 mcg/day, ⇧ in case of haemolytic diseases & exfoliative skin disease.

Clinical picture: similar to Vit. B_{12} def. but nervous system function remain normal.

Diagnosis: •***CBC:*** ⇩ Hb & ⇧ MCV. •***Blood smear:*** hyper segmented polymorphnuclear cells. •***Low folate.*** •⇧ ***Serum homocysteine*** •***Normal methylmalonic acid.***

Management: Folic acid 5 mg tab./day.

HEREDITARY SPHEROCYTOSIS

Spherocytosis is an autohaemolytic anaemia characterized by the production of spherocytes- RBCs, that are sphere-shaped, rather than biconcave disk shaped. Spherocytes are found in hereditary spherocytosis & autoimmune haemolytic anaemia. The hereditary spherocytosis is an AD disorder in ẃ the corpuscular membrane is abnormally less deformable & more permeable to sodium. This is due to abnormality of the protein spectrin in the corpuscular membrane ẃ causes water imbibition & rupture RBCs. It was first described in 1871 & is the most common cause of inherited haemol-

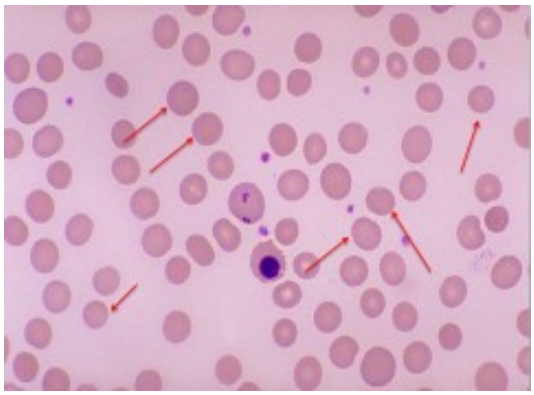
ysis in Europe & North America within the Caucasian population é an incidence of 1 in 5000 births.

Clinical picture

Symptoms usually appear during the first decade of life as:-

- Slight or moderate enlargement of the spleen.
- Pigment biliary stones in long standing cases.
- Chronic leg ulcers may be seen.

Investigations



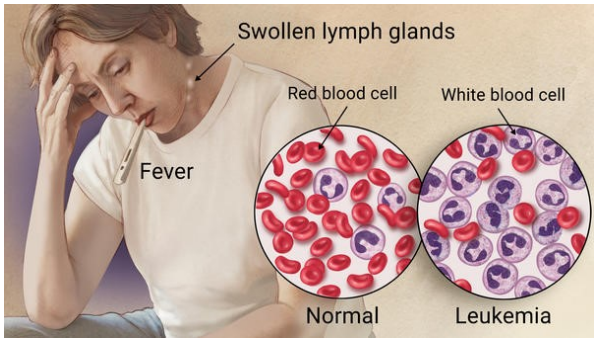
Arrows indicate non biconcave RBCs (Hereditary Spherocytosis)

- **CBC:** spherocytosis, reticulocytosis & anemia of moderate degree.
- **Osmotic fragility:** characteristically ⇧, hemolysis usually begins at sodium chloride concentration of 0.6% or higher.
- **Direct comb's test:** is -ve in case of hereditary spherocytosis, this exclude an auto-immune or hemolytic cause of sphereocytosis.

Treatment

The principal Rx is splenectomy although this should not be performed unless clinically indicated because of anemia. Splenectomy lengthens the life span of RBCs & correct anemia, also will prevent haemochromatosis, but does not affect the character of RBC.

LEUKAEMIA



Leukaemia are neoplasms of hematopoietic cells proliferating in bone marrow initially & then disseminate to peripheral blood, LNs, spleen & liver etc.

Etiology

Unknown in most of the cases, but studies have demonstrated that both genetics & environmental factors are important in the causation of these diseases.

Genetic factor: there is greatly ⇧ incidence of leukaemia in identical twin of pt é leukaemia. Also ē in people é chromosomal abnormalities as Down's sy.

Environmental factors: ionizing radiation, the relation between acute leukaemia & ionizing radiation, has been established in those having occupational radiation exposure or pts receiving radiotherapy & the Japanese survivors of atomic bomb explosions. Radiation exposure ⇧ the risk of CML, AML & ALL but no known relation é CLL. Chemicals like benzene, aromatic hydrocarbons, Rx é alkylating agents & other chemotherapeutic drugs, the exposure to such chemicals is associated é ⇧ risk of developing AML. The RNA based retroviruses, HTLV-I implicated as a causative agent of adult T-Cell leukemia. Another related virus HTLV-II was isolated from pt é atypical hairy cell leukemia while EBV linked to Burkett's Lymphoma.

Epidemiology: globally the incidence of all Leukaemia is 13/100,000/year. Usually affecting men **>** women. Certain leukaemia are more common in a particular age group than the other, for example; ALL is common in children & young adults whereas AML, CLL & hairy cell leukaemia are common in adults.

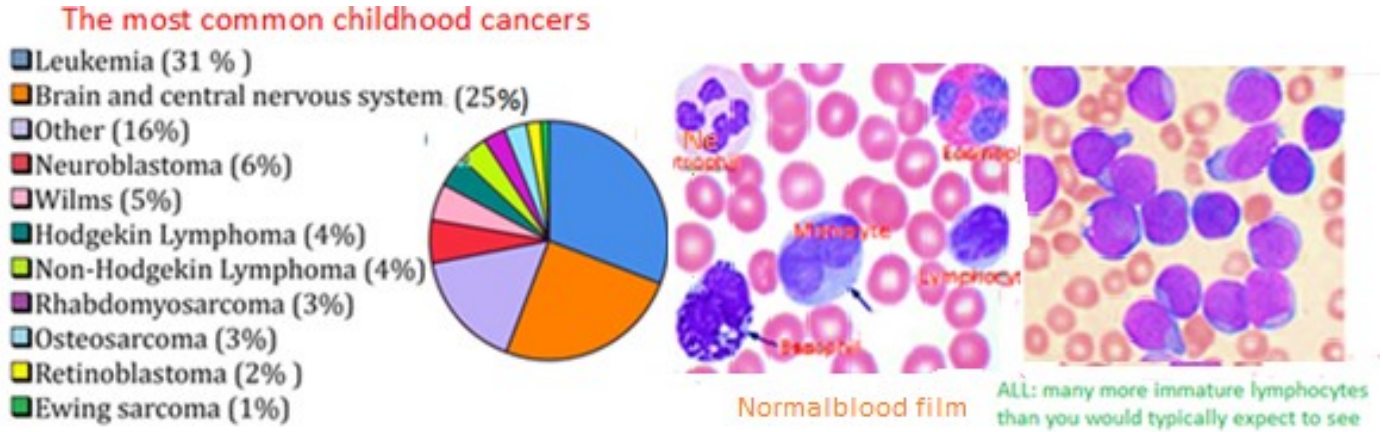
ACUTE LEUKAEMIA

Characterized by presence of immature WBCs in the marrow & peripheral blood. There are 2 types (ALL & AML). Such classification & the further subtyping is done by using the following techniques:-

- Morphology of the cells.
- Immunophenotypic characteristics.
- Cytochemical characteristics.

The differentiation between ALL & AML is critical because each have different; natural history, prognosis & response to Rx. ALL is common in children, 85% of cases of ALL occur in children. The lymphoblasts are found both in bone marrow & blood in case of ALL & are characterized by the following feature microscopically:-

- Smaller size (10-15 mm) than myeloblasts.
- Thin rim of dark blue cytoplasm é no granules.
- Nucleus is round or convoluted, centrally located & has 1-2 nucleoli.



Classification

Morphological classification (FAB):-

① **L 1:** small monomorphic cells (childhood), é small nucleolus.

② **L 2:** large heterogeneous cells (adults) é ≥ 1 prominent nucleoli.

③ **L 3:** uncommon (constituting <5% of ALL), Burkett cell-type, large. vesicular nucleus é basophilic often vacuolated cytoplasm.

Immunological classification

①**Common ALL:** 75% of ALL, derived from precursors of B-cell.

②**T-ALL:** 20% of ALL, common in adolescent males, associated é high WBC count, anterior mediastinal mass &CNS involvement.

③**B-cell ALL:** 5%, extramedullary presentation & metabolic abnormal.

Classification of AML

Myeloblasts predominantly make up AML. These cells are larger than lymphoblasts & are characterised by:-

- Lower nuclear to cytoplasmic ratio.
- Prominent multiple nucleoli.
- Auer rods (stick like structures in cytoplasm) seen in 50% of AML.
- Granules in cytoplasm.

The FAB group divided AML into 8 subtypes based on the followings:-

- Degree of differentiation.
- Maturation of predominant cells towards granulocytes, monocytes, erythrocytes or megakaryocytes.

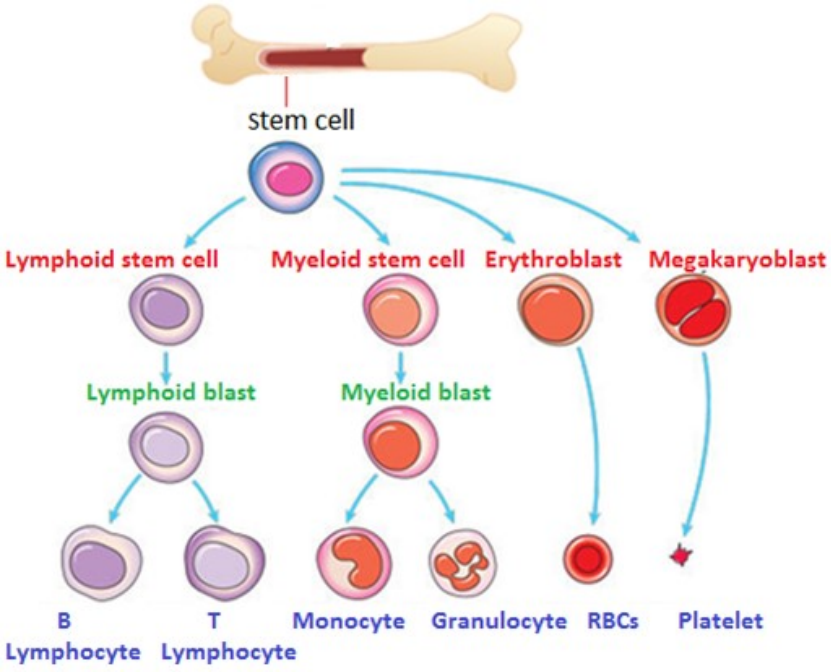
The 8 subgroups nominated as:-

- M0 (undifferentiated): primitive cells éout cytochemical stains (3% of AML).
- M1 (éout maturation): few if any azurophilic granules (20% of AML).
- M2 (é maturation): blasts é promyelocytic granules, Auer rods, present strong avidity to peroxidase & Sudan black (25% of AML).
- M3 (promyelocytic): hypergranular promyelocytes often é Auer rods per cell.
- M4 (myelomonocytic): monocytoid appearing cells in peripheral blood, strong avidity to nonspecific esterase (20% of AML).
- M5 (monocytic): M5**a** -undifferentiated & M5$_{\mathbf{b}}$-differentiated é 80% promyelocytes

& monocytes. Both have avidity to nonspecific esterase (20% of AML).

- M6 (erythroleukemia): erythroblasts >50% of all nucleated cells, avidity to peri odic acid Schiff stain (5% of AML).
- M7 (acute megakaryocytic): megakaryoblasts are >30% of all nucleated cells, activity to PAS (5% of AML).

Pathophysiology



Acute leukaemia characterized by clonal proliferation of immature hematopoietic cells. The most important characteristic is the defect in maturation beyond lymphoblast in ALL or beyond myeloblast or promyelocyte in AML, the proliferation of these immature cells in the bone marrow leads to appearance of blast cells in circulation where they aren't normally seen & occlusion of microcirculation by blast cells (leukostasis). Infiltration & enlargement of the tissues i.e. LNs, liver, spleen, skin, gum, viscera & CNS. Accumulation of blasts in bone marrow has 2 major effects on haematopoiesis causing bone marrow failure through suppression of the normal haematopoiesis & replacement of the normal elements in the bone marrow. The bone marrow changes lead to ⇩ of normal blood cells in circulation causing; infection from ⇩ WBCs, anaemia from ⇩ RBCs & bleeding from ⇩ of platelets.

Clinical Features

The Bone marrow failure, in both ALL & AML share many clinical features. In the majority of cases the initial symptoms are present for <3 months, including:-

Symptoms of anaemia: tiredness, weakness, shortness of breath on exertion.

Recurrent infection from ⇩ count & functionally abnormal neutrophils.

Bruising &/or Bleeding related to ⇩ platelet count.

LNs enlargement occasionally.

Enlargement of the liver & spleen.

Symptoms related to hypoperfusion of lungs & brain due to occlusion of microcirculation of these organs by blast cells.

Physical findings

•Pallor. •Bruises, petechial Hge & purpura. •Signs of infection like fever. •Peripheral/generalized lymphadenopathy in ALL, uncommon in AML. •Hepatosplenomegaly in ALL & small % in AML. •Weight loss. •Testicular involvement in ALL. •Bone pain & sternal tenderness due to expanding malignant cell mass, occur in ›50% of pts é acute leukaemia. •Symptoms related to CNS (meningitis).

Investigation

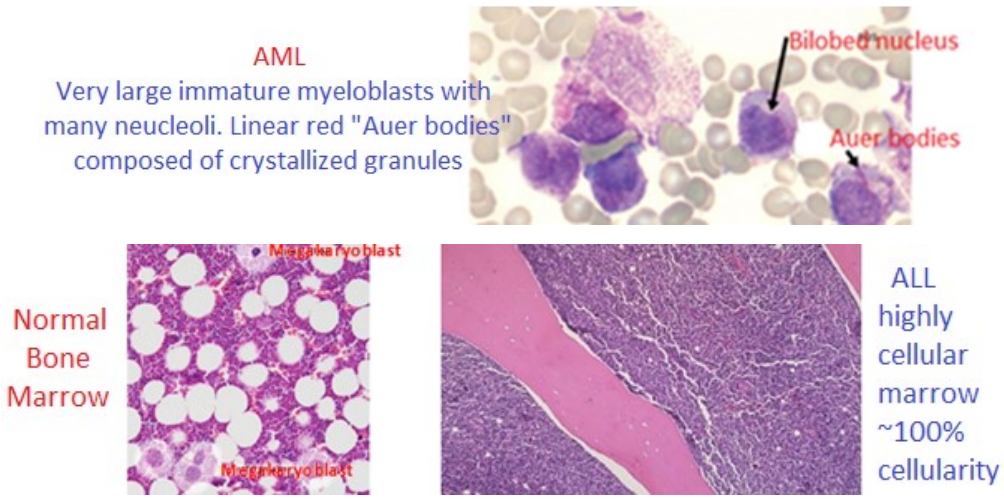
CBC: will show ⇩ Hb, while the WBC count often very high, but occasionally ⇩ or normal, in addition to ⇩ of platelet count.

Blood film

	Lymphoblast (ALL)	Myeloblast (AML)
Cell size	Smaller	Larger
Nucleus shape	Round, central	Irregular, eccentric
Nucleoli	1- 2 in number, not prominent	> 2, prominent
Auer rods	Absent	Present in 50%
Cytoplasm	Dark blue rim	Pale blue, granular

will show characteristic leukemic cells, ẃ are distinct from each other morphologically through the following:- **Type of cells;** lymphoblast/myeloblast. **Cell size;** smaller or larger. **Shape of nucleus;** round/central/irregular or eccentric. **Nucleoli number**; 1 or 2 & not prominent, or >2 & prominent. **Auer rods;** absent/or present. **Cytoplasm;** dark/or blue rim, pale blue/or granular.

Bone marrow biopsy & aspirate: the normal cellularity of bone marrow range from 30-70%, ẃ include many mature red & myeloid cells in variant stages of differentiation, also the presence of megakaryocytes, erythroid islands & granulocytic precursors.



The above right microscopic picture shows high cellularity of bone marrow smear in ALL where 30% or more of all nucleated cells are blast cells. The left picture shows the normal bone marrow cellularity. Notice that the marrow between the pink bone trabeculae seen (in the right slide) is nearly 100% cellular & consists of leukemic cells. Thus, though the marrow is quite cellular, there can be peripheral cytopenia. Biopsy mostly done on the sternum using special needle, smear prepared & stained é wright stain, shows; ⇧ cellularity é abnormal lymphoid or myeloid blast cell population.

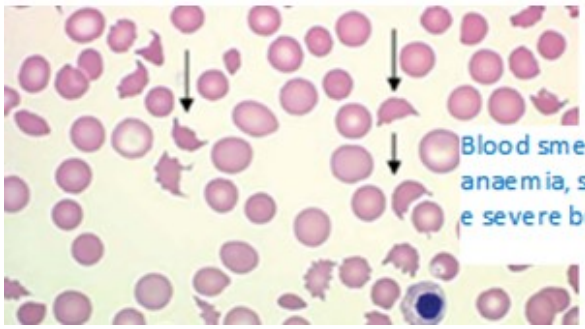
Hypermetabolism: ⇧ Uric acid in 50% of pts due to rapid cellular turnover.

Radiology: mediastinal mass in T-cell ALL. Osteopenia or lytic lesion in 50% of pts.

Blood electrolytes: ⇩ or⇧ K^+, ⇩Mg^+, ⇩Ph^+.

DIC: é consumption of all clotting factors & ⇧ of FDP is most common é promyelocy

tic leukaemia & in small % of monocytic leukaemia & ALL.



Disseminated intravascular coagulopathy

Blood smear of a patient e Microangiopathic haemolytic anaemia, schistocytes (arrows) are also noted in patient e severe burns, DIC, dysfunctional prosthetic valves.

Management

The aim of Rx for ALL is to destroy the leukemic cells &enable the bone marrow to work normally again. Chemotherapy is the main Rx for ALL. Usually a combination of chemotherapy & steroids are given according to a Rx plan.

Chemotherapeutic agents: drugs that have the capacity to kill leukemic cells. Chemotherapy of ALL is divided into 4 phases:-

① ***Remission induction phase:*** this phase aimed at destroying as many leukemic cells as possible. This phase lasts 4-6 wks. Bone marrow test is taken at end of this phase to confirm whether or not the pt. still has leukaemia. The sample is looked for under microscope & when there is no evidence of leukaemia, the pt condition referred to as being in remission. In this phase 2 or 3 drugs used:- Vincristine 1.4 mg/m^2 IV once weekly for 4 wks. Prednisone 1 mg/kg BW, PO daily. -L. Asparaginase or Adriamycin.

②***Intensification phase:*** after complete remission if there is no further Rx given, leukemic cells will expand & lead to relapse, so in this phase intensive chemotherapy is given to ⇩ the total number of residual malignant cells to 10 G cells or less. The drugs used include:- MTX 15 mg/m^2 IM daily for 3-5 days. followed by Cystarabine 100 mg/m^2 IV twice daily for 3-5 days.

③ ***Maintenance phase:*** next phase of Rx aim to maintain remission & prevent spread of leukemic cells into brain & spinal cord. Here lower dose chemotherapy is given over several yrs, it include:- -MTX 15 mg/m^2 once or twice weekly IM -6 MP 1-2.5 mg/

kg daily PO & Cyclophosphamide: 200 mg/m^2 PO weekly.

④ ***CNS & Testicular prophylaxis:*** involves injecting a drug, usually MTX, directly into spinal fluid (intrathecally) during lumbar puncture. Occasionally, radiotherapy to the brain is also necessary. In this phase local chemotherapy or radiation is given to sites of frequent relapse. This phase include; intrathecal MTX 6-12 mg/m^2 as 5 injections (twice weekly). Cranial irradiation 1800-2400 R. If child is < 2 yrs age, he will not be given this treatment. The testicular radiotherapy in some situations may be necessary for boys.

Side effects of treatment for ALL

Many cancer treatments will cause side effects. This is because while treatments are killing cancer cells, they can also damage some normal cells. The side effects of chemotherapy are; hair loss, reduction of the number of blood cells produced by bone marrow result in ⇧ risk of bruising, bleeding & infection. Loss of appetite & BW., feeling nauseated & vomiting. The steroid can also cause side effects as; ⇧ appetite, weight gain, mood changes.

Summary of Rx of ALL & AML

Phase	ALL	AML
Remission	Vincristine +Prednisolone+L-Asparag-inase for 4 wks	Daunorubucin+ Cytosine Arabinoside, for 4 wks
Intensification	Combination of 6-MP & MTX + BMT.	2-3 intensive cycles or high dose of Cytosine Arab-inoside + BMT.
Maintenance	Oral 6 MP & MTX	No benefit
Prophylaxis	Brain radiation combined é intrathecal MTX	No benefit because CNS relapse occurs only é sys-temic relapse

Supportive treatment: applicable for both ALL & AML including:-

①***For pts é severe anaemia &thrombocytopenia:*** especially when platelet ﹤20.000 /ml é the risk of bleeding may be transfused é whole blood & platelet concentrate.

② *Infections are common in acute leukaemia:-*

•Isolation of staff & visitors by the use of face masks.

•Careful hand washing before coming in contact é a pt.

•Advise the pt to eat only cooked foods.

•When infections occur, G -ve sepsis is the commonest presentation, ẃ requires prompt evaluation & use of empirical antibiotic until definitive diagnosis made by blood culture, after ẃ the antibiotic can be modified depending C/S results.

③ *Bone marrow treatment*

Bone Marrow or stem cell transplants for children's cancers, only used for children é ALL that's likely to come back following standard chemotherapy. Can also used for children whose leukaemia reoccurred following standard treatment.

Drug doses & duration	Dose	Route	Regimen
Induction (4weeks)			
Vincristin	1.5 mg/m^2	IV	Weekly for 4 wks
Prednisolone	40 mg/m^2	Oral	Daily for 4 wks
L-Asparaginose	6000 u/m^2	IM	3 x weekly for 3 wks
Daunorubicin	45 mg/m^2	IV	Daily for 2 days
Intensification (1 week)			
Vincristine	1.5 mg/m^2	IV	1 dose
Daunorubicin	45 mg/m^2	IV	Daily for 2 days
Prednisolone	40 mg/m^2	Oral	Daily for 5 days
Etoposide	100 mg/m^2	IV	Daily for 5 days
Cytarabine	100 mg/m^2	IV	2 x daily for 5 days
Thioguanine	80 mg/m^2	Oral	Daily for 5 days
CNS prophylactic (3 wks)			
Cranial irradiation	24 Gy		
Methotrexate	I.T.weekly (3 wks)		
Maintenance (2 years)			
Methotexate	20 mg/m^2	Oral	Weekly
6-Mercaptopurine	75 mg/m^2	Oral	Daily
Prednisolone	40 mg/m^2	Oral	5 days/month
Vincrisitin	1.5 mg/m^2	IV	Monthly

CHRONIC LEUKAEMIA

Acute Vs Chronic Leukemia

	Acute	Chronic
Age	All ages	Adults
Clinical onset	Sudden	Insidious
Leukemic cells	Immature	Mature
Anaemia	Mild to Severe	Mild
Thrombocytopenia	Mild to Severe	Mild
WBCs	Variable	Increased
Organomegally	Mild	Prominent

CHRONIC LYMPHOCYTIC LEUKAEMIA

It is an incurable disease of older people characterized by an uncontrolled proliferation & accumulation of mature B-lymphocytes (in 98% of CLL). In most cases, the cells are monoclonal B lymphocytes that are CD5+. The T-lymphocytes are seen in rare instances. Although, the disease remains asymptomatic in a proportion of cases; symptoms of anaemia, infections & bleeding resulting from bone marrow failure are common in the majority of cases.

Classification

FAB suggested 3 types of CLL:

①Typical CLL: >95% of lymphocytes in blood are small lymphocytes.

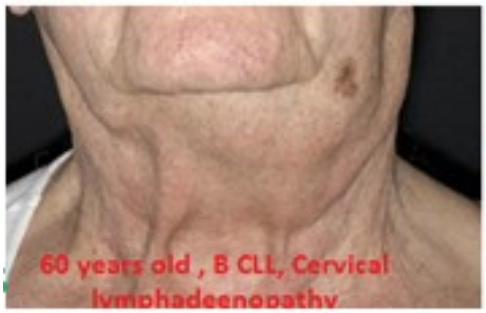
② Prolymphocytic CLL: ≥ 51% lymphocytes are prolymphocytes.

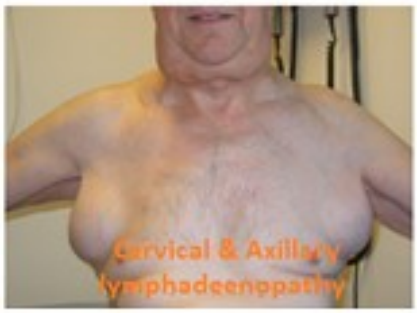
③ Atypical CLL: <10% of lymphocytes are small lymphocytes.

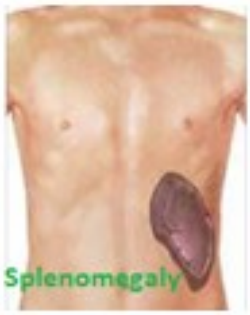
Clinical Features

In 25% of cases, the diagnosis made incidentally in asymptomatic individuals when WBC count is done for other reasons. However, the majority will have signs & symptoms resulting from:- •Tissue infiltration by leukemic cells. •Bone marrow failure é blood cytopenias & immunosuppression. •Recurrent infections resulting from neutropenia. •Reduced immunoglobulin levels. •Symptoms of anaemia. •Painless LNs enlar-

gement. •Spleen &/or liver enlargement (may be huge).







Pt present é severe anemia, or any of the above

Investigation

•***CBC:*** Hb low or normal, WBC >15.000/mm^3 of ẃ 40% are lymphocytes é minimum of 5000/mm^3 mature lymphocytes in the circulation. Platelets are low or normal.

•***Bone marrow:*** 30% of the cellular elements are mature B cells.

•***Serum immunoglobulins:*** are low or normal.

•***Coomb's test:*** +ve in the presence of haemolysis.

Staging of CLL

Clinical course of the disease is variable & prognosis is correlated directly é the stage of the disease. There are 2 different classifications:-

① RAI classification

This is used more often in the United States, it include:-

Stage 0: Lymphocytosis only (in blood & bone marrow).

Stage I: Lymphocytosis é lymphadenopathy.

Stage II: Lymphocytosis é liver &/or spleen enlargement.

Stage III: Lymphocytosis & Hb <11 gm/dl.

Stage IV: Lymphocytosis é thrombocytopenia (platelets <100,000 /L). N.B.: Lymphocytosis is defined as WBC count >15.000/L, of ẃ 40 % are lymphocytes.

② Binet classification

This is used more widely in Europe, it include:-

Stage A: <3 involved lymphoid areas & Hb >10 gm/ dl.

Stage B: **>**3 involved lymphoid areas & platelets **<** 100,000/dl.

Stage C: any number of involved lymphoid areas & Hb **<**10 gm/dl &/or platelets **<** 100,000/dl. (NB: the cervical, axillary, inguinal LN groups (either unilateral or bilat-eral), spleen & liver each of them is counted as one area.

Prognosis

•Stage 0 &1: has good prognosis. If pt has stage 0 éout other poor prognostic fact-ors, the median survival would be **>**10 yrs éout treatment.

•Stage II: has intermediate prognosis, median survival is 5 yrs.

•Stage III & IV: median survival is 3 yrs.

Treatment

The disease may remain stable for several years éout Rx.

Indication for treatment:- ◉Haemolytic anaemia. ◉Cytopenia é recurrent infections, or bleeding. ◉Disfiguring lymphadenopathy. ◉Symptomatic organomegally. ◉Mark-ed systemic symptoms. ◉Advanced disease.

①Chlorambucil: is given as small daily doses or larger (intermittent)/3-6 wks. Or

②Cyclophosphamide is also used in the same way (daily or pulses).

③Steroids can be used in CLL if the pt develops autoimmune haemolytic anaemia, or thrombocytopenia.

Other modalities of treatment ẃ are rarely employed:-

•Combined chemotherapy (similar to lymphoma) is used for advanced disease.

•Splenectomy/splenic irradiation.

•IV immunoglobulin for life threatening infection.

Response to Rx can be assessed by:-

- ⇩ WBC count.
- ⇧ Hb.
- ⇧ Platelet count.
- ⇩ Size of LNs.

CHRONIC MYELOCYTIC LEUKAEMIA

It is disease of older adults & characterized by clonal expansion of he-matopoietic cells of myeloid origin, possessing *Philadelphia chromosome*. It has a progressive clini-cal course é 3 phases starting é chronic phase & evolving to accelerated, then to blast transformation phase.

Epidemiology

The incidence of CML is 1.3/100.000 population/yr é men more affected than women, incidence ⇧ slowly é age until middle forties when it rises rapidly. In the majority of cases the aetiology is unknown. However, CML has been one of the leukaemia ob-served ē ⇧ prevalence following atomic explosion at Hiroshima.

Clinical Features

Clinical features of CML depend on the stages of the disease & range from early asymptomatic phase to severe manifestations of the accelerated phase & blast trans-formation. Therefore, manifestation can be described as:-

Chronic phase

The onset is insidious & some pts diagnosed while asymptomatic during health screening visits. Others may present é fatigue, anaemia, night sweating, fever, wt loss & symptoms related to enlarged spleen as left upper abdominal dull pain & early sa-tiety. A few cases may show symptoms related to granulocytic or platelet dysfunction as recurrent infections & thrombosis manifesting commonly é painful erection of pe-nis (priapism) & cerebral vascular accidents.

Accelerated phase & blast transformation

Progression of CML from chronic to the accelerated phase & then to blast transfor-mation (blast crisis). The pt will present é severe symptoms as unexplained fever, progressive Wt loss, bone & joint pain, bleeding/thrombosis & recurrent infections.

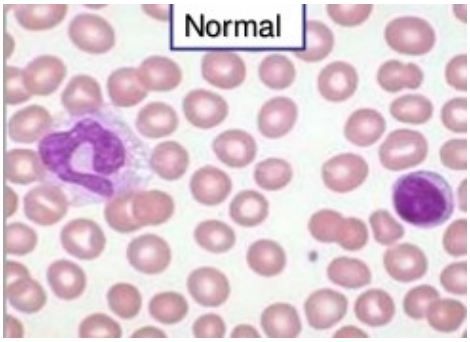
10-15% of pts may present for the first time é either the accelerated phase or blast transformation.

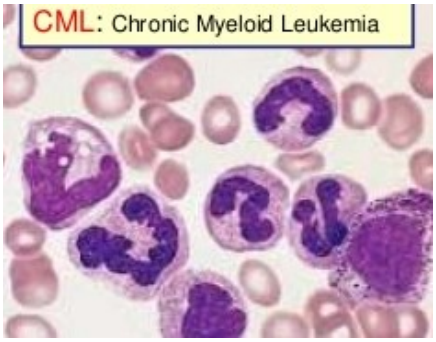
Physical examination

In the early stage ≥ 90% of cases may show; moderately pale conjunctivae, enlarged spleen & mild liver enlargement. Late in the disease pt may develop; LNs enlargement , chloromas (leukemic deposits on the skin) & tender sternum.

Laboratory Findings

- ***CBC:*** ⇧ of the granulocytic series é variable degrees of maturity i.e. mature neutrophils & band forms are seen in the peripheral blood film. More over immature granulocytes such as promyelocytes, myelocytes & metamyelocytes are seen in the peripheral film é increased number. Some myeloblasts are also seen, the % of blasts varies according to the stage of the disease, i.e. in the chronic phase the blasts <5% of granulocytes in blood. In the accelerated phase the blasts are 15-30 % of granulocytes in blood & In Blast crisis the blasts account for > 30% of granulocytes in blood. Other findings include; ⇧ Platelet count, ⇩ RBC count & ⇩Hb.





- ***Bone marrow:*** aspiration shows ⇧ cellularity primarily of the myeloid & megakaryocytic lineage, but the % of marrow blasts remains normal or slightly ⇧.

Treatment

The goal of Rx is complete molecular remission (i.e. achieving prolonged, durable non-neoplastic & non clonal haematopoiesis). Treatment include the following (used singly or in combination):-

(1)Hydroxyurea or Busulphan. (2)α-Interferon (3)Tyrosine Kinase Inhibitors. (4) BMT is the only curative Rx, involves the introduction of donor (allogeneic) or the pt's own treated (autologous) stem cells into the pt in the hope that the procedure will replace the damaged stem cells causing the CML. In this procedure, the pt is first treated é high doses of chemotherapy &/or radiation to destroy all bone marrow cells (cells used for autologous transplant are withdrawn prior to this step). Stem cells from the donor's marrow or peripheral blood are then transfused into the pt, é the intent of repopulating the pt's marrow. In the case of CML, autologous transplantation has generally been unsuccessful because many of the pt's stem cells contain the genetic defect causing the disease.

PLASMA CELL NEOPLASM

B-cell malignancy characterised by abnormal proliferation of plasma cells "able to pr-oduce a monoclonal immunoglobulin"(M protein). Plasma cell is terminally differenti-ated B-Lymphocytes that are capable of producing immunoglobulins. The paraprotein are structurally identical & homologous (the same clone i.e. monoclonal).

Incidence & Epidemiology

1% of all malignancies. 10% of haematological malignancies (2nd most common). 3-4/100,000 population. Incidence higher in African populations. Africa is 2-3 times the risk in whites. 16,000 new cases/yr & 11,000 deaths/yr. The median age for plas-ma cell neoplasm is 65 yrs & 3% are < 40 yrs age. The disease is slightly more frequent in men than in women (1.4 : 1).

Clinical Presentations

✶Anaemia -normocytic normochromic, present in 73% at diagnosis & in 97% at some time during the course of the disease. This anaemia can be related to: bone marrow replacement, Kidney damage, dilution in the case of a large M-protein, B_{12} deficiency

in 14%. ✶Bone pain in 58%. ✶Elevated creatinine in 48%. ✶Fatigue/ generalized weakness in 32%. ✶Hypercalcemia in 28%. ✶Wt loss- in 24 % (1/2 of them lost ≥ 9 kg)

Classification of plasma cell neoplasm

① Monoclonal Gammopathy of undetermined significance

Occurs in 3% of people >70 yrs & in 15% of people >90 yrs. The condition is diagnosed in 67% of pts é an M protein. 10% of pts develop multiple myeloma. The condition characterized by; M protein (stable), normal CBC & immunoglobulins, bone marrow plasmacytosis < 5%, no lytic bone lesions & no signs of disease.

②Macroglobulinemia

Tumour of lymphoplasmacytoid cells producing Monoclonal immunoglobulins most commonly (IgM). Include; Essential Macroglobulinemia & Waldenstrom macroglobulinemia. Presented é wt loss, fatigue, bleeding usually epistaxis, bone marrow infiltration by the lymphoplasmcytic cells “less mature than plasma cells”, anaemia, thrombocytopenia, or leucopenia.

③Multiple Myeloma

MM is related to malignant behaviour of plasma cells & abnormalities produced by M protein. Plasma cell proliferation result in; multiple osteolytic bone lesions, hypercalcaemia, BM suppression result in pancytopenia, monoclonal M protein, ⇩ level of normal immunoglobulins & hyperviscosity.

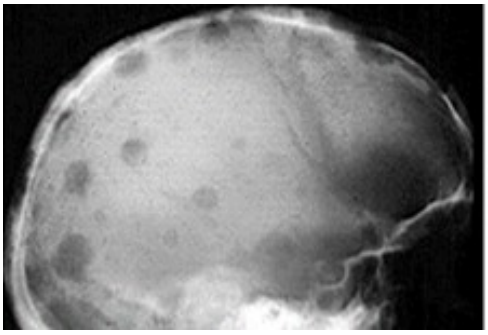
Asymptomatic MM: serum monoclonal protein ≥ 3 gm/dl &/or bone marrow plasma cells ≥ 10% & No end organ damage related to plasma cell dyscrasia.

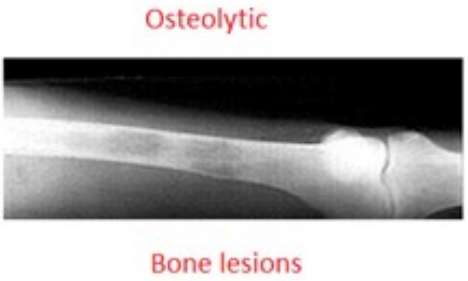
Symptomatic MM: bone pains, pathologic fractures, weakness & fatigue, serious infection, renal failure & bleeding diathesis.

Diagnostic criteria for MM: all of the following 3 criteria must be met:-

- Presence of a serum or urinary monoclonal protein.

- Presence of clonal plasma cells in bone marrow or plasmacytoma >10%.
- Presence of end organ damage felt related to the plasma cell dyscrasia, such as: ⇧ calcium conc, lytic bone lesions, anaemia or renal failure.
- Other investigations include: ESR > 100, thrombocytopenia.





Management:

Pts < 65 yrs: high-dose therapy é autologous BMT. Allogeneic BMT (conventional & „mini"). ***Pts > 65 yrs:*** conventional chemotherapy. Non-myeloablative therapy é allogeneic transplantation („mini")

Conventional chemotherapy

- Melphlan + Prednisone.
- Vincristine, Melphalan, Cyclophosphamide, BCNU, Prednisone.
- Vincristine, Adriamycin, Dexamethasone (VAD).

The response rate 50-60% of pts. Long term survival 5-10% of pts.

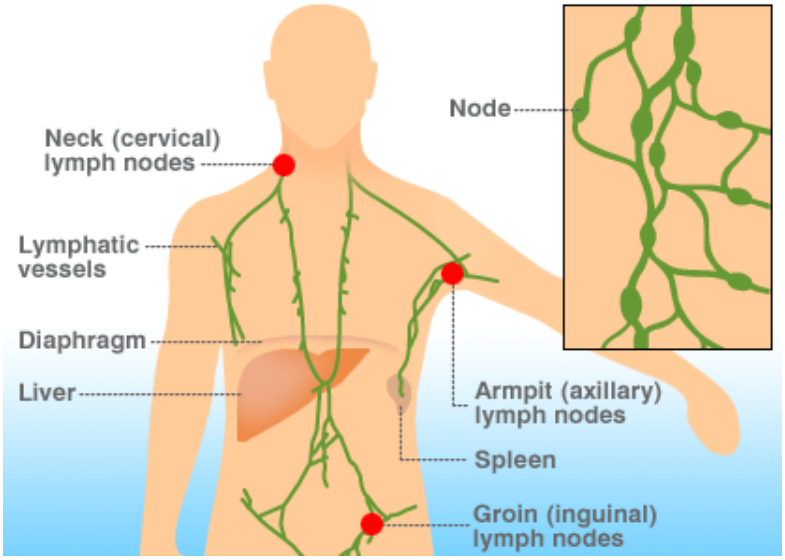
Autologous transplantation: for pts <65-70 yrs. Rx related mortality 10-20%. Response rate 80%.

Conventional allogeneic transplantation: for pts <45-50 yrs é HLA- identical donor. Treatment related mortality 40-50%. Long term survival 30%.

New method: non-myeloablative Rx & Allogeneic transplantation. Thalidomide.

Supportive treatment: Biphosphonates. Calcitonin. Recombinant Erythropoietin. Immunoglobulins. Plasma exchange & Radiation therapy.

LYMPHOMAS



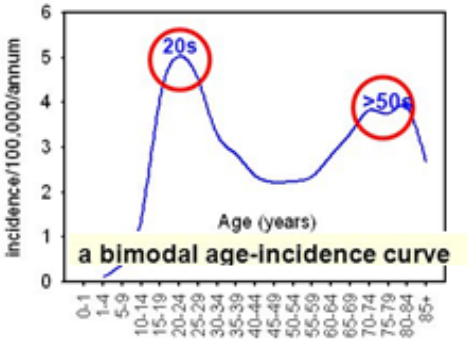
Lymphoma are cancers originating from the lymphatic cells of the immune system, typically seen as solid tumours. The lymphatic system is part of the body`s immune system & helps fight infections & other diseases. The lymph system is made up of thin tubes that branch into all parts of the body. Lymph vessels carry lymph, a colourless, watery fluid that contains lymphocytes. Along the network of vessels are groups of small, bean-shaped organs called LNs, found in clusters in the under arm, pelvis, neck & abdomen. Because lymphatic tissue is found in many parts of the body, lymphoma can start almost anywhere. In 1832, Thomas Hodgkin, a British pathologist published the 1st description of lymphoma, a specific form ẃ is named after him: 'Hodgkin lymphoma'. Since then many other form of lymphoma have been described, all are grouped under a single label "non Hodgkin lymphoma".

HODGKIN'S DISEASE

Epidemiology

less frequent than non- Hodgkin lymphoma

A bimodal peaks at the 3rd and from the 6th decades.



Hodgkin`s lymphomas has bimodal age incidence (20-30 yrs & > 50 yrs). The Male to Female ratio is 2:1.

Clinical manifestations

Most pts present é non-tender asymmetrical, firm, discrete & rubbery enlargement of superficial LNs: cervical (in 60-70%), axillary(in 10-15%), inguinal (in 6-12%). Has waxing & waning feature. Mild splenomegaly (50%), mediastinal lymphadenopathy (6-11%) é/éout pleural effusion. Superior vena caval syndrome may present. Constitutional symptoms like fever, weight loss & sweating are common in widespread disease. Fever found in 30% of pts described as pelebsteins fever characterized by wks. of febrile period, interspersed by several wks of afebrile period. Purities seen in 25% of pts. Also alcohol induced pain in the affected area.

Haematological findings

•CBC: normocytic normochromic anaemia. 30% of pts may have leucocytosis, wh-ile eosinophilia, lymphopenia found in advanced cases. Platelets count is variable (normal or ⇧ in the early stage & ⇩ later).

•⇧ ESR. •Bone marrow: involvement occur late in the course.

Immunologic findings

Progressive loss of immunologically competent T-lymphocytes leads to impaired cell mediated immunity ẃ ⇧ susceptibility to viral infection (herpes zoster, CMV)& fungal infections (cryptococcus, candida), moreover pt will have ⇧ risk of reactivation of latent TB infection.

Biochemical findings: ⇧ Ca, ⇩ Ph, ⇧ Liver transaminases, Hyperuricemia & ⇧ SB.

Diagnosis

LN biopsy: the distinctive multinucleated, polyploidy cell é characteristic Owel-eye appearing. Reed-Sternberg cells on an appropriate inflammatory background.

Classification

Depending on worsening order of prognosis (4 groups) as follows:- (1) Lymphocytic predominant. (2) Nodular sclerosis. (3) Mixed cellularity. (4) Lymphocytic depleted.

Stages

- ***Stage I:*** only affecting one LN area.
- ***Stage II***: 2 or more LNs on the same side of diaphragm.
- ***Stage III:*** involving LNs above & below diaphragm; splenic involvement included
- ***Stage IV:*** extranodal site involvement (Liver, bone marrow). Depending on presence or absence of constitutional symptoms the stage is further classified as A (no constitutional symptoms) & B (é constitutional symptoms)

Treatment

Radiotherapy: mainstay for stage I & II diseases. In stage III & IV radiotherapy used é chemotherapy.

Chemotherapy: for stage III & IV diseases, or pt in stage I & II é bulky disease e.g. mediastinal widening by $1/3^{rd}$ or LN **>**10 cm in diameter. include:-

MOPP: Mustine, Vincristine, Procarbatine, Prednisolone. or

ABVD: Adriamycin, Bleomycin, Vinblastine, Decarbazine. or

MOPP-ABVD hybrid given for 6 cycles (or 4 cycles after full remission).

Relapse cases

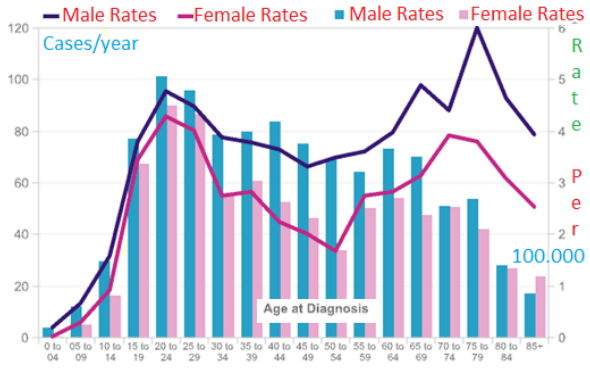
Are better treated é autologous BMT é total body irradiation & high dose CT.

Prognosis: The 5 years survival:-

- Stages I, II is 85%
- Stage III_A is 70%
- Stage III_B & Stage IV are 50%.

NON HODGKIN'S LYMPHOMA

Incidence & Predisposing factors



In HIV infected pts there is an ⇧ incidence of lymphoma often at unusual sites like CNS; usually of B-cell origin é high or intermediate grading. Immunosuppression ⇧the risk of developing NHL. Others include celiac disease, dermatitis herpetiformis & autoimmune diseases predispose to T-cell lymphomas, helicobacter infection is associated é ⇧ frequency of maltomas.

Clinical features

Constitutional symptoms are encountered less commonly when compared é HD & if present indicates dissemination. Oropharyngeal involvement in 5-10% cases: have involvement of Waldeyer's ring including tonsils, adenoids & paratonsilar areas. Anemia ,neutropenia, thrombocytopenia may follow bone marrow involvement or may be autoimmune in origin. Abdominal organs & LNs involvement is more common in NHL than HD. Other organs as; skin, brain, testis, GIT, or thyroid involvement is frequent.

Laboratory findings

Haematological findings: normocytic normochromic anaemia (autoimmune haemolysis). cytopenias, lymphoma cells may be seen in the peripheral blood.

Bone marrow biopsy may show focal or diffuse involvement.

Blood chemistry: ⇧ Uric acid, ⇧ Liver enzymes, ⇧ LDH (in rapidly proliferating & extensive disease hence has prognostic implication).

Immunologic markers: used for classification.

Chromosomal findings: various forms of translocations identified.

Prognostic features

Depends upon many factors:-

•Histology.

•Stage of the disease.

•Age > 60 yrs (unfavourable).

•Poor performance status.

•Multiple sites of extra-nodal involvement.

•⇧ LDH. •Bulky disease (mass >5 cm in diameter).

•Prior history of low grade disease.

•AIDS or other causes of immunosuppression related.

Treatment

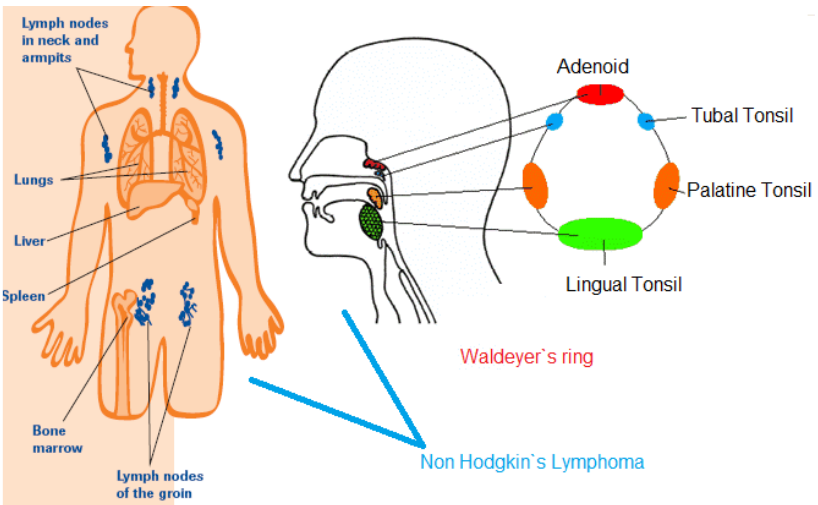
Low grade malignancy

•No need of Rx if pt is asymptomatic. Local radiotherapy is indicated for stage I, II.

•Combination chemotherapy for advanced cases (Chlorambucil or Cyclophosphamide or repeated courses of Fludarabine). •BMT & α INF.

***Intermediate grade* malignancy**

*Localized disease: initial therapy (Cyclophosphamide, Adriamycin, Vincristine & Prednisolone) followed by irradiation. *Disseminated disease, combined chemotherapy.



DISORDERS OF HAEMOSTASIS

Abnormal bleeding may be due to:-

*1ry haemostatic disorders: including:-

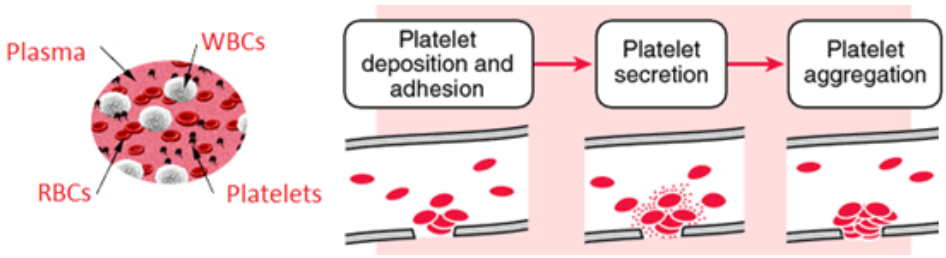
- Thrombocytopenia.
- Functional platelet defect or
- Vascular disorders.

*2ry haemostatic disorder: resulting from problem in the coagulation pathway.

DISORDERS OF PLATELET & VESSEL WALL

Pt é platelet or vessel wall disorder usually bleed into superficial sites as the skin, mm, genitourinary or GIT. Bleeding begins immediately after trauma. Either responds to simple measures as pressure &packing or requires systemic therapy é Glucocorticoids, Desmopressin, Plasma Fractions & Platelet concentrate.

PLATELET DISORDERS



Platelets are produced from fragmentation of megakaryocytes in the bone marrow results in platelets of ẃ 1/3 sequesters in the spleen & 2/3 circulates in blood for 7-10 days. Platelet count in normal adult is 150.000-450.000/ml. When platelet count ⇩ there will be reactive marrow megakaryocytosis. Platelet count varies during menstruation i.e.⇧ during ovulation & ⇩ during the onset of menses. It is also influenced by nutritional state: ⇩ in sever Fe^{++}, or Folic acid, or Vit B_{12} deficiencies. Platelets are acute phase reactants hence may be ⇧ in pt. é systemic inflammation, tumour, bleeding & mild iron deficiency. Hence the term secondary or reactive thrombocytosis is used. It is mediated by cytokines IL-3, 6 & 11.

THROMBOCYTOPENIA

Deficiency of platelets in the blood. This causes bleeding into the tissues, bruising & slow blood clotting after injury. May follow any of the following mechanisms:-

•⇩ Bone marrow production. •⇧ Splenic sequestration. •Accelerated destruction.

Causes

①**Impaired production of platelets:** commonly associated é stem cell injury. Affect multiple hematopoietic cell lines, hence there is varying degree of accompanying anaemia & leucopoenia. Bone marrow aspirate/biopsy show ⇩ number of megakaryocytes. Commonly caused by marrow aplasia or fibrosis or infiltration é malignant cells, or due to cytotoxic drug use, or rarely may be congenital.

②**Splenic sequestration:** usually follows conditions causing splenomegaly such as; portal hypertension, or splenic infiltration é tumour cells as in myeloproliferative or lymphoproliferative disorders.

③***Accelerated destruction:*** immunologic**:** platelets coated é antibody, immune complexes, or compliments, may follow viral or bacterial infections or drugs. Non immunologic; associated é abnormal vessels, fibrin thrombi, heart valve prosthesis, vasculitis, haemolytic uremic syndrome, TTP, or DIC.

④**Drug induced thrombocytopenia:** chemotherapeutic agents-especially Carboplatin, Alkylating agents, Anthracyclines & Antimetabolites, Antibiotics as Sulphonamides, Penicillins, Cephalosporines, Heparins- highest incidence is é the unfractionated products, Thiazide diuretics. Most of these drugs induce thrombocytopenia by eliciting an immune response in ẃ platelets are innocent bystanders. The best proof of drug induced thrombocytopenia is prompt ⇧ in platelet count when the suspected drug is discontinued. Most pts recover within 7-10 days of discontinuation of the causative drug, some pts é platelet count of 10.000-20.000/ml may have severe Hge

& hence need temporary support é glucocorticoid, plasmaphoresis, or platelet transfusion & pt should be instructed to avoid the offending drug.

⑤**Idiopathic/Immunologic Thrombocytopenic Purpura**

Acute ITP: usually follows viral URTI & is common in children aged 2-6 yrs (90% of paediatric cases), 60% of them recovers in 4-6 wks & >90% recover within 3-6 mo.

Chronic ITP: common in adults &run a more indolent course. Women age 20-40 yr are afflicted most commonly & outnumber men by a ratio of 3:1. It presents acutely or more often é prior history of easy bruising & menorrhagia. There is immune mediated platelet destruction as well as functional platelet dysfunction.

ITP vs. TTP vs. DIC

Parameter	ITP	TTP	DIC
Pathogenesis	Antiplatelet AB.	Endothelial defect	Thrombin excess
Clinical condition	Not sick	Sick	Sick
Red cells	N	Schistocytes	Schistocytes +/-
PT(INR)	N	N/Slightly ⇧	⇧
PTT	N	N/Slightly ⇧	⇧
Fibrinogen	N	N	⇩
Fibrin Monomers	N	Slight ⇧	⇧
Fibrindegradation	N	Slight ⇧	⇧
D-dimers	N	Slight ⇧	⇧
Therapy	Steroids, IVIG, Splenectomy	Plasma Exchange. Vincristine	Plasma/Platelet ATIII (?)

Investigation

- **CBC & Platelet count.**
- **PT, PTT, Fibrinogen, FDP.**
- **D-dimers:** is a fibrin degradation product, a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis, it is so named because it contains 2 cross linked **D** fragments of the fibrin protein.
- **Serology for HIV** commonly cause immunologic thrombocytopenia in young pt.

•**Screening for SLE.** •**BM aspirate** to look for reactive ⇧ of megakaryocyte.

•**U/S abdomen** to look for splenomegaly.

Treatment: depends upon age, severity & anticipated natural history. Specific treatment may not be necessary unless platelet count is **<** 20.000/ml.

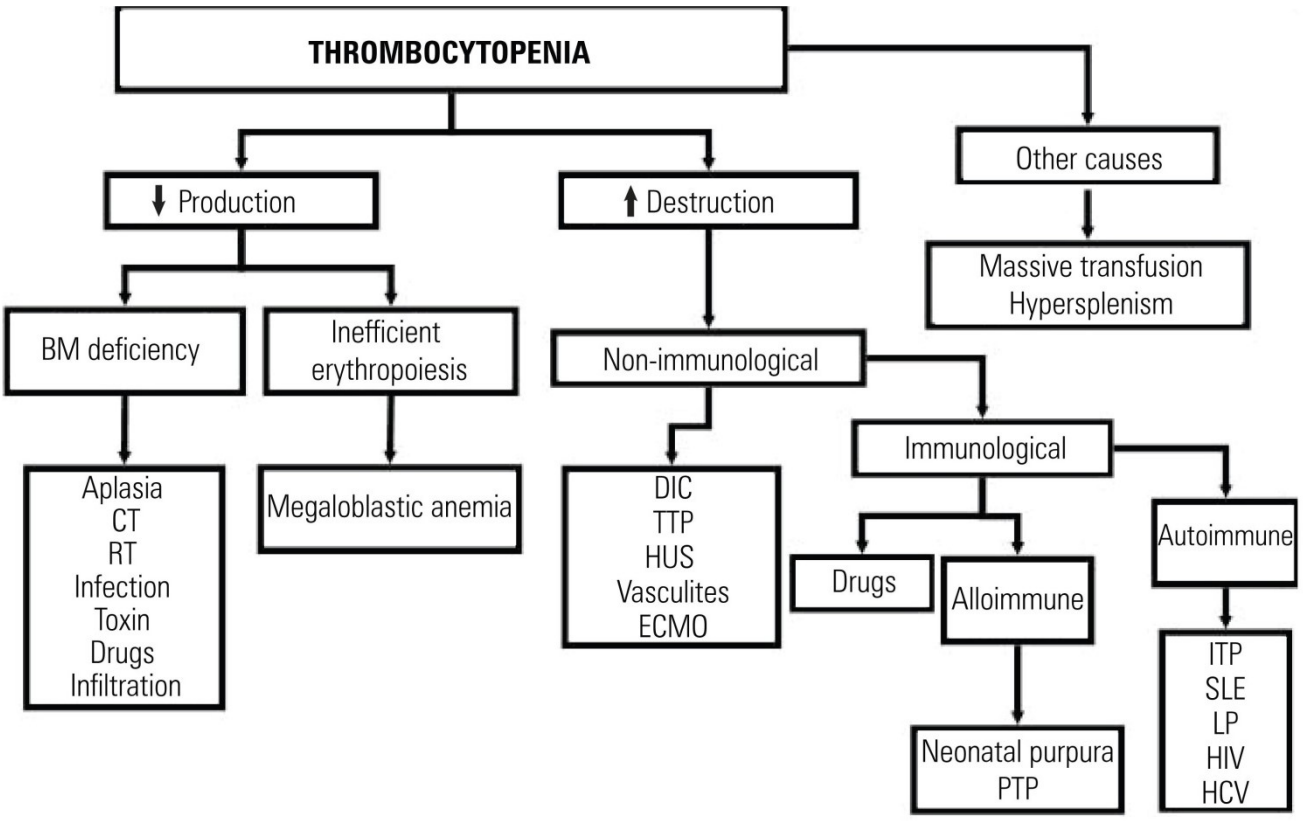
Steroids: used for symptomatic pt é chronic ITP, in a dose of 60 mg/day for 4-6 wks, then to be tapered slowly over another few wks, those pts who fail to maintain a normal platelet count after a course of steroid are eligible to splenectomy.

IV Immunoglobulins: reserved for those é severe thrombocytopenia & clinical bleeding who are refractory to other measures.

Platelet transfusion: for those é eminent CNS bleeding as a temporary measure.

Emergency splenectomy: done for those who are desperately ill & refractory to medical measures, failure to respond to splenectomy may signify presence of acce ssory spleen ẃ may be evidenced by peripheral blood smear examination for Howell jelly body ẃ appears in the circulation.

Antiretroviral Rx: for those dually infected é HIV.



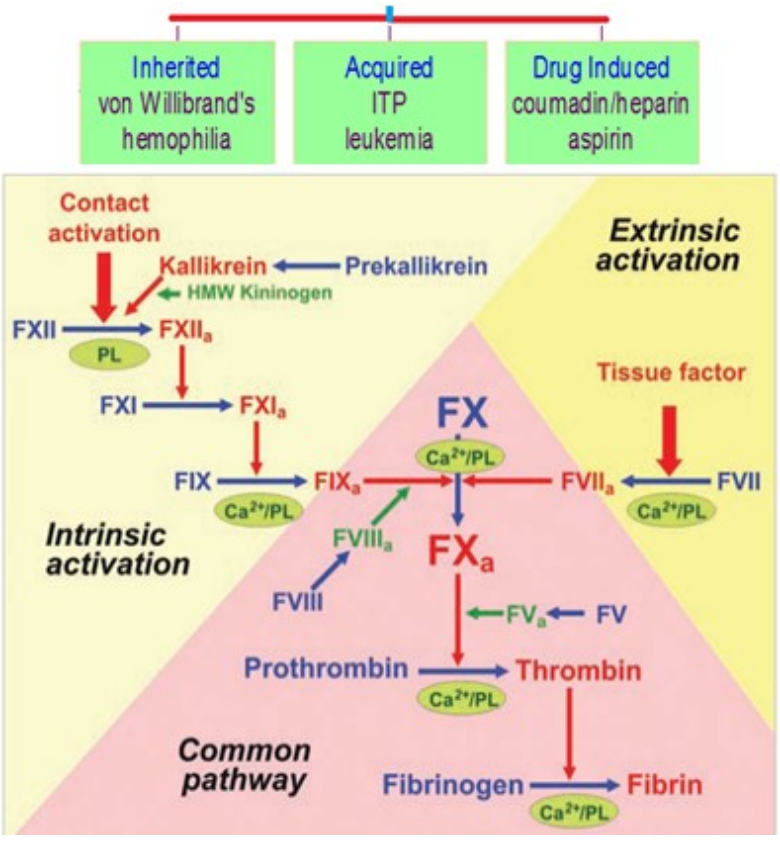
VASCULAR BLEEDING DISORDERS

✳Hereditary Haemorrhagic telangiectasia: (is AD disorder).

✳Acquired vascular defects: include the following:-

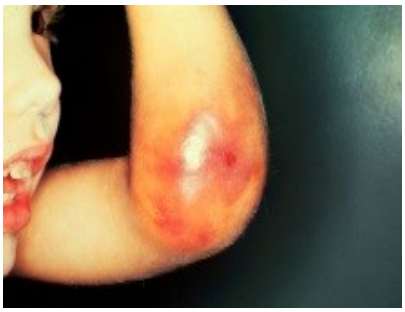
- **Simple easy bruising:** is benign disorder seen in women of child bearing age.
- **Senile purpura:** due to atrophy of the connective tissues of cutaneous vessels.
- **Purpura associated é infection:** result from vascular damage by infecting organism or immune complex deposit e.g. Meningococcemia, Marburg, Ebola, Lassa, Dengue Haemorrhagic Fever, Typhoid Fever, Yellow Fever, Malaria.
- **Leukaemias.**
- **Henoch-Schonlein's sy.:** is immune complex (type III) hypersensitivity, characterized by purpuric rash on the buttock &extensor surfaces of L.L., abdominal/joint pain, haematuria, usually self-limiting; however, sometimes may cause RF.

COAGULATION DISORDERS



It is important to understand the coagulation disorders to remember the intrinsic cascade, extrinsic cascade & the common pathway ẃ are illustrated above.

HAEMOPHILIA A



The commonest hereditary disorder, related to X Chromosome, Gene F 8, Location X q 28. Haemophilia A is sex linked AR but 33% may not have family history & results from spontaneous mutations. Its incidence is 1/5000 male births. Haemophilia A result from absence or low level of plasma factor VIII & is classified into:

- Mild: when FVIII 5-20% of normal.
- Moderate: FVIII 1-5% of normal.
- Severe: FVIII <1% of normal.

Clinical picture

70% of cases not bleed from circumcision during the 1st yr of life, later on, the child is easily traumatized, bruising especially in knees, elbows when he start to crawl (at 6-9 months age). Repeated Hemarthrosis is common & bleeding may be internal if FVIII < 5%, may cause damage to any internal organ & may be life threatening. In the NN period, baby may develop IC Hge as FVIII does not cross placenta.

Activity	Clinical manifestation
< 1%	Sever disease. Frequent spontaneous bleeding, episode from early life. Joint deformity & crippling.
1-5%	Moderate disease. Post traumatic bleeding. Occasional spontaneous episodes of bleeding.
5-20%	Mild disease. Post-traumatic bleeding.

Investigations

- **Prolonged APTT** ẃ measure the intrinsic pathway of coagulation ẃ include the common pathway (F I,II, V, X) in addition to F VIII, IX, XI, XII. The APTT is ⇧ to double the normal value.
- **Low level of factor VIII** is diagnostic, mother of such child usually have low F VIII (30-70%). In case of VWD the BT is prolonged (due to associated ⇩ of platelets).
- **All other coagulation profile tests are normal.**

Management

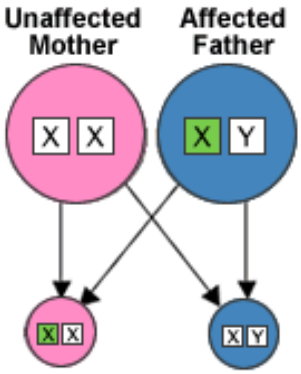
Prophylactic measures: for avoidance of trauma. In normal situation we aim to raise FVIII level to 30%, but é major operation we have to raise FVIII level to 100% & to maintain it above 60% until healing occurs after the operation.

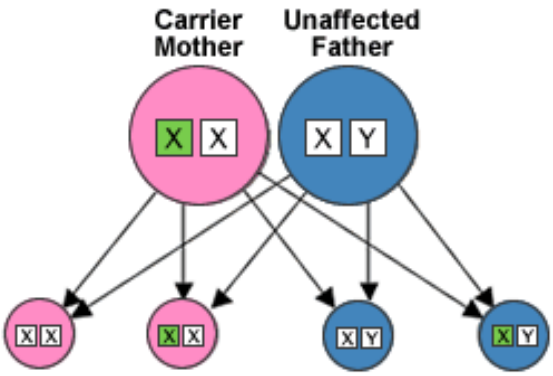
Fresh plasma; ẃ rise FVIII up to 5%, 10-20 ml/Kg/12 hrs. Or

Cryoprecipitate; rise FVIII up to 25% (contain FVIII 100u+ fibrinogen), 1 bag/5/Kg.

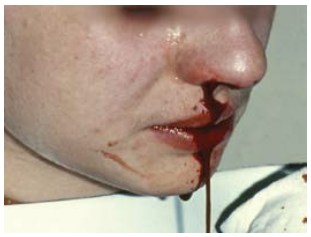
FVIII conc. infusion, the amount needed can be calculated according to the formula: % of FVIII needed to be raised ÷ 2 X BW (Kg) or roughly as 20 u/Kg twice daily, each bottle of FVIII labelled é the number of units it contain.

You have to measure the post infusion level FVIII. No aspirin. No Antihistaminics. Measuring FVIII antibodies & 40 days to be passed between repeated FVIII transfusions or until AB disappear.





VON WILLEBRAND'S DISEASE



Related to chromosome 12, Gene VWF, Location p13.3. Named after Dr. Adolf Von Willebrand, a Finnish paediatrician in 1926.

Incidence

1/100 population. Is AD disorder, result from def. of VWF. é variable degree of penetrance. Has both functional platelet abnormality & ⇩ synthesis of VWF ẃ facilitates platelet aggregation & act as a carrier of FVIII.

Clinical picture

•Epistaxis. •Mucocutaneous bleeding. •Skin bleeding. •Women may have heavy menses or excessive blood loss during labour.

Comparison between different coagulation disorders

Features	Haemophilia	Factor IX deficient	Von Willebrand's
Inheritance	Sex linked AR	Sex linked AR	AD
Site of bleeding	Body cavities, Joint & intramuscular spaces	Body cavities, joint & intramuscular spaces	Mucocutaneous & other mentioned sites
Platelet count	N (normal)	N	N
Bleeding time	N	N	Prolonged
PT	N	N	N
PTT	Prolonged	Prolonged	Prolonged or N
VIII	Low	N	Low
VWF	N	N	Low
Factor IX	N	Low	N

Treatment

Intermediate-purity FVIII conc. containing F VIII & VWF. Desmopressin.

Chapter III

DISEASE OF THE RESPIRATORY SYSTEM

- Introduction
- Common cold
- Influenza
- Bronchitis
- Pneumonia
- Bronchial Asthma
- Chronic Obstructive Pulmonary Diseases
- Bronchiectasis
- Lung Abscess
- Pleurisy & Pleural Effusion
- Pulmonary Hypertension
- Neoplasms of Lung

INTRODUCTION

Cough

Is an explosive expiration that provides a protective mechanism for clearing the tracheobronchial tree of secretions & foreign material. Cough can initiated by a variety of airway irritants, ẃ enter the tracheobronchial tree by inhalation (smoke, dust, fumes) or by aspiration (upper airway secretions, gastric contents, foreign bodies) or any disorder resulting in inflammation, constriction, infiltration, or compression of airways. Inflammation commonly results from airway infection, ranging from: inflammation-infection (viral, bacterial) as bronchitis, bronchiectasis etc. Constriction- as é asthma. Infiltration as é TB, neoplasm, granuloma, or sarcoidosis. Parenchymal lung disease potentially producing cough- as pneumonia, interstitial lung disease & lung abscess, or CHF as a result of interstitial oedema.

Approach to the pt é cough

History: frequently provides the most valuable clues for aetiology of the cough. Particularly important questions include:- is the cough acute or chronic ? What are the factors influencing it? Were there associated symptoms suggestive of respiratory infection? Is it seasonal or associated é wheezing ? Dyspnoea? Is there nasal discharge or gastroeosophageal reflux (heartburn)? Is there fever? What its character of sputum if present? Is there is associated disease or risk factors (as smoking, pollution, HIV)?

Examination: may point to a non-pulmonary cause of cough, such as HF, malignancy, or AIDS. Auscultation of the chest may demonstrate; inspiratory stridor (indicative of upper airway disease), respiratory wheezing (indicating lower airway disease) or inspiratory crepitations (process involving the pulmonary parenchyma, as interstitial lung dis- ease, pneumonia, TB or pulmonary oedema).

Complications of cough: may ppt syncope, fracture of the ribs.

Treatment

Depends on determining the underlying cause, then initiating specific different cough suppressants can used in addition to the specific Rx to ⇩ cough duration.

Chest discomfort/Pain

Is one of the most frequent complaints for ẃ pt seek medical attention. There is little relation between the severity of chest discomfort & the gravity of its cause.

Causes

Pleuritic chest pain: is usually brief, sharp, knife like pain, ppt by inspiration or coughing. Is very common & generally results from inflammation of parietal pleura. Typical example is pneumonia.

Myocardial ischemia: angina pectoris is usually described as a heaviness, pressure, squeezing or sensation of strangling or constriction in the chest, but it also may be described as an aching or burning pain or even as indigestion. Typically, angina develops during emotion or physical exertion. The pain typically resolves within 5-50 minutes & is more prolonged in MI.

Pericarditis: the pain arises from parietal pericardium & adjacent parietal pleura. Infectious diseases & inflammation are the main causes of pain. Pericarditis can cause pain in several locations like the tip of the shoulder & neck, more often the pain is located in the anterior part of the chest & is relieved by bending forward; but pain may also be in upper part of abdomen or at corresponding region of the back. Pericardial pain commonly has a pleuritic component; i.e. it is aggravated by cough & deep inspiration, because of pleural irritation. Sometimes there may be steady substernal discomfort that mimics AMI.

Vascular causes of chest pain: pain due to acute dissection of aorta usually begins abruptly, reaches an extremely severe peak rapidly. It is felt in the centre of chest &/or

the back, lasts for hours & requires unusually large amounts of analgesics for relief of pain. Pain is not aggravated by changes in position or respiration & is usually associated é low blood pressure.

Chest pain due to pulmonary embolism: may resemble that of AMI, be cause in massive embolism pain is located substernally. In pt é smaller emboli, pain is located more laterally, is pleuritic in nature & sometimes associated é haemoptysis. Gastrointestinal causes of chest discomfort: oesophageal pain commonly presents as deep thoracic burning pain, ẃ is the hallmark of acid-induced pain. Oesophageal spasm has acute pain that may be indistinguishable from MI. Other diseases like Biliary disease, Pancreatitis may present as chest discomfort or pain.

Emotional cause of chest pain -Cardiac neurosis: usually,the discomfort is experienced as sense of "tightness" & sometimes called "aching". It is confused é myocardial ischemia. Ordinarily, it lasts for half an hour or more & usually associated é emotional strain or fatigue.

Haemoptysis

Defined as expectoration of blood from the Resp. tract, ẃ could be scanty & mixed é sputum or large amount of frank blood. Massive haemoptysis defined as expectoration of >600 ml of blood in 24 hrs.

Causes

Tracheobronchial: •Neoplasm •Bronchitis •Foreign body • Airway trauma.

Pulmonary parenchymal: •Pneumonia •TB •Lung abscess.

Primary vascular source: •Mitral stenosis •Pulmonary embolism.

Others causes: Nasopharyngeal or GIT bleeding. TB & pneumonia are the commonest causes of haemoptysis in developing countries. But bronchitis & bronchogenic carcinoma are common in developed regions. Up to 30% of pts. may not have identifiable

cause even after complete investigation.

Approach to the pt é Haemoptysis

- Blood streaked, mucopurulent sputum suggests bronchitis.
- If haemoptysis associated é fever pneumonia should be suspected.
- If sputum smell is putrid, lung abscess is likely.
- If occurs suddenly é chest pain & dyspnoea suggests pulmonary embolism.
- If associated é previous history of renal disease, SLE, or malignancy, are important for suggesting diagnosis & Rx.

Physical examination

- Pleural friction rub.
- Localized or diffuse crackles (lung parenchymal damage).
- Wheezing (air flow obstruction, chronic bronchitis).
- Cardiac examination may reveal pulmonary hypertension, MS or HF.

Diagnostic evaluation

- CXR: may show lesion suggestive of bronchiectasis or pneumonia. - CBC.
- Sputum examination: for Gram & AFB stain. - Coagulation profile. - Urine analysis.
- BUN & - Creatinine. - Bronchoscopy, useful in localizing, managing bleeding site.

Treatment

The rapidity of bleeding & its effects on gas exchange determine the urgency of Rx. If there is only blood streaking sputum é mild haemoptysis, first establish diagnosis; put the pt at rest & giving cough suppressant may help to subside the bleeding. If haemoptysis is massive: pt should be referred to a hospital. pt may require ETT & mechanical ventilation. If bleeding side is known, position the pt so that the source of bleeding is placed in dependent position to protect suffocation.

COMMON COLD



Common cold or acute coryza is an acute, usually afebrile, viral infection of the respiratory tract é inflammation in any or all airways (the nose, paranasal sinuses, throat, larynx & often trachea & bronchi).

Etiology

Many viruses cause the common cold including; Picornavirus (Rhinovirus), Influenza, Para influenza, RSV, Corona & Adenovirus group. Infections may facilitated by excessive fatigue, emotional distress, or allergic nasopharyngeal disorders & during the mid phase of the menstrual cycle.

Symptoms & Signs

Onset is abrupt after short IP (1-3 days). Illness generally begins é nasal or throat discomfort followed by sneezing, rhinorrhoea & malaise. The disease is afebrile & pharyngitis is usually present. Nasal secretions, watery & profuse during 1^{st}-2^{nd} day, become more mucous & purulent. Hacking cough associated é scanty sputum often on 2^{nd} wk. When no complications occur, symptoms resolve within 4-10 day.

Diagnosis

Nonspecific symptoms & signs. many other disorders also cause URT symptoms at onset. Differentiation depends on the season & course of the symptoms. Fever & more severe symptoms usually indicate influenza.

Prophylaxis

Immunity is virus type-specific. Because of numerous types & strains of known viruses causing URT, it is difficult to produce useful vaccine.

Treatment

•A warm, comfortable environment & measures to prevent direct spread of infection are recommended for all persons.

•Antipyretics & analgesics to control fever.

•Nasal decongestants used if pt have nasal congestion. Steam inhalation also used in nasal congestion to help mobilize secretions & relieve chest tightness.

•Treat persistent cough é cough suppressants.

•Vit C/high doses of citrus juices have no scientific benefit.

•Antibiotics not effective against viruses so not recommended unless a specific bacterial complication develops.

INFLUENZA

Specific acute viral resp. disease. Usually occurs as an epidemic in rainy seasons.

Etiology: caused by influenza viruses, there are types A, B & C.

Epidemiology

Influenza type A virus is the most frequent single cause of clinical influenza; other causes include influenza B, paramyxovirus, pneumoniavirus & rhino & echoviruses. Spread is by person to person contact through airborne droplet infection. Persons of all ages are affected, but prevalence is highest in school children. Persons at highest risk of developing severe disease are those é chronic pulmonary disease, those é valvular heart disease, pregnant women, the elderly or very young & the bed ridden. Influenza A is associated é significant morbidity & mortality.

Symptoms & Signs

During the 48 hrs of the IP, transient asymptomatic viremia occurs. Chills & fever 39-39.5 ^{0}C developing over 24 hrs. Generalized aches & pain (most pronounced in back & legs). Headache is prominent. Respiratory tract symptoms may be mild initially but become prominent later. The soft palate, posterior hard palate & tonsillar pillars may be reddened. Usually after 2-3 days, acute symptoms rapidly subside & fever ends. Weakness, sweating & fatigue may persist for several days or occasionally for wks. In severe cases, haemorrhagic bronchitis & pneumonia are frequent & can develop within hrs. Fulminant, fatal viral pneumonia may occur & death may follow as soon as 48 hrs after onset. This is usually during a pandemic caused by a new virus or in high-risk people.

Complications

- Secondary bacterial infection of the bronchus & pneumonia. é pneumonia, cough worsens & purulent or bloody sputum is produced. Crepitations can detected over the affected segment.
- Encephalitis, Myocarditis & Myoglobinuria may occur, usually during convalescence.

Diagnosis

- Clinical influenza is a common experience & can be easily diagnosed. Chest examination usually normal in mild cases & may look like common cold. Pulmonary symptoms may be similar to those of bronchitis or atypical pneumonia. Fever & severe constitutional symptoms differentiate influenza from the common cold.
- WBCs count is normal in uncomplicated cases.
- Isolating the virus can make specific diagnosis of influenza.
- Serologic tests are also used.

Prognosis: recovery is the rule. Viral pneumonia may cause death.

Prophylaxis

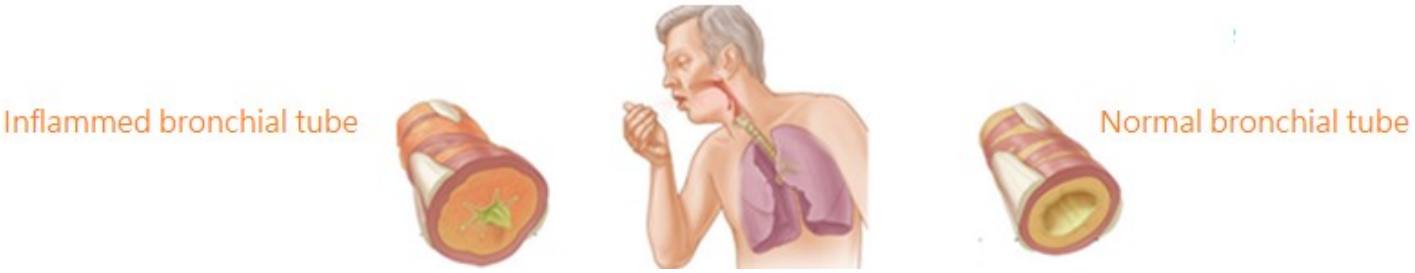
Vaccines that include the prevalent strains of influenza viruses effectively ⇩ the incidence of infection. Amantadine 100 mg PO bid (for adults) can be used prophylactically against influenza A.

Treatment

•Basic Rx for most pts is symptomatic é bed rest, antipyretics, nasal decongestants & steam inhalation.

•Amantadine has beneficial effect on fever & respiratory symptoms if given early in uncomplicated influenza, it inhibits penetration of the virus into the host cell (it has no virucidal actions), 100 mg tab, 4-8mg/kg/D for 5 D. adult 1 tab daily X 5D.

ACUTE BRONCHITIS



Is acute inflammation of the tracheobronchial tree, generally self-limiting & é eventual complete healing & return to normal function. It could be caused by infecti- ons or irritants.

Etiology

Acute infectious bronchitis is often part in acute URTI. It may develop after a common cold or other viral infection of the nasopharynx, throat or tracheobronchial tree, often é secondary bacterial infection. Acute irritative bronchitis is caused by various mineral & vegetable dusts, volatile solvents, tobacco & smoke.

Symptoms & signs

Acute infectious bronchitis is often preceded by symptoms of URTI, coryza,malaise

,chilliness, slight fever, back & muscle pain, sore throat. The onset of cough usually signals onset of bronchitis. Cough is initially dry but progresses to be productive. Purulent sputum suggests bacterial superinfection. In uncomplicated case, fever to 38.8 ^{0}C may be present up to 3-5 days, following ẃ acute symptoms subside (thou- gh cough may continue for several wks). Persistent fever may suggest complication like pneumonia. Pulmonary signs are few in uncomplicated acute bronchitis. Scattered rhonchi & wheezes may be heard, as well as occasional crepitations at the bases. Serious complications are usually seen only in pt é underlying chronic respiratory disorder or immunocompromised pt.

Diagnosis

- CXR taken only to R/O serious condition like pneumonia.
- In pt who do not respond to antibiotics, gram stain & sputum culture to be done.

Treatment

General management

- Rest until fever subsides.
- Oral fluids to be ta-ken more: facilitates sputum expectoration.
- Antipyretics & analgesics (Aspirin/Paracetamol) are given if there is fever or myalgia (Aspirin not indicated for children < 5 yrs for the risk of Reye`s sy.).

Symptomatic Rx

Of cough may shorten cough duration.

Specific Rx

As antibiotics should be given when purulent sputum & persistent fever are present. Ampicillin given for 7-10 days.

PNEUMONIA

Is an acute infection of lung parenchyma including alveolar spaces & interstitial tissue. Involvement may be confined to entire lobe (lobar) or segment of a lobe (segmental) or to alveoli contiguous to bronchi (bronchopneumonia) or interstitial tissue (interstitial). These distinctions based on CXR findings.

Predisposing factors

The usual mechanisms to develop pneumonia are either to inhale droplets small enough to reach alveoli, or to aspirate secretions from the upper airways. Other means include haematogenous dissemination, or via the lymphatics, or directly from contiguous infections. Predisposing factors include; preceding respiratory viral infections, alcoholism, cigarette smoking, underlying diseases such as HF or COPD, age extremes, immunosupressive therapy & disorders, or é ⇩ consciousness, coma, seizure, surgery & aspiration of secretions.

Microbial pathogen that cause pneumonia

Community-acquired pneumonia: streptococcus pneumonia is the commonest, others include; mycoplasma, chlamydia, haemophilus influenza, oral anaerobic bacteria, staphylococcus aureus, legionella pneumophila & mycobacterium TB.

Aspiration pneumonia: this occurs when large amount of oropharyngeal or gastric contents are aspirated into the lower respiratory tract. Aspiration pneumonia occur more frequently in pts é ⇩ consciousness level (alcoholism, seizure, stroke, general anaesthesia), or é neurologic dysfunction of oropharynx & swallowing disorders, or people é periodontal disease. Common etiologic agents of aspiration pneumonia; often polymicrobial. Anaerobic organisms in the oral cavity, enterobateriacae, streptococcal pneumonia, staphaphylococcal aureus. Pt present é cough & foul smelling sputum. Cough may be chronic forming lung abscess & may resemble TB. There will be

signs of cavity on physical examination & CXR. It is treated é Crystalline Penicillin & Metronidazole IV for several wks if lung abscess develops.

Community acquired pneumonia in Immunocompromised hosts: as transplant recipients, HIV infected pt & pt on chemotherapy are prone to develop pneumonia. The etiologic agents are: Streptococcal, H. Influenza, Mycoplasma, G-ve organisms (Enterobacteriaceae), Funguses as Pneumocystis Carinii (Jerovecii), C. Neoformans , Histoplasmosis, Aspergillus, MycobateriumTB & Viruses as HSV, CMV.

Hospital-acquired pneumonia: pt is said to have HAP if symptoms begin 48 hrs after hospital admission & not incubating at the time of admission. Common organisms are ; G-ve bacilli (Pseudomonas Aeroginosa & K. Pneumonia), Stphylococcus Aureus (may be drug resistant) & Oral Anaerobes.

Clinical presentation of community acquired pneumonia

Typical CAP: characterized by sudden onset, high grade fever(up to 40.5^{0}C), cough is productive é purulent, blood streaked or rusty sputum, pleuritic chest pain on the involved side, worsened during inspiration or coughing, shortness of breath, headache, myalgia & fatigue. Pt will have tachycardia (100-140/min) & tachypnea (**>**20/min). There will be pulm signs of consolidation (lobar) ẃ are ⇧ tactile fremitus & vocal fremitus, dullness on percussion & bronchial breath sound.

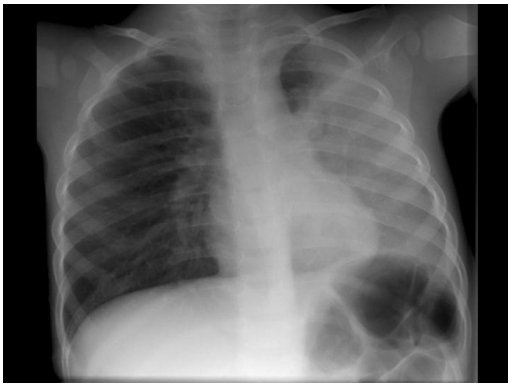
Atypical CAP: more gradual onset of symptoms, dry cough, shortness of breath. Prominence of systemic symptoms as headache, fatigue, nausea, vomiting & diarrhea. Chest findings on physical exam are minimal even though CXR changes are marked.

Complications

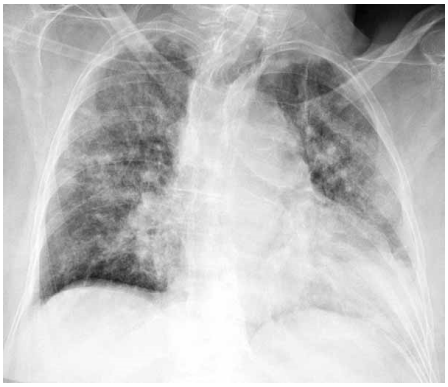
- Local: Para pneumonic effusion or pus in pleural space (empyema).
- Distant: septic arthritis & meningitis. Pneumonia can progress to sepsis, sometimes é septic shock.

Laboratory findings

- ***CBC***: leucocytosis é ⇧ neutrophils seen in most cases.
- ***Gram stain sputum:*** may show predominant pathogen.
- ***Sputum culture.***
- ***CXR:*** shows pulmonary infiltrates or homogeneous opacity indicating lobar pneumonia. Very early in the course CXR may be normal.



Lobular pneumonia



Bronchopneumonia

Diagnosis

Pneumonia should be suspected in pt é acute febrile illness associated é chest pain, dyspnoea &cough. Presumptive diagnosis can made from history, changes on CXR, blood, sputum gram stain &culture. Absolute diagnosis requires demonstration of bacteria or other etiologic agents in pleural fluid, blood, lung or tracheal aspirate.

Prognosis

The overall mortality rate is low, if treated early. Factors that herald a poor prognosis include the following:-

- Extremes of age, especially <1 yr or >60 yrs.
- +ve Blood culture •Involvement of >one lobe.
- Peripheral WBC <5000/ml.
- Presence of associated diseases as liver cirrhosis, CHF, immunosuppression.
- Development of extrapulmonary complications like meningitis & endocarditis.

Management

Mild form of CAP: pt é uncomplicated "Typical" pneumonia" can treated at OPD. Amoxicillin 500 mg PO TID or Ampicillin 500 mg PO QID for 7-10 days, or Procaine penicillin 600,000 IU IM/12 hrs. If "Atypical" pneumonia is suspected" Erythromycin 500 mg PO QID for 7-10 days or Doxycycline 100 mg PO BID. Pt should also get bed rest, adequate fluids & antipyretics & analgesics for pleuritic chest pain. In mildly ill pt who is treated early, fever subsides in 24-48 hrs. Others may require 4 days to re-spond. If pt is allergic to Penicillins, Cephalosporins, Erythromycin & Clindamycin can be given. If pt not improve, the following factors should be considered; wrong etiolog-ic diagnosis, adverse drug reaction, far advanced case or super infection, inad-equate host defences due to associated condition, noncompliance to the drug regimen in outpatients, antibiotic resistance of the strain & complications like emp-yema requir-ing drainage, or metastatic foci of infection requiring higher doses (e.g. Meningitis, Endocarditis or Septic Arthritis). The persistent cough & infiltration on CXR for > 6 wks after Rx suggests possibility of underlying bronchogenic neoplasm or TB.

Severe CAP: if pt seriously ill, he should be admitted, treated as inpatient. The criteria for hospitalization of such pt are:- •Tachypnea (RR > 28/min), tachycardia (HR of >140 /min).•SBP < 90 mmHg. •Hypoxemia (P_aO_2 < 60 mmHg) while breathing room air or O_2 saturation < 90 % (é pulse oximeter). •New onset of confusion or impaired level of consciousness. •Unstable/Significant comorbidity e.g. HF, uncontrolled DM, CRF, alco-holism or immunosuppression. •Multilobar pneumonia é hypoxemia. •Pleural effusi-on é analysis showing characteristics complication. •Other conditions in ẃ inpatient management advisable include:- elderly pt > 65 yrs of age, leukopenia < 5000 WBC /ml, pneumonia caused by S. aureus or G -ve bacilli, suppurative complications (emp-yema, meningitis, endocarditis), failure of outpatient treatment, inability to take oral

medication. The admitted pt should started on antibiotics empirically, high dose of Crystalline Penicillin 3-4 million IU IV/4-6 hrs. Alternatives are Ceftriaxone 1 gm IV daily or 2 X /day or Ampicillin 500 mg IV QID or Cefotaxime. In severely ill pt add Erythromycin or Fluoroquinolone. Choice of antibiotics may be modified based on C/S results. If the pt improves, IV Rx can be changed to oral after 3-4 days to complete 7-10 days course. Ensure adequate oxygenation to pt é cyanosis, or significant hypoxemia, or severe dyspnoea, or circulatory disturb- nce or delirium. Pt should be well hydrated. Fever & pain should be managed.

Prevention: of CAP through cessation of smoking & alcoholism. Vaccination agai-nst influenza & pneumococcus.

Pneumonia in the compromised pt

This include pt é AIDS, acute leukaemia, cancer chemotherapy, DM, Sickle cell disease, Hodgkin disease or pt on corticosteroid therapy. The potential pathogens in compromised hosts are many, as it stated above. Pathogens like streptococcus, are still responsible for the majority of pneumonia in compromised pt.

Diagnosis

Sputum examination & culture are used but they are not specific. Trans tracheal aspirate, bronchoscopy & biopsy have high accuracy, however these are done only in specialized hospitals. High index of suspicion from clinical presentation is important to diagnose pneumonia in immunocompromised hosts.

Treatment

Acutely ill pt who have suspected bacterial infection is often treated é antibiotics selected on the basis of probabilities & the findings é sputum gram stain & culture. Later Rx adjusted on the basis of more definitive diagnostic evaluation. Pt é AIDS & suspected atypical pneumonia should be treated é high dose of Cotrimoxazole.

Hospital Acquired Pneumonia

As mentioned before, a pt is said to have HAP if symptoms begin 48 hrs after hospital admission & not incubating at the time of admission. Presence of a new or progressive infiltrates of CXR in addition to at least 2 of the following:-

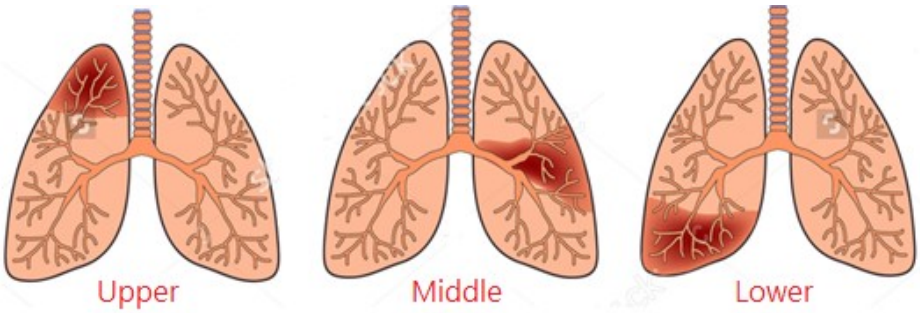
- Fever>37.8 ^{0}C.
- Leucocytosis>10.000/ mm^{3}.
- Purulent sputum.
- Others: dyspnoea, hypoxemia & chest pain.

Treatment

Antibiotics should initiated empirically & latter on may be modified based on culture/sensitivity results. Selection of drugs should be guided by understanding of local patterns of antibiotics resistance. Antibiotics should cover at least G-ve & Staph Aureus. Ceftriaxone 1 gm IV daily or BID **+** Cloxacillin or Methicillin or Levofloxacin 500mg IV/day. When resistant organisms are suspected use Cefotaxime 750 mg IV TID **+** Vancomycin 1gm IV BID.

Prevention

Strict hand washing protocols by health care providers. Extubate an intubated pt as soon as the pt is stable. Removal of the NG tube when the pt is stable. Proper aseptic handling of IV lines.



BRONCHIAL ASTHMA

Chronic inflammatory disease of airways characterized by ⇧ responsiveness of the tracheobronchial tree to a multiplicity of stimuli. Is associated é widespread airway obstruction that is reversible (but not completely in some pts) either spontaneously or é treatment.

Epidemiology

Asthma is a common disease, its prevalence is rising in different parts of the wor-ld. It can occur at any age; but usually starts early in life. About 50% of pts develop asthma before age of 10 yrs & another 35% before the age of 40 yrs. Males are affected twice as common as females in early life; this sex difference equalizes by age 30 yrs. Most cases of asthma are associated é personal or family history of allergic disease such as eczema, rhinitis & urticaria.

Etiology

	Allergic	Non allergic
Age of onset	Early in life	Late in life
Family or personal history of allergy	Yes	No
Skin test é ID injection of allergens	+ve	-ve
Serum IgE level	⇧	Normal
Response to inhalation provocative tes	+ve	-ve

Asthma can be classified into 2 types; allergic & non-allergic. Many pts have disease that does not fit into either of the 2 categories, but instead fall into mixed group é some features from each group. In general asthma ẃ has its onset early in life tends

to have strong allergic component, whereas asthma that develops late in life tends to be non-allergic or mixed aetiology.

Factors important for the genesis of asthma

- ***Genetic:*** there is strong genetic predisposition or familial tendency.
- **Allergens:** seasonal allergens such as pollen green, non-seasonal animal feathers, dust mites, molds.
- **Pharmacologic stimuli**: Aspirin, Tatrazin (colouring agent), ß blockers.
- **Environmental & air pollution**: industrial/heavily populated areas. Common pollutants are ozone, nitrogen dioxide & sulphur dioxide.
- **Infections**: respiratory infections are the most common of the stimuli that evoke acute exacerbation of asthma. Respiratory viruses are the major factors.
- **Exercise:** very common precipitant of acute episodes of asthma.
- **Emotional stress:** psych ological factors can worsen or ameliorate it.

Pathophysiology

Asthma results from a state of persistent subacute inflammation of the airways. The airways obstruction in asthma is due to combination of factors. The cells thought to play important part in the inflammatory response are mast cells, eosinophils, lymphohocytes, airway epithelial cells. These cells release inflammatory mediators result in:-

- Bronchoconstriction (spasm of airways smooth muscles).
- Vascular congestion & oedema of airways mucosa.
- ⇧ Mucus production, injury & desquamation of airways epithelium & impaired mucociliary transport.

Symptom & Signs

The symptoms of each asthmatic pt differ greatly in frequency & degree. Some asthmatics are symptom free é an occasional episode that is mild & brief, others have

mild coughing & wheezing much of the time, punctuated by severe exacerbations of symptoms following exposure to known allergens as viral infection, exercise or psychological factors particularly those associated é crying, screaming or hard laughing may ppt symptoms. An asthmatic attack usually begins acutely é paroxysms of wheezing, coughing & shortness of breath, or insideously é slowly increasing manifestations of resp. distress. The asthmatic first notices dyspnea, tachypnea, cough & chest tightness & may even notice audible wheezes.

Physical examination

Varying degrees of resp. distress; tachypnoea, tachycardia & audible wheezes are often present. Dehydration may be present because of sweating & tachypnea. Chest examination shows prolonged expiratory phase é relatively high pitched wheezes throughout inspiration & most of expiration. In more severe episodes, pt may be unable to speak more than few words éout stopping for breath. Cyanosis is usually a late sign of hypoxia. Confusion & lethargy may indicate the onset of progressive respiratory failure. Less wheezing (silent chest) might indicate mucous plug. Pt fatigue é less airflow is sign of impending respiratory failure. The presence, absence, or prominence of wheezes does not correlate precisely é the severity of the attack. The most reliable clinical signs include; the degree of dyspnoea at rest, cyanosis, difficulty in speaking & the use of accessory muscles of respiration. This is confirmed by ABG analysis. Between acute attacks, breath sounds may be normal during quiet respiration. However, low grade wheezing may be heard at any time in some pts, even when they claim to be asymptomatic.

Complications

- **Pneumothorax**: may present as sudden worsening of respiratory distress accompanied by sharp chest pain &on examination hyper resonant lung é shift of mediastinum

& CXR confirms the diagnosis.

- **Mediastinal & subcutaneous emphysema:** from alveolar rupture.
- **Atelectasis:** due to obstruction.
- **Dilated right heart chambers** (cor-pulmonale): from chronic hypoxemia & pulmonary hypertension.
- **Respiratory failure.**

Laboratory Findings

- **Eosinophilia:** is common finding.
- **Sputum:** is tenacious, rubbery & whitish or may be yellowish; eosinophils are present in the sputum.
- **CXR:** varies from normal to hyperinflation. Atelectasis & pneumothorax may be seen in complicated cases.
- **Pulmonary function tests:** are valuable in differential diagnosis & in a known pts to assess the degree of airways obstruction.

Differential diagnosis

In children: foreign body obstruction, or viral URTI involving the epiglottis (croup), or bronchiolitis (RSV infection).

In adults: COPD, HF, endobronchial TB &malignancies. Physical examination should search for HF & signs of chronic hypoxemia (clubbing). Unilateral wheezes usually indicate obstruction by foreign bodies or tumour.

Prevention of attacks

The role of environmental factors (animal dander, dust, airborne moulds, pollens) in acute exacerbations is clear. Allergens that can be controlled by avoidance should be eliminated. Nonspecific precipitating factors as cigarette smoke, odours, fumes, change in temperatur or atmospheric pressure & humidity should also be investigated.

Treatment

General principles: assessing severity of the attack is paramount in deciding Rx. Bronchodilators should be used in orderly progression. Decide when to start steroids.

Treatment of the acute attack: mild acute attack: most pts can managed as an OP, to be given:- •Salbutamol aerosol (Ventolin) 2 puffs / 20 min for 3 doses is 1st line.

•Adrenaline 1:1000 can be given in doses up to a maximum of 0.2 ml in children & 0.3 ml in adults, repeated once or twice in 20-30 minutes (if there is no hypertension or any other contraindication).

•If the initial Rx fails, Aminophylline 250 mg IV diluted in dextrose in water should be given slowly over 10-15 minutes, once. If the pt does not respond to one dose of Aminophylline, then the pt is declared to have severe asthma & should be admitted to the hospital.

Hospital admission: pt who diagnosed to have severe & life threatening asthma need inpatient management & even admission to ICU.

The signs of severity of acute asthmatic attack include:-

Severity	Symptoms	Medication	Alternative Rx
Mild Intermitnet	≤ 2 days/week & ≤ 2 nights /month	No daily Rx. Rx é acute exacerbate.	
Mild Persistent	>2 day/wk but <1/ D & >2 nights/month	Low dose. Inhaled steroid or Cromolyn.	Theophedrine or Salbutamol tab.
Moderate Persistent	Daily symptoms & > 1 night/wk	Low-medium dose. Inhaled steroid & long acting B-agonist inhaler.	Theophylline sustain release/ Salbutamol or Prednisolone ta. low dose
Severe Persistent	Continual daily Symptoms & frequent night symptoms	High dose. Inhaled steroid & long acting inhaled B-agonist & oral steroid (if needed)	Theophylline sustained release/Salbutamol tab. Prednisolone tab. (high dose)/ Celestamine tab.

•Tachycardia HR >120/min. •Tachypnea RR >30/minute. •Presence of pulsus paradoxus. •Use of accessory muscles of respiration. •Cyanosis •Altered state of consciousness (confusion, drowsiness). •Silent chest. •Paradoxical movement of the chest & abdomen. •Presence of complications; as pneumothorax, atelectasis. •Unable to finish a sentence é single breath (frequent interruption of speech to take a breath). •Laboratory parameters include; FEV <60%, PaO_2 <60 mmHg or SaO2 < 90 % (pulse oximeter) or $PaCO_2$ (arterial sample) >42 mmHg.

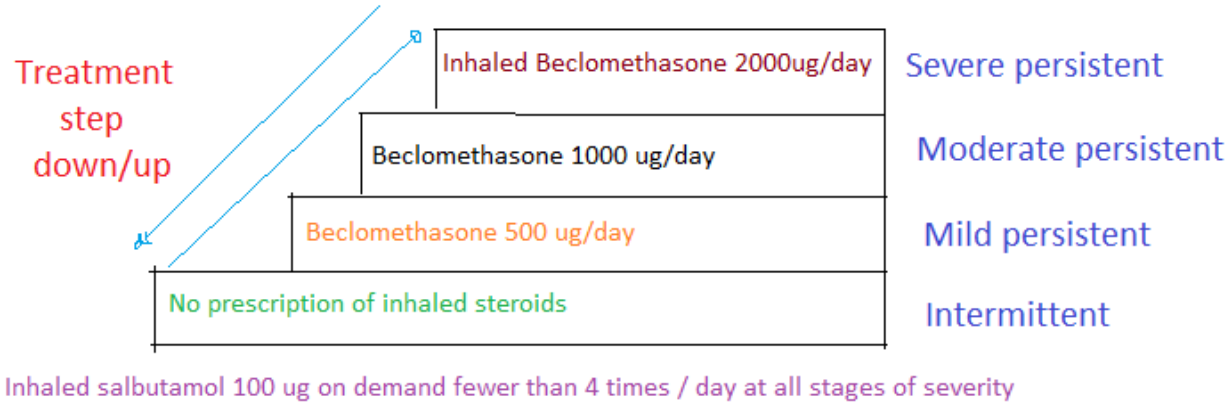
Specific drug treatment

Aminoplylline: in doses of 1 mg/kg/hr in a continuous IV infusion.

Corticosteroids: should also be given IV e.g. Hydrocortisone 4 mg/kg/4 hrs. When the pt improves the hydrocortisone to be changed to Prednisolone PO& dosage should be tapered up on discharge. Pt who does not respond to aggressive drug Rx is candidate for endotracheal intubation & mechanical ventilation for ẃ they should be admitted to an ICU.

Antibiotics: respiratory tract infection precipitating acute asthmatic attack is predominantly viral; but if pt expectorates yellowish, green or brown sputum, antibacterial Rx is indicated. Ampicillin is the first line; alternatives are Erythromycin or Cotrimoxazole. CXR to be taken if there is suspicion of pneumonia/complication.

Stepwise approach for managing asthma in adults



Supportive Treatment

O_2 therapy always indicated for hospitalized pts. Fluid & electrolyte balance requires special attention because of frequent occurrence of dehydration during acute asthmatic attack. However, over hydration may cause pulmonary oedema & one should be cautious in fluid administration. Also anxiety is common in pt é severe attack. However this can be overcome when underlying hypoxia & feeling of asphyxiation is treated.

Maintenance therapy for asthma

The goal of maintenance therapy is to achieve a stable, asymptomatic state é the best pulmonary function, using the least amount of medication. Drug selection is based upon the severity of illness. Antileukotriens & prophylactic therapy. Ketotifen/Montelukast; prevent the bronchoconstriction & mucous secretion of leukotrienes (leukotrienes are mediators released from mast cells during asthma) by competitive binding to leukotrienes receptors found in the airway. It can used é corticosteroids or B-agonists or theophylline.

SEVERE ACUTE RESPIRATORY SYNDROME

Viral infection, IP is 2-16 days, presented ē fever, cough, rigors, muscle pain, may associated ē nausea, vomiting, diarrhoea in 20% of cases.

Investigations

- CXR: solitary, multiple lesions near pleura.
- CBC: leucopenia, thrombocytopenia.
- Serum electrolytes: ⇩ Na, ⇩ K.
- LFTs: ⇧ Enzymes.
- Isolation of the virus.

Management

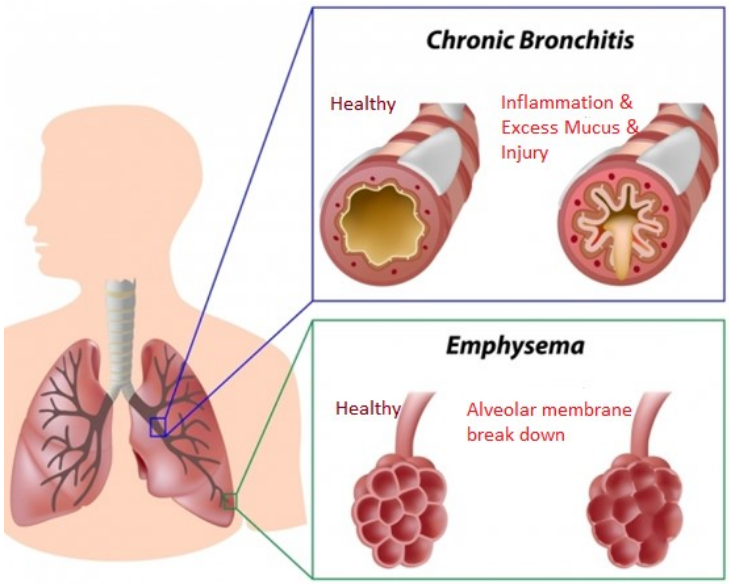
- Antiviral: Ribavirin tab 200mg, or Acyclovir tab 200mg, 15 mg/Kg/D÷3 for 5 days.
- Prophylactic antibiotic: Claforan amp 500, 1000mg, 50 mg/Kg÷2 IV/IM "3rd gene. Cephalosporine".
- With marked deterioration, transfer to ICU.

CHRONIC OBSTRUCTIVE PULMONARY DISEASES

COPD are conditions characterized by chronic irreversible airway obstruction caus- ing ⇧resistance to outflow of air due to chronic bronchitis & emphysema. Both th-ese diseases occur together in the same individual in variable proportion but the manifes- tations of one often predominates the clinical picture.

Chronic Bronchitis: is a condition associated é excessive tracheobronchial mucus pro- duction sufficient to cause cough é expectoration of sputum for at least 3 mon-ths in a year for over 2 consecutive yrs.

Pulmonary Emphysema: is distension of the airspaces distal to the terminal bronchi- oles, accompanied by destructive changes of the alveolar septa.



Aetiology

Chronic Bronchitis: sufficient exposure to bronchial irritants, particularly cigarette smoke, most persons develop some degree of chronic bronchitis é signs of inflam- mation of the airways. In developing countries household smoke from fire wood is a major contributing factor.

Pulmonary Emphysema: any factor leading to chronic alveolar inflammation wou- ld encourage development of emphysematous lesion. Smoking has adverse effects on lung defences, leading to emphysematous changes. Congenital enzyme defects

such as α 1-antitrypsin deficiency are also risk factor.

Prevalence

COPD is a major health problem. Males are affected >females, ẃ could be attribu-ted to the higher prevalence of smoking in males. Nowadays, the incidence in females ⇧ because of ⇧ smoking habit.

Pathological changes & Pathophysiology

Chronic Bronchitis: characterized by hypertrophy of mucus glands in both large & small airways é thickening of walls & accompanying excess production of mucus & narrowing of airway lumen. Alveoli are often spared & no vessel loss & lung perfusion remains normal but ventilation is very much reduced. This cause abnormal V/Q & pt usually suffer from hypoxemia (manifested é cyanosis) & acidosis, ẃ cau-ses pulmo-nary hypertension & right side heart failure in long term.

Pulmonary Emphysema: characterized by destruction of alveolar septa & distension of alveoli resulting in reduced surface area & loss of vessels, the later (loss of vessels) cause reduced perfusion. Moreover, emphysema cause mucus production & airway narrowing é accompanying reduction in ventilation. This leads to retention of Co_2 in blood & severe dyspnoea from reduced tissue perfusion. However, those pts do not suffer from hypoxia & acidosis & have less chance of development of pulmonary hy-pertension & cor pulmonale. However, pts usually have a mixed picture of emphyse-ma & chronic bronchitis.

Clinical features

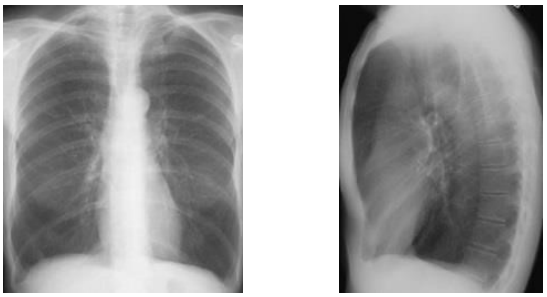
COPD is thought to begin early in adult life, significant symptoms & disability do not appear until middle age. A mild "smoker's cough" is often present many yrs before the onset of excertional dyspnoea. Gradual progressive excertional dyspnoea is the most common presenting complaint. Cough, wheezing, recurrent respiratory

infections or occasionally weakness, wt loss,⇩ sex libido may be initial manifestations of COPD.

Physical findings

COPD physical findings are very variable especially in early stages. A consistent abnormality is obstruction to expiratory airflow manifested by prolonged forced expiration (normally <4 sec.). Typical findings of COPD include: gross pulmonary hyperinflation, prolonged expiration during quiet breathing, pursed-lip breathing, stooped posture & marked use of accessory muscles of respiration seen in later stages. Other findings are rhonchi, ⇩ vesicular breath sounds, tachycardia, distant heart sounds & ⇩diaphragmatic excursion. The chest may be "quiet"remarkably in advanced stages of emphysema but is usually "noisy" in pts é chronic bronchitis. In advanced cases, frank cyanosis may be there from hypoxemia; a plethoric appearance associated é secondary erythrocytosis & signs of right sided heart failure in pt é cor-pulmonale. Mild oedema may be there even éout heart failure.

Diagnosis



CXR PA & L: note bilateral flattening of the diaphragms & significant hyperinflation as demonstrated by visualization of 11 posterior ribs.

- **CXR** findings are very variable, in early stages it is normal. Hyperinflation (e.g. depressed diaphragm, generalized radiolucency of the lung fields) is common usually late in disease process. In pt é recurrent chest infections, a variety of non-descriptive post-inflammatory abnormalities (referred to as "dirty lung") may be noted on CXR. COPD should be suspected in any pt é chronic productive cough &/

or exertional dyspnoea of uncertain etiology or whose physical examination reveals evidence of prolonged forced expiration.

- **Pulmonary function tests:** (spirometric testing) are done at specialized hospitals to determine the type of pulmonary obstruction.
- **CBC:** may reveal erythrocytosis & ⇧ Hct in chronic hypoxemic pts.
- **ABG:** the pattern of physiologic abnormality in each pt depends to some extent on the relative severity of intrinsic bronchial disease & emphysema. In pts é severe emphysema, resting hypoxemia usually is mild (i.e. no or less cyanosis).

In pts é chronic bronchitis, severe hypoxemia may be noted relatively early.

	Predominant Emphysema	Predominant Ch. Bronchitis
Age	60 +/-	50+/-
Body	Thin	Obese
Cough	After dyspnoea	Before dyspnoea
Sputum	Scanty, mucoid	Copious, purulent
Appear	Pink, tachypneic (pink puffers)	Cyanosed, normal RR
P/E	⇧ AP diameter. Use of accessory mus. Silent chest. Hyperresonant.⇩ Cardiac dullness	+/- use of accessory muscles. No hyper-resonance. Rhonchi (changing), Wheezing é cough
CXR	Long, narrowed heart. Low diaphragm,translucent lung, loss of periph vasc. markings	Enlarged heart. Large pulm. A ⇧ bronchovascular markings
CBC	Normal Hct	⇧ Hct
ABG	PaO_2 65-75 & $PaCO_2$ 35-40 mmHg.	PaO_2 40-60 & $PaCO_2$ 50-60 mmHg.
Complic.	Less bronchial infection.	Frequent bronchial infection.

Course & Prognosis

In the early stage of COPD, some reversal of airway obstruction & considerable symptomatic improvement can often be obtained é Rx, but the long-term prognosis is less favourable.

Treatment

So far no curative Rx. The Rx directed at relieving symptoms,controlling potentially

fatal exacerbations & slowing of the progression of the disorder. Avoidance of bronchial irritants, especially cessation of smoking. Thus, Rx is outlined as follows:-

①**Rx of infection:** COPD pt é purulent sputum should be treated é broad spectrum antibiotic. Cotrimoxazole 960 mg, PO BID or Ampicillin 500 mg X 4 times a day for 10 days. The course can be repeated at the first sign of recurrence.

②**Control of bronchospasm:** β-agonists like salbutamol, or one of the Theophyllines can used. Corticosteroids do not have major role in maintenance Rx.

③**Facilitation of drainage of bronchial secretion:** hydration é oral fluids to prevent drying of secretions. Inhalation of mist, postural drainage & chest exercise.

④**Hypoxemia:** this will lead to cor-pulmonale in pt é predominant chronic bronchitis. O_2 should be given to such pt & in severe cases portable O_2 (16 hrs/day) for home use is recommended.

⑤**Control of HF:** the most important measures are correction of hypoxemia, administration of diuretics & restriction of sodium.

⑥**Exercise:** prolonged inactivity leads to exercise intolerance. Regular exercise as long as there is no severe heart disease is recommended.

⑦**Depression:** the nature of the disease should be well understood by both pt & family, psychological support is important. Antidepressants may be necessary but should be used cautiously to avoid sedation.

⑧***Rx* of exacerbation:** exacerbation requires prompt Rx. If sputum becomes purulent, course of broad spectrum antibiotics should be given.

⑨**Phlebotomy:** Hct is usually high because of the chronic hypoxemia (polycythaemia) especially in pt é predominant chronic bronchitis. Phlebotomy should be done when the Hct level very high (**>** 55%) & the pt is symptomatic.

BRONCHIECTASIS

It is a pathologic, irreversible destruction & dilatation of the wall of bronchi & bronchioles, usually from suppurative infection of obstructed bronchus.

Etiology & Pathogenesis

Small bronchi of children are susceptible to recurrent infections & obstruction by foreign body, LNs, or impacted secretions, all of ẃ lead to persistent infection & development of bronchiectasis. However, bacterial pneumonia is the commonest cause. Predisposing conditions include congenital disorders (e.g. bronchial stenosis), cystic fibrosis & immunosuppression.

Clinical features

Chronic cough, productive of copious & offensive purulent sputum is the cardinal feature of bronchiectasis. The sputum typically forms 3 layers when collected in a glass container: the upper layer is foam (mucus), the middle is liquid & the lower one is sediment. In the early stage of the disease, cough & sputum production are related to cold exposure é occasionally haemoptysis. In advanced disease pt have progressive dyspnoea, massive haemoptysis & cough at any time of the day & produces large volume of khaki coloured sputum é accompanying cyanosis & clubbing. Complications in advanced cases include recurrent haemoptysis, cor-pulmonale, Respiratory failure, amyloidosis & recurrent pneumonia.

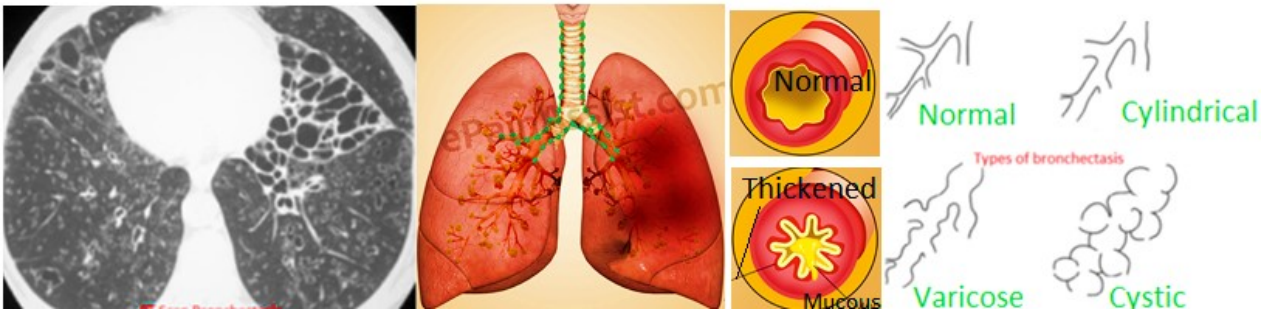
Diagnosis

Largely based on clinical features. Obtaining a history of recurrent pulmonary infections ultimately followed by chronic recurrent cough & production of copious purulent sputum may suggest the diagnosis. Physical exam of the chest may show only rales in early stages. Additional findings like cyanosis, clubbing & signs of right sided HF appear late. Pulmonary function test may be normal in early disease.

CXR: usually shows peribronchial fibrosis or honey comb appearance. Segmental lung collapse may observe in parts of the lung affected by bronchiectasis.

CT scanning: is often identifies the lesions, eliminating the need for bronchoscopy & contrast studies.

Bronchography: for definitive diagnosis of bronchiectasis.



Treatment

Generally, pt should avoid smoking & exposure to dust. Living in warm & dry climatic condition is advisable. However, medical therapy is the mainstay of Rx

1) Control of respiratory infections: broad spectrum antibiotics that should be given whenever signs of pulmonary infection appear & symptoms are exacerbated (Ampic-illin, Tetracycline or Erythromycin). Immunization for influenza & Strept pneumonia also recommended.

2)Improve drainage of secretion: postural drainage, liquefaction &bronchodilators

3) O_2 therapy: may be given to pt é hypoxemia.

4) Surgical resection: for the affected part is indicated when bronchiectasis is local-ized & in those é recurrent massive haemoptysis that fails to respond to conservative Rx. Is effective if done early in life.

RECURRENT CHEST INFECTION

Causes

May be; •*TB*, •Abscess • Immune deficiency •TOF • ą-1- antitrypsin deficiency.

Investigations

▲CBC ▲Chest X ray & thin film barium swallow ▲Sweat test ▲Tuberculine test ▲Immunoglobulins level ▲Seriological test for HIV infection ▲α-1- antitrypsin in blood especially ē associated endocrinal diseases.

LUNG ABSCESS

Collection of pus within a destroyed portion of the lung. May develop following necrotizing infections of the lung (bacterial pneumonia, TB, or fungi) or loss of blood supply to a part of the lung causing cavitory infarction due to septic or bland embolism, or due to obstruction to airways or cavitations of malignancy. The anaerobic abscess is the commonest & usually follows periodontal diseases as gingivitis, pyorrhoea or aspiration of oropharyngeal/gastric contents.

Aetiology

Commonly caused by pyogenic bacteria: Staph aureus, Klebsiella, mixed anaerobes & Nocardia. Common risk factors are; alcoholism, immunodeficiency, loss of consciousness & periodontal diseases.

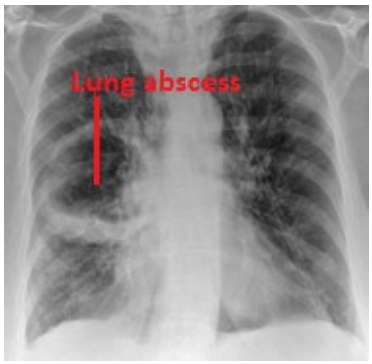
Clinical features

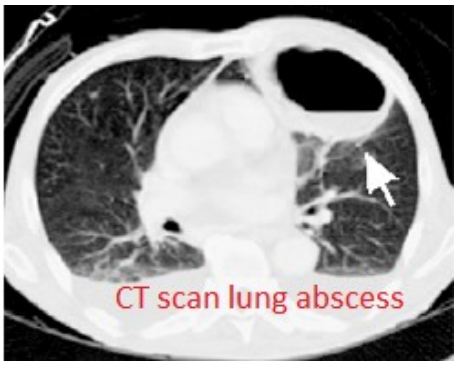
In the early stage manifestations may resemble that of pneumonia. The development of features of lung abscess within 1-2 wks after bacterial pneumonia, possible aspiration or bronchial obstruction is usually reported. Pt will have cough é sudden expectoration of massive purulent, foul smelling sputum, high grade fever & sweating é occasional haemoptysis.

Diagnosis

When pt present é the typical manifestations outlined above, the diagnosis of lung

abscess may not be difficult, but it should be confirmed by ***CXR***, by demonstrating parenchymal infiltrates é cavity containing air-fluid level. The ***Gram stain & culture of sputum*** help to make etiologic diagnosis.





Complications

- Metastatic brain abscess.
- Empyema.
- Fatal haemoptysis.
- Secondary amyloidosis.

Treatment

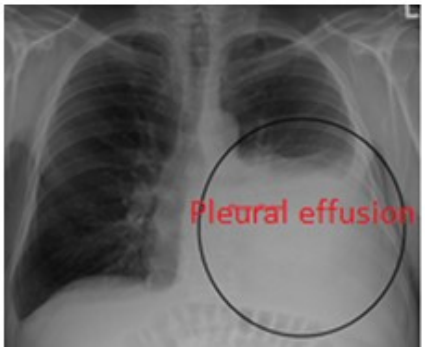
Medical Rx is the main stay of Rx. Admit the pt to hospital & the following modalities of therapy can be given:-

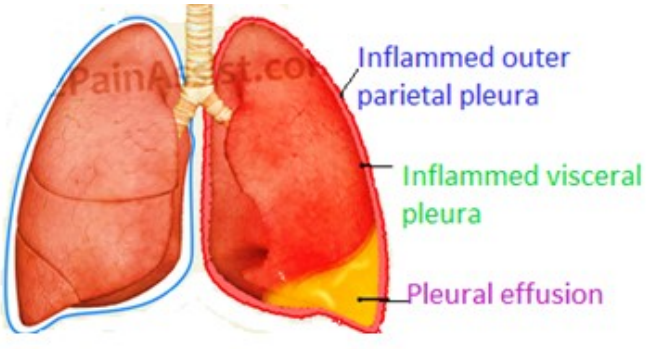
1) Antibiotics: start empirical antibiotics until lab results are available & adjust drugs accordingly. Start both Crystalline Penicillin & Chloramphenicol high doses IV. Rx should be given for 4-8 wks.

2) Drainage of abscess: postural drainage can be effective but bronchoscopic drainage may be used when airway obstruction by foreign body or mass hinders drainage of pus by postural means.

3) Surgical Rx: indicated in pt é:- persistent or massive haemoptysis, empyema or bronchopleural fistula or in case of failure of medical treatment, or in case of lung cancer.

PLEURISY & PLEURAL EFFUSION





Pleural effusion is the presence of excess fluid in the pleural space. Normally 10-20 ml of fluid is spread in a thin layer between the 2 layers of pleurae. Pleural effusio- ns are classified as transudates & exudates based on lab analysis of the fluid.

Transudative effusion: results from ⇧ in hydrostatic pressure or ⇩ in oncotic pressure, the following are some of the causes:- •HF •Liver cirrhosis • Nephrotic sy. •Myxoedema •Hypoproteinaemia.

Exudative effusion: due to pleurisy é ⇧ permeability of the pleural surface to protein. Pleurisy commonly occurs é infections as pneumonia, or infection of the oesophagus, mediastinum or sub-diaphragmatic areas or traumatic injuries or extension of infections from adjacent organs. Initially pleurisy tends to be dry but fluid starts to collect subsequently. Exudative effusion is found in association é:-•Para-pneumonic effusions •Empyema •Pulmonary embolism •Neoplasms •SLE & Rh^{ed} pleural effusion •Sub-diaphragmatic abscess •Pancreatitis •Uremic pleural effusion •Hemothorax •Chylothorax (thoracic duct injury) & •Radiation or drugs.

Clinical findings & diagnosis

Pleuritic chest pain & dyspnoea are the most common symptoms, but many pleural effusions are asymptomatic & discovered on physical examination or CXR. The underlying causes should suspected from the history. Physical examination of the affected side discloses the presence of ⇩ chest motion, absent tactile fremitus, percussion dullness & ⇩ or absent breathes sounds.

Laboratory findings & diagnosis

CXR/U/S: the X ray is the most precise way to confirm the physical findings. It demonstrates the presence of pleural fluid as homogenous opacity é a meniscus sign & obliteration of the costophrenic angle. Large pleural effusions may result in complete opacification of the hemithorax & mediastinal shift to the opposite side. ***Pleural thoracentesis:*** the best way to identify & localize pleural effusion. (aspiration of fluid) should be performed to confirm the presence of fluid & to determine its characteristics, including; colour & consistency. Clear yellow fluid described as serous, while bloody or blood tinged fluid described as sanguineous or serosanguinous, the translucent/opaque, thick fluid described as purulent. Microscopic examination of the fluid is important including; Gram stain & Culture, Total & Differential cell counts should be obtained. The predominance of PMN leukocytes suggests an underlying pneumonia é a parapneumonic effusion, while the presence of many small mature lymphocytes, particularly é few mesothelial cells, strongly suggests TB. It is important to determine whether pleural fluid is an exudate or transudate; this gives a clue to the underlying cause. Exudative effusions have at least one of the following characteristics, whereas transudates have none of these characteristics:- •Pleural fluid protein/serum protein > 0.5 (exudative) •Plural fluid LDH/serum LDH >0.6 (exudative) •Pleural fluid LDH >2/3 normal upper limit for serum LDH (exudative). If effusion is exudative, gross description of fluid, glucose level, amylase level, WBC & differential count, microbiologic studies & cytology should be obtained.

Treatment

•Therapeutic Thoracentesis should be done in massive effusion to relieve Resp. Dist. Removal should be limited to 120-1500 ml at a time.

•Definitive Rx. of pleural effusion requires identifying the underlying condition and

administration of specific therapy. TB effusion is treated é course of anti-TB drugs. Parapneumonic effusions & other bacterial infections in the pleural space should be treated é long course of antibiotics. Empyema (purulent fluid) treated é high doses of parenteral antibiotics coupled é surgical drainage (chest tube).

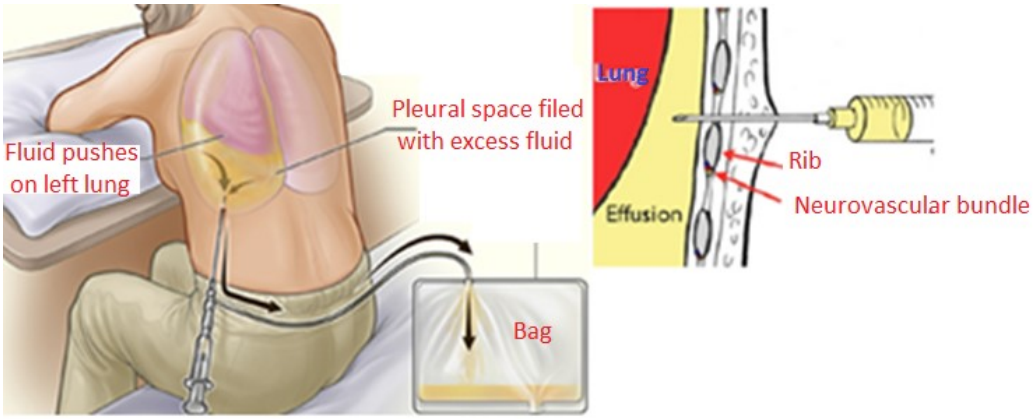
Diagnostic Thoracentesis

*__Indications:__ •Pleural effusion ẃ needs diagnostic work-up •Symptomatic Rx of a large pleural effusion.

*__Contraindications:__ •Uncooperative pt •Chest wall cellulitis at site of puncture.

*__Relative contraindication:__ •Bullous disease, e.g. emphysema •+ve EEP mechanic- al ventilation only one functioning lung •Small volume of fluid (< 1 cm thickness on a lateral decubitus film).

Technique



Chest tube size F 28 is recommended. Physical examination should guide selection of the puncture site. U/S guidance should be employed. The operator should adhere strictly to sterile technique. 1% Lidocaine used to anesthetize the skin. Needle should be inserted 1-2 ICS below the level where the percussion note becomes dull & fremi- tus is absent. When the effusion is free-flowing, a site midway between the spine & the posterior axillary line should be selected, as the ribs are easily palpated in this lo- cation. Needle should be passed over the superior aspect of the rib to ⇩ the risk of injury to the neurovascular bundle (inferior to the rib).

PULMONARY HYPERTENSION

High BP that affects pulmonary arteries & capillaries in the lungs, ẃ become narrowed, blocked, or destroyed, this make it harder for blood to flow through the lungs & ⇧ pressure within the arteries in the lungs, this put burden on right ventricle, ẃ must work harder to pump blood through the lungs.

Grading of pulmonary arterial hypertension*	Systolic	Diastolic	Mean
Grade 1 (Mild)	30-50	20-25	>30
Grade 2 (Moderate)	50-70	26-35	>40
Grade 3 (severe)	70-110	36-45	>50
Grade 4 (Systemic or supra systemic)	>110	46-55	>60

Hemodynamic definition

Resting mean pulm artery pressure (adults) ›30 mmHg (normally it is 8-20 mmHg).

Causes

•Liver diseases as chronic liver, liver cirrhosis. •Rheumatic disorders as scleroderma, SLE. •Lung diseases as COPD, pulmonary fibrosis. •Heart diseases as congenital heart, valvular defect, Heart failure. •Thromboembolic diseases. •Others as high altitude living, obesity & genetic predisposition in small number of pts or it may be Idiopathic.

In neonates pulmonary hypertension is not defined by a specific pressure of the pulmonary circulation & the diagnosis is confirmed regardless of the pulm arterial pressure as long as it is accompanied by Rt ⇨ Lf shunt. Persistent pulmonary hypertension of neonates is syndrome of marked pulmonary hypertension that causes hypoxemia & Rt ⇨ Lf shunt, it is seen in 1/1000 births. Causes in neonates include:- HMD. Meconium aspiration. Transient tachypnea. Congenital pneumonia. Hypoplastic lungs. Polycythaemia. Heart failure. Or Idiopathic.

Clinical picture

Symptoms usually not specific & delay in diagnosis is very common. Early present é dyspnea é activity. Late symptoms include; syncope, chest pain/pressure, leg edema (signs of RHF). In neonates: signs of respiratory distress (dyspnoea, tachypnea, inter-costal & subcostal recession, working alanasi) cyanosis & grunting.

Diagnosis

(1) ***ECHO:*** to determine right ventricular size, systolic function, estimation of right ventricular systolic pressure & EF.

(2) ***CXR & ECG:*** abnormal findings.

Management

New onset exertional dyspnea…think of pulmonary hypertension. Screen by transtho-racic Doppler ECHO but make sure you tell the cardiologist that you are thinking of PH! Definitive diagnosis is through right heart catheterization. Treat any underlying disease as: cardiac or pulmonary, hypoxemia or obstructive sleep apnea.

NEOPLASMS OF THE LUNG

Metastatic tumours are more common than primary tumours of the lungs; the com-monest primary sites being the breasts, stomach, prostate & ovary. The majority of primary lung tumours are malignant epithelial tumours collectively called bron-chogenic carcinomas (90-95%). The remaining are bronchial carcinoids, mesenchymal tumours (lymphomas, sarcomas, liomyomas, lipomas, fibromas, liomyosarcomas) & bronchial hamartomas, the last being tumours é aberrant differentiation of the bron-chial tissues. The disease is common between the age 65-75 yrs & affects men >women é M : F ratio of 2:1.

Etiology

Lung cancer kills more people than colon, breast & prostate cancer combined. Fac

tors associated é lung cancer & include:-

•**Cigarette smoking:** cigarettes contain at least 55 carcinogens & the risk of lung cancer⇧ to 20 fold for people who smoke >40 cigarettes/day. Smokers have 10 times more risk of dying from lung cancer than non-smokers.

•**Exposure to radon in underground miners** (occupational).

•**Exposures to other carcinogens**: Ni, Co, Cr, asbestos, polycyclic aromatic hydrocarbons, silica, mustard gas (world war I).

Pathologic features of bronchogenic carcinomas

Originate from bronchial epithelium & have the following types:-

•Adenocarcinoma (including bronchoalveolar carcinoma) account for 60% of bronchogenic carcinoma.

•Squamous cell carcinoma accounts for 25-30%.

•Small cell (oat cell) carcinoma accounts for 15-25%.

•Large cell carcinoma accounts for 10-15%.

•Mixed cell type (squamous & small cell or squamous cell & adenocarcinoma) account for 5-10%.

•Pleomorphic type (mixed carcinoma & sarcomatoid pattern) 0.5%.

The differentiation between small cell & non-small cell carcinoma (adenocarcinoma, squamous cell, large cell carcinoma) is very important because small cell carcinoma is responsive (at least initially to chemotherapeutic Rx). All lung neoplasms are very aggressive, invasive & widely metastasizing commonly to liver, adrenals brain & bones; they also produce bioactive hormones & other products. Cigarette smoking is closely linked to squamous cell, small cell & large cell carcinomas.

Adenocarcinoma

Is more common in women than men & develop in the periphery of the lung & is

the commonest lung cancer in non-smokers. Some adenocarcinoma arise from an area of pulmonary fibrosis or scar (old infarcts, Asbestosis, or on healed TB scars) ẃ are referred to as scar cancers. Distant organ metastases occurs in over 50% of cases, especially to the brain & have poor prognosis -the 5 yrs survival is 10-12%.

Squamous cell carcinoma

More common in males than females & strongly associated é cigarette smoking. Arise centrally in the major or segmental bronchi & spread to hilar LNs in 70-90% of cases or to distant LNs in 50-60% of cases or to viscera. Has poor prognosis - the 5 yrs survival is only 5-8%.

Small cell carcinomas

Very aggressive, early metastasizing, more common in males than females & strongly associated to cigarette smoking. Centrally located. Commonly associated é paraneoplastic syndromes & carries poor prognosis - the 5 yrs survival is only 5%.

Large cell carcinomas

Undifferentiated tumours. Occur in smokers. Central or peripheral locations. Metastasizes very rapidly.

Clinical features

The clinical features are variable. Some present é local pulmonary symptoms. Others present é symptoms referable to metastasis before pulmonary symptoms. About 10-15% of lung tumours are detected by chance (coin shaped lesion on CXR). Manifestations could be related to local obstruction, local tumour invasion, distant metastasis or ectopic hormone secretions by tumour cells (paraneoplastic sy.). Local symptoms depend on the location of tumour. When tumour is endobronchial; cough, haemoptysis, stridor, wheezes, dyspnoea & non-resolving pneumonia may predominate. Pleuritic chest pain is common é peripheral tumours.

Local tumour invasion & obstruction may result in: recurrent laryngeal nerve palsy causing hoarseness of voice. Phrenic nerve paralysis é diaphragm paralysis. Oesophageal obstruction causing dysphagia. Superior vena cava obstruction presenting é oedema of face. Pancoast syndrome is said to exist when apical lung tumour infiltrate the spinal nerves (C8-T1) causing shoulder pain & cervical sympathetic nerves causing Horner's sy. ẃ is characterized by absence of sweating, eyelid drooping & pupillary constriction on the affected side. Pericardial or pleural effusions & bronchial obstruction leading to atelectasis, pneumonia & lung abscess. The paraneoplastic sy.: occur in 10-15% of bronchogenic carcinoma, the manifestations are related to ectopic hormone secretion by tumour cells & the manifestations could be systemic, or related to different systems. The systemic symptoms as anorexia, cach-exia, weight loss & fever may occur in 30% of cases. Another third of pts may present é endocrine manifestations like hyper/or hypocalcaemia (from ectopic secretion of PTH or calcitonin), Cushing sy. (from ectopic secretion of ACTH), gynecomastia (from ectopic secretion Gonadotrophins) & inappropriate release of ADH causing sodium + water retention. Additionally pts may present é clubbing, migratory thrombophlebitis, cerebellar degeneration, neuropathies & myopathies such as Eaton-Lambert sy or myasthenia gravis, anaemia & thrombocytopenic purpura.

Diagnosis

- ***Screening:*** is mandatory for men >45 yrs & those smoking >40 cigarettes/day, screened tumours were resectable in 62% of cases while the non-screened tumours were resectable only in 20%. Screening can be done by sputum cytology (malignant cells).
- ***CXR:*** usually demonstrates solitary pulmonary nodule & about 35% of such cases are due to bronchogenic carcinoma.

•***C-T scan:*** visualize a white nodule, its size, adjacent tissue penetration, presence or absence of pleural effusion, presence or absence of metastasis to other organs; spleen, liver, adrenals.

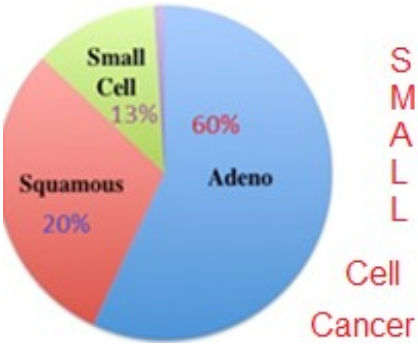
•***LNs biopsy:*** from enlarged scalene or supraclavicular LNs to detect metastasis.

•***Mediastinoscopy.***

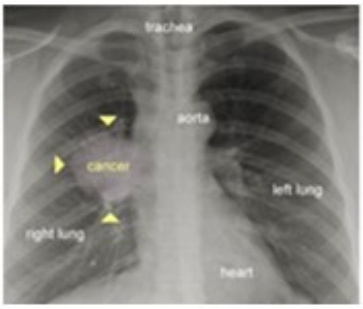
•***Bronchoscopy.***

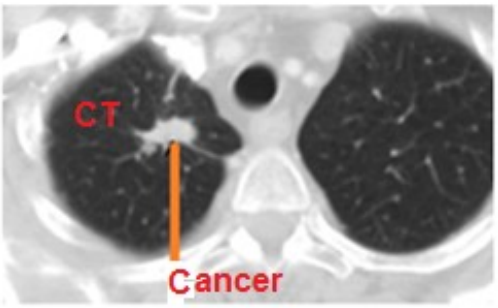
•***Thoracentesis:*** to collect fluid for cytology.

•***Pleural biopsy:*** all are other investigations for diagnosis.



SMALL Cell Cancer





Management

•Non-small cell carcinoma: surgical excision is curative for pt é ipsilateral LN involvement but éout local/distant spread or contralateral LN involvement.

•Intrathoracic disease- radiotherapy is palliative.

•Pancoast syndrome: radiotherapy/chemotherapy.

•Extrathoracic disease: analgesics, radiotherapy, dexamethasone, obliteration of pleural cavity.

•Small cell carcinoma: by the time of diagnosis 95% of cases have metastasized. Responsive for chemotherapy +/- radiotherapy.

•Bronchial adenomas, carcinoids: need surgical resection.

CHAPTER IV

DISEASES OF THE CARDIOVASCULAR SYSTEM

- Introduction
- Rheumatic Fever
- Congestive Heart Failure
- Valvular Heart Diseases
- Infective Endocarditis
- Myocarditis
- Pericarditis & Pericardial Effusion
- Cardiomyopathies
- Hypertension
- Ischemic Heart Diseases
- Angina Pectoris
- Myocardial Infarction
- Familial Hypercholesterolemia
- Cardiac Arrhythmias
- Deep Venous Thrombosis
- Heart & Electrolytes
- Hyperventilation Syndrome
- Practical Points

INTRODUCTION

The epidemic of CVDs is accelerating globally over all regions & social classes. This is reflected in the high burden as well as the estimated escalation of those burdens over the next 2 decades. CVD contributes to a large proportion of morbidity & mortality. As many as 39% of pts é acute rheumatic fever may develop varying degrees of pan-carditis é associated valve insufficiency, HF, pericarditis & even dea- th. A number of reasons underlie the expected rise in CVDs as:-

- An overall ⇧ in the population.
- Improved life expectancy is leading to more person living to the middle age & beyond, ẃ ⇧ the risk of CVDs.
- Lifestyle transition; ⇧ urbanization, industrialization, globalization & change in nutritional habit.
- Past or current nutrition deprivation in utero & early childhood may affect cardiovascular health trend.
- Lack of weight gain in the 1st yr of life & LBW in spite of maternal weight gain have been linked to coronary disease in adult life.

The causes of CVDs in developing countries include:-

- Chronic rheumatic heart disease.
- Hypertension & IHD.
- Cardiomyopathies.
- Congenital disease.

There are indicators of ⇧ prevalence of IHD due to the existence of risk factors in some segment of population these includes:-

- Hypertension. Hypercholesterolemia
- DM. Obesity.
- Smoking.

RHEUMATIC FEVER

RF cause chronic progressive damage to the heart & its valves. The association between sore throat & RF was not made until 1880. The dramatic decline in the incidence of RF in the developed world is thought to be largely owing to antibiotic Rx of streptococcal infection, though it stated to decline before the era of antibiotic, probably due improvement of socioeconomic status. It thought that 40-60% of pts é ARF will develop RHD. The commonest valves affected are the mitral & aortic, in that order. However all four valves can be affected.

Epidemiology

Even though the overall incidence of RF & RHD in developed countries has sharply declined, RF is the commonest cause of Ht disease in the developing countries. In those countries >50% of heart diseases is accounted for RHD. Even in developing countries, the prevalence of RF & RHD varies between rural & urban areas. As many as 39% of pts é ARF may develop varying degrees of pancarditis é associated valve insufficiency, HF, pericarditis & even death. Worldwide, there are >15 million cases of RHD é 282.000 new cases & 233.000 deaths from this disease each year. The incidence in developed countries 0.5-3/100.000 & in developing countries is as high as 100-200/100.000. The overall mean incidence of RF worldwide: 5-50/ 100.000. The age 5-15 yrs are most susceptible & it is rare in age < 3 yrs. The girls are affected ›Boys. The incidence more during fall, winter & early spring. The high attack rate of group A streptococcal pharyngitis in families, institutions & military recruits is the result of contact among susceptible persons living closely enough to ensure droplet transmission. The risk factors for RF include low socioeconomic status é associated over crowded living condition. However, RF is not associated é streptococcal skin infection (pyoderma)?.

Pathophysiology

ARF is a sequel of a previous group A streptococcal infection, usually of the URT. One ß-streptococcal serotype (e.g. M types 3, 5, 18, 19, 24) is linked directly to ARF. Rheumatogenicity of GAS is important factor as not all GAS pharyngitis is associated é development of RF. RF follows Lancefield β haemolytic streptococcus pharyngitis within the interval of 2-3 wks. The mechanism is elusive, but the followings are proposed ones:-

- Dysfunction of the immune response.
- Antigenic mimicry: similarity between the carbohydrate moiety of GAS & glycoproteins of heart valve. Molecular similarity between some streptococcal antigens & sarcolemma or other moiety of human myocardial cells.
- Several host related factors have been identified to have operated in relation to specific genetic function & difference in the immune response of individuals.
- The disease characterized by an exudative & proliferative inflammatory lesion of the connective tissue especially that of the heart, joints, blood vessels & subcutaneous tissues.

Clinical manifestation

ARF is associated é 2 distinct patterns of presentation:-

- First pattern of presentation is sudden onset, typically begins as polyarthritis 2-6 wks after streptococcal pharyngitis & usually characterized by fever & toxicity.
- Second pattern is insidious or subclinical & the initial abnormality is mild cardities. The age at onset influence the order of clinical picture, younger children tend to develop cardities first, older pt tend to develop arthritis first.

Diagnosis

RF is mainly a clinical diagnosis. *No single diagnostic sign or specific laboratory test*

available for diagnosis. 50% of cases of RHD **don`t remember** having ARF. Diagnosis requires high index of suspicion. Jones criteria developed by the American Hea- rt Association is used to make the diagnosis include the following;

Major criteria	Minor criteria
Pancarditis (pericarditis, endocarditis, myocarditis)	Fever
Polyarthritis	Arthralgia
Sydenham Chorea	Prolonged PR interval
Subcutaneous Nodules	Increased ESR or CRP*
Erythema marginatum	Leukocytosis

2 major or 1 major + 2 mino
must be present for diagnosis of Rheumatic Fever

Diagnosis of ARF *requires 2 major or 1 major + 2 minor criteria*

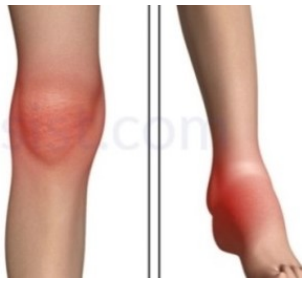
1) Cardities (pancarditis here): occurs in as many as 50% of pts & may manifest as; (a) New murmur (b) Cardiomegaly (c) CHF (d) Pericarditis é/éout a pericardial rub & resolve éout constriction (e) Valvular disease: mitral & aortic valves are commonly af- fected. Healing of rheumatic valvulitis will lead to fibrous thickening & adhesion, re- sulting in progressive valvular damage. But, about 80% of mild valv- ulitis would re- solve. There is a risk of developing endocarditis on a damaged valve.

2) Migratory polyarthritis: occurs in 75% of cases, fleeting arthritis é all signs of in- flammation on the joint, the larger joints are mainly affected, lasts for 2-3 days then migrate to other joints. Arthritis do not progress to chronic disease. Involves many joints at a time.

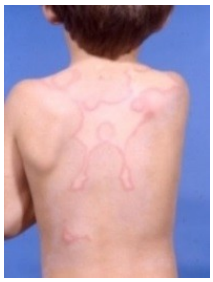
3) SC nodules: occur in 10% of pts & are oedematous fragmented collagen fibres. They are firm painless nodules on the extensor surfaces of wrists, elbows & knees, seen over bony prominence or in heart (Aschoff nodules) & associated é cardities.

4) Erythema marginatum: occurs in 5% of cases. The rash is serpiginous & long last- ing, occur in the trunk or lower limbs, clear from centre & spread peripherally.

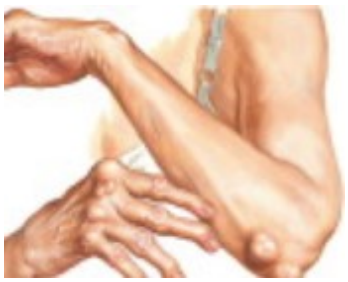
5) Sydenham's chorea: "St Vitus 'dance", is characteristic movement disorder occ-urs in 5-10% of cases. Consists of rapid purposeless movements of face & upper extremities. Onset may be delayed for several months to years & may cease when the pt is asleep & seen mainly in girls.



Typical appearance of Arthritis



Erythema Marginatum



Subcutaneous Nodules

Laboratory studies

No specific confirmatory laboratory tests exist. However, several laboratory findings indicate continuing rheumatic inflammation. Some are part of the Jones minor criteria. ASOT is +ve in 80% of cases. Anti DNAase β & Anti hyaluronidase +ve in 95% of cases. Isolate GAS via throat culture ẃ has 20-40% yield. ESR &CRP. Leucocytosis may be seen. Anaemia from suppression of erythropoiesis. Prolonged P-R interval in 25% of all cases but is neither specific nor diagnostic.

Treatment

1. Treat group A streptococcal infection: regardless of organism detection, all pts é ARF should be given appropriate antibiotic. Penicillin V 250.000 u/5 ml or Cliacil 1.200.000 u/tab., at a dose of 100.000 u/Kg/day ÷ 4 for 10 days. Or Benzathin Penicillin 1.2 million u IM as single dose, or Erythromycin 500 mg PO QID for 10 day (for Penicillin allergic pt).

2. Therapy for manifestation of ARF

Arthritis: ASA is given at dose 2 gm 4 times/day for 4-6 wks, at a dose of 100 mg/ Kg/day÷4, maximum dose 10gm/day **+** antacid. ⇩ the dose according to the resu- lts of ESR, or after 1 wk to 50% & continue for 1 month. No indication for steroids.

Cardities: severe cardities é CHF should be treated é prednisolone 60-80 mg/day, I mg /Kg/day÷4 for 4 wks, to be tapered as pt improves. Start ASA during tapering phase to be given for 4-6 wks, but both have no influence on future development of valvular heart disease.

CHF: conventional Rx such as Digoxin & Diuretics.

Sydenham's chorea: the majority of cases are self-limiting, but in symptomatic pt Benzodiazepines (Diazepam) or Phenothiazines (Haloperidol) may be helpful in contr-olling symptoms.

3. Complete rest in bed 10 days.

4. Administer secondary prophylaxis: indicated for all pts é RF. Benzathin Penicillin is the 1st choice for better compliance & longer prevention, 1.2 million IU IM/4 wks, but if there is high risk of recurrence, it can be given every 3 wks, or Penicillin V syrup (250 mg twice/D), or Sulfadiazine (1 gm/D), or Erythromycin for those allergic to Peni-cillin. In pt é an established RHD, it is advisable to be given life long.

Epidemiology	• Peak incidence age 5-15 • Twice as common in girls	
Clinical features	Major	•Joints (migratory arthritis). • Carditis. •Nodules (subcutaneous). •Erythema Marginatum. •Sydenham chorea.
	Minor	•Fever. •Arthralgia. • Elevated ESR./ C- reactive protein. •Prolonged PR interval.
Late sequelae	Mitral regurgitation/stenosis	
Prevention	Penicillin for group A strept (pyogenes) pharyngitis	

CONGESTIVE HEART FAILURE

Heart failure is a clinical syndrome characterized by inadequate systemic perfusion to meet the body's metabolic demands as a result of abnormalities of cardiac structure or function. This may be further subdivided into systolic or diastolic HF:

oSystolic HF: there is reduced cardiac contractility.

oDiastolic HF: there is impaired cardiac relaxation & abnormal ventricular filling.

In HF the body, sensing inadequate organ perfusion, activates multiple systemic neurohormonal pathways ẃ compensate initially by redistributing blood flow to vital organs, but later exacerbate the pt's symptoms & lead to deterioration.

Etiology

HF is the most common reason for hospitalization in adults ›65 yrs old. About 30% of pts experiencing MI also develop HF. The most common cause of HF is systemic hypertension (60-70% of pts). The following are some of the underlying causes:-

- ⇩ ***Of the contractile function of the heart:*** as é valvular or coronary heart disease (myocardial ischemia, MI) or myocardial disease (cardiomyopathy & myocarditis).
- ⇧ ***Of the afterload:*** acute systemic hypertension.
- ***Abnormalities in the preload:*** as é excessive or reduced preload.
- ⇩ **Compliance**: as é constrictive pericarditis or restrictive cardiomyopathy.

Preload: is the end diastolic pressure that stretches the Rt or Lf ventricle to its greatest geometric dimensions under variable physiologic demand. It depends upon venous return & compliance.

Afterload: is the force needed to eject blood into circulation. The pressure in ventricles must be ›the systemic & pulm pressures to open the aortic & pulm valves.

The afterload ⇧ é valvular diseases.

Precipitating factors for CHF

These are relatively acute disturbances that place an additional load on a myocardium that is chronically & excessively burdened. In compensated state pt is asymptomatic; however as pt have little additional reserve, he become symptomatic in the presence of these ppt factors. Knowing the precipitating factors is important because most of the time they are treatable & the cardiac function improves when these precipitating factors are treated or avoided. The most important precipitating factors may be represented é the mnemonic, "HEART FAILES";

•H- Hypertension (systemic) •E-Endocarditis (infections) •A-Anaemia •R-RF & myocarditis •T-Thyrotoxicosis & pregnancy •F-Fever (infection) •A-Arrhythmia •I-Infarction •L-Lung infection •E-Embolism (pulmonary) •S-Stress (Emotional, Physical, Environmental, Dietary & Fluid excess).

Pathophysiology

In Lf ventricular systolic dysfunction, regardless of the aetiology, the COP is low & pulmonary pressures are high, leading to pulmonary congestion. As a result, a series of adaptive mechanisms are activated. Initially, as direct result of inadequate COP & systemic perfusion, the body activates several neurohormonal pathways in order to ⇧ the circulating blood volume & é continuous neurohormonal stimulation, the LV undergoes remodelling é LV dilatation & hypertrophy, such that stroke volume is ⇧ éout an actual ⇧ in ejection fraction (EF). This is achieved by myocyte hypertrophy & elongation. However, LV chamber dilatation causes ⇧ wall tension, worsens subendocardial myocardial perfusion & may provoke ischemia in pt é coronary Atherosclerosis. Furthermore, LV chamber dilatation may cause separation of the mitral leaflets & mitral regurgitation é worsening of pulmonary congestion. Enhanced neurohormonal stimulation of the myocardium also causes apoptosis or programmed cell death, lead-

ing to worsening of ventricular contractility.

Clinical manifestations

- **Progressive dyspnoea:** ẃ initially occurs é exertion & later occurs at rest. Found to be the most sensitive complaint, yet the specificity for dyspnoea is **<** 60%,
- **Orthopnoea & PND:** specific symptoms, sensitivity is only 20-30%.
- **Cough:** productive of pink, frothy sputum is highly suggestive of CHF.
- **Peripheral oedema & ascites.**
- **Nonspecific complaints:** easy fatigability, light headiness, malaise, anxiety.
- **Past medical history**: of RF, Alcohol use, Hypertension, Angina, previous history of MI & +ve family history.

Physical findings

- ***Tachycardia, Tachypnea, signs of RD***: use of accessory muscles of respiration.
- ***Jugular venous distension*** frequently present & engorged neck veins.
- ***Pulses alternans:*** weak &strong pulse indicative of depressed LV function.
- ***Wheezing or rales:*** may heard, bilateral basal dullness may elicited.
- ***Apical impulse frequently displaced:*** laterally.
- ***Cardiac auscultation:*** may reveal aortic or mitral valvular abnormalities, S3 or S4.
- ***Skin may be diaphoretic or cold,grey &cyanotic peripheral oedema*** may noticed.

Grades of CHF

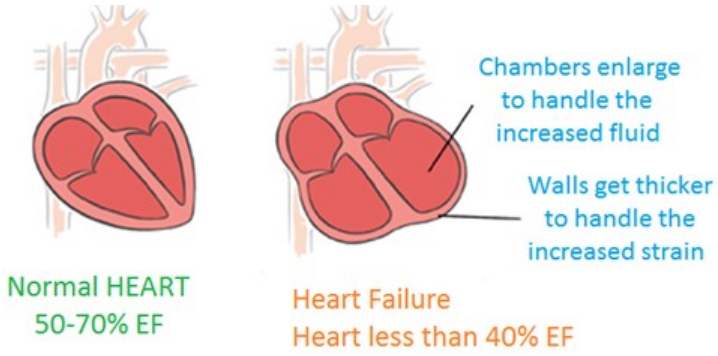
Grade	Symptoms
I	No symptom limitation é ordinary physical activity.
II	Ordinary physical activity somewhat limited by dyspnoea (i.e. long distance walking, climbing 2 flights of stairs).
III	Exercise limited by dyspnoea at mild workloads (i.e. short distance walking, climbing one flight of stairs).
IV	Dyspnoea at rest or é very little exertion.

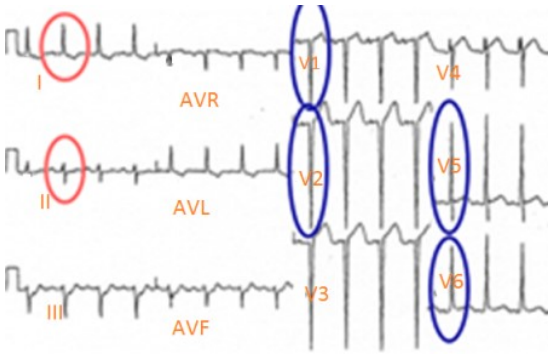
Diagnostic workup

- ***CXR***: cardiomegaly, pulmonary oedema & pleural effusion.
- ***ECHO***: Key indicator for diagnosing. The EF is the % of blood that is pumped out of the heart during each beat. EF normally 50-70%, ⇩ é HF to ‹40%. ECHO also help to detect valvular abnormalities, ventricular dysfunction, cardiac tamponade, pericardial constriction & pulmonary embolus.
- ***ECG***: useful in diagnosing concomitant cardiac ischemia, prior MI, cardiac dysrhythmias & LVH.

☆ **To Diagnose *LVH*** you can use the following criteria*:-*

R wave in V_5 or V_6 + S wave in V_1 or V_2 are ›35 mm & the R wave in AVL ›13 mm.

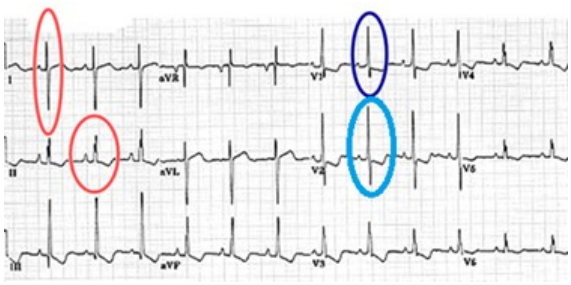




The above ECG strip shows left axis deviation (R wave is +ve in lead I & -ve in lead II) & ***LVH*** (there are tall R waves in V_5,V_6. Deep S waves in V_1,V_2). The deep S waves seen in leads over the Rt ventricle are created because the heart is depolarizing (away from leads V_1, V_2).

☆ **To Diagnose *RVH*** you can use the following criteria:-

Rt axis deviation + R wave in V_1 › 7 mm tall.



The above ECG strip shows Rt axis deviation (R wave -ve in lead I & + ve in lead II)

& there are tall R waves >7 mm tall in V_1, V_2 = RVH.

☆ **To Diagnose *Left Atrial Enlargement,*** you can use the following criteria:-

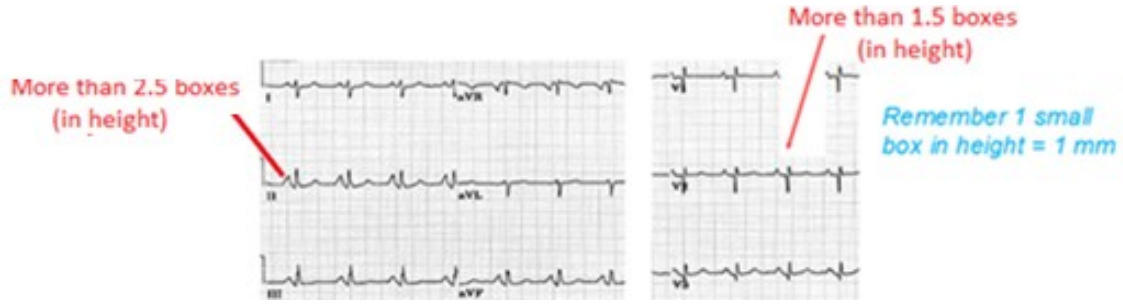
Lead II: P wave >0.04 sec. (>1 small box) between notched peaks, or Lead V_1: -ve deflection >1 box wide X 1 box deep.

Take a look at this ECG. What do you notice ?

The P waves in lead II are notched (>1 small box) & in lead V_1 they have deep & wide -ve deflection (>1 box wide X 1 box deep).

☆ **To diagnose *Right atrial enlargement,*** you can use the following criteria:-

Lead II: P > 2.5 mm, or Lead V_1 or V_2: P > 1.5 mm



The next ECG strip shows RAD (R wave -ve in lead I, +ve in lead II), peaked P wave P> 2.5 mm in lead II, P >1.5 mm In Lead V_1, V_2.

Management

(A) General measures

Dietary sodium restriction: should be implemented in all pts é CHF to < 3 gm/day. ***Activity & life style modification***: meals should be small in quantity but more frequent, reduce anxiety/emotional stress, avoid excess physical exertion (exercise may be advised within the limit of the pt's cardiac function), Wt loss is encouraged in obese pts, cessation of smoking & avoidance of other CVD risk factors.

(B) Control of the congestive state

Diuretics: useful in relieving congestion & reduce or prevent oedema. Most pts é HF have some degree of symptomatic congestion & benefit from diuretic therapy. Usually a loop diuretic is required é the addition of thiazide diuretic in pts refractory to the loop diuretic alone. *Furosemide*: initial dose 20-40 mg PO 1-2 tab daily or 20 mg IV, maximum dose 400 mg PO/day or 80 mg IV/day. *Hydrochlorothiazide*: initially 25 mg PO/ day, maximum dose 100 mg PO/day. The Loop & Thiazide diuretics are useful for symptomatic relief, however they have not been shown to improve survival. Their side effects include: azotaemia, hypokalaemia, metabolic alkalosis & elevation of neurohormones. *Spironolactone*: is an Aldosterone inhibitor, reduces mortality in pts é advanced HF. This drug should be reserved for pts é moderate to severe HF (class IV symptoms), 25 mg PO/day or every other day, maximum dose 50 mg PO BID. Side effects; Hyperkalaemia is common so monitoring K^+ level is essential. As a result, this drug should not be used in pts é a creatinine level >2.5 mg/dl. Gynecomastia in men is another side effect of this drug.

(C) Enhancement of myocardial contractility

Digoxin: is a drug ẃ has: *Inotropic effect;* acts by inhibiting the Na^+- K^+ ATPase &⇧ intracellular Ca^{++}, this ⇧ myocardial contractility. In addition to *Neurohormonal modulation* of centrally mediated parasympathomimetic & sympatholytic activity, by doing so it blocks the AV node & delays AV conduction. Initially 0.125 mg PO/ day, maximum 0.25 mg PO/ day, tab 0.25 mg, syrup 0.05 mg%, amp 0.5 mg/2 ml. Start é digitalizing dose over 24 hrs, 20 ug/Kg/day, 1^{st} dose is 50%, after 8 hrs 2^{nd} dose 25%, after 8 hrs 3^{rd} dose 25%, then maintenance dose equal to ¼ of the digit-alizing dose (5ug/Kg÷2/day). It take about 1 wk to digitalize pt. The IV digitalizing dose is 80% of oral dose. The tab. is well absorbed through GIT & initial effect can

be seen within 30 minutes after oral administration, adjust the dose in pt é renal failure, give ½ total digitalizing dose immediately & the succeeding 2 quarter doses at 12 hrs intervals & do ECG monitoring. The dose of digoxin almost never ⇧ but may ⇩ in presence of toxicity or RF. The signs of cardiac toxicity include; arrhythmia, bradycardia, AV block, PVCs, (premature QRS complex of abnormal shape & duration), also hypokalaemia & hypercalcaemia ⇧ the toxicity of digoxin & in such condition discontinue the drug. The use of digoxin can improve symptoms, reduce the duration & the need for hospitalization in pt é HF, but has no effect on long term survival. Digoxin is renal excreted &so the dose adjustment is necessary in RF as mentioned above. A low dose of the drug (0.125mg daily) should be prescribed, especially in women. The Digoxin use is recommended for pt é LV systolic dysfunction, particularly if they have AF & it is relatively contraindicated in some cardiac disease e.g. cardiac outflow obstruction in MS (in absence of AF) or corpulmonale. Because of its narrow window of safety, digoxin is associated é different side effects including:- anorexia, nausea, vomiting, wt loss, neuralgia, delirium, yellow vision, gynecomastia, arrhythmias of different types. If toxicity occurs, drug should be withheld & pt to be observed for some days before reinitiate é a lower dose. Electrolyte disturbances should be suspected & one should also give KCl, as hypokalaemia ⇧ toxicity.

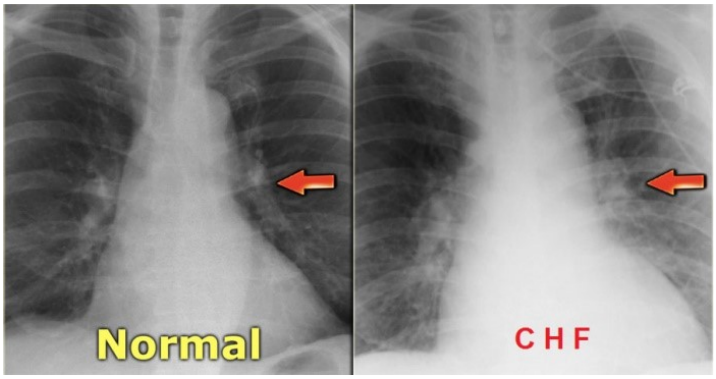
Vasodilators: may be useful in pts é severe acute HF who demonstrate systemic vasoconstriction despite ACEIs therapy. The vasodilators reduce the peripheral resistance & after load & improve cardiac performance. Hydralazine: initially 25 mg PO TID, maximum dose 150mg PO QID. Isosorbide Dinitrate: initially 10 mg PO TID, maximum dose 80 mg PO TID. Hydralazine & nitrates in combination are effective afterload reducing agents used in ACEIs intolerant pts.

(D) Prevention of deterioration of myocardial function

The following drugs prevent deterioration in myocardial function by inhibiting the neurohumeral mechanism ẃ causes cardiac remodelling & progression of HF. ***1)Angiotensin converting enzyme inhibitors:*** cause reduction of the afterload & neurohormonal modulation as; *Captopril, Enalapril*, etc., have been shown to improve mortality, symptoms & hospitalizations. The dose of ACEIs should be titrated to the maximum that can tolerated symptomatically or the target dose. Initial dose of Captopril 6.25 mg PO/day or every other day & its maximum dose 50-100 mg PO QID. Enalapril 2.5 mg PO BID & maximum dose 10-20 mg PO BID. The side effects of ACEIs include, angioedema, ARF in pt é bilateral renal artery stenosis. Other side effect is cough. The first two side effects are serious & necessitate immediate cessation of the drug. ACEIs are contraindicated é; angioedema, anuric RF, pregnancy & hypotension.

2) Angiotensin-II Receptor blocker: useful in pts who cannot tolerate ACEIs due to different side effects like cough, angioedema & leukopenia. *Losartan*: 25-50 mg 1-2 tab/day.

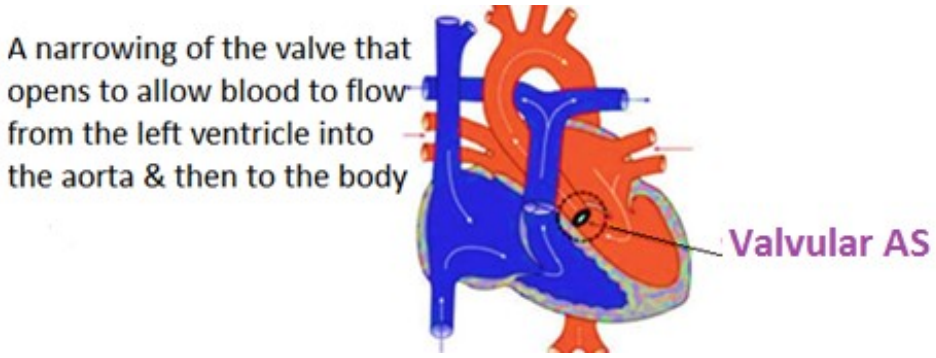
3) ß-adrenoreceptors blockers: administration of these drugs é gradual ⇧ of the dose has been reported to improve symptoms of HF, the need for hospitalization & reduce mortality. Indicated for moderate to severe HF. Contraindicated in unst-able HF, hypotensive states, severe fluid overload, sinus bradycardia, AV block & asthma. *Metoprolol*: initial 6.25 mg PO BID & maximum dose 75 mg PO BID.



VALVULAR HEART DISEASES

VHD from chronic RF is still the commonest cardiac disease in the developing world, occurring at the younger age. It causes significant morbidity & mortality due to lack of appropriate preventive & therapeutic intervention. Generally, pt é stenotic valvular lesion can be monitored clinically until symptoms appear. In contrast, pts é regurgite valvular lesions require careful ECHO monitoring for LV function & may require surgery even if no symptoms are present. Aside from antibiotic prophylaxis, very little medical Rx is available for pts é valvular heart disease. Surgery is the Rx for most symptomatic lesions or for lesions causing LV dysfunction even é absence of symptoms.

AORTIC STENOSIS



AS could be caused by: •Rheumatic cardities. •Congenital stenosis of aortic valve. •Senile/calcific AS ẃ is idiopathic results in calcification & degeneration of the aortic leaflets. •Persons born é bicuspid aortic valve are predisposed to develop AS. The aortic valve area must be reduced to one-fourth of its normal size before significant changes in the circulation takes place. Occasionally, the obstruction does not involve the aortic valve itself but consists of narrowing of the passage either above (supravalvular) or below it (subvalvular) caused by accumulation of fibroela- stic tissue, or calcification.

Clinical features

Initially there is an extended latent period during ẃ the pt is asymptomatic. This is

followed by the classic symptoms of AS including:-

- Angina.
- Exertional syncope.
- Dyspnoea & PND.

Physical examination

Systolic ejection murmur at 2nd LICS that radiates to the neck. In mild AS, the murmur peaks early in systole, but as the severity of AS ⇧, the murmur peaks progressively later in systole & may become softer as COP ⇩. As the stenosis worsens, the aortic component of the 2nd HS may become diminished. The timing & amplitude of the carotid pulse correlate é the severity of AS. Later in the disease, the carotid upstrokes become diminished & delayed.

ECHO: provides an accurate assessment of AV area & transvalvular gradient & also can be used to estimate LVH & EF.

CXR: may demonstrate valve calcification.

Management

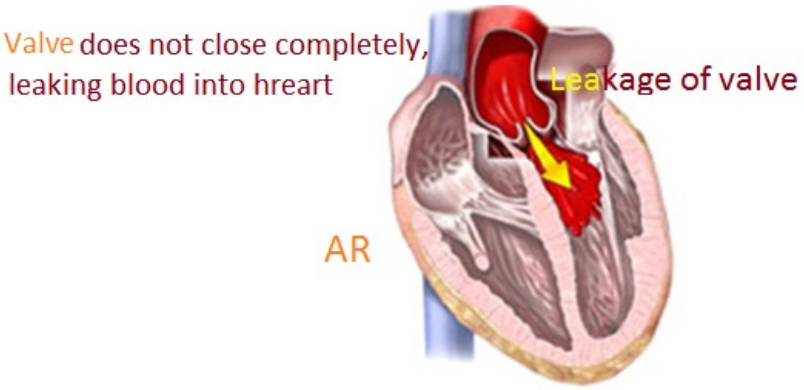
Medical Rx: is not effective & Rx é Digitalis or cautiously administered diuretics may only reduce symptoms. Pts é severe AS should limit vigorous physical activity. Pts é AS are at moderate risk for development of endocarditis & should receive endocarditis prophylaxis before selected procedures.

Surgical Rx: aortic valve replacement is the only effective Rx.

Prognosis

The survival of pt é AS is nearly normal until the onset of symptoms, when survival rates ⇩ sharply. Although the rate of progression of AS is variable & difficult to predict, about 75% of pts é AS will be dead 3 yrs after the onset of symptoms if the aortic valve is not replaced.

AORTIC REGURGITATION



Defect in aortic root or aortic leaflets, preventing their normal closure. In chronic AR, the stroke vol-ume⇧, ẃ in turn causes systolic hypertension, ⇧ pulse pressure & ⇧ afterload ẃ may be as high as that occurring in AS. The pt may be asymptomatic until severe LV dysfunction occur.

Causes

•Endocarditis. •Rheumatic fever. •Collagen vascular diseases. •Aortic dissection. •Syphilis. •Bicuspid aortic valves are also prone to AR.

Clinical features

The initial signs are subtle & may include ⇩ functional capacity or fatigue. As the dis-ease progresses, the typical presentation is that of left-sided heart failure:-

•Orthopnoea •Dyspnoea •PND.

Physical examination

Diastolic blowing murmur heard along the LSB is characteristic of AR.

Diastolic rumble may also be heard over apex.

Peripheral signs of hyperdynamic circulation indicate severe disease, some of these signs include:- oWide pulse pressure oCollapsing pulse oQuincke's pulse (alternating blanching & erythema of the nail bed é gentle pressure applied). oDe musset's sign (head bobbing) oPistol shot over the femoral artery.

ECHO: provides information about aortic valve & aortic root size & semi quantitative estimate of the severity of AR & information about LV size & function.

Management

Systolic dysfunction is initially reversible é full function after AV replacement. Over time, however, progressive chamber enlargement é ⇩ contractility make recovery of LV function impossible, even é surgery.

Medical Rx

•**Diuretics** •**Salt restriction** •**Digoxin**: may be indicated in pt é severe regurgitation & dilated LV éout frank LV failure **Vasodilators**: afterload reduction é vasodilators has been shown to improve LV performance & reduce AR. The ACEIs are the preferred vasodilators. Rx é long acting **Nifedipine** in particular has been shown to delay the need for surgery by 2-3 yrs. Endocarditis prophylaxisis essential for all pts.

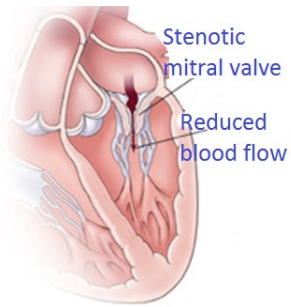
Surgical Rx

Aortic valve replacement is definitive Rx for pt é AR. Two important points to consider in deciding timing of surgery:-

a) Pt é AR usually don't become symptomatic until after the development of myocardial dysfunction.

b) When delayed too long, surgical Rx often does not restore normal LV function. Therefor appropriate timing is necessary for surgical intervention. AR should be corrected if the symptoms are more than mild.

MITRAL STENOSIS



MS is squealy of RH primarily affecting women. MS has a progressive, life long course that is slow & stable in the early years é rapid acceleration later in life. It is very common in the developing countries manifesting below the age of 20 years. Elevated left

atrial pressure eventually causes pulmonary vasoconstriction, pulmonary hypertension & compromise of right ventricular function.

Clinical features

Many pts remain asymptomatic until AF develops or until pregnancy occurs, when there is ⇧ demand on the heart. Symptoms are generally those of left sided HF.:-

•Orthopnoea •Dyspnoea •Fatigability & PND.

Pt may also present é haemoptysis, signs of right-sided HF & embolic like stroke.

Physical examination

Apical rumbling, mid-diastolic murmur are characteristic & will immediately follow an opening snap, if present. The rumble is loudest in early diastole, but in pt é mild MS or MS é low COP, the murmur may be difficult to hear. It can accentuated by placing the pt in the left lateral decubitus position & using the bell of the stethos- cope. Brief exercise (as walking in the hallway) may also accentuate the murmur. Loud 1st HS is common.

A right ventricular lift, elevated neck veins, ascites & oedema are later signs of right ventricular overload é pulmonary hypertension.

Complication

•AF •Thromboembolism •Right sided heart failure.

Investigations

ECHO: the study of choice for diagnosing &assessing severity of MS.

CXR: may show left atrial enlargement & sign of pulmonary congestion.

Management

Asymptomatic pt.

•Annual evaluation (history, physical exam, CXR & ECG) •Endocarditis prophylaxis •Prophylaxis for rheumatic fever

Symptomatic pt.

Diuretics are helpful in reducing left atrial pressure.

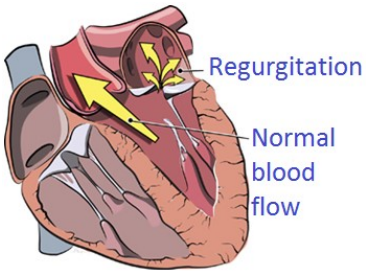
Digoxin indicated for pt é AF to control HR, since tachycardia will further ⇩ left ventricular filling, ⇩ COP & ⇧ left atrial pressure.

Anticoagulants warfarin indicated in pt é AF.

Surgical Rx

Improves survival & reduce symptoms, include, open commissurotomy, mitral valve reconstruction or replacement.

MITRAL REGURGITATION



Causes

•Rheumatic fever •Infective endocarditis •Degenerative valvular disease (mitral valve prolapse) •MI affecting papillary muscles.

Pathophysiology

Chronic MR is a state of volume overload leading to development of LVH. The Lf. atrium also enlarges to accommodate the regurgitate volume. This compensated phase of MR varies in duration but may last many yrs. The prolonged state of volume overload may eventually lead to decompensate MR. This phase is characterized by impaired LV function,⇩ EF + pulmonary congestion.

Clinical features

•Left sided HF: Fatigue, Excertional dyspnoea, Orthopnoea are the most common.

•Right sided HF é painful hepatic congestion.

•Peripheral oedema may occur in pt who have associated pulm hypertension.

Physical Examination

Soft 1st HS & wide split of the 2nd HS may present.

S3 gallop indicates severe disease but does not necessarily indicate HF. There may be displacement of the LV impulse.

Holo systolic murmur that may radiate to axilla & upper sternal border or the subsc-apular region.

Investigations

**ECHO:* used to determine the aetiology & morphology of MR, ẃ are important in de-termining suitability for M. valve repair.

**CXR:* enlargement of LA & LV, pulmonary venous congestion, interstitial oedema & Kerley-B lines.

Management

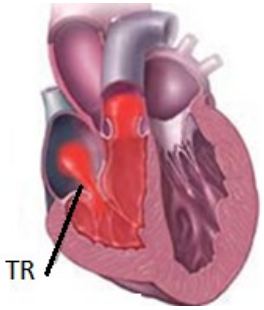
Medical treatment

- Diuretics.
- Salt restriction.
- Digoxin: may be indicated for pt é sever MR & dilated LV éout frank LVF.
- Vasodilators; afterload reduction é vasodilators has been shown to improve LV per-formance. ACEIs are the preferred vasodilators.
- Rx of AF if it occurs.
- Endocarditis prophylaxis is important essential.

Surgical Treatment

MV replacement is the definitive Rx. In pt é chronic MR, LV damage can occur wh-ile the pt remains asymptomatic. Therefore, surgery is indicated if LV dysfunction has begun to develop, even in the absence of symptoms. Pt é MR who is asymptomatic & whose LV function are normal are not considered for surgical Rx.

TRICUSPID REGURGITATION



TR is functional & secondary to marked dilatation of tricuspid annulus. It`s most common cause is pulmonary hypertension as a result of:-

☆ **LHF or pulmonary parenchymal/vascular disease**

☆**Less common causes include; Rheumatic Heart, Right side MI, or Endocarditis.**

Clinical features

Symptoms of right sided heart failure, peripheral oedema & ascites.

Pt will have prominent jaguar venous distension.

Presence of Holosystolic murmur at the LLSB.

Pulsatile liver & prominent ascites than oedema is common.

Diagnosis

•**Clinical examination** •**ECHO:** very useful study & differentiates 1ry from 2ry TR.

Management

- Rx of the underlying cause of HF usually reduces the severity of functional TR.
- Surgical treatment as indicated for primary TR.

MITRAL VALVE PROLAPSE

MVP occurs when varying portions of one or both leaflets of the mitral valve exte-nd or protrude abnormally above the mitral annulus into the left atrium. MVP has

different causes as redundant or excessive MV tissue, or congenital diseases as Marfan's sy or Osteogenesis Imperfecta. Although the prevalence of MVP was once thought to be as high as 15% of the general population, more recent studies using new ECHO criteria have suggested a prevalence of approximately 2.4%.

Clinical features

MVP is more common in females & in the age group of 14-30 yrs. The clinical course is often benign. Most pts are asymptomatic, may remain so for entire lives. Some pts may manifest é features of MR. Arrhythmias like PVCs & ventricular tachycardias may occur as complications. The mid-systolic click, often accompanied by late systolic murmur, is the auscultatory hallmark of MVP.

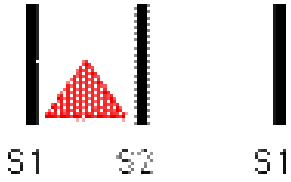
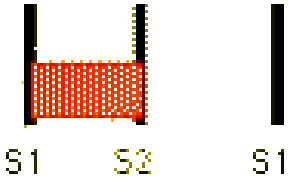
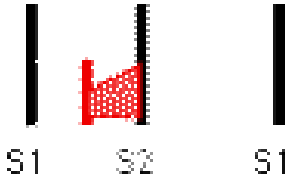
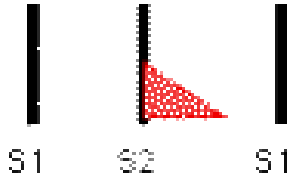
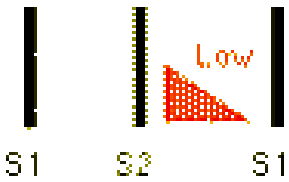
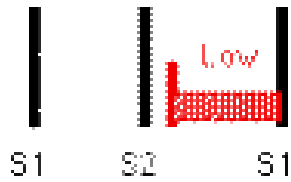
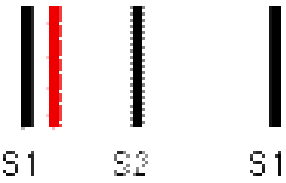
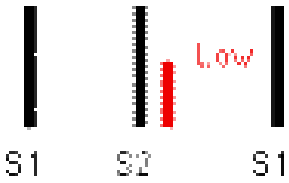
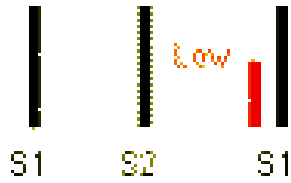
Management

Asymptomatic pts may need only reassurance. Symptomatic pt é thickening of MV will need endocarditis prophylaxis. ß-blockers sometimes may relive chest pain. Pt é severe symptoms from secondary MR, surgical Rx may be needed (mitral valve repair & or rarely replacement).

SUMMARY of VALVULAR HEART DISEASES

Even though the definitive Rx for most valvular heart diseases is surgical intervention to correct the underlying valvular abnormality. The onset of symptoms in the developing world occurs at an earlier age because of repeated attack of recurrent rheumatic fever. ⇧ Lf atrial pressure &⇩ COP produce the symptom. Therefore both 1ry & 2ry preventions are paramount importance to ⇩ the morbidity & mortality. In fact great progress has been made in improving rates of morbidity & mortality in pts é valvular Ht disease. Successful Rx of pts é valvular Ht disease requires an evidence-based approach to ECHO & to surgical intervention. ECHO should assess not only the valvular lesion but also the compensatory changes of the heart in

response to the lesion. The timing of surgical Rx often correlates é outcome. Most pts é acquired valvular Ht disease are at risk for endocarditis.

Systolic Ejection  Innocent/Physiologic Aortic/Pulmonic Stenosis	**Pansystolic**  Mitral/Tricusp Regurgitation	**Systolic Click Late Systolic**  Mitral Valve Prolapse
Early Diastolic  Aortic Regurgitation	**Mid Diastolic**  Mitral/Tricusp Stenosis	**Opening Snap Diastolic Rumble**  Mitral Valve Stenosis
Ejection Sound  Aortic Valve Disease Aortic/Pulmonic	**S3**  Normal in Children Heart Failure	**S4**  Physiologic Various Diseases

INFECTIVE ENDOCARDITIS

Infection of the endocardial surface of the heart. The intracardiac effects of this infection include; severe valvular insufficiency, ẃ may lead to intractable CHF & myocardial abscesses. IE affects not only the heart, but also produces a wide variety of systemic signs & symptoms through several mechanisms, including both sterile & infected emboli & a variety of immunological phenomena. Common site of infection is heart valve, but may occur at septal defect or on chordae tendinae or in the mural endocardium.

Epidemiology

Incidence: **<**1% of the general population & it is more common in men, median age 50 yrs. Population groups at greater risk include the following:-

•RF history (most often involving aortic & mitral valves). •Hemodialysis. •Previous history of endocarditis or Pt é prosthetic valves. •IV drug users; 30% risk in in 2 yrs.

Etiology

Streptococcus viridans: is a bacterium ẃ is a normal flora of oral cavity. Accounts for 50-60% of cases of SIE. Group D streptococci; the source for this bacterium is the GIT or genitourinary tract. Most cases of IE due to this organism are SIE.

Staph Aureus is the leading cause of prosthetic valve IE & endocarditis in IV drug abusers. 35-60% of staph bacteraemia is complicated by IE. In **>** half of cases of IE due to staph aureus occurs in the absence of underlying valvular disease, the mortality rate may range 40-50%.

Coagulase -ve Staph Aureus accounts for 30% of prosthetic valve IE & fewer than 5% of native valve endocarditis cases, causing SIE.

HACEK organisms accounts for 5% of IE. Include; Haemophilus, Actinobacillus, Cardiobacterium hominis, Eikenella corrodens, Kingella species. Usually cause SIE.

Fungus may cause IE, the most frequent cause is Candida Albicans.

Pathophysiology

All cases of IE develop from a commonly shared process include:- (1) Bacteraemia (nosocomial or spontaneous) that delivers the organisms to the valve's surface.

(2) Adherence of the organisms to valvular structures.

(3) Eventual invasion of valvular leaflets & formation of vegetations.

IE develops most commonly on the mitral valve, closely followed in descending or-der of frequency by the aortic valve, the combined mitral & aortic valves, tricuspid valve & rarely pulmonic valve. Mechanical prosthetic & bioprosthetic valves exhibit equal rates of infection. Turbulence in blood flow damages valvular surface & endocardium ẃ creates favourable situation for formation of sterile thrombus(ve-getation) made of platelets & fibrin. The microorganisms that most commonly pr-oduce IE (strept viri-dans, staph aureus, group A, C, D strept & enterococci) resist the bactericidal action of complement. The result of an invasive procedure gives access to the bacteria to adhere to the sterile platelet/fibrin vegetation. Most cases of SIE are secondary to the bacteraemia that develop from the activities of daily living (brushing teeth, bowel movements). The complications of acute IE result fr-om intracardiac disease & meta-static infection produced by suppurative emboli.

When to suspect?

(a) Sepsis of unknown origin.

(b) Fever coexisting é:- •Intracardiac implantable material. •Congenital heart or valve disease. •Presence of IE risk factors •Presence of CHF symptoms. •New heart block. •Positive blood cultures. •Peripheral abscesses (of kidney, spleen…).

Classification

Native Valve Endocarditis (NVE): develop on natural valve. The affected valve may

be damaged or normal.

Prosthetic Valve Endocarditis: develops on prosthetic 'artificial' valve.

Endocarditis in IV Drug Abuser: marked ⇧ in cases of prosthetic valve endocarditis

Clinical course

Subacute Infective Endocarditis

Typically affects only previously damaged valves, has insidious course ẃ may exte- nd over many months. The pt suspected to have SIE should be asked about invasi- ve procedures that may cause bacteraemia. Mostly caused by St. Viridans & related to dental disease. Symptoms of early subacute NVE usually are subtle/nonspec-ific, sug- gested by a history of a slowly progressive process characterized by fever, fatigue, anorexia, back pain & wt loss. Less commonly are stroke or CHF. When appropriate Rx is delayed for wks or months, additional clinical features, either embolic or immu- nological in origin, develop. The embolic manifestations include:-

•Acute meningitis é sterile spinal fluid.

•Hemiplegia due to embolization in the distribution of the middle cerebral artery.

•Renal regional infarcts producing painless haematuria.

•Splenic infarction. •Unilateral blindness caused by occlusion of a retinal artery. •MI from embolization to coronary artery. The risk is related to type of organism, size of the vegetation & rate of growth or resolution & location of vegetation.

The immunologic manifestations include:-

•Acute glomerulonephritis. •Osler's nodes. •Roth spots. •Presence of Rh^{ed} factor.

Physical findings

Fever: most pts have low grade fever; however 3-15% of pts may have normal or subnormal temperature.

Murmurs**:** the vast majority of pts have detectable murmurs (99% of cases). The

absence of murmur should cause clinician to reconsider the diagnosis of IE. The major exception is right sided IE in ẃ only 1/3 of cases have a detectable murmur. ***The peripheral lesions:*** observed in only 20% of pts as compared to 85% in the preantibiotic era, including:-

Petechiae ẃ is the most common (result of fragmentation & microembolization of vegetative lesions), may occur on the palpebral conjunctivae or dorsum of hands & feet, or anterior chest & abdominal wall or oral mucosa & soft palate.

Subungual He: black longitudinal streaks not extending to the entire length of nails

Clubbing of fingers & toes: may be seen primarily occurs in pts who have an extended course of untreated IE.

Arthritis: is asymmetrical, limited to 1-3 joints.

Splenomegaly: observed more commonly in pts é long standing SIE & may persist long after successful therapy.

Osler nodes: are small tender nodules pea-size lesions that range in colour from red to purple, located primarily in the pulp spaces of terminal phalanges of fingers, toes, soles of feet, thenar & hypothenar eminences of the hands.

Acute Infective Endocarditis

Frequently involves healthy valves, is a rapidly progressive é destruction of valvular structures. History of antecedent procedures/illicit drug use must investigated. Is a much more aggressive disease. The onset of illness is abrupt é rapidly progre-ssive destruction of the infected valve. The valvular leaflets are destroyed rapidly by bacteria that multiply very fast within the ever growing friable vegetations.

The clinical symptoms of AIE result from either embolic or intracardiac suppurative complications. The disease characterized by:

Acute onset of ***high-grade fever, chills*** & rapid onset of ***CHF.***

Complications of AIE

Develop within a wek, include:-

Dyspnoea & Fatigue of severe CHF.

Neuropsychiatric complications: resulting from involvement of the CNS.

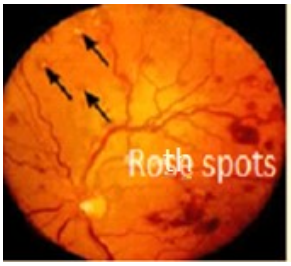
Roth spots: retinal Hge é pale centres. Litten sign "cotton-wool exudates".

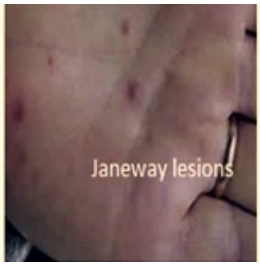
Murmurs: present in 2/3 of pts. The most common is murmur of AR. Because of the rapid onset, the LV does not have chance to dilate. In this situation, the classic findings of ⇧ pulse pressure that are seen in chronic AR are absent.

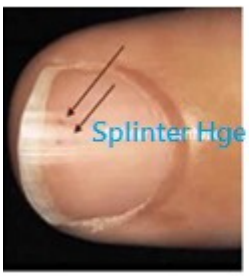
Janeway lesions: irregular erythematous & painless macules (1-4mm in diameter). Most often located on the thenar & hypothenar eminences of hands & feet. They represent an infectious vasculitis of AIE resulting from staph aureus infection.

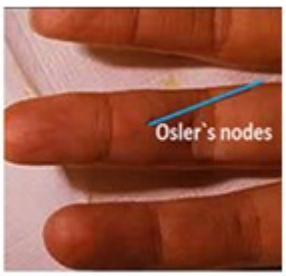
Acute septic monoarticular arthritis: most often caused by staph aureus infection.

Purulent meningitis: observed in pt é AIE, as compared to the aseptic type observed in pt é SIE.









The right-sided infective endocarditis

Is associated é a very low rate of CHF & valvular perforation. Pulmonary infarcts may result from emboli of right-sided IE.

The percentage of occurrence of clinical & laboratory manifestations

Clinical manifestations	*% of occurrence*
Fever	> 95
Arthralgias &/or myalgias	25-45
Murmur	> 85
Splenomegaly	25-60
Splinter haemorrhages	20-40
Roth's spots	< 5
Osler's nodes	10-25
Janeway lesions	< 5
Clubbing	10-20
Clinically apparent emboli	25-45
Neurologic manifestations	20-40
laboratory manifestations	%
Anaemia	70-90
Leucocytosis	20-30
Proteinuria	50-65
Microscopic haematuria	30-50
Elevated s. creatinine level	10-20
Elevated ESR.	>90
Rheumatoid factor	50
Circulating immune complexes	65-100
⇩ serum complement level	5-40

Diagnostic work up

Blood Culture: gold standard test for diagnosis of IE is documentation of a continuous bacteraemia (**>**30 min in duration) through blood culture. For making diagnosis of SIE, draw 3-5 sets of blood cultures, at 3 different sites, over 24 hrs. This detects 92-98% of cases in pts whom did not receive antibiotics recently. In the case of AIE, 3 sets may be drawn over 30 min (é separate vein punctures) to document a continuous bacteraemia.

ECHO: Has become the indirect diagnostic method of choice, especially in pt who presents é clinical picture of IE but who have non diagnostic blood cultures. TTE & TEE to see vegetation's on mitral or aortic valve, or other findings as abscess, pseudoaneurysm, perforation, fistula, valve aneurysm, dishence of prosthetic valve.

TEE is 1st choice to find IE complications. Sensitivity of TEE is bigger than TTE (90-100% vs 40-63%). But diagnosis of IE can never excluded by -ve ECHO.

ECG: detect 10% of pts who develop conduction delay (prolonged P-R interval).

Rh^{ed} factor: becomes +ve in 50% of pts é SIE, it becomes -ve after successful Rx.

WBCs é differential.

ESR & CRP.

Duke criteria

Major Criteria
•Positive Blood culture: for typical microorganism that causes IE from 2 separate blood cultures (strept. viridans, strept bovis, HACEK group, or community-acquired staph aureus or enterococci in the absence of a primary focus). •Positive ECHO: include:-Definitive vegetation (oscillating intracardiac mass on valve) or Abscess, or New partial dehiscence of prosthetic valve, or New valvular regurgitation (not changes in pre-existing murmur).
Minor Criteria
•Predisposing heart condition or IV drug abuse. •Fever >38.0 °C. •Embolic phenomena: major arterial emboli, septic pulmonary infarcts, mycotic aneurysm, ICHge, conjunctival Hge, Janeway lesions. •Immunologic phenomena: Glomerulonephritis, Osler's nodes, Roth's spots, or Rh^{ed} factor. •Microbiologic: positive blood culture but not meeting major criterion. •ECHO: consistent é IEbut not meeting major criterion.

**Definitive diagnosis made by documentation of: 2 major or 1 major + 3 minor or 5 minor.*

Management

General measures

Diet: no special diets recommended for pt é IE, however if the pt has CHF, sodium

restriction may be necessary.

Activity: activity limitations are determined by the severity of IE, complications (e.g., stroke) & by the presence of significant CHF.

Medical treatment

The major goals of therapy for IE are:-

•Eradicating the infectious agent from the thrombus: antibiotics remain the mainstay of Rx for IE. In the setting of AIE, antibiotic Rx should be instituted as soon as possible to minimize valvular damage. 3-5 sets of blood cultures should be obtained within 60-90 minutes, followed by the infusion of the appropriate antibiotic regimen. By necessity, the initial antibiotic choice is empiric, determined by clinical history & physical examination. In the case of SIE, Rx may be safely dela- yed until cultures & sensitivities are available. Waiting does not ⇧ the risk of complications in this form of the disease. Eradicating bacteria from the fibrin-platelet thrombus is extremely difficult. IV administration is the preferred to ensure reliable serum therapeutic levels. The antibiotics should be bactericidal & should administered at higher dose for prolonged period of time. The *Empirical antibiotic Rx of SIE are:* Crystalline Penicillin 3-4 million U IV/4 hrs for 4-6 wks + Gentamicin 1 mg/ kg IV TID for 2 weeks. For *Prosthetic, valve endocarditis:* Vancomycin 1 gm IV BID for 6 wks + Gentamicin 1 mg/kg IV TID for 2 wks + Rifampicin 300 mg PO/ TID for 6 wks. For *AIE: where staph aureus is suspected:* Naficillin 1.5-2 gm IV/4 hours or Vancomycin 1 gm IV BID for 6 weeks + Gentamicin 1 mg/kg IV TID for 2 wks. When the result of blood culture is made available the choice of antibiotics depend on the type of the organism identified & sensitivity.

•Dealing é the complications of valvular infection: includes both the intracardiac & extracardiac consequences of IE. Mild CHF resulting from valvular insufficiency or

myocarditis may be managed é the standard medical Rx for CHF. Although thrombosis is a key element of IE, anticoagulation é Heparin or Warfarin is controversial & it should be avoided.

Surgical treatment

15-25% of pts é IE require surgery. The indication for surgery include:-

- AR é severe HF.
- Fungal endocarditis.
- Mobile vegetation >10 mm in size.
- Evidence of valve ring or myocardial abscess.
- Recurrent embolization despite adequate antibiotic Rx.
- Poor response to antibiotics.
- Prosthetic valve dysfunction associated é CHF or valve ring abscess near a prosthetic valve.

Admission to hospital

Pt should be treated in the hospital to allow adequate monitoring of the development of complications & the response to the antibiotic.

Complications

- CHF: ~60% of IE pts.
- Systemic embolism: 30% of pts (brain, spleen, lungs).
- Uncontrolled infection.
- Neurologic events.
- ARF. •Rheumatic problems. •Myocarditis.

Prophylaxis

First & most important- Proper oral hygiene & Regular dental review.

Antibiotics reserved for narrow group of high risk pt.

Inflammation of the myocardium often resulting from infectious process, ẃ subsequently leads to myocardial destruction & a dilated cardiomyopathy. The acute picture is nonspecific unless overt CHF develops. Although the causes are numerous, the most common association is an antecedent viral syndrome.

Etiology

Infectious causes

- **Viral**: Coxackie virus B, HIV (overt involvement seen in 10% of HIV pts).
- **Bacterial**: not common, usually occurs as a complication of IE. Diphtheric myocarditis may occur in 25% of pts é diphtheria.
- **Fungal.**
- **Protozoal**: Chagas disease caused by a trypanosoma cruzi & transmitted by an insect & is one of the common causes of heart disease in central & south America.
- **Rickettsial**: associated é Typhus, Lyme disease.
- **Spirocheatal**: associated é relapsing fever.
- **Hypersensitivity & toxic reaction*:*** Doxorubicin (antineoplastic) or radiation.

Giant cell myocarditis: is a rare form & of unknown aetiology.

Pathophysiology

Myocarditis defined as inflammatory changes in heart muscle & characterized by an interstitial mononuclear cell infiltrate é an attendant myocyte necrosis. It is not known whether the infiltrate is caused by direct invasion of the infective agents or by a systemic immune response. In the chronic stage, cytotoxic T lymphocytes infiltrate the myocardium & mediate an autoimmune response é myocardial autoan- tibody activity directed against cardiac myosin. This process persists after the viral particles are no longer detected. Coronary artery thrombosis, luminal obstruction, ischemia & dysrhythmias compound the deleterious effects of inflammation.

Clinical features

The clinical presentation is variable. Pt may present é nonspecific illness characterized by fatigue, mild dyspnoea, or fulminant CHF. Myocarditis may even cause sudden death in some pts. The majority of cases of myocarditis are subclinical; therefore, the pt rarely seeks medical attention during acute illness. An antecedent viral syndrome documented in 60% of cases. The typical time interval between the onset of viral illness & cardiac involvement is 2 wks. Fever is present in 20% of cases. Fatigue, myalgia & malaise are common. Chest pain or discomfort is reported in 35% of cases, it is often pleuritic quality é precordial pain of a sharp stabbing nature. Sometimes it may be substernal & squeezing, more typical of ischemic pain. Dyspnoea on exertion is common & orthopnoea & shortness of breath at rest may be noted if CHF is present. Palpitations are common. Syncope signals development of AV block or malignant dysrhythmias & may lead to sudden death.

Physical examination

Pt é mild myocarditis have a nontoxic appearance & simply may appear to have a viral syndrome. Tachypnea & tachycardia are common. Tachycardiais often out of proportion to fever. More acutely ill pt have signs of LVF including: ⇧ JVP, bilateral basal crepitations, ascites & peripheral oedema. S3 gallop may be noted é significant cardiac enlargement (displaced apical impulse). S1 is soft or muffled & cyanosis may be noticed. Hypotension caused by LV dysfunction is uncommon in the acute setting. A poor prognosis is indicated when hypotension is present. Cardiogenic shock observed in fulminant cases é high mortality. Murmurs of mitral or tricuspid regurgitation may be present due to ventricular dilatation .In cases where a dilated cardiomyopathy has developed, signs of peripheral or pulmonary thrombo-

embolism may be found. Associated pericarditis may manifest é a pericardial fricti-

on rub. Pericardial effusion is common, but signs of tamponade (hypotension, jugular venous distension, muffled Heart sounds) are rare. Pleural friction rub might be heard as pleuritis can occur é acute myocarditis.

Diagnostic workup

Since many cases of myocarditis are not clinically obvious, a high degree of suspicion required for making diagnosis.

•***ESR*** is ⇧ in 60% of pts é acute myocarditis.

•***Leucocytosis*** is present in 25% of cases.

•***CXR:*** often reveals normal cardiac shadow, but pericarditis or overt clinical CHF may be associated é cardiomegaly. Vascular redistribution, interstitial & alveolar oedema & pleural effusion may be seen on CXR.

•***ECHO:*** dilated chambers & ⇩ EF indicating LV systolic dysfunction.

•***ECG:*** sinus tachycardia is the most frequent finding. ST-segment elevation éout reciprocal depression, particularly when diffuse, is helpful in differentiating myocarditis from acute MI.

Treatment

Pt é mild symptoms & no signs of cardiac failure or dysrhythmia may be treated on an outpatient basis. The medical Rx is directed towards amelioration of associated complications including CHF, cardiogenic shock, arrhythmias & thromboembolism. ***Lf vent. dysfunction é signs of CHF should be treated é;***

•Low sodium diet. •Limitation or avoidance of exercise. •Diuretics. •Digoxin: sho-uld be given é caution as pt é myocarditis is sensitive for digitalis toxicity. •ACEIs & vasodilators. In general, sympathomimetic & B-blocker drugs should be avoided because they ⇧ the extent of myocardial necrosis & mortality.

Arrhythmias: detection of dysrhythmia é inpatient cardiac monitoring. Medical Rx

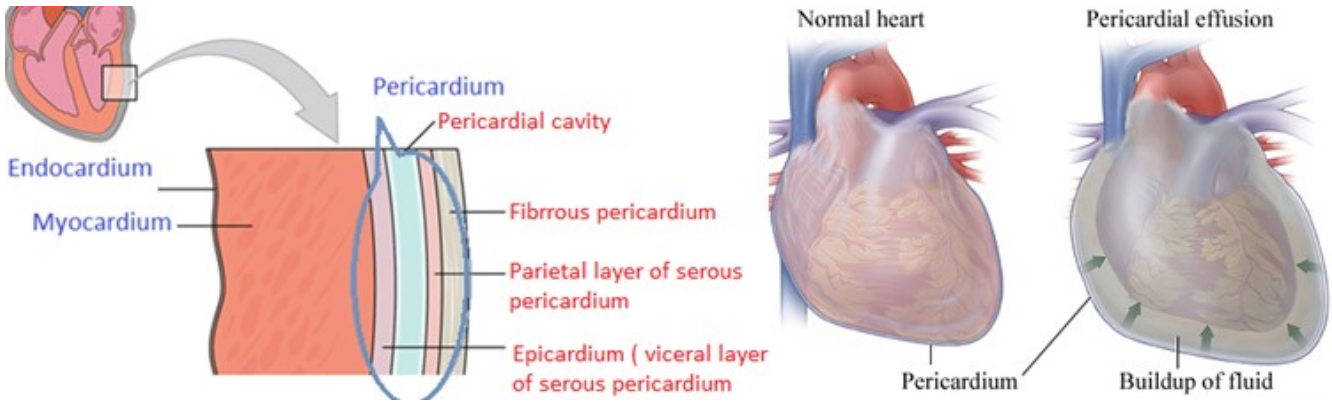
for arrhythmias or implantation of pacemakers.

Avoiding risk of thromboembolism: anticoagulants such as warfarin or heparin may be given. NSAID are contraindicated in the early course of the disease because of inhibition of prostaglandin production, worsened myocyte function & ⇧ myocardial necrosis.

Prognosis

Majority of cases are believed to be clinically silent & resolve spontaneously éout sequealy; therefore, it is difficult to make accurate statements concerning the prognosis of myocarditis. Pt presenting é CHF experience morbidity & mortality based on the degree of LV dysfunction & the presence of arrhythmias & thromboemblic complications ẃ ⇧ the risk of mortality.

PERICARDITIS & PERICARDIAL EFFUSION



Inflammation of the pericardium surrounding the heart. Pericarditis & cardiac tamponade are clinical problems involving the potential space surrounding the heart or pericardium. Pericarditis is one cause of fluid accumulation in this potential space & cardiac tamponade is hemodynamic result of fluid accumulation.

Pathophysiology

The pericardium consists of an outer fibrous layer (parietal pericardium) & an inner serous layer (visceral pericardium). Normally the 2 layers are separated by a

small quantity of fluid (15-50 ml). The pericardium serves as a protective barrier from the spread of infection or inflammation from adjacent structures. It also prevents sudden dilatation of the cardiac chambers during exercise & hypervolemia. It restricts the anatomic position of the heart & minimizes friction é the surrounding structures. Approximately 120 cc of additional fluid can accumulate in the pericardium éout ⇧ in pressure. Further fluid accumulation can result in marked ⇧ in pericardial pressure, eliciting ⇩ in COP &⇩ BP (cardiac tamponade). The rapidity of fluid accumulation influences the hemodynamic effect.

Classification of pericarditis

Clinical classification	Etiologic Classification
I. Acute pericarditis (< 6 weeks)	I. Infectious pericarditis
Fibrinous - Effusive (serous or sanguineous)	Viral - Pyogenic - Tuberculous - Fungal
II. Subacute pericarditis (6 weeks- 6 months)	II. Noninfectious pericarditis
Effusiveconstrictive - Constrictive	Uremia - Acute MI - Neoplasm - Idiopathic.
III. Chronic pericarditis (> 6 months)	III.Hypersensitivity/autoimmune
Constrictive - Effusive - Adhesive	Rh fever - Rh^{ed} arth - SLE - Posttraumatic.

N.B. TB pericarditis is quite common in HIV +ve pts. The viral & autoimmune causes represent ﹥50% of acute pericarditis.

Clinical picture

The most common symptom of acute pericarditis is precordial or retrosternal **chest pain**, usually described as sharp or stabbing. Pain may be of sudden or gradual onset & may radiate to the back (left trapezial ridge), neck, left shoulder, or arm. Movement or inspiration may aggravate the pain. Pain may be most severe when pt is supine & can be relieved when pt leans forward while sitting. **Kussmaul sign**-neck veins distend é inspiration (constrictive type). **Low-grade intermittent fever, cough, dyspnoea & dysphagia.** In TB pericarditis, fever, night sweats & wt loss seen in 80% of cases.

Cardiac tamponade: as the volume of pericardial fluid ⇧, the capacity of atria & ventricles to fill is mechanically compromised, leading to ⇩ stroke volume & tamponade. It is influenced by volume & rate of accumulation. ***Beck triad:*** jugular venous distension + hypotension + muffled HS. ***Neck vein distension:*** is common finding: but Kussmaul`s sign is -ve. ***Hypotension:*** to the extent of shock: may occur when cardiac stroke volume significantly ⇩ & tissue perfusion is compromised. ***Pulsus paradoxus:***⇩ in BP ›10 mmHg during inspiration. ***Narrow pulse pressure*** indicates ⇩ LV stroke volume. ***Cyanosis. Altered consciousness:*** pt may present subacutely é symptoms of anxiety, dyspnoea, orthopnoea, fatigue. Pt may have a history of medical illnesses associated é pericardial involvement, particularly end-stage renal disease. A waxing waning clinical picture may be present in intermittently decompressing tamponade. ***Ewart sign:*** dullness & bronchial breathing between the tip of the left scapula & the vertebral column. ***Hepatomegaly & ascites*** may be found.

Diagnosis

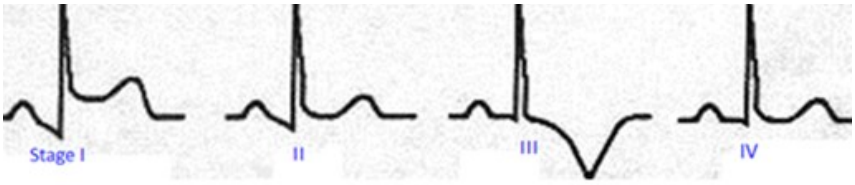
2 of the following features including the ECG changes are necessary for diagnosis:-

Chest Pain: described in detail é the clinical picture above.

Pericardial friction rub: highly specific é variable sensitivity. A high-pitched scratchy or squeaky sound best heard é the diaphragm at the LSB é the pt leaning forward. Have 3 components, ẃ correspond to atrial systole, ventricular systole & early diastole. Audible throughout the respiratory cycle, whereas the pleural rub disappears when respirations are on hold. Friction rub may be transient from one hour to the next & is present in approximately 50-85% of cases. Friction rub may distinguished from a cardiac murmur by its changing character from heart beat to another & pt position changes, in addition that it is closer to the ear on auscultation than a murmur.

ECG changes

Acute pericarditis: widespread upward concave S-T segment elevation & P-R segment depression. If the ratio of S-T segment elevation to T wave amplitude in V6 **>** 0.24, acute pericarditis is almost always present. The ECG changes have 4 phases during the course of illness; each phase lasts from few days to few weeks, while phase IV lasts for several months for gradual resolution of T wave changes. Typical diffuse ST elevation not seen é uremic pericarditis, in ẃ fibrin is deposited in parietal layer é no epicardial inflammation.



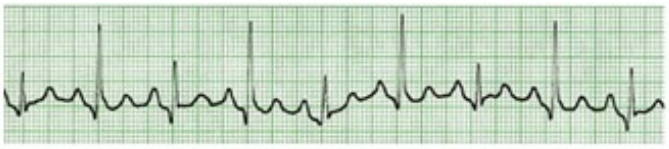
Stage I: everything is UP (i.e., ST elevation in almost all leads)

Stage II: transition (i.e., "pseudonormalization").

Stage III: everything is DOWN (inverted T waves).

Stage IV: normalization.

Cardiac tamponade or massive effusion: electrical alternans is pathognomonic & is characterized by alternating levels of ECG voltage of P wave, QRS complex & T waves. This is a result of heart swinging in a large effusion.

Electrical pulsus alternans 

CXR: recommended in all cases. It is typically normal, or associated é enlarged cardiac silhouette in effusion (é clear lung fields). Bottle shaped heart may be seen é excessive pericardial fluid accumulation. In cardiac tamponade (or large effusions), CXR may demonstrate enlarged cardiac shadow after 200-250 ml of fluid accumulation. The chronicity of effusion may suggested by the huge cardiac shadow.

ECHO: minimal pericardial effusion in pericarditis. Significant pericardial effusion in

chronic pericarditis or cardiac tamponade. Presence of effusion supports the diagnosis, but absence does not exclude it.

Laboratory abnormalities: ⇧ **WBC** (purulent pericarditis). ⇧ **ESR & CRP**. ⇧ **Uric acid** (uremic etiology). **HIV** in selected cases. **ANA & Rh^{ed} Factor. Blood cultures** if febrile. Viral cultures & antibody testing not indicated. **Cardiac isoenzymes**? helpful, **MB fraction of CK** & **Troponin 1:** are modestly ⇧ it is related to the extent of myocardial inflammation. Features associated é rise in (Tn-I) are younger age, male gender, presence of effusion & a recent infection. The enzyme rise is transient, resolving within the 1st wk, it`s persistent rise suggest myopericarditis. **TB skin test**

Differential Diagnoses

•MI •Myocarditis •Pulmonary embolism •Pneumothorax •Pneumopericardium & •Musculoskeletal cause.

Need for hospitalization

Many physicians tend to admit them, but this may not be necessary. Uncomplicated acute pericarditis can undergo initial evaluation in a same day hospital facility or clinic é an outpatient follow-up**.**

Features of high risk

•Subacute symptoms (e.g. developing over several days or wks). •Fever (**>**38^{0}C) & leucocytosis. •Evidence of cardiac tamponade. •Large pericardial effusion •Immunosuppressed state. •History of oral anticoagulant therapy. •Acute trauma •Failure to respond within 7 days to NSAID. •⇧ Cardiac tr-1.

Complications

•Recurrence in 15-32% of pts, mostly in cases of autoimmune etiology.

•Pericardial effusion/cardiac tamponade.

•Chronic constrictive pericarditis: can be “transient”- 10% may have transient wit-hin

the 1st month & resolves by 3 months.

•Cardiac perforation at time of pericardiocentesis.

•Bronchopericardial fistula: noted as complication of multi drug-resistant TB inHIV pt.

Management

Goals of acute therapy

•Relieve pain. •Treat inflammation. •Prevent cardiac tamponade. •Treat underlying disease •Drain purulent effusions. •Symptomatic treatment.

Treating pain & inflammation

NSAIDs are effective in reducing the inflammation & reliving chest pain. May require wks to months of Rx é high doses. The choice of NSAND is usually empiric, based on the physician's familiarity é the agent &/or its availability. Rapidly titrate the dose within 1-2 days to achieve maximum symptomatic relief. Evaluate for a response within 1-2 wks, symptoms usually subside in a wk. If adequate clinical response, continue NSAIDs for 1 wk after complete resolution of symptoms, then taper in 2-3 days.

Aspirin: 2-6 gm daily, preferred in pt é coronary artery disease.

Ibuprofen: 400-800 mg q 6-8 hrs.

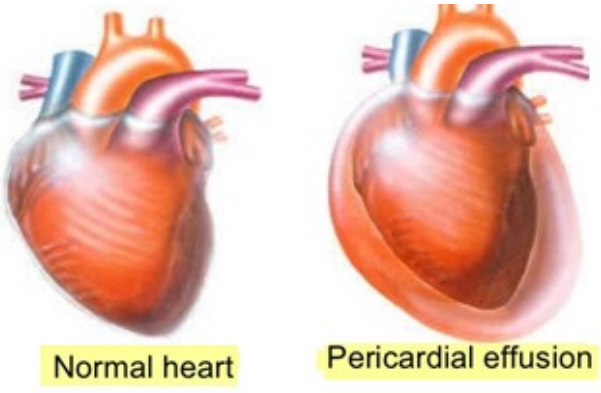
Indomethacin: 75-225 mg daily, try to avoid, unless absolutely needed, it can ⇩ coronary blood flow.

Colchicine: prospective, randomized, open-label design was used. 120 pts é a first episode of acute pericarditis were randomly assigned to conventional Rx é Aspirin (group I) or conventional Rx plus colchicine 1.0-2.0 mg for the first day & then 0.5-1.0 mg/day for 3 months (group II). Colchicine significantly ⇩ the recurrence rate (10.7 % vs 32.3 %; P= 0.004) & presence of symptoms at 72 hrs (11.7 % vs 36.7%;P= 0.003). Based upon this, addition of it to the Rx regimen for an initial episode of acute pericarditis is an option.

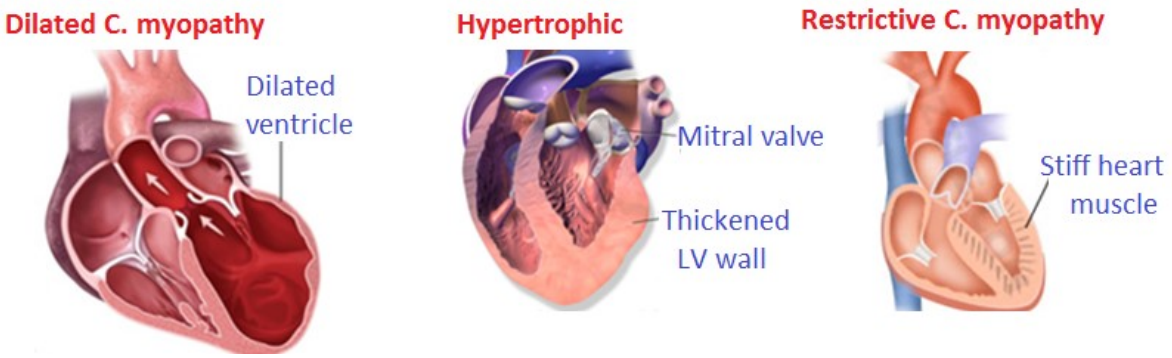
Steroids: in pt refractory to NSAID & Colchicine. Steroid Rx é initial episode is more likely associated é recurrent episodes. Evidence available argues against the routine administration of corticosteroids during the 1st episode of acute pericarditis. Specific conditions that will benefit from steroids include; acute pericarditis due to connective tissue diseases, or autoimmune pericarditis & Uremic pericarditis.

Specific therapy

- ***TB pericarditis*** should be treated é anti TB along é steroid.
- ***Cardiac tampon*ade:** pt will need emergency pericardiocentesis.
- ***MI associated pericarditis:*** early post MI pericarditis is a consequence of trans-mural MI. Aspirin is drug of choice in this setting. Late MI associated pericarditis (Dressler sy.) occurs days– months after MI, is autoimmune in aetiology & NSAIDs are the Rx of choice. Colchicine seems to be most effective if NSAIDs fail. Corticosteroids seem to provide symptomatic benefit (not prevent recurrence). Pericardiectomy is only rarely curative.



CARDIOMYOPATHY



Group of diseases that affect the myocardium & are not the result of; hypertension, valvular, coronary or pericardial abnormalities. frequently associated é myocardial dysfunction & subsequently HF. Histologic findings are nonspecific é myocyte hypertrophy, cellular necrosis & fibrosis.

Etiologic classification

Primary myocardial involvement: •Idiopathic. •Familial. •Eosinophilic endomyocardial diseases. •Endomyocardial fibrosis.

Secondary myocardial involvement: •Infective (viral, bact., fungal, protozoal, spirochatal). •Metabolic (thyrotoxicosis). •Peripartum heart diseases. •Familial storage diseases (glycogen). •Deficiencies (Electrolyte, Vit B_1). •Connective tissue diseases (SLE, Rheumatoid). •Infiltration & granulomas (sarcoidosis, malignancies). •Neuromuscular (muscular dystrophies, myotonic dystrophies). •Sensitivity & toxicity.

Classification

Type	Description
Dilated	Dilatation & impaired contraction of the Lf or both ventricles. Caused by familial/ genetic, viral, immune, alcoholic, toxic or unknown factors, or associated é cardiovascular disease
Hypertrophic	LVH &/or RVH, often asymmetrical, usually involves the interventricular septum. Mutations in sarcoplasmic proteins cause the disea-se in many pts.
Restrictive	Restricted filling & reduced diastolic size of either or both ventricles é normal or near-normal systolic function. Is idiopathic or associated é other disease.

DILATED CARDIOMYOPATHY

Impaired left &/or right ventricular systolic function. characterized by an EF ﹤40% in the presence of ⇧ LV dimensions (LV end-diastolic size ﹥115% of that calculated for age & body surface area).

Pathophysiology

Dilated cardiomyopathy represents the final common morphologic outcome of a variety of biological insults. It is a combination of myocyte apoptosis & necrosis é ⇧ myocardial fibrosis, producing ⇩ in mechanical function. Many causes are a result of direct toxicity (e.g. alcohol) or mechanical insults (e.g. chronic volume overload in MR), or infection (e.g. in myocarditis).

Clinical manifestations

Careful history is essential é particular emphasis on; family history of similar illness. Exposure to cardiotoxins such as alcohol. Protracted "flulike illness" or RTI may suggest previous myocarditis. History of recent delivery or being in last TM of pregnancy. Some pts may have LV dilatation for months or even yrs & may remain asymptomatic & diagnosed only by screening or post-mortem examination. Symptoms of **Lf & Rt sided CHF** develop gradually in most cases. Unfortunately, the commonest clinical presentation is one of progressive deterioration é worsening HF & death occurring over a variable time course. **Syncope** may result from **arrhythmias**. **Systemic embolization**, often emanating from ventricular thrombus..

Physical examination

•Hypotension. •Tachycardia. •Cardiomegaly. •Findings of CHF: narrow pulse pressure , ⇧ JVP & S3, S4 gallops. •Functional mitral or tricuspid regurge.

Diagnostic work up

•**CXR:** cardiac enlargement, evidence of pulmonary congestion.

•**ECG:** sinus tachycardia or AF, ventricular arrhythmias, ST segment abnormalities.

•**ECHO:** LV dilatation & dysfunction (EF ˂40%).

•**Other investigations :-**CBC, RFTs, FBS, PPBS, lipid profile & TFTs.

Treatment

Medical Rx: standard Rx of HF include:-

•Salt restriction. •Diuretics (spironolactone). •Digitalis. •ACEIs or ARBs. •Alcohol should be avoided. •Identify &treat the underlying cause if it is treatable.

Surgical Rx: cardiac transplantation provides median 10 yrs survival & is effective palliation in appropriately selected individuals.

Prognosis

In the absence of a specific remediable aetiology (e.g. peripartum or alcoholic cardiomyopathy), the overall outcome is poor. The majority of pts have downhill course & particularly those ˃55 yrs, die within 3 yrs of onset of symptoms. The 5 yrs survival rate of pts diagnosed é HF is 50%. The blacks are more likely to suffer from progressive heart failure & death than whites.

HYPERTROPHIC CARDIOMYOPATHY

HCM is characterized by LVH (myocardial thickness ˃1.5 cm), typically of none dilated chamber éout obvious causes. Other aetiologies of LVH, as long-standing hypertension & AS need to be excluded before one can diagnose HCM.

Genetic predisposition

HCM is the most common genetic CV disease. 50% of cases have +ve family history é AD transmission. The prevalence in the general adult population for people é phenotypic evidence of HCM is estimated at 1 per 500.

Pathophysiology

Generally, ventricular hypertrophy involves the proximal portion of the interventricul-

ar septum. As the septum thickens, it may narrow the outflow tract. In addition, systolic anterior motion of the mitral valve may occur & result in LV outflow tract obstruction & mitral regurgitation. When systolic anterior motion occurs, the mitral valve leaflets are pulled or dragged anteriorly toward the ventricular septum, producing the obstruction. Consequently, the LV has to generate much higher pressures to overcome the out flow obstruction & to pump blood to systemic circulation. Premature closure of the aortic valve may occur & is caused by the decline in pressure distal to the LV outflow obstruction.

Clinical features

Clinical course is variable. Most pts are asymptomatic. The most common symptom of HCM is dyspnoea on exertion. The pt may also complain of chest pain é exertion, syncope or near syncope, or palpitations. CHF & AF along é their accompanying symptoms may be part of the natural history of HCM. Unfortunately, the first clinical manifestation may be sudden cardiac death, frequently occurring in young children/adults, often during or after physical exertion.

Physical examination

Unless CHF has developed, the **lungs are usually clear & JVP is normal. Bisferiens pulse**: rapidly rising carotid pulse followed by collapse in the pulse & then a 2ry rise. **Point of maximal impulse:** may be double or triple & sustained. **S4 gallop:** may be present. **Systolic murmur:** the classic finding for HCM is crescendo-decrescendo systolic murmur along the LSB that ⇧ é the valsalva manoeuvre. In young adults, HCM is the most common aetiology for sudden death.

Diagnosis

- **CXR:** may suggest LVH but will often be normal because hypertrophy in HCM involves the ventricular septum

- **ECG*:*** often shows LVH & occasionally have a pseudo infarct pattern. Left atrial abnormality may be present if the pt has had long-standing MR from systolic anterior motion of the mitral valve. AF may be present as a complications
- **ECHO:** is the gold standard for diagnosis. On transthoracic ECHO, the clinician should note the thickness of the septum; location & pattern of hypertrophy, degree of LV outflow tract obstruction, presence of systolic anterior motion of the mitral valve, presence of premature closure of the aortic valve & any change in severity associate é Amylnitrite.

Treatment

Medical Rx: competitive sport & strenuous exercise should avoided. Dehydration should avoided & diuretics should be used é caution. ß-blockers are considered as first line of Rx, by decreasing contractile force, ß-blockers ⇩ outflow gradient & ⇩ O_2 demand. ß-blockers also lengthen diastolic filling by slowing the heart rates. They help to control chest pain. Ca.Ch.Bl. is the 2nd line of Rx including Verapamil & Diltiazem can be used. But Nifedipine, Amlodipine & Felodipine should be avoided because they cause peripheral vasodilatation, ẃ may result in ⇩ LV filling & worsening of symptoms of outflow tract obstruction. AF is common complication of HCM. Rx of persistent AF in HCM includes anticoagulation & rate control é ß-blockers. Digoxin should be avoided in HCM pts, particularly in those é resting or latent obstruction, because of its +ve inotropic effect. Pts é HCM should receive prophylactic antibiotics for endocarditis prevention before dental or invasive procedures. The turbulent flow through the LV-outflow tract striking the aortic valve as well as mitral regurge from systolic anterior motion of the mitral valve predispose to endocarditis.

Surgical Rx: septal myomectomy/myotomy may cause lasting symptomatic relief in 3/4 of severely symptomatic pts. Alcohol ablation: Ethanol injection into septal artery

has reported to ⇩ obstruction.

Prevention: the first degree relatives of pt should be screened for ECHO.

RESTRICTIVE CARDIOMYOPATHY

Disease of myocardium, characterized by restrictive filling & ⇩ diastolic volume of either or both ventricles é normal or near-normal systolic function.

Pathophysiology

These conditions result in impaired ventricular filling & primarily diastolic HF. They present é clinical HF syndrome, that is frequently indistinguishable from that caused by systolic dysfunction. AF is poorly tolerated. It simulates other right side HF like cor-pulmonale & constricted pericarditis.

Clinical features

Exercise intolerance & dyspnoea are the prominent symptoms. Peripheral oedema é predominant ascites. Enlarged tender & pulsatile liver. ⇧ JVP ẃ does not fall normally during inspiration (Kussmaul sign). Ht sounds may be distant but apical impulse is easily palpable unlike in constrictive type.

Differential diagnosis: very similar to constrictive pericarditis.

Diagnostic work up

- **CXR:** mild cardiac enlargement.
- **ECG:** low voltage & conduction defects
- **ECHO:** ⇧ LV wall-thickness, ⇩ systolic function.

HYPERTENSION

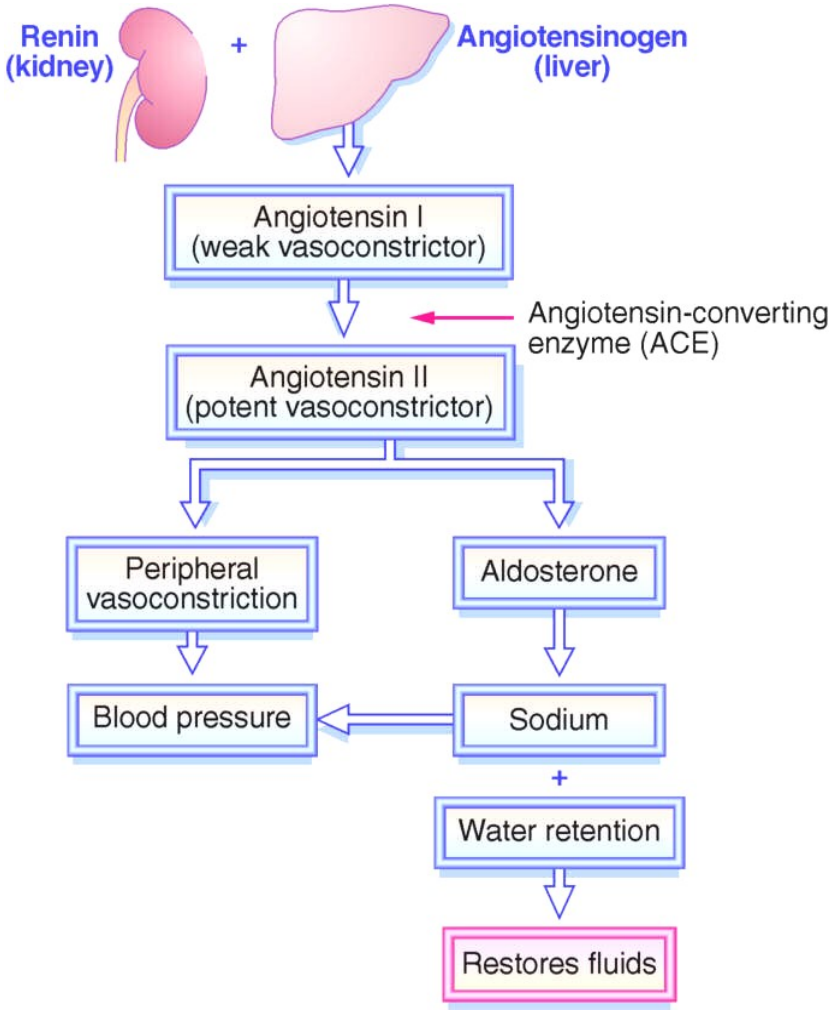
Renin-Angiotensin-Aldosterone system

The kidney & blood vessels strive to regulate & maintain a normal BP, kidney regulate BP via the renin angiotensin system. Renin secreted from renal cells (jucsta glomerular apparatus) act on Angiotensinogen (produced by liver) changing it to Angiotensin I. In the lung Angiotensin I acted upon by angiotensin converting enzyme to form Angiotensin II ẃ is a potent vasoconstrictor & stimulant to adrenal gland to secrete Aldosterone. The aldosterone is steroid hormone (mineralocorticoid) secreted by zona glomerulosa of adrenal cortex, is under control of renin-angiotensin-aldosterone system & K^+ level in blood, also is under control of ACTH & the stretch receptors located in the atria of heart & the baroreceptors located in the large blood vessels. The aldosterone act on the renal tubules causing Na^+ & H_2O retention + ⇧ K^+ excretion in urine. Atrial Natriuretic Peptide is powerful vasodilator, secreted by atrial myocytes in response to ⇧ BP, act by dilating the afferent glomerular arteriole & constrict efferent glomerular arteriole so it cause ⇩ Na reabsorption in distal convoluted tubules & in the collecting duct, in addition to inhibition of renin secretion & ⇩ aldosterone secretion & inhibition of the effect of catecholamines in blood vessels causing relaxation of vascular smooth muscles in arterioles & venules (the opposite action of aldosterone).

Hypertension is defined as arterial BP that exceeds 140/90 mmHg at several determinations. This is an arbitrary definition because a diastolic pressure of even 85 mmHg may be associated é ⇧ cardiovascular morbidity &mortality. Hypertension is one of the most common diseases affecting humans throughout the world.

Because of the associated morbidity & mortality & the cost to society, hypertensi on is an important public health challenge. It is easily detectable, usually easily treatable & often leads to lethal complications if left untreated. Hypertension is the most impo-

rtant modifiable risk factor for CHD, stroke, CHF, end-stage renal disease & peripheral vascular disease. Therefore, health care professionals must not only identify & treat pts é hypertension but also promote a healthy life-style & preventive strategies to ⇩ its prevalence in the general population.



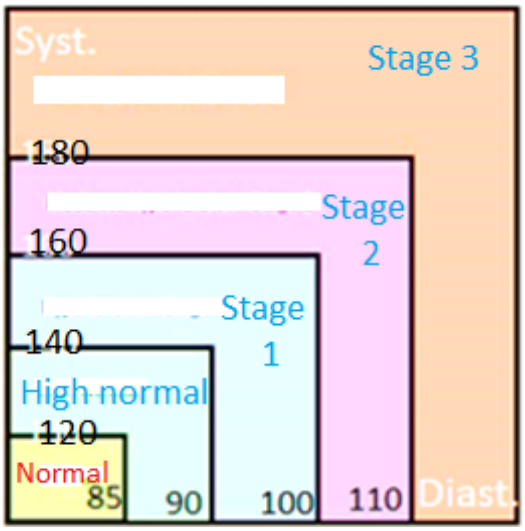
Epidemiology

Overall, 20% of the world's adults are estimated to have hypertension in excess of 140/90 mmHg. Some studies in developed countries show 50% of population have hypertension. The prevalence dramatically ⇧ in pts > 60 yrs. Prevalence is higher among blacks than whites. The age-adjusted prevalence of hypertension is slightly higher in men than in women. The prevalence in women is closely related to age, é substantial ⇧ occurring after age 50. This may be related to hormonal changes associated é menopause.

Classification

Because the risk to an individual pt may correlate é the severity of hypertension, a classification system is essential for making decision about aggressiveness of Rx or therapeutic interventions. When systolic & diastolic BP levels fall into different categories, the higher category should be selected to classify the individual's BP status e.g. 160/92 mmHg should be classified as stage "II" hypertension & 174/120 mmHg should be classified as stage "III" hypertension. Isolated systolic hypertension defined as systolic BP ≥ 140 mmHg & diastolic BP ˂90 mmHg & staged approximately (e.g 170/82 mmHg is defined as stage "II" isolated systolic hypertension). In addition to classifying stages of hypertension on the basis of average BP levels, clinicians should specify the presence or absence of target organ damage & additional risk factors. This specificity is important for risk classification & Rx. Optimal BP é respect to cardiovascular risk is ≤ 120/80 mmHg. Hypertension should be diagnosed based on the average of 2 or more readings taken at 2 or more visits after an initial screen.

	Blood Pressure mmHg		
Category	Systolic		Diastolic
Optimal	<120	&	< 80
Normal	<130	&	< 85
High-normal	130–139	or	85–89
Hypertension stages			
*Stage 1	140–159	or	90–99
*Stage 2	160–179	or	100–109
*Stage 3	>180	or	N > 110



Etiologic classification

Hypertension may be classified as either essential or secondary.

(I) Essential hypertension (90-95%): is diagnosed in individuals in whom generalized or functional abnormalities may be the cause of hypertension but no specific second-

ary causes are identified. The pathophysiology of essential hypertension is multifactorial & highly complex. A number of factors modulate the BP, including; humeral mediators, vascular reactivity, circulating blood volume, vascular calibre, blood viscosity, COP, blood vessel elasticity & neural stimulation. Contributing factors for essential hypertension include the following:-

- ***Genetic predisposition:*** the exact mechanism not established.
- ***Environment***: number of factors implicated as dietary salt intake & salt sensitivity, obesity, occupation, family size & crowding.
- ***Pregnancy-induced hypertension:*** toxaemia of pregnancy.

(II) Secondary hypertension (5-10%): 2ry to an identifiable disorder include:-

- Renal (2.5-6%): variety of renal diseases may be accompanied by hypertension; Renal parenchymal disease: CRF, chronic pyelonephritis, acute & chronic glomerulonephritis, polycystic kidney, renin-producing tumour, Hyperuricaemia.
- Renovascular hypertension (0.2-4%) including; hyperlipidaemia, coarctation of aorta, renal artery stenosis, vasculitis & collagen vascular disease.
- Endocrinal (1-2%): DM. Oral Contraceptives. Adrenocortical hypertension- Primary Aldosteronism, Conn`s syndrome, Cushing syndrome, Congenital Adrenal Hyperplasia, Pheochromocytoma. Acromegaly. Myxoedema. Thyrotoxicosis.
- Neurogenic: psychogenic, ⇧ ICP, acute spinal cord section.
- Drugs & Toxins: alcohol & adrenergic medications.

Predisposing factors

- Strong F/H of hypertension.
- Age: secondary hypertension often develops before the age of 35 or after 55 yrs.
- Associated CV risk factors as; cigarette smoking, lipid abnormality or hypercholesterolemia, DM, family history of early deaths due to CV diseases & alcoholism.

Prevalence

Age (years)	Hypertension
18-29	4%
30-39	11%
40-49	21%
50-59	44%
60-69	54%
70+	64%

Effects of hypertension

Pt é hypertension die prematurely, the most common cause of death is heart disease, stroke & renal failure also frequent, particularly in pt é retinopathy.

1. Effects on heart: •LVH as a compensatory mechanism •Coronary artery disease/ IHD as; angina pectoris or MI which may lead to HF.

2. Neurologic effects: ■Retinal changes: exudates: hard & soft exudates. Hge include; dot & bloat Hge. Thickening of arterioles: copper wiring/silver wiring. Abno- rmalities on arteriolovenular crossings, or papilledema.

■CNS dysfunction: cerebrovascular disease: TIAs; episodic dizziness, unilateral blind-ness, hemiparesis. Stroke either; ischemic due to atherosclerosis of cerebral vessels, or haemorrhagic stroke as a result of ⇧ arterial pressure & formation of vascular mi-croaneurysms. Hypertensive encephalopathy is another effect of hypertension is con-sists of severe hyprtension, altered state of consciousness, ⇧ ICP é papilledema & sei-zure. The focal neurologic deficits are uncommon.

3. Effects on the kidneys: arteriolosclerosis of the afferent & efferent arterioles & the glomerular capillary tuft impairs renal function. Pt may have proteinuria & microscop-ic haematuria & later on CRF.

Risk factors for an adverse prognosis in hypertension

•Black race. •Youth. •Male sex. •Smoking. •Obesity. •DM. •Hypercholesterolem-ia. •Excess alcohol intake. •Evidence of end organ damage.

Approach to a pt é hypertension

Hypertension is confirmed after an elevated BP ≥ 140/90 mmHg, properly measured, has been documented on at least 3 separate occasions (based on the average of 2 or more readings taken at each of 2 or more visits after initial screening).

An accurate measurement of BP is the key to diagnosis

Several determinations should make over period of several wks. At any given visit, an average of 3 BP readings taken 2 min apart using a mercury manometer is preferable. BP should be measured in both the supine &sitting positions, auscultating é the bell of the stethoscope. On the 1st visit, BP should be checked in both arms &in one leg to avoid missing coarctation of aorta or subclavian artery stenosis. The improper cuff size may influence BP measurement, wider cuffs preferable, particularly if pts arm circumference ›30cm. Pt should rest quietly at least 5 min before measurement. Although somewhat controversial, the common practice is to document phase V (disappearance of all sounds) of Korotkoff sounds as diastolic BP.

Practical points

•Normally there is diurnal variation of BP. We may hear 4th HS in hypertension.

•Isolated systolic hypertension seen in elderly (atherosclerosis).

•Hypertension may associated é steroids, NSAID, cough syrup, contraceptive pills, erythropoietin, liquorice ẃ contain natural mineralocorticoids causing Na & H_2O retention, or vitamins especially Vit B.

•White coat hypertension (⇧ BP of pt during doctor examination).

•Reduction of BP by 5-6 mmHg ⇩ the risk of stroke by 40% & the risk of coronary heart diseases by 15-20%.

•Most hypertensive pts will require combination of antihypertensive drugs to achieve recommended target of BP **<** 140/80.

•Hypertension in neonate occur in 2% of admission to NNICU, BP is usually 85 /60 mmHg. In children, BP calculated as follow: SBP = Age in yrs X 2 + 80. & DBP = 2/3 of the SBP. Causes of hypertension in infants, children include: IC He, Neuroblastoma, Congenital adrenal hyperplasia, Congenital anomalies kidnyes, Coarctation of aorta, Renal vein thrombosis, & Vesicoureteric reflux.

Patient evaluation

In evaluating a pt é hypertension the initial history, physical examination & laboratory should be directed at:-

(1) Establishing pre-treatment base line hypertension.

(2) Identifying correctable secondary cause of hypertension.

(3) Determining if target organ damage is present: pts may have undiagnosed hypertension for yrs éout having their BP checked. Therefore, a search for end organ damage should be made through proper history, physical exam & investigations.

(4) Determining whether other CV risk factors are present.

(5) Assessing factors ẃ may influence the type of Rx or changed adversely by Rx.

Clinical symptoms & history

Most pts é hypertension has no specific symptoms & are identified only in the course of physical exam. If pt develops symptoms, this may be attributable to: elevated BP itself, or due to the end organ damage associated é hypertension, or the underlying secondary disease. Some of the symptoms may be:-

*Headache: though popularly considered symptom of high BP, it is a characteristic of only severe hypertension. Such headaches are localized to the occipital region & present when the pt awakens in the morning but subsides spontaneously after several hrs. *Dizziness. *Palpitation. *Easy Fatigability. *Impotence. *Symptoms referable to vascular or target organ damage: include; Epistaxis, Haematuria, blurring of vision.

Cerebrovascular damages; TIA, episodes of weakness, dizziness or stroke (haemorrhagic or ischemic). Cardiovascular damages; angina, MI, Pain due to dissecting aorta.

**Symptoms/history suggesting underlying disease:* include:-

•History of known renal disease, abdominal masses, anaemia.

•History of repeated UTI may suggest chronic pyelonephritis.

•History of sweating, labile hypertension, headache, nervousness, postural dizziness, palpitations & wt loss may suggest pheochromocytoma.

•History of polyuria, polydipsia & muscle weakness may be suggest hypokalaemia associated é aldosteronism.

•History of wt gain, emotional labiality may suggest Cushing syndrome.

•History of cold/heat tolerance, sweating, lack of energy, bradycardia or tachycardia may indicate hypo or hyperthyroidism.

•History of intake of contraceptives pills, liquorice & sympathomimetics should be looked for. Obtain a history of over-the-counter medication use or unsuccessful antihypertensive Rx trials.

Physical examination

Compare BP & pulse in the 2 upper extremities & in supine & standing position & the ⇧ in DBP when pt goes from supine to standing.

General appearance: round face & truncal obesity suggests Cushing syndrome.

Proper measurement of BP: a rise in DBP when the pt goes from supine to standing position is compatible mostly é essential hypertension while ⇩ BP in the absence of antihypertensive medications suggests 2ry hypertension.

Funduscopic evaluation of eye: for evidence of hypertensive retinopathy. Flame-shaped Haemorrhage, cotton wool exudates, papilledema & other neurologic signs raises the possibility of ⇧ intra cranial pressure.-

Palpation of all peripheral pulses should be performed: mainly palpation & auscultation of carotid arteries. Femoral pulse should be felt & compared é radial pulse. Radial femoral delay suggests COA.

Careful cardiac examination: to evaluate signs of LVH. These include displacement of apex, a sustained & enlarged apical impulse & presence of S4, occasionally, a tambour S2 is heard é aortic root dilatation.

Abdominal examination: look for renal artery bruit over the upper abdomen; the presence of a unilateral bruit é both a systolic & diastolic component suggests renal artery stenosis. Palpate for an abdominal aneurysm, enlarged kidneys of polycystic kidney diseases.

Diagnostic workup

Laboratory investigations: unless a 2ry cause for hypertension is suspected, only the following routine laboratory studies should be performed including:-

- CBC, Hct.
- Urine analysis including microscopy, protein, blood, sugar.
- FBS, 2HPPBS • Electrolytes (K^+, Na^+).
- Lipid profile (cholesterol, LDL, HDL, triglycerides).
- Creatinine & Uric acid
- **ECG & Imaging studies:** ECHO to detect LVH.

Special studies: requested only when 2ry hypertension strongly suspected.

- U/S & doppler flow study for renovascular disease.
- 24 hrs urine assay of metanephrines & catecholamine for pheochromocytoma.
- Overnight dexamethasone suppression test or 24hr urine cortisol for Cushing sy.
- Plasma aldosterone for 1ry aldosteronism.
- Thyroid function (TSH, T3, T4) for thyrotoxicosis/Myxoedema.

Complications of Hypertension

- Hypertensive Cardiomyopathy: HF, LVF (congested lung, pt unable lie flat on bed) .RVF (enlarged congested liver, ⇧ of JVP, oedema of lower limbs & sacrum), MI.
- Hypertensive Nephropathy: chronic renal failure, in diabetic pt é hypertension, the early sign of development of diabetic nephropathy is the presence of microalbuminurea in urine.
- Hypertensive Encephalopathy: confusion, headache, convulsion), CVA (stroke).
- Hypertensive Retinopathy.

Management

Indication for Rx are; SBP >140 & DBP >90 mmHg repeatedly. Isolated systolic hypertension SBP >160 & DBP <89 mmHg, if pt is >65 yrs.

General measures

***Sodium restriction:** intake <100 mmol/day (2.4 gm Na or 6 gm of Nacl).

***Lifestyle modifications:** Wt. reduction in obese pt. Limitation of alcohol intake: as alcohol potentiates the action of catecholamines & may exacerbate hypertension. Regular physical exercise:⇧ aerobic activity (30-45 minutes most days of the wk). Stop smoking. The DASH diet (Dietary Approach-es to Stop Hypertension) include; adequate intake of dietary K, Ca & Mg (healthy diet like fruits, vegetables) & reducing the intake of dietary saturated fat & cholesterol.

Medications

Diuretics: also called water pills, often the 1st line drugs, reduce ECF volume. Act by flushing of excess H_2O & Na from the body, thus lowering the BP, may be enough along é life style changes to control BP in the start, include:-

Thiazide diuretics: are more effective antihypertensive agents than loop diuretics. Block Na & Cl reabsorption predominantly in the distal convoluted tubules,⇧ urine

excretion of Na, Cl, K & Mg. **Chloro/Hydrochlorothiazide** 25 mg PO daily & may be ⇧ gradually. Side effects: Hyponatraemia, hypokalaemia, hypomagnesaemia, Hypercalcaemia, hyperuricemia, hyperglycaemia, weakness, muscle cramps, impotence, hyperlipidaemia (⇧ LDL & triglyceride), thiazide induced pancreatitis. Thiazide contraindicated in pt é Gout.

Loop diuretics: block Na, Cl & K reabsorption in the thick ascending loop of Henle & the most effective agent in pt. é renal insufficiency (Cr. >2.5 mg). **Furosemide** 20, 40 mg tab/amp, 20-320 mg/day. Side effects: hypo k/Ca/Mg, & ototoxicity.

Potassium-sparing diuretics: is competitive inhibitor of aldosterone on kidney, may be used in 1ry hyperaldosteronism (as additional therapy in combination é thiazide diuretics). **Spironolactone** 25, 50, 100 mg tab, 25-100 mg/day. Side effects: hyperkalaemia, gynecomastia in males & breast tenderness in females.

Angiotensin Converting Enzyme Inhibitor

Block the production of Angiotensin II by preventing conversion of Angiotensin I to Angiotensin II. By doing so ACEI reduce peripheral resistance. In addition they reduce Aldosterone production, reducing the retention of Na^+ & ⇧ GFR. Effective in pt é hypertension associated é HF, kidney disease, DM, or CT diseases.

Captopril 12.5-75 mg PO BID.

Enalapril: 2.5-40 mg daily. Side effects include; cough, leucopenia, angioedema, hyperkalaemia, hyponatraemia, taste disturbance & first dose hypotension. Contraindicated in bilateral renal artery stenosis & renal failure.

Angiotensin II Receptor Blockers (ARBS)

Prevent Angiotensin II (ẃ is potent vasoconstrictor causing smooth muscles surrounding blood vessels to contract) from binding to angiotensin receptors, block vasoconstriction & block release of aldosterone. Used in hypertensive pt é renal impairment,

diabetic nephropathy, AF, HF & those unable to tolerate ACEIs as result of marked cough or development of angioedema.

Irbesartan tab 1500 mg/day. **Losartan** tab 25-50 mg once or twice daily.

Side effects include: hyperkalaemia, headache, cough, hypotension, angioedema, dizziness, allergic reaction. Are contraindicated during pregnancy.

Action of ACEI & ARBS: vasodilatation, ⇩ BP, ⇩ peripheral resistance, diuresis, no changes in HR, no reduction of COP.

β-Blockers

The β-receptors are found on cells of the heart muscles, arteries, smooth muscle, airway, kidneys & other tissues that are part of the sympathetic nervous system. β-receptors blockers block the action of catecholamines epinephrine (adrenaline) & norepinephrine (noradrenalin) in particular, on β-adrenergic receptors by competitive inhibition. There are 3 types of β-receptors:-

- β1-adrenergic receptors: are located mainly in heart & kidneys.
- β2-adrenergic receptors: are located mainly in lungs, GIT, liver, uterus, vascular smooth muscles & skeletal muscles.
- β3 adrenergic receptors: are located in the fat cells.

The β-blockers used mainly for the Rx of cardiac arrhythmia, protecting heart from 2nd heart attack, angina & hypertension. The **β1-Receptor Blocker** is cardioselective preferred,⇩ HR, COP & contractility of heart, also prolong P-R interval, ⇧ prostaglandine ẃ is potent vasodilator & ⇩ renin release from the kidneys & cause no bronchospasm compared by the non-selective β-blocker ẃ act on both β_1 (he-art) & β_2 (bronchial) receptors. **Propranolol** is non-selective β-Blocker, 20 mg PO/ day to maximum of 120 mg PO 4 X/day. **Metoprolol** is selective β-Blocker, 25-150 mg PO BID or **Atenolol** (Tenormin/ Blokium tablet), 25-100mg PO/day.

The side effects of β-blockers: bradycardia, worsening of HF, AV block, dry mouth, depression, ⇧ serum lipids, hypoglycaemia, hyperkalaemia, bronchospasm, aggravate bronchial asthma & COPD, insomnia, night mares, hallucination, impotence & psychosis. The contraindications for β-blockers are; bronchial asthma, or peripheral vascular disease (severe).

Calcium channel blockers

Inhibit inward movement of calcium ions through the slow channels of active membrane in myocardial & vascular smooth muscle cells, causing -ve inotropic effect in the heart, prolong depolarization, ⇩ myocardial O_2 consumption, coronary & peripheral vasodilatation (smooth muscle cells relaxation). Used in elderly pt é hypertension, angina or é cardiac arrhythmia. The Ca Ch BLs pharmacodynamics include: ⇩ BP, ⇩ HR, ⇩ of strokevolume, ⇩ COP, ⇩ total peripheral resistance.

The Ca Ch Bls include 2 groups:-

① **Dihydropyridines** (vascular effect): **Nifedipine** 30-90 mg PO/ day. **Amlodipine** 2.5-10 mg PO daily. Contraindicated é heart block or HF.

② **Non Dihydropyridines** (cardiac effect): **Diltiazem & Verapamil**. **Isoptin** 80, 120, 240 mg tab 80-480 mg/day, have cardio depressant effect & their use may be problematic é CHF.

Side effects of Ca Ch BLs: constipation, headache, peripheral oedema, palpitation, dizziness, fatigue, visual disturbances & mental depression.

Centrally acting agents

These agents inhibit sympathetic out flow from the CNS. Are vasodilators: dilate arterioles & arteries, ⇩ peripheral vascular resistance ẃ in turn reduces high BP. **α blockers;** block the effect of sympathetic nerves on blood vessels by binding to α-adrenoreceptors located in the vascular smooth muscle, most of these drugs act as competit-

ive antagonists to the binding of norepinephrine that is released by sympathetic nerve synapsing in smooth muscle. Therefore sometimes referred to as sympatholytic. The side effects of α blockers include; weakness, fainting when standing up suddenly, nasal congestion & headache.

Prazosin 1, 2 mg tab, dosage range 1-20 mg/day.

Methyldopa 250-1000 mg PO BID, TID or QID. Side effects: postural hypotension, depression, gynecomastia.

Hydralazine 10-75 mg PO QID, 10-50 mg IV. Side effects: headache, SLE like sy.

Minoxidil 2.5-4.0 mg PO BID. Side effects: orthostatic hypotension.

Stepwise prescription of anti-hypertensive medication

Diuretics are often prefered as first line drugs. They may be effective alone in mild hypertension. However most of the time they are used in combination é other drugs as β-blockers, ACEI or Ca Ch BL. Hydrochlorothiazide will potentiate the activity of a number of antihypertensive drugs, particularly ACEI. Such combination has an additive effect, controlling BP in up to 85% of pts. The dosage of antihypertensive drugs should be escalated till BP is well controlled. If BP still uncontrolled consider using multiple drugs acting at different sites & have additive effect. Most drug combinations, using agents that act by different mechanisms, have an additive effect. The combination of Ca Ch Bls é an ACEIs has additive effects. Some combinations may not be additive, including β-blockers & ACEIs or βblocker & α1 blocker or α 2 stimu-lant. Some combinations may have additive adverse effects; these include β-blocker combined é Verapamil or Diltiazem (Ca Ch Bl), ẃ leads to cardiac depression bradycardia, or AV block. If the BP is still resistant to Rx add direct vasodilators.

For summary of the stepwise prescription:-

Elderly hypertensive (**>** 60 yrs): generally pt have ⇧ vascular resistance, ⇩ plasma

renin & greater LVH than younger pt, so use diuretics as first line, or Ca Ch Bls ẃ ⇩the peripheral resistance & has no adverse effects on lipid level.

Diabetic hypertensive pt: usually have diabetic nephropathy, proteinurea & renal insufficiency, use ACEIs or ARBs as first line, they shown to ⇩ rate of progression to end stage renal disease & ⇩ retinal complications.

Hypertensive é chronic renal insufficiency: diuretics used to deal é the Na & H_2O retention, loop diuretics are the most effective class, ACEIs are shown to slow the rate of deterioration of renal function.

Hypertensive é coronary artery disease: pt is at high risk for development of MI & angina. β-blockers used as first line of Rx. ACEIs or ARBs are also useful in such pt é LV dysfunction.

Hypertensive é HF: ACEIs or ARBs is beneficial in ⇩ the mortality. β-Blockers & Aldactone also improve outcome. Don`t use NHPor α-Blockers.

Hypertensive é Ht block: never use β-Blockers or NHP.

Hypertensive é asthma or COPD: never use β-Blockers.

Hypertensive é Gout: never use diuretics as it worsen the condition, ARBs are good choice to reduce serum urates.

Hypertensive é benign prostatic hyperplasia: α- blockers is good choice.

***Thiazides:** preferred therapy for uncomplicated hypertension, or é systolic hypertension in elderly people & older diabetic pt éout nephropathy.

***ACEIs:** should be the initial Rx in situations in ẃ hypertension is associated é CHF, or DM é proteinuria or post MI é systolic LV dysfunction, or in pt who develop persistent cough while on ACEIs Rx, an ARBs may be substituted, but these agents' efficacy in lowering cardiovascular mortality rates has not yet been proven.

***B-Blockers:** often preferred in post-MI & uncomplicated hypertension.

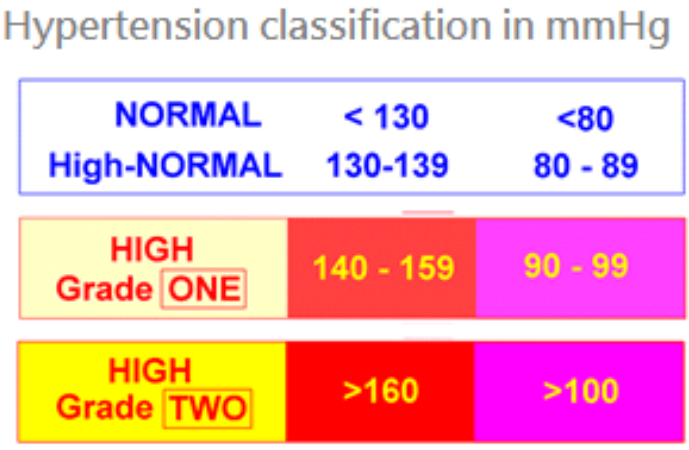
Diuretic or long-acting Ca Ch Bls: effective in elderly é isolated sys. hypertension.

Ca.Ch.Bl.: Nifedipine is preferred Rx for systolic hypertension & alternative therapy in uncomplicated hypertension.

Central acting agents (e.g. Methyldopa): may be used as alternative Rx for uncomplicated hypertension.

Side effects of commonly used drugs

Diuretics	Hypokalaemia, hypomagnesaemia, ototoxicity, orthostatic hypotension, hyperuricemia
B- Blockers	Bradycardia, hypotension, AV block, dizziness, fatigue, depression, diarrhoea, nausea, vomiting, bronchospasm, hypoglycaemia, hyperglycaemia
ACEIs	Angioedema, dry cough, hyperkalaemia, dizziness, hypotension, fatigue, syncope, rash, nausea, vomiting
ARBs	Orthostatic hypotension, diarrhoea, hyperkalaemia, dizziness, fatigue, myalgia, nasal congestion, insomnia, syncope
Ca Ch Bls	Bradycardia, hypotension, tachycardia, ventricular fibrillation, dizziness, fatigue, peripheral oedema, nausea, vomiting, constipation, anorexia, flushing, ⇧ liver enzymes, AV block
α- blockers	Orthostatic hypotension, dizziness, sinus bradycardia, vertigo, syncope, diarrhoea, fatigue, peripheral oedema, nausea, vomiting, priapism, impotence, floppy iris syndrome



HYPERTENSIVE CRISIS

Defined as severe hypertension characterized by DBP >130 mmHg. The BP elevation to such degree can cause vascular damage, encephalopathy, retinal Hge, renal damage & death. 1-2 % of the hypertensive population develop this complication. It is categorized into:-

(1) Hypertensive emergency: there is acute impairment of an organ system (CNS, CVS, Renal). In these conditions, BP should lowered aggressively over minutes.

(2) Hypertensive urgency: BP is high & there is potential risk but not yet caused acute end-organ damage. These pts require BP control over several days to wks.

Diagnosis: DBP of 130 mmHg, funduscopic finding of papilledema, change in neurologic & mental status & abnormal renal sediments are the hallmarks.

Approach to pt é hypertensive crisis rapid assessment of the pt é brief history & targeted physical examination (of the CNS, CVS & Retina).

Laboratory investigations

▲CBC. ▲Urine analysis. ▲Renal function test. ▲ECG.

Treatment "treats the pt not the number".

General measures: look if the pt is in stressful situation. Place pt in quiet room & re-evaluate after initial interview. Some pt's BP ⇩ below a critical level after relaxation.

Pharmacologic Rx: if pt has hypertensive emergency, lower the BP rapidly by 25% of the diastolic BP & not <95 mmHg. Use rapidly acting drug as IV Sodium Nitroprusside, Hydralazine, or sublingual Nifedipine.

Sodium Nitroprusside 0.5-8 ugm/kg/min IV infusion till BP is lowered to normal or

Hydralazine 10-20 mg IV stat to be repeated every 20-30 min or

Labetalol 2mg/min through continuous IV infusion.

As the pt BP stabilizes start long term oral medications.

ISCHEMIC HEART DISEASES

Myocardial ischemia occurs when the blood flow demands of the heart exceed the blood supplied by the coronary arteries.

Epidemiology

IHD is the leading cause of morbidity & mortality in developed countries & it incurs greater economic cost. The prevalence of IHD is on the rise in developing countries as there is change in the life style associated é urbanization including sedentary life style, smoking, obesity, high fat & energy diet & the associated ⇧ prevalence of DM. Larger ⇧ in prevalence of IHD throughout the world are projected & is likely to become the most common cause of death worldwide by year 2020.

Etiology/Pathophysiology

Myocardial ischemia reflects an imbalance between the myocardial O_2 supply & demand. Myocardial O_2 demand is mainly determined by heart rate, the force of ventricular contraction & ventricular wall tension, ẃ is proportional to the ventricular volume & pressure. Unless there is a proportionate rise in O_2 supply, conditions that ⇧ O_2 demand such as physical exertion result in ischemia. Atherosclerosis is another factor.

Risk factors

Age: the risk of CAD ⇧ progressively é age. The risk of death from coronary artery disease is 1.5/1000 individuals at age 50.

Gender: IHD is more prevalent in men than women. The difference is more marked in premenopausal women compared to men of similar age.

Lipid abnormalities: ⇧ serum LDL & ⇩ HDL é hypertriglyceridemia favours the deposition of lipids &cholesterol in atherosclerotic plaques (hypertriglyceridemia commonly is associated é DM).

Smoking: the smokers are 60% more likely to develop CAD than the non-smokers.

Hypertension: ⇧ the risk of CAD both in men & women. DM is associated é significant ⇧ in the risk of CAD.

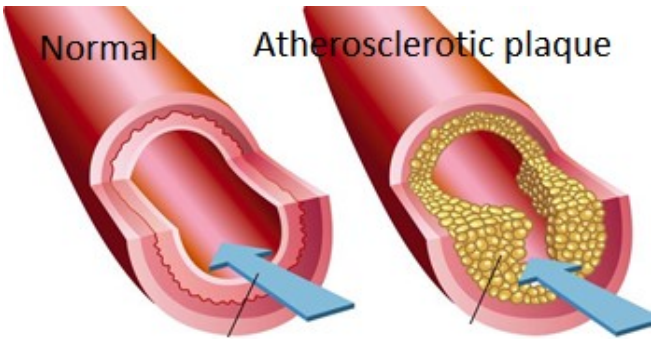
Family history: a familial predisposition to CAD exists.

Oral contraceptive pills: associated é ⇧ risk of CAD.

Other risk factors: gout & obesity.

Atherosclerosis

Is focal narrowing of arteries ẃ results from plaque formation. CAD & atherosclerosis risk factors such as hyperlipidaemia, smoking, DM & hypertension apparently disrupt the normal functioning of the vascular endothelium. Plaques are formed as a result of:- intimal smooth muscle proliferation probably as a result of endothelial damage, or due to lipids (cholesterol esters) deposition at the centre of plaque & also within smooth muscle cells. A fibrous cup made of connective tissue covers the plaque. As the stenotic lesions grow, perfusion pressure distal to the lesions ⇩; in response, coronary arterioles dilate to maintain adequate blood flow preventing ischemic symptoms at rest. During exertion the myocardial O_2 demand ⇧ ẃ could not be matched by the perfusion via narrowed coronary artery. The resulting myocardial ischemia results in chest pain, ẃ is relieved by taking rest. Sometimes atherosclerotic plaques may rapture & a fibrin thrombus is formed over the plaque ẃ completely blocks the narrowed coronary artery & result in MI.



ANGINA PECTORIS

Is a chest pain or pressure produced by myocardial ischemia. Anginal pain is often ppt by exertion or other factors that ⇧ myocardial O_2 demand (e.g. emotional stress, eating meal, sexual intercourse) may ppt angina. Chest pain in angina is squeezing in type or a feeling of pressure or tightness in the chest. Sometimes it can be burning in nature or felt as epigastric discomfort. The pain radiates to the left shoulder, left jaw, teeth or to the left arm & sometimes may radiate to the right arm.

The pain in angina is often reproducible é the same degree of physical exertion. The symptom usually begins é low intensity, ⇧ over 2-3 min & often lasts ‹15 min. An episodes lasting ›30 min suggest MI may have occurred.

Types

Classic or excertional angina: pain ppt by ⇧ workload on the heart. May be caused by exercise, emotions, stress & cold exposure. Symptoms may remain "stable" for a number of yrs or progress in severity.

Silent ischemia: is particularly dangerous form of myocardial ischemia as there is a lack of clinical symptoms, i.e. ischemia éout angina. For every episode of symptomatic ischemia that the pt suffers, there are usually 4-5 episodes of silent (asymptomatic) ischemia. Can be detected by ECG including stress ECG or Holter monitor. Such episodes are less severe in nature & shorter in duration.

Unstable Angina: is angina that occurs at rest. Also referred to as "pre infarct angina" since it usually associated é extensive blockage of the coronary arteries. The coronary blood flow does not meet the needs of the heart even at rest. Unstable angina is progressive & may be ominous feature of imminent MI. So physicians & pts should be aware that close observation & intensive therapy are required. It represents a more serious situation than chronic stable angina.

Variant angina (vasospastic angina, prinzmetal's angina): this is type of angina resulting from transient coronary spasm, usually associated é fixed atherosclerotic lesion. The spasm produces total but transient coronary occlusion. Usually occurs at rest (often at night) & frequently complicated é ventricular arrhythmias.

Diagnosis

In pt presenting é history of recurrent chest pain, obtain detailed history including onset, quality, location, duration, radiation, ppt & relieving factors. Determine presence or absence of each of the 3 following symptom complex characteristics:-

① Substernal discomfort é characteristic quality & duration.

② Symptoms provoked by exertion or emotional stress.

③ Symptoms relieved by rest or nitroglycerine.

Based on the number of symptom complex present, angina can be classified as:-

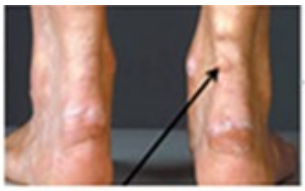
- ***Typical (definite) angina:*** all the above 3 characteristics are present.
- ***Atypical (probable) angina:*** only 2 of the above 3 characteristics are present.
- ***No cardiac chest pain:*** 1 or none of the 3 characteristics is present.

If the pt's symptoms are consistent é definite angina, sub classifies the angina as **stable** (unchanged for 2 or more months) or **unstable** (at rest, or new-onset, or increasing angina). In pt é definite or probable angina, ask about functional limitations. Ask about any episodes of dyspnoea, palpitations or dizziness é/éout chest pain. If the pt has experienced any such episodes, ask about the same symptom variables applicable to typical (definite) angina. Assess potential risk factors for CAD, including those related to lifestyle, habits (smoking), medical history, family history, hormone therapy. Ask about history of symptoms such as excertional dyspnoea, orthopnoea & bilateral leg swelling, that suggest LV dysfunction or HF. Ask about nocturia. Ask about other potential causes of chest pain, especially if symptoms have changed or new symptom

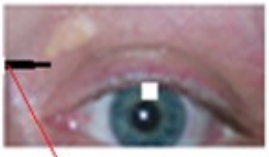
have arisen, or pt is at low risk for CAD.

Physical examination

In pt presenting é suspected stable angina (unchanged for 2 or more months), perform complete physical examination to help identify the cause of the chest pain & any combined disorder(s). Assess vital signs, especially for hypertension, tachycardia, bradycardia, arrhythmia & tachypnea. Closely examine the head & neck, especially for signs of anaemia (mucous membrane pallor), thyroid disease (exophthalmos, thyromegaly), hypercholesterolemia (xanthelasma ẃ is lipid deposit in the skin of the eyelids) or atherosclerosis (carotid brut). Examine the lower extremities for dependent (ankle) oedema, tendinous xanthomas (lipid deposit), weak pulses, or cutaneous signs of ischemia or necrosis. Perform general & peripheral vascular examination to identify signs of generalized or peripheral atherosclerosis (e.g. inequality of BP in arms, diminished pedal pulse & abdominal aneurysm). Carefully examine the heart for evidence of hypertrophy, murmur & 3rd or 4th heart sounds. Examine lungs for rales & abnormal sounds



Tendinous xanthomas

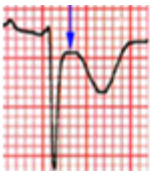


Xanthelasma

Diagnostic workup

ECG: if taken when pt is not in pain may be normal. The presence of new horizontal or down sloping of ST segment & new T-wave inversion are suggestive of myocardial ischemia. ST segment elevation associated é pain ẃ returns to normal as the pain wanes suggest variant angina. There are some things you should bear in mind before you can say if the pt really has angina or not. You need to see T wave changes on 2 or more consecutive leads (not including AVR) for you to get worried about it. The other

thing you can see on angina ECG is that the T wave (the last wave) is upside down. T wave inversion or even flattening is another sign of angina, but it is not a good one. It could also signify an old or current heart attack (MI).



ST depression

But clue like this is useful when you become more experienced & you are trying to interpret more difficult ECG's. Remember that history & change on the ECG is more important than a ECG by itself. ECGs are not fool proof - If you convinced that the pt has angina from the history but the ECG is normal then you should still contact some one senior. ECGs can be normal when really something awful happening.

Stress ECG: recording ECG during exercise ⇧ the sensitivity & specificity of ECG. This helps to quantify the pt's exercise tolerance. Presence of new horizontal or down sloping of ST segment depression has sensitivity of 70% & specificity of 90%.

Holter monitoring: 24 hrs ambulatory ECG, for different types of angina.

Radiologic/Imaging: **CXR** in pt é CHF.

Stress radionuclide ventricuography, *Stress ECHO* & *Cardiac catheterization.*

Other laboratory tests: CBC, FBS & lipid profile.

Differential Diagnosis

Consider other causes of chest pain like; pleurisy, pneumonia, pericarditis, ischemia associated é AS or hypertrophic cardiomyopathy.

Treatment

Therapy for angina should be directed either towards reducing myocardial O_2 demand, or to compensate for impaired flow through diseased coronary arteries or ⇧ myocardial O_2 supply (blood flow).

Life style measures: •Counsel pt about cessation of smoking.•Diet: ('healthy' diet like

low fat, low caloric diet é ⇧ habit of eating fruits & vegetables). •Regular exercise. •Wt reduction.

Organic nitrates: this class of drugs produce venodilatation & to lesser extent arteriolar dilatation. Dilate peripheral veins & so ⇩ preload. Dilate coronary arteries & so ⇧ myocardial blood flow. Dilate peripheral arteries & so ⇩ the afterload (afterload is the force that contracting heart must generate to eject blood, the afterload is affected by peripheral vascular resistance & BP). These effects of organic nitrates ⇩ the BP & cardiac size. You should instruct pt about how & when to use the short-acting nitrates (e.g. 0.4mg sublingual nitroglycerin) for the acute attacks, unless nitrates are contraindicated. Consider the long-acting nitrates in pt who have refractory chest pain despite maximal tolerated ß-blocker therapy, or in pt. who would benefit from after load reduction. To avoid nitrate tolerance in pt requiring long-acting nitrates, prescribe a 10-12 hrs nitrate-free period daily.

Nitroglycerine: 0.3-0.6 mg sublingual as soon as the pain starts or 5 min before a stressful activity.

Isosorbide dinitrate slow release: 10-60 mg PO TID or 2.5-10 mg sublingual/4-6 hrs. Major adverse effects of nitrates are headache, hypotension & tolerance.

β- Blockers: act by blocking myocardial β-adrenergic receptors. ⇩ HR & COP, also ⇩ myocardium workload (contractility). By doing so ⇩ cardiac O_2 demand.

Propranolol- is non-selective β1 & β2 blockers 20-80 mg PO BID-QID.

Metoprolol- is selective β1 blocker, 25-200 mg Po BID.

Atenolol- selective β1 blocker, 50-150 mg PO daily.

Consider the pt concomitant health problems when selecting a specific ß-Blocker.

β-Blockers are contraindicated in pt é asthma or severe CHF.

Side effects: bradycardia,⇩ COP & bronchoconstriction é the nonspecific drugs.

Ca Ch Bls.: act by ⇩ smooth muscle tone of coronary arteries, especially effective in preventing coronary spasm that cause variant angina. Also used for hypertension & arrhythmia. Mechanism of action is through blocking the calcium channels in vascular smooth muscles, dilate coronary arteries & ⇧myocardial blood flow, also dilate peripheral arteries & ⇩ the afterload. Consider Ca Ch Bls when ß-blockers are contraindicated or not tolerated. Consider using combination therapy cautiously (e.g. ß-blocker + Ca Ch Bl or nitrate) for pt who fail to respond adequately to monotherapy.

Nifedipine XL 30 mg PO daily.

Verapamil 180-240 mg daily.

Amlodipine 5-10 mg daily. Side effect: headache, hypotension, reflex tachycardia, risk of heart block& HF particularly é verapamil.

Antiplatelet agents: Aspirin prevent platelet aggregation, use for prophylaxis of blood clots particularly in unstable angina, small dose is recommended for pt é angina to prevent the occurrence of MI. 75-150 mg PO daily. Alternative is Plavix.

Lipid lowering drugs: generally, prescribe a lipid-lowering medication (Statins) & a low-fat, low-cholesterol diet for pt é CAD & elevated LDL levels to achieve an LDL level of ⟨100 mg/dl.

ACE inhibitor: may be beneficial in pt é significant CAD by angiography or for those é previous MI who have DM &/or LV dysfunction.

Treat comorbidities: that can provoke or exacerbate angina (e.g., hypertension, DM, hyperthyroidism, pulmonary disorders, anaemia). Always refer pt presenting é new-onset angina, or rest angina, or increasing angina to an emergency department & hospitalize pt é clinical evidence of unstable angina or MI.

Coronary angioplasty: uses a balloon catheter to open occluded blood vessels. Performed under local anesthetic. Carries 5% mortality & high rate of vessel reoccusion.

Use of "stents" in opened vessel ⇩ the rate of occlusion. Stent is effective during the first 3 hrs after occurrence of MI, new stents include; drug impregnated & self-absorbable one. Up to 6 or 8 stent may be used sometimes.

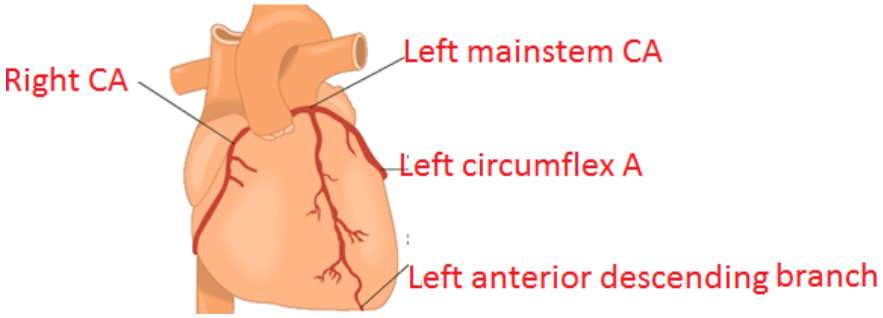
Coronary artery bypass: revascularization procedure in ẃ a blood vessel is taken from elsewhere in the body & surgically sutured around a blocked coronary artery. May involve multiple (1-5) vessels. Reocclusion of transplanted vessel is possible.

Prognosis: depends upon status of coronary arteries & LV function.

MYOCARDIAL INFARCTION

AMI or "heart attack" is an irreversible injury to & eventual death of myocardial tissue result from ischemia & hypoxia, is a leading killer of both men & women. Most heart attacks result from occlusion of coronary blood vessel by lipid deposit. These lipid deposits may accumulate to the point where they completely block a coronary vessel or, more commonly, accumulated lipid plaques may break off from the vascular endothelium & act as thrombus that blocks coronary artery at a narrower point downstream. Prolonged vasospasm might also ppt a AMI.

Coronary blood flow



The location of a MI will be largely determined by ẃ coronary blood vessel is occluded. The 2 main coronary arteries supplying the myocardium are:-

*left coronary artery: subdivides into left anterior descending & circumflex branch.

*Right coronary artery.

When myocardial blood supply is abruptly ⇩ or cut off to a region of the heart, a seq-

uence of injurious events occur beginning é ischemia (inadequate tissue perfusion), followed by necrosis & eventual fibrosis if the blood supply is not restored in an appropriate period of time.

Types of Myocardial infarction

- Transmural: involves full thickness of ventricular wall, tend to have a greater effect on cardiac function & pumping ability.
- Subendocardial: involves inner 1/3 to 1/2 of the ventricular wall.

Symptoms

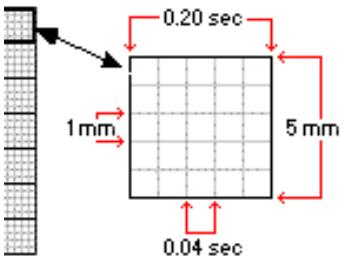
Chest pain: sever squeezing or crushing type of chest pain that lasts for **>** 30 min & not relived by rest or sublingual nitroglycerine. Pain radiates in a similar pattern to angina. Usually occurs when pt is at rest or involved in minimal activity. Emotional stress may also ppt AMI. Pt deny presence of a problem & try to find an explanati- on. Also significant % of AMI are "silent" é no symptoms & may be discovered on doing routine ECG.

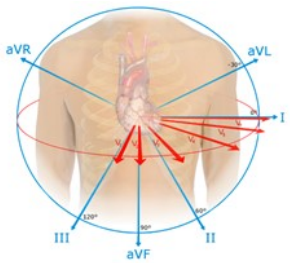
Other associated symptoms: Nausea. Vomiting. Excessive sweating. Shortness of breath. Anxiety & Sense of impending doom.

Physical examination

Pt is in pain &quite apprehensive often appears ashen. ⇩BP & ⇧HR, seen é extensive infarction, signs of CHF may be seen. A new murmur of MR may be present.

Diagnostic work up



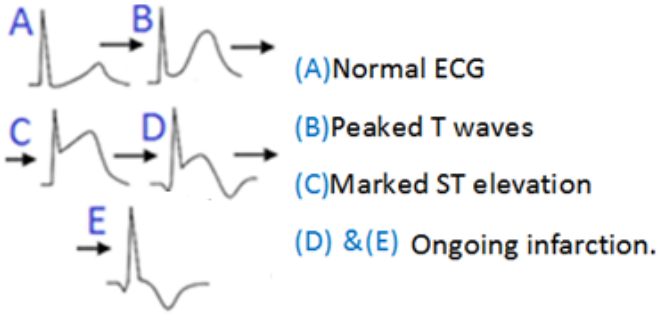


① ***ECG:*** diagnostic in ~85% of cases. To diagnose MI you need to go beyond looking at a rhythm strip & obtain a 12-Lead ECG. The 12-Lead ECG sees the heart from 12 differ-

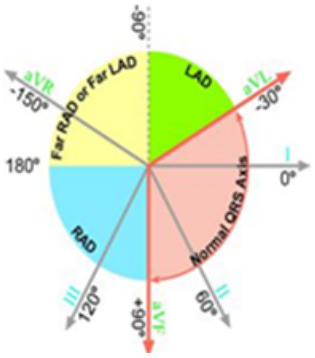
ent views. Therefore, the 12-Lead ECG helps you see what is happening in different portions of the heart.

Clue: look at AVL & AVF, if no changes of both ⇨ Anterior MI. If AVF show changes ⇨ Inferior MI. If AVL shows changes ⇨ Lateral or Anterolateral.

ECG changes over time é AMI occurs as follow:-



Determination of axis deviation



I	II	Axis
+	+	Normal
+	-	Left axis deviation
-	+	Right axis deviation
-	-	Right superior axis deviation

A quick way to determine the QRS axis is to look at the QRS complexes in leads I & II.

Normal axis deviation: the QRS axis falls between -30^0 ⇨ $+90^0$ because ventricular depolarization is leftward & downward.

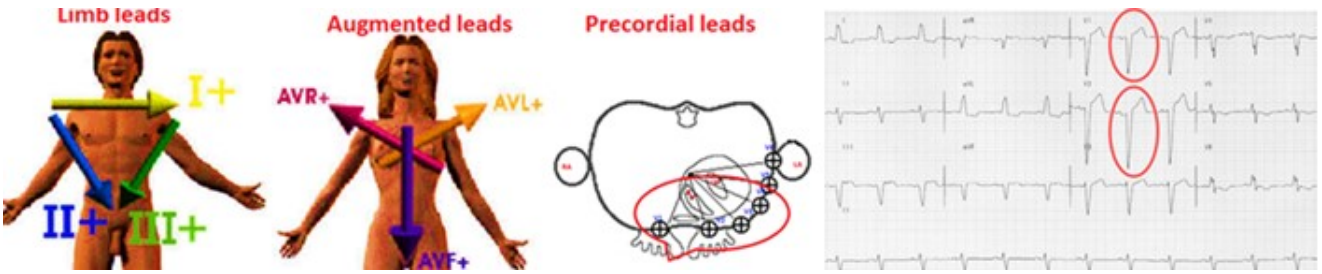
◍ LAD: occurs when axis falls between -30^0 - 90^0.

◍ RAD: occurs when axis falls between $+90^0$ ⇨ $+150^0$.

◍ RSAD: occurs when axis falls between $+150^0$ ⇨ -90^0.

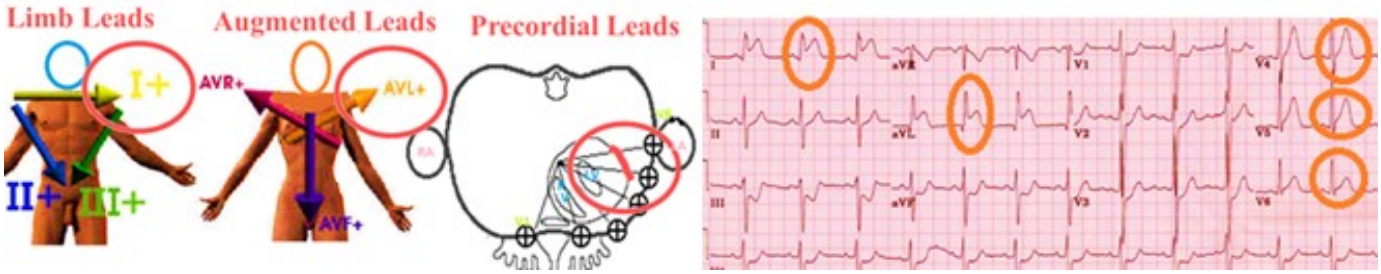
ECG changes on MI:

***Anterior MI: If you see changes in leads V1, V2, V3, V4 that are consistent é MI, you can conclude that it is an anterior wall MI.



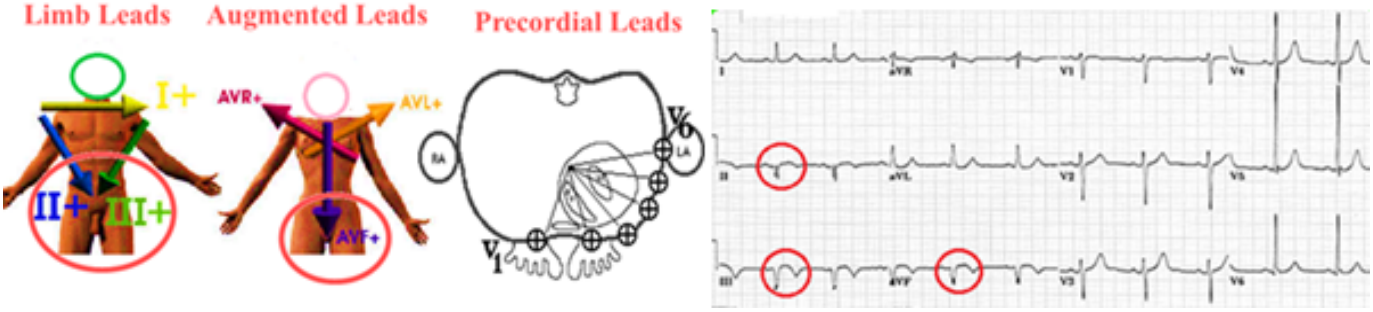
Interpretation: Yes, this person is having MI involves the anterior wall. Note the ST elevation in leads V1, V2.

*** Lateral MI: If you see changes in leads: I, AVL, V4, V5,V6



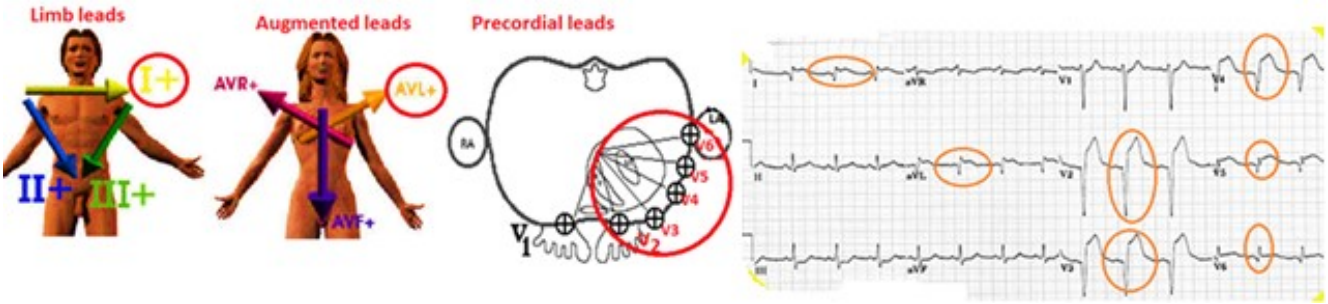
Interpretation: Yes, this person is having MI involves lateral wall (I, AVL, V4- V6)!

*** Inferior MI: If you see changes in leads: II, III, AVF



Interpretation: Yes, this person is having MI involves the inferior wall. Note the ST elevation in leads II, III, AVF.

*** Anterolateral MI: If you see changes in leads: I, AVL, V5, V6 + V2, V3, V4.



Interpretation: Yes, this person is having MI involves both the anterior wall (V2, V3, V4) & lateral wall (I, AVL, V5, V6)!

② ***Cardiac enzymes:*** as the myocardial necrosis occurs, the myocardial damaged cells releases cardiac enzymes into the circulation. CPK elevation appears 6 hrs aft- er MI. SGOT elevates 12 hrs after MI. LDH starts to elevate 24 hrs after MI. Cardiac specific troponin-T & troponin-I, are also elevated, starts to elevate during the first few hrs, both are very specific to cardiac muscles, these proteins normally undetectable in the blood of healthy individuals, but rise ›20 X in pt é AMI.

③ ***Cardiac Imaging:*** ECHO: ⇩ myocardial function (⇩ EF) & significant wall motion abnormality may be detected. Radionuclide imaging.

Complications of MI

Depending on the extent of the area involved in MI, a number er of complications might arise, including the following:-

- ***Arrhythmias:*** is common on as result of hypoxia, acidosis & altered electrical con- duction through damaged & necrotic areas of myocardium, may be life-threat- ening & lead to fibrillation. Lethal ventricular arrhythmia are the commonest cause of death in the first hour. This include; ventricular tachycardia or ventricular fibrillation. Atrial arrhythmias also may be seen as AF or atrial flutter.
- ***Acute conduction system abnormality:*** the conduction system may be part of the myocardium affected during infarction. This may lead to bradycardia & heart block. Inferior wall MI occurs when the right coronary artery is occluded. Since it supplies the AV node, sinus bradycardia & varying degrees of AV block may occur. In case of Anterior MI right or left bundle branch block may occur.
- ***Pump failure:*** CHF is most likely, when 30% of the myocardium is infarcted. Cardio- genic shock is defined as SBP ‹90 mmHg: occurs if ›40 % of the myocardium is affect- ed by infarction. Cardiogenic shock is associated é a mortality rate > 80%.
- ***Mitral regurgitation:*** may occur if papillary muscles are affected.

- ***Ventricular septal defect:*** LV septum may become infracted either in anterior or inferior AMI, leading to rapture of the septum.
- ***Rupture of weakened myocardial wall:*** bleeding into pericardium may cause cardiac tamponade & further impairment of cardiac pumping function. Most likely to occur é Transmural MI (involvement of full thickness of ventricular wall). Rupture of the septum between the ventricles might also occur if the septal wall is involved
- ***Left ventricular aneurysm:*** the infracted myocardium may evaginate & heal é fibrous tissue. May be a source for cardiac emboli.
- ***Pericarditis:*** post AMI pericarditis (Dressler's sy.), is believed to be autoimmune in origin. Often occurs 1-2 days after the MI.
- ***Formation of thromboembolism:*** from blood pooling in ventricles.
- ***Pulmonary infarction:*** is common on 2^{nd}-3^{rd} wk after infarction, pain, fever, haemoptysis, heart failure & pleural rub.

Management of MI

A main goal of intervention for MI is to limit the size of infarcted area & thus preserve cardiac function. Early recognition & intervention in a MI have been shown to significantly improve the outcome & reduce mortality in pts if employed in the early stages of MI. Antiplatelet-aggregating drugs such as Aspirin & clot dissolving agents such as streptokinase & tissue plasminogen activator may be very effective at improving myocardial blood flow & limiting damage to the heart muscle. Other drugs such as vasodilators, β-adrenergic blockers & ACEIs can also improve blood flow & reduce workload on the injured myocardium & thus reduce the extent of myocardial damage. The development of potentially life-threatening arrhythmias is also common during MI as consequence of hypoxia, acidosis & enhanced autonomic activity & must be treated é appropriate antiarrhythic drugs & immediate referral to hospitals é ICU facility.

Management is outlined as follows:-

- ***Emegrency management***

Should start before pt reaches the hospital emergency room. A main goal of intervention is to limit the size of infarcted area & thus preserve cardiac function. Early recognition & intervention in MI have been shown to significantly improve the outcome & reduce mortality in pts. Oxygen used to maintain blood oxygenation as well as tissue & cardiac oxygen.

- ***General measures***

Reassure & make the pt comfortable. Supply O_2 by mask. Secure IV line. Give Aspirin 160-325 mg tab, if administered when MI is detected, the antiplatelet properties of aspirin may ⇩ the overall size of infarction & prevent further aggregation.

- ***Treat pain***

Nitroglycerin: sublingual up to 3 doses of 0.4 mg should administered at about 5 min interval. Morphine sulphate: very effective analgesic for pain associated é AMI, administered in small dose of 2-4 mg IV/5 min.

- ***Limitation of infarct size through reperfusion/revascularization***

Thrombolytic agents: as Streptokinase, t-Plasminogen activator, Urokinase: these drugs are given to dissolve the occlusive thrombus & promote reperfusion of the infarct related artery, reduces mortality from MI when administered within 6 hrs of the onset of chest pain, but contraindicated é history of cerebrovascular Hge or marked hypertension or bleeding disorder. The direct per-cutaneous transluminal coronary angioplasty is the preferred method to restore perfusion of occluded coronary artery. The short & long term outcomes are much better than what can
be archived through thrombolysis/or fibrinolysis.

- ***Hospital phase management:*** include, General & Specific measures;

General measures

***Activity:** absolute bed rest for the first 12 hrs, sitting on their bed in the 1st 24 hrs, the pt may ambulate in their rooms by the 2nd or 3rd day.

***Diet:** because of the risk of emesis & aspiration soon after MI, pt should receive either nothing or only clear liquids PO for the first 4-12 hrs. Diet should be low in fat & calories & rich in potassium.

***Bowel motion:** constipation is common & straining may ppt AMI. Fibrous diet & stool softeners like Bisacodyl, Dioctylsodium Sulfosuccinate 200 mg/day are recommended. If pt. remains constipated laxatives can be prescribed.

***Sedation:** many pts require sedation during hospitalization to withstand the period of enforced inactivity é tranquillity. Diazepam 15-30 mg or Lorazeam 0.5-2 mg given 3-4 X daily.

Pharmacological therapy

1) ***Antithombotic & Anti platelet agents:*** unfractionated heparin: may be given in pts where there is a risk of cardiac thrombus formation &subsequent emboli. **Heparin** prevent clotting of blood through its action on ant thrombin 3, also inhibit formation of stable fibrin clot & has antilipaemic effect, starting dose 5000-10000 u IV followed by 1000 U/hr as continuous infusion using syringe pump é monitori-ng PT, APT. The IN to be kept 1.5-2 times of the normal value. or ***Calexane*** 40, 60, 80 u, SC/12 hrs. ***Calciparine*** 12.500 u, SC/12 hrs. ***Fraxiparine*** 0.6 ml, SC/12 hrs.

Fibrinolytic: are contraindicated for pt above 75 yrs, or pt é peptic ulcer, or bleeding disorder or major surgery in the last 2 wks, can be used é heparin during the 1st 24 hrs. Major side effects are; internal/GIT Hge, stroke & allergic reactions. Streptokinase derived from β-hemolytic streptococcus bacteria; involved in the activation of plasmin. **Kabikinase/Sidonase** during the 1st 6 hrs, 1.5million u IV infusion pump over 1hr.

Anistreplase complex of human lysplasminogen & streptokinase; administered as a prodrug. ***Alteplase*** "Rt-PA" 10 mg stat followed by 40 mg over one hour.

Urokinase endogenous human enzy that converts plasminogen to active plasmin.

2) ***Vasodilator:*** Nitroglycerin IV, ⇧blood flow to myocardium &⇩myocardial work. **Isordil/Dinitra/Angesid** 10 mg tab sublingual.

Isordil 10 mg tab 1X1 (long acting vasodilator).

Tridil: 50 mg/10 ml amp (glycerine trinitrate) IV diluted é G 5%, 1 ug/Kg/min. é careful monitoring for ⇩ of BP.

3) ***β-Blockers:*** have short & long term benefits for pts:-short term benefit as; relive pain & ⇩ the risk of arrhythmia. Long term benefits as; improving myocardial performance & facilitate healing process in post MI pts. ***Metoprolol****:* 25-200 mg BID. ***Atenolol****:* 50-150 mg PO daily. Contraindicated é severe CHF, AV block.

4) ***ACEIs:***⇩ mortality rate & improve long-term survival in post AMI by preventing cardiac remodelling ẃ may have led to progressive HF. Their effect is additive to what is archived é aspirin & β-blockers. The maximum benefit is seen in high-risk pts (elderly pt, significant LV dysfunction).

Captopril: start é smaller dose 12.5mg PO/D to gradually escalate to 75mg PO BID.

Enalapril: start é 12.5 mg PO daily, escalate gradually to 40 mg PO/day.

5) ***Aspirin/Plavix:*** inhibits the cyclooxygenase pathway for the synthesis of prostaglandins, prostacyclins & thromboxanes. Inhibits aggregation of platelets & is effective in reducing MI, stroke & mortality in high-risk pts.

Aggrex 75 mg tab. 1 X 1 daily, or ***Plavix*** tab. 1X1 daily.

6) ***Marevan*** after discharge from hospital, maintenance therapy 1 mg tab daily, follow up by INR to keep INR from 2-3.

7) Ca.Ch.Bls, ***Delaytiazim*** 90, 120 mg tablet 1 X 1.

8) ***Antioxidant: Omega 3*** 1 X 1 daily.

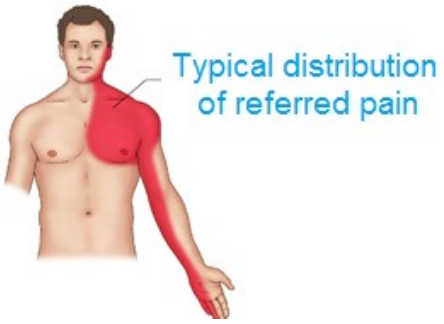
9)***Lipid regulating agent, Zocor*** tab. 1 X 1 daily to keep cholesterol < 250 & triglyceride <200 & LDL <100, & HDL >35. Lipid profile to be repeated monthly.

Management of complications

- ***Malignant arrhythmias:*** cardiac defibrillation. Prophylactic lidocaine. Other antiarrhythmic agent as; Bertyluim, Tosylate & Procainamide.
- ***Serious conduction disturbances:*** sinus bradycardia: Atropine 2 mg IV may restore heart rate. AV block: transcutaneous pace makers.
- ***Heart failure:*** diuretics, salt restriction, ACEIs, vasodilators. The use of Digoxin is controversial.
- ***Cardiogenic shock:*** do ECHO to assess the ventricular function. IVF to maximize LV filling. Use of vasopressors (Dubutamine, Dopamine) in IV infusion. Intra-aortic balloon pumping. Percutaneous transluminal angioplasty.

Prognosis

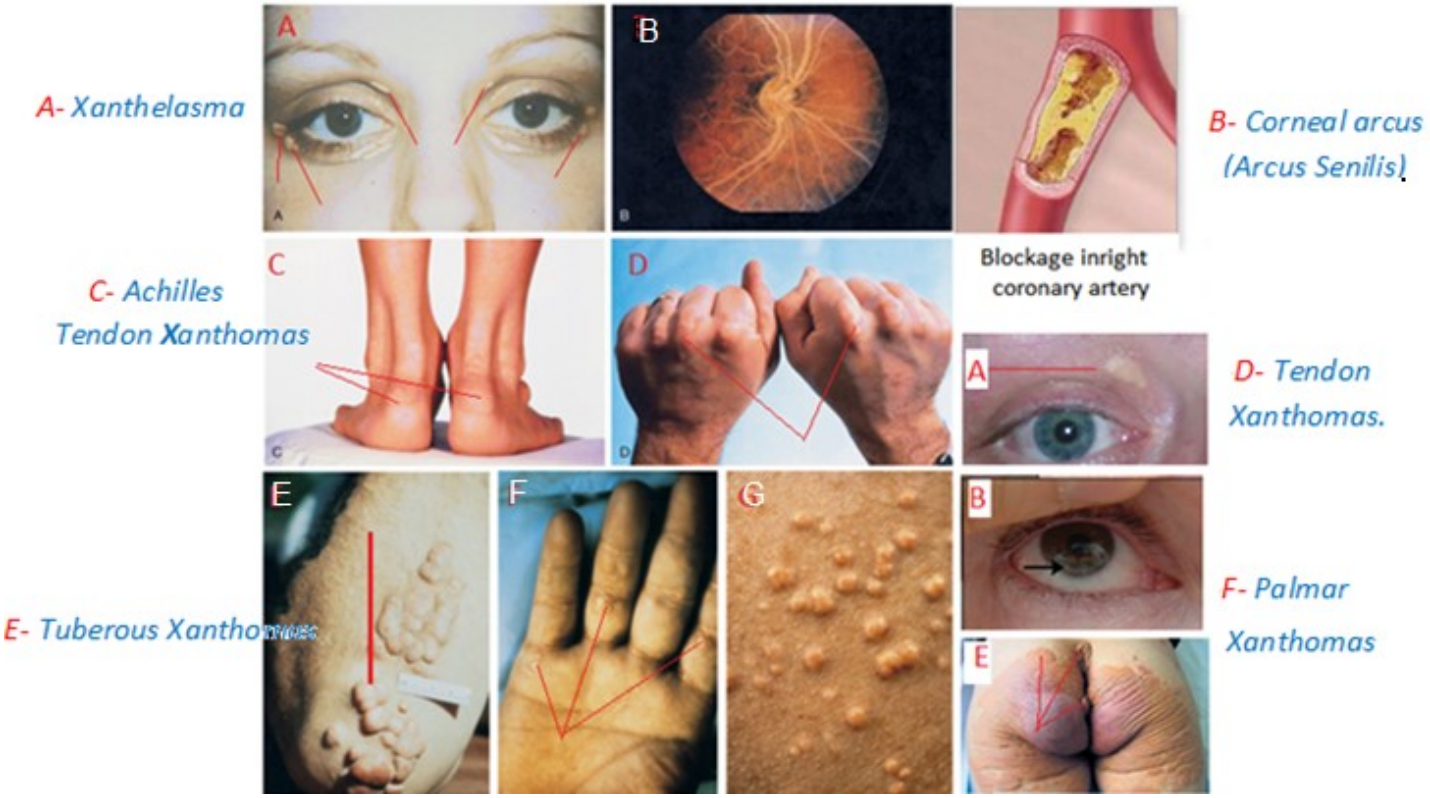
Depends upon number of vessels affected & extent of ventricular damage. Pt é uncorrected main left coronary artery disease have 20% mortality in the 1st year. Single vessel coronary artery has 2% annual mortality. Double vessel disease has 2-4 % annual mortality. Triple vessel disease has 5-8% annual mortality. The left ventricular EF of **<** 40% doubles the yearly mortality.



FAMILIAL HYPERCHOLESTREMIA

AD disorder, characterized by high levels of LDL & early coronary artery disease. Heterozygous ~1 in 500 & Homozygous ~1/1,000,000. Greater risk of heart disease (100 X for males 20-40 yrs). 85% of affected individuals remain undiagnosed.

Diagnosis: in addition to ⇧ cholesterol, the following manifestations may be seen:



Suspicions & Screening:

Who to screen? ▲Anyone é high cholesterol by age 20. ▲All children aged 9-11 ▲Children as young as 2 yrs é family history of premature cardiovascular disease or very high cholesterol levels.

Who to suspect?

- Adults aged 20 or older é LDL cholesterol >190 mg/dl.
- Children aged 9-11 yrs é LDL cholesterol 160 mg/dl.

Management

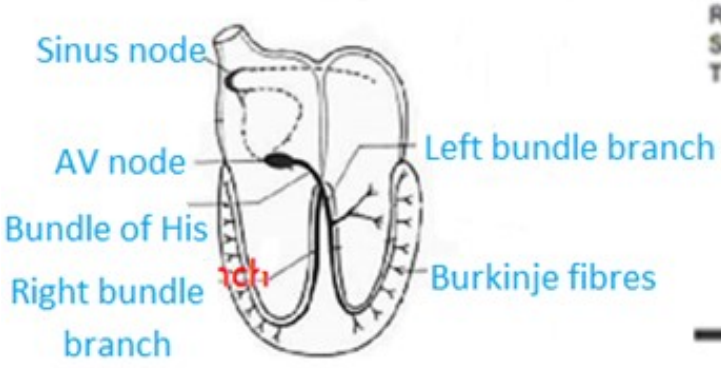
•Early identification •Reduction in morbidity through changes in the lifestyle. Diet, exercise & no smoking • Use of statins to lower cholesterol.

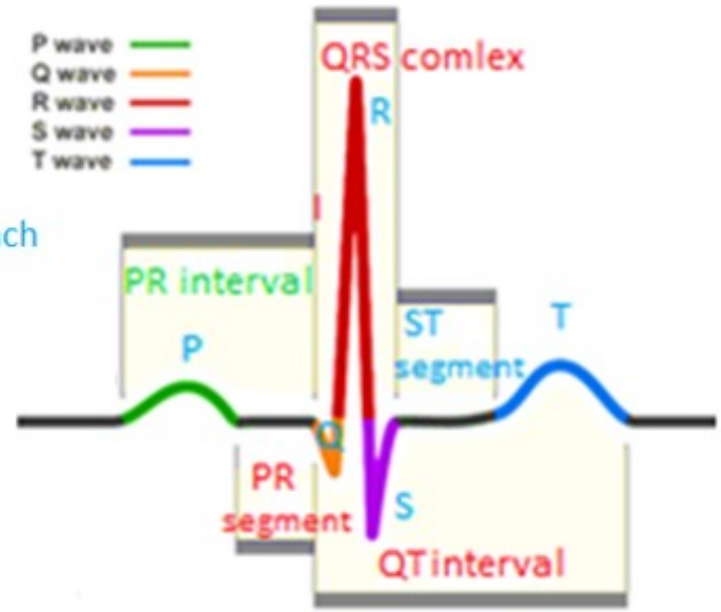
CARDIAC ARRHYTHMIAS

Cardiac arrhythmias are changes in the regular beating of the heart. The heart may seem to skip a beat or beat irregularly or beat very fast or very slow. Normal heart beat of a person ranges from 60-100/min. Many arrhythmias occur in people who do not have underlying heart disease. Most of the time, there may not be a recognizable cause of an arrhythmia. Heart disease may cause arrhythmias. Other causes include; stress, caffeine, tobacco, alcohol, cough & cold medicines. In a very small number of people é serious symptoms, arrhythmias themselves are dangerous. These arrhythmias require medical Rx to keep the heart beat regular. Arrhythmias occur commonly in middle age adults. As people get older, they are more likely to experience an arrhythmia. Pts é arrhythmias often complain that they felt their heart beat very fast, experienced a fluttering in their chest, or noticed that their heart skipped a beat. Almost everyone has also felt dizzy, faint, or out of breath or had chest pain at one time or another. Also arrhythmia seen in 40% of premature babies.

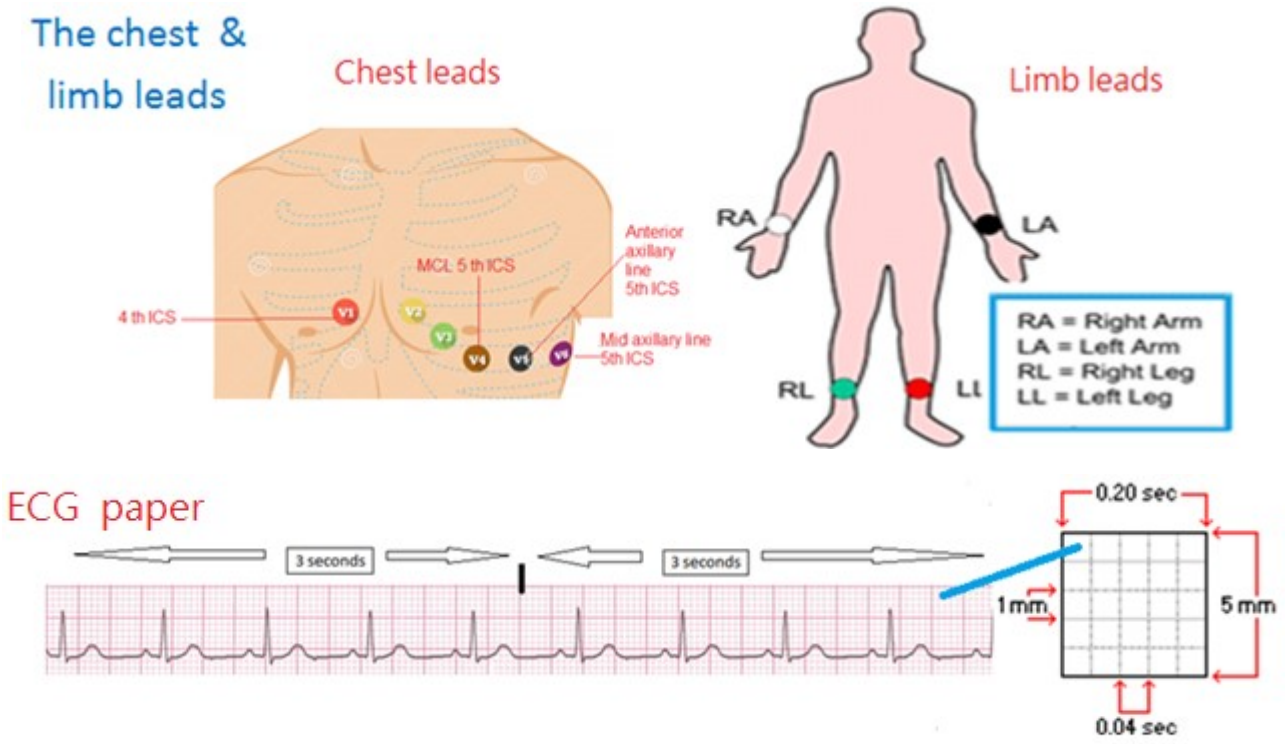
Normal impulse conduction

SAN ⇨ AVN ⇨ Bundle His ⇨ Bundle branch ⇨ Purkinje Fibres





Doing an ECG



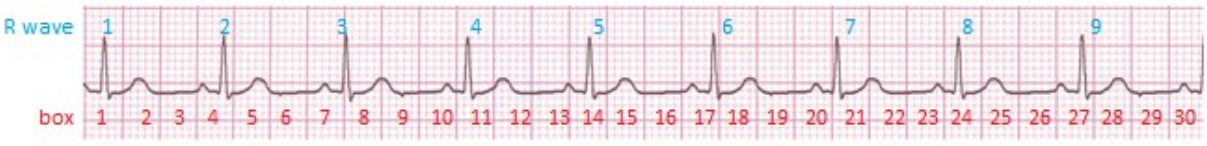
Practical point to remember on interpretation of an ECG:-

- P wave: represent atrial depolarization.
- QRS: represent ventricular depolarization.
- T wave: re-present ventricular repolarization.
- Small box = 0.04 sec. (1 mm).
- Large box = 0.2 sec. (5 mm or ½ mv).
- Every 15 large boxes in the strip =3 sec. This helps when calculating the HR.
- P wave: normally < 2 small squares & its peak is < 2 small squares. A Wider bifid P wave means LAH. A peak of P wave> 2 small square means RAH.
- P-R interval: normally < 4 small squares (4 mm).
- R wave: normally 2 mm height.
- QRS wave: normally 3 mm width, become broader in Heart Block.
- S-T segment elevation: seen in MI, Pericarditis, or Ventricular Aneurysm.
- S-T segment depression: seen in Hypertension, IHD, LVH, Hypokalaemia, Hypocalcaemia, or Digitalis toxicity

How to read an ECG

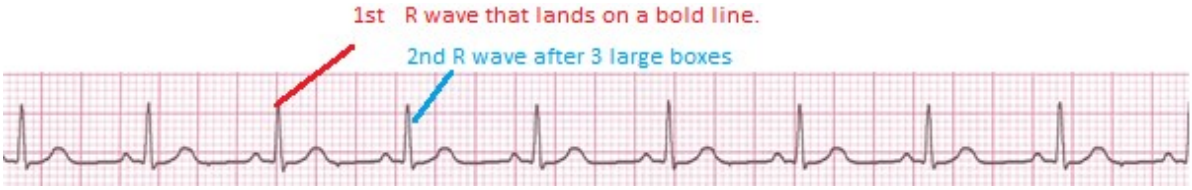
Step 1: Calculate Rate

Option 1:



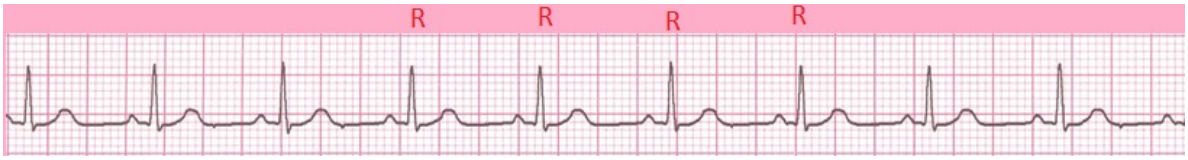
Count number of R waves in 6 second rhythm strip, (30 large boxes) then multiply by 10. Interpretation of the above strip rate *9 x10 = 90 bpm.*

Option 2:



Find a R wave that lands on a bold line. Count number of large boxes to the next R wave. If the 2nd R wave is 1 large box away the rate is 300, 2 boxes away the rate is 150, 3 boxes -100, 4 boxes -75, etc.

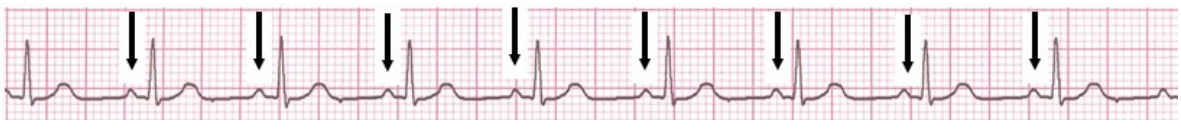
Step 2: Determine regularity



Look at the R-R distances (using markings on a pen or paper). Is it regular ? or occasionally irregular? or regular irregularity ? or it is irregular irregularity?

Interpretation of the above strip: regular rhythm.

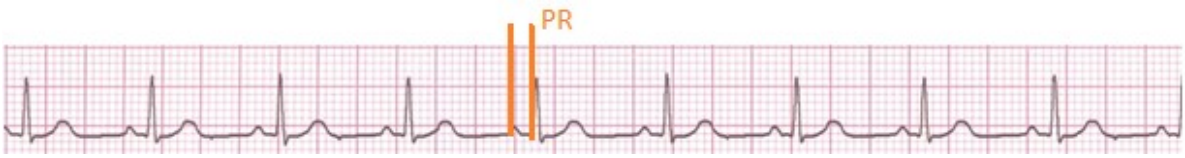
Step 3: Assess the P waves



Are there P waves ? Do the P waves all look alike ? Do the P waves occur at a regular rate? Is there one P wave before each QRS?

Interpretation: the above ECG shows normal P waves é one P wave for every QRS.

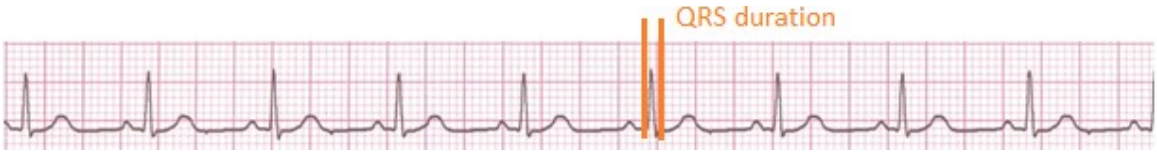
Step 4: Determine PR interval



Normal PR interval = 0.12-0.2 seconds (3-5 small boxes = 3-5 mm).

Interpretation: normal PR interval (0.12 seconds).

Step 5: Determine QRS duration



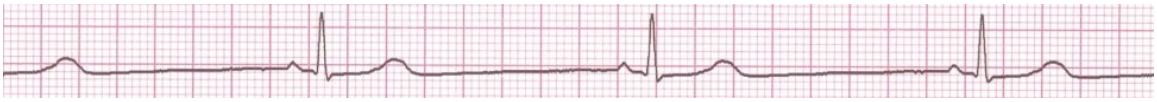
Normal QRS= 0.04-0.12 seconds (1-3 small boxes = 1-3 mm).

Interpretation: normal QRS (0.08 seconds).

RECOGNIZE THE 13 MOST COMMON RHYTHM DISTURBANCES.

Look to each of the following strips & try to interpretate.

1-Sinus Bradycardia



Rate: 30 bpm. -Regularity: regular. -P waves: normal. -PR interval: 0.12 second. - QRS duration: 0.10 second.

Interpretation: *Sinus bradycardia*

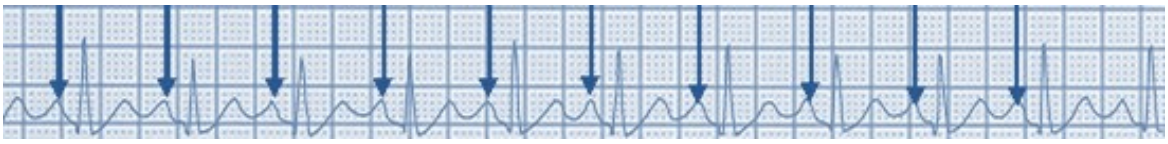
Comment: deviation from normal sinus rhythm, the HR is ˂60 bpm, SA node is depolarizing slower than normal, impulse conducted normally (i.e. normal PR & QRS interval).

Causes: •Physical conditioning in professional athletes. •Hypothyroidism. •Sinus node dysfunction.

Therapy: •If it is physiologic no need for treatment. •If it is due to sinus dysfunction & severe (the HR is **<** 35 bpm):- o Atropine: 1 mg IV may temporarily ⇧ the si-

nus rate. o Cardiac pacemaker implantation.

2- Sinus Tachycardia



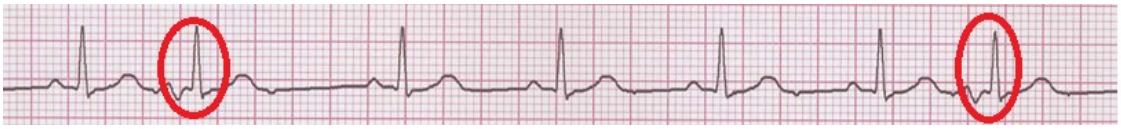
Rate: 130 bpm. -Regularity: regular. -P waves: normal. -PR interval: 0.16 sec.-QRS duration: 0.08 second.

Interpretation: Sinus tachycardia

Comment: the SA node depolarizing faster than normal, impulse is conducted normally (SA node sends out electrical signals faster than usual, speeding HR).

Causes: it represents physiologic sinus tachycardia in response to physical or psychological stress. Rate rarely exceeds 200 bpm.

3-Premature Atrial Contractions

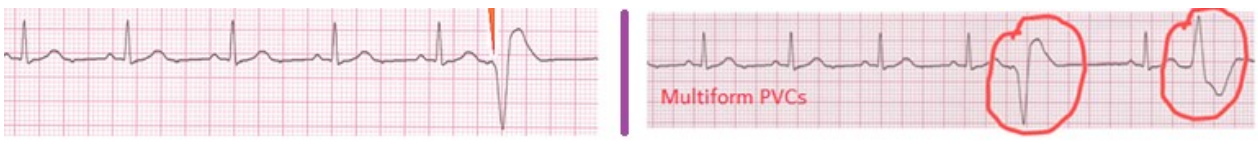


Rate: 70 bpm -Regularity: occasionally irregular -P waves: beat 2 & 7 have different contour -PR interval: 0.14 second (except beat 2 & 7) -QRS duration: 0.08 second.

Interpretation: Normal sinus rhythm é PACs.

Comment: these ectopic beats originate in the atria (but not from SA node), therefore the contour of P wave, PR interval & the timing are different than a normally generated pulse from SA node. The excitation of an atrial cell forms an impulse that is then conducted normally through the AV node & ventricles.

4- Premature Ventricular Contractions



Rate: 60 bpm. -Regularity: occasionally irregular. -P waves: 6 are normal & no P wave

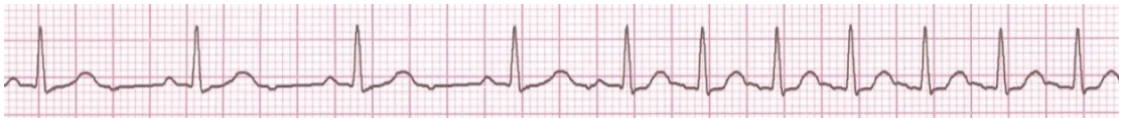
for the 7th QRS. -PR interval: 0.14 sec. QRS: duration is 0.08 sec. & the 7th QRS is wide.

Interpretation: *Sinus Rhythm é one PVC. (in left strip & multiform in the right)*

Comment: ectopic beats originate in the ventricles resulting in wide & bizarre QRS complexes. When there are ›1 PVCs & look alike, they called "uniform". When they differ they called "multiform". One or more ventricular cells are depolarizing & the impulses are abnormally conducting through the ventricles. When an impulse originates in a ventricle, conduction through the ventricles will be inefficient & the QRS will be wide & bizarre. PVCs are among the commonest arrhythmias.

Therapy: most of the isolated PVCs are benign & need no treatment.

5- Paroxysmal Supraventricular Tachycardia



Rate: variable, 74 ⇨ 148 bpm - Regularity: regular ⇨ irregular. - P waves: normal ⇨ none. - PR interval: 0.16 sec. ⇨ none. - QRS duration: 0.08 sec.

Interpretation: Paroxysmal Supraventricular Tachycardia

Comment: series of early beats in the atria speed up the heart rate. Heart rate of 150-250 bpm, occur as repeated periods, begin & end suddenly. Often occurring in pt é otherwise normal heart. The incidence ⇧ é age & é the presence of cardiovascular diseases. The Incidence of new cases is 35/100.000 persons/year.

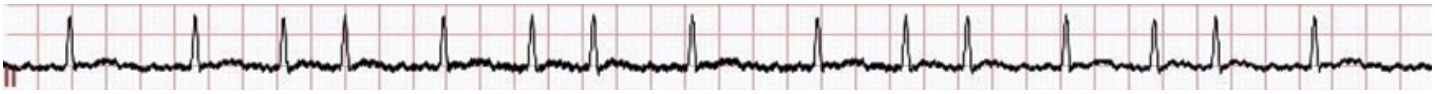
Causes: •Exercise •Fever •Anxiety •Thyrotoxicosis •Hypoxemia or •Hypotension.

Clinical picture:Palpitations: trigger is usually not identified. Feeling of heart pounding in chest & neck. Anxiety, light headedness, dyspnea. Syncope & chest pain are uncommon, but may indicate coronary artery disease, especially in older pts. Psychological stress is very common.

Diagnosis: •ECG. •Holter 24 hrs monitor.

Treatment: •***If pt is stable:*** Identify & treat the underlying cause. •***If pt hemodynamically unstable:*** Mechanical Rx; carotid massage, to one side of neck because massage to both sides may cuse cerebral stroke, valsalva manoeuvre, head immersion in cold water. Medical Rx; β-blockers, Ca Ch BL. (Verapamil & Diltiazem). Digoxin 20 ug/Kg/D÷3 IM effective in 60-80% of pts. For chronic SVT, class 1A or 1C or Amiodarone work well. Inderal 40 mg 1X2 also effective. Ablation will cure it too, but usually done for young pts.

6- Atrial Fibrillation



Rate:? 100 bpm. - Regularity: irregular irregularity. - P waves: none. PR interval: none - QRS duration: 0.06 second.

Interpretation: Atrial Fibrillation

Comment: electrical signals in the atria are fired in very fast, uncontrolled manner. The electrical signals arrive in the ventricles in a completely irregular fashion & heart beat is completely irregular. No organized atrial depolarization, so no normal P waves as the impulses are not originating from the SA node. The atrial activity is chaotic resulting in irregular irregularity rate. Recent theories suggest that it is due to multiple reenterant wavelets conducted between the Rt & Lf atria. Either way, impulses are formed in totally unpredictable fashion. The AV node allows some of the impulses to pass through at variable intervals. 25% of people aged 40 yrs or older develop AF. Men affected > women & the number of people é AF is expected to double by year 2050. The heart beats are completely irregular, often too fast or too slow.

Causes: whilst some cases of AF have no known cause, conditions & life style factors known to lead to AF include:- •Age > 40 yrs. •Poorly controlled hypertension •HF. •DM. •Atherosclerosis. •Thyrotoxicosis. •Stress. •Fever. •Excessive alcohol intake.

•Hypotension. •Endocarditis. •Pericarditis. •CAD. •MI. •Open heart surgery. •Pulmonary embolism. •Cold •Mitral valve diseases. •Rheumatic heart. •Sick sinus syndrome •Obesity. •Iatrogenic or •Idiopathic.

Symptoms

May be experienced on regular basis, intermittently or not at all. **>50%** of episodes of AF are not felt by the pt. Symptoms include; fatigue, palpitations, dizziness, chest pain & breathlessness. Asymptomatic AF is substantial problem for individual health & the health care system: it may cause stroke. it is frequent despite antiarrhythmic drug Rx or catheter or surgical ablation. It may cause cognitive dysfunction & dementia.

Complications

- Stroke.
- Mesenteric ischemia.
- Claudications of lower limbs.

How does AF lead to stroke?

Blood pools in the atria ⇨ Blood clot forms ⇨ Whole or part of the blood clot breaks off ⇨ Blood clot travel to the brain & closes a cerebral artery ⇨ Stroke.

What is a stroke?

Stroke is the brain equivalent of MI. Blood must flow to & thro-ugh the brain for the brain to work properly. If this flow blocked by clot, brain los-es its energy &O_2 supply, causing brain damage that can lead to disability or death. People é AF are 5 times more likely to have stroke, while 20-30% of strokes are related to AF.

Classification of AF

⊙ ***Paroxysmal AF***: terminates in <7 days. ⊙***Persistent AF***: fails to terminate within 7 days. ⊙***Permanent AF***: >1 yr. ⊙***Lone AF***: individuals éout structural heart disease, & <60 yrs.

EHRA score for AF (according to symptoms)

	Explanation
EHRA I	No symptoms
EHRA II	Mild symptoms, normal daily activity not affected
EHRA III	Severe symptoms, normal daily activity affected
EHRA IV	Disabling symptoms, normal daily activity discontinued

Diagnosis

HR 100-175/min, irregular, can`t count 4 consequent regular heart beats. Pulse deficit ≥ 10 beats difference between the radial pulse & auscultation. Difference in intensity of the 1st HS, absence of A wave in JVP & the ECG changes.

Management

The goal is to achieve rest HR 60-80 bpm & activity HR 80-110 bpm.

If pt hemodynamically unstable: direct current synchronous cardioversion: 2 watt /Kg/second, may repeated 2-3 times é duplication of dose.

If pt hemodynamically stable: identify & treat the underlying cause. Control the ventricular rate: β-blockers, Ca Ch BL, Digoxin. Restore sinus rhythm: Quinidine.

Antithrombotic therapy: anticoagulant & Antiplatelet medications. The Anticoagulant should be recommended in every pt é persistent or paroxysmal AF unless clinically contraindicated. The INR control goal is to keep it at a range of 2-3.

Reasons for not prescribing anticoagulation

•Advanced Age. •High falls risk. •Dementia. •Poor INR control. •Atrial Flutter. •Frailty. •History of previous significant Hge or risk factors for bleeding.

Antiplatelet: near-complete platelet inhibition is achieved ē Aspirin 75 mg daily.

Major issues at present

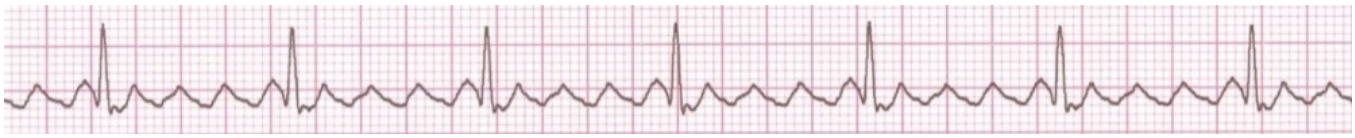
▲Early Rx by rhythm control therapy?

▲Anti-arrhythmic drugs Vs catheter ablation?

▲Better prevention by novel drugs, health care costs.

Category	Drug	IV dose	Oral (maintenance)
B Blockers	Metoprolol CR/XL	2.5-5 mg bolus over 2 min up to 3 doses	100-200 mg
	Bisoprolol		2.5-10 mg
	Atenolol		25-100 mg
	Esmolol	50-200 ug/kg/min	
	Propranolol	0.15 mg/kg over 1 min	10-40 mg tid
	Carvedilol		3.125-25 mg bid
Ca Ch Bls	Verapamil	0.0375-0.15 mg/kg over 2 min	40-360 mg bid
	Diltiazem		60 -360 mg tid
Digitalis	Digoxin	0.5- 1 mg	0,125 mg- 0.5 mg
	Digetoxin	0.4 – 0.6 mg	0.05 mg-0.1 mg
Others	Amiodarone	5 mg/kg in 1 hour	100mg-200 mg

7-Atrial Flutter



Rate: 70 bpm -Regularity: regular. -P waves: flutter waves. -PR interval: none. -QRS duration: 0.06 sec.

Interpretation: Atrial Flutter

Comment: no P waves, instead flutter waves (note saw tooth pattern) are formed at a rate of 250-350 bpm. Only some impulses conducted through the AV node (strip: every 4 P waves one QRS regular.

Etiology: reentrant pathway in right atrium é every 2nd, 3rd or 4th impulse generating a QRS, others are blocked in the AV node as the node repolarizes. Sometimes there may be a varying block resulting in irregular ventricular beat.

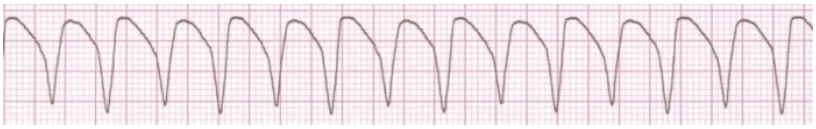
Causes: often associated é antecedent heart diseases:-

•Coronary artery diseases. •Pericarditis. •Valvular heart diseases. •Cardiomyopathy.

Therapy: •***Direct current cardioversion:*** if pt is hemodynamically unstable.

•***Drugs:*** Digoxin, Esmolol or Verapamil. Quinidine to restore sinus rhythm.

8. Ventricular Tachycardia



Rate: 160 bpm. -Regularity: regular. -P waves: none. -PR interval: none. -QRS duration: wide (> 0.12 sec).

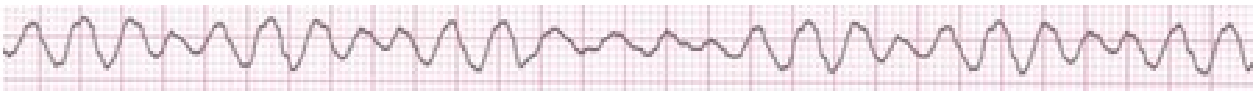
Interpretation: Ventricular Tachycardia

Etiology: there is a reentrant pathway looping in a ventricle (the most common cause). It occurs paroxysmal & exceeds 120 bpm é regular rhythm. There is AV dissociation & the ventricular arrhythmia proceeds independently of the normal atrial rhythm. During ventricular tachycardia, the ventricles do not have enough time to relax, ventricular filling is impaired & COP significantly ⇩. Ventricular tachycardia can sometimes generate enough COP to produce pulse; at other times no pulse can be felt. When ventricular tachycardia lasts for ›30 sec or requires control because of hemodynamic collapse it is called sustained ventricular tachycardia. Ventricular tachycardia may quickly degenerate to ventricular fibrillation & death.

Therapy: since this is a life threatening situation, urgent intervention needed.

Anti-arrhythmic drugs: IV Beretylium, Lidocaine or Procainamide may be useful in returning the pt's rhythm to normal while preparation is being made for ***DC cardioversion*** ẃ urgently required.

9. Ventricular Fibrillation



Rate: none. -Regularity: irregular irregularity. -P waves: none. -PR interval: none.

- QRS duration: wide, if recognizable.

Interpretation Ventricular fibrillation

Etiology: electrical signals in the ventricles are fired in a very fast uncontrolled mann-

er, causing the heart to quiver rather than beat. It is characterized by lack of ordered contraction of the ventricles. Therefore there is no COP, thus ventricular fibrillation synonymous é death unless urgent conversion to effective rhythm can be accomplished.

Therapy

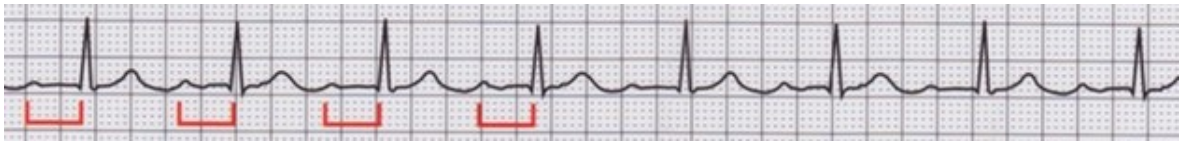
•Cardiac resuscitation.

•Mechanical ventilation.

•Intracardiac adrenalin.

•DC cardioversion using high voltage.

10- First Degree AV Block



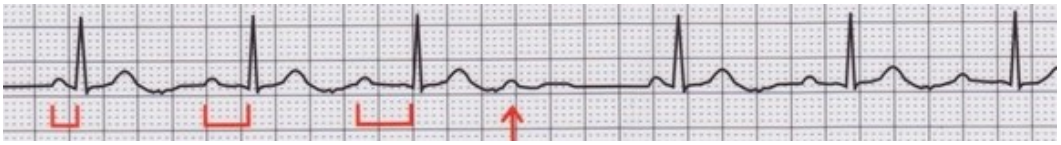
Rate: 60 bpm. -Regularity: regular. -P waves: normal. -PR interval: 0.36 sec. -QRS duration: 0.08 second.

Interpretation: First degree AV Block

Etiology: prolongation of PR interval > 0.2 second.

Therapy: we use Dopamine, or Isuprel.

11- Second Degree AV Block, Mobitz Type I (Wenckebach)

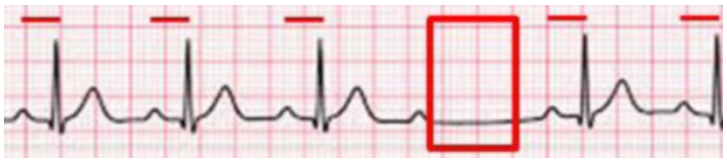


Rate: 50 bpm - Regularity: regular-irregularity - P waves: normal, but no QRS on the 4th beat - PR interval: progressively lengthens - QRS duration: 0.08 sec.

Interpretation: Second degree AV Block, mobitz type I.

Comment: PR interval progressively lengthens,then the impulse is completely blocked (P wave not followed by QRS).

12. Second Degree AV Block, Mobitz Type II

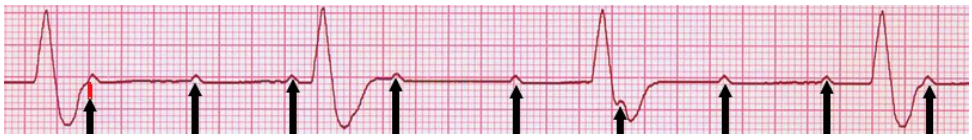


Rate: 40 bpm -Regularity: regular -P waves: normal & on the 4th beat no QRS - PR interval: 0.14 sec. - QRS duration: 0.08 sec.

Interpretation: 2nd degree AV Block Type II

Comment: occasional P waves are completely blocked (the P wave not followed by QRS). - Intermittent drop of QRS, can rapidly progress to complete heart block. No prolongation of PR interval before the dropped beat. Typically block occurs in the bundle of His.

13. Third Degree AV Block



Rate: 40 bpm. -Regularity: regular. -P waves: no relation to QRS. PR interval: none. - QRS: wide (> 0.12 sec). -The atrial rate > 100 bpm & ventricular rate is 38 bpm.

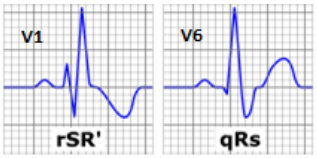
Interpretation: 3rd Degree AV Block

Comment: no atrial impulses conducted. Both atria & ventricles are contracting independen- tly. The ventricles own intrinsic pace maker kicks in at around 30-45 bpm & pts become symptomatic. No relation between P & QRS.

Therapy: pharmacologic therapy reserved only for acute situations for temporarily ⇧ of the ventricular rate. Atropine 0.5-2 mg IV or Isoproterenol 1-4 microgram/ min IV. Permanent cardiac pacemakers for most symptomatic AV blocks.

Right Bundle Branch Block

Right bundle branch block

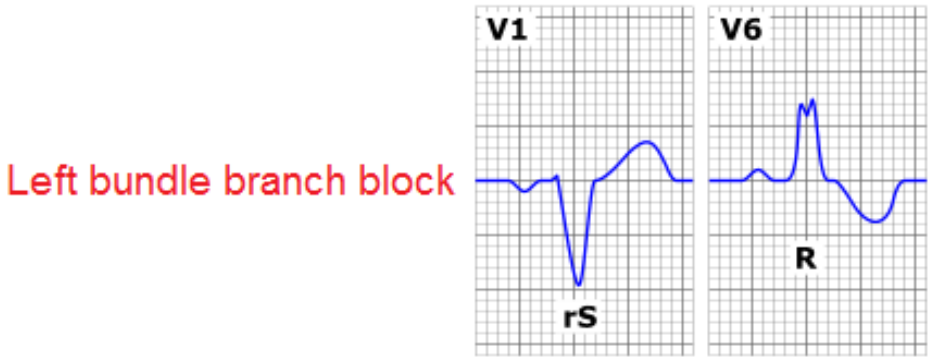


How is the right ventricle depolarized in RBBB? Impulses from the left ventricle; the septum depolarizes from left to right, the left ventricle is depolarised as norm al, the right ventricle is depolarized late & in an anterior direction. The QRS is wide due to slow conduction through myocardial cells.

ECG changes in RBBB: QRS duration exceeds 0.12 sec. RSR1 complex in V1. Delayed slurred S wave in I, aVL, V5 & V6. ST/T components are opposite in direction to the terminal QRS (this is 2ry to the block & does not predispose primary ST/T).

Significance of RBBB: Normal subjects "occasionally". Pulmonary embolus. Corona ry artery disease. ASD. Active cardities. Right ventricular diastolic overload.

Left Bundle Branch Block



How is the right ventricle depolarized in RBBB? the left ventricle is activated from the RBB & right ventricle. From the above diagram;

1a. Impulses pass to the left of the septum, therefore depolarizing it from Rt to Lf.

1b. Impulses travelling down the RBB simultaneously depolarize paraseptal region.

2. RV depolarization follows, small magnitude.

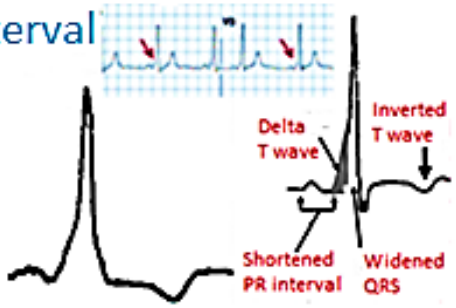
3. Delayed LV depolarization due to slow conduction through myocardium.

ECG changes in LBBB: QRS duration exceeds 0.12 sec. Wide, notched (M shaped) QRS in I, aVL, V5 & V6 (LBBB is best seen in V6). Wide, notched QS complexes in V1. Small r in V2 & V3 - paraseptal depolarization.

Occurs in? always indicative of organic heart disease. In IHD. In hypertension.

Wolf Parkinson White Syndrome

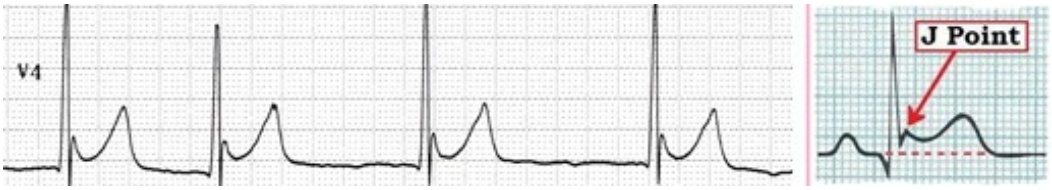
ECG shows: delta wave, short P-R interval widened QRS complex.



WPW is an abnormal band of atrial tissue connects the atria & ventricles & can electrically bypass the normal pathways of conduction. A reentry circuit can develop causing paroxysms of tachycardia.

Management: drugs includes Flecainamide, Amiodarone or Disopyramide. Digoxin & Verapamil are contraindicated. Transvenous catheter radiofrequency ablation (is the treatment of choice).

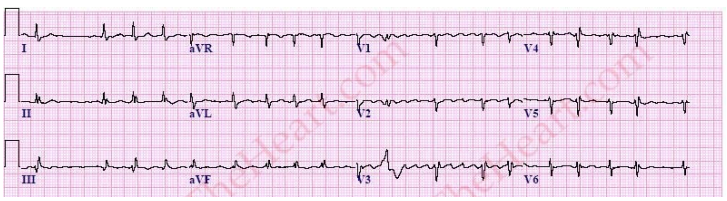
J Wave



ECG shows hump like wave superimposed on QRS distal limb (J Point). Bradycardia & Osborn waves (J-waves) all over.

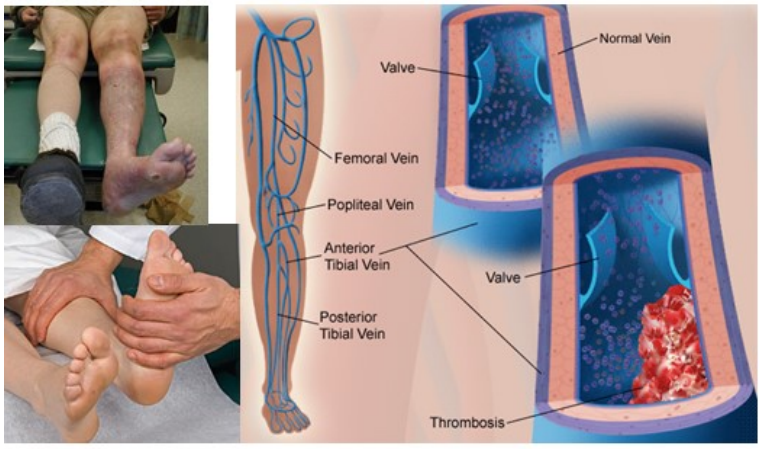
Causes: •Hypothermia (temp < 30 ^{0}C), but not pathognomonic, as J waves may be seen as a normal variant. •Hypercalcaemia. •Medication. •Head injury. •SAHge.

LOW VOLTAGE ECG



Seen in case of:- •Myxedema. •Pericardial effusion. •Constrictive pericarditis. •Emphysema. •Incorrect standardization.

VENOUS THROMBOEMBOLISM



Is a spectrum include (1) Deep venous thrombosis. (2) Pulmonary embolism.

Incidence: 1/1000 (⇧ é age).

Risk factors: •Stroke •Heart disease •Hyperlipidemia •Smoking in females •Obesi- ty •Cancer •+ve family history •Recent surgery, particularly orthopaedic, within past 4wks •Serious illness: sepsis, severe infection, ulcerative colitis •Polycythemia •Spinal cord injury, burns, lower extremity fractures •Contraceptives/oestrogen Rx & preg- nancy •Paralysis or immobility for 〉3 days •Plane or car travel (〉4 hrs).

Deep venous thrombosis in upper & lower extremities

Formation of a blood clot that does not break down, in a deep vein of the body. It can become large & obstruct the normal flow in the vein. Deep veins of the LL are the most common sites. If the clot breaks into smaller pieces, it becomes an embolus, travel to vital organs & cause heart attack, stroke, or pulmonary embolism.

Clinical picture

•Sudden swelling in the affected limb. Calf tenderness or limb pain.

•+ve Homan's sign (discomfort in calf muscles on forced foot dorsiflexion é knee straight, but Homan's sign is neither sensitive nor specific & is present only in 〈1/3 of pts é confirmed DVT & found in 50% of pts éout DVT.

•Dilated superficial collateral veins, minute petechiae/ecchymosis.

•Cyanosis or pallor of the leg.

•Leg may be cool é diminished arterial pulsation (distal pulse of dorsalis paedis, posterior saphenous & anterior tabialis).

•The skin over the area of thrombosis may be warm. Often difficult to differentiate from non-thrombotic disorders.

Diagnosis

•Pt risk factors/medical history physical examination.

•Specific limb symptoms (oedema, pallor). •Duplex U/S. •MRI. •Venography.

•D-dimer is a fibrin degradation product, a small protein fragment present in the blood after a blood clot is degraded by fibrinolysis. It is so named because it contains two cross linked D fragments of the fibrin protein.

Complications

•Pulmonary embolism (in 1/3 of pts) •Post-thrombotic syndrome leading to chronic venous insufficiency or ulcers & critical limb ischemia.

Management

Anticoagulation: (Heparin, Warfarin, LMWH). Reduces occurrence of a pulmonary embolism, can ⇩ symptoms. Its disadvantages include; bleeding from long-term use & it does not ⇩ the thrombus burden. ***Thrombus removal:*** catheter directed thrombolytic therapy. ***Compression stockings*** prevent post-thrombotic sy.

HEART & ELECTROLYTES

The electrolytes potassium, magnesium, sodium & calcium play a crucial role in the function of the myocardium, the muscular tissue of the heart. Movement of these ions across the semi-permeable myocardial cell membrane causes the voltage across the membrane to exceed a threshold & generate an action potential, resulting in muscle contraction. Electrolytes carry electrical charge & are maintained to tight physiological concentrations through various mechanisms to ensure appropriate heart function. An imbalance of these electrolytes can have detrimental effects on the heart, causing or contributing to arrhythmia & cardiac arrest. Life-threatening arrhythmias are commonly associated é potassium disorders, particularly hyperkalaemia in ẃ the potassium level is elevated, less com-monly é disorders of serum calcium & magnesium. Electrolyte imbalances also ha-ve wider effects in the body.

Electrolytes

Work é fluids to keep the body healthy & in balance. They are solutes that are found in various concentrations & measured in terms of mille equivalent (mEq) units. Are either +ve charged (cations), as (Na^+), (K^+), (Ca^{++}), (Mg^{++}) & (H^+), or -ve charged (anions), as (Cl^-), (PO_4^-), (HCO_3^-) & (SO_4^-). For homeostasis body needs: total body anions = total body cations. The Non-electrolytes include; Glucose, Urea, Protein, Lipids etc….

Body fluids

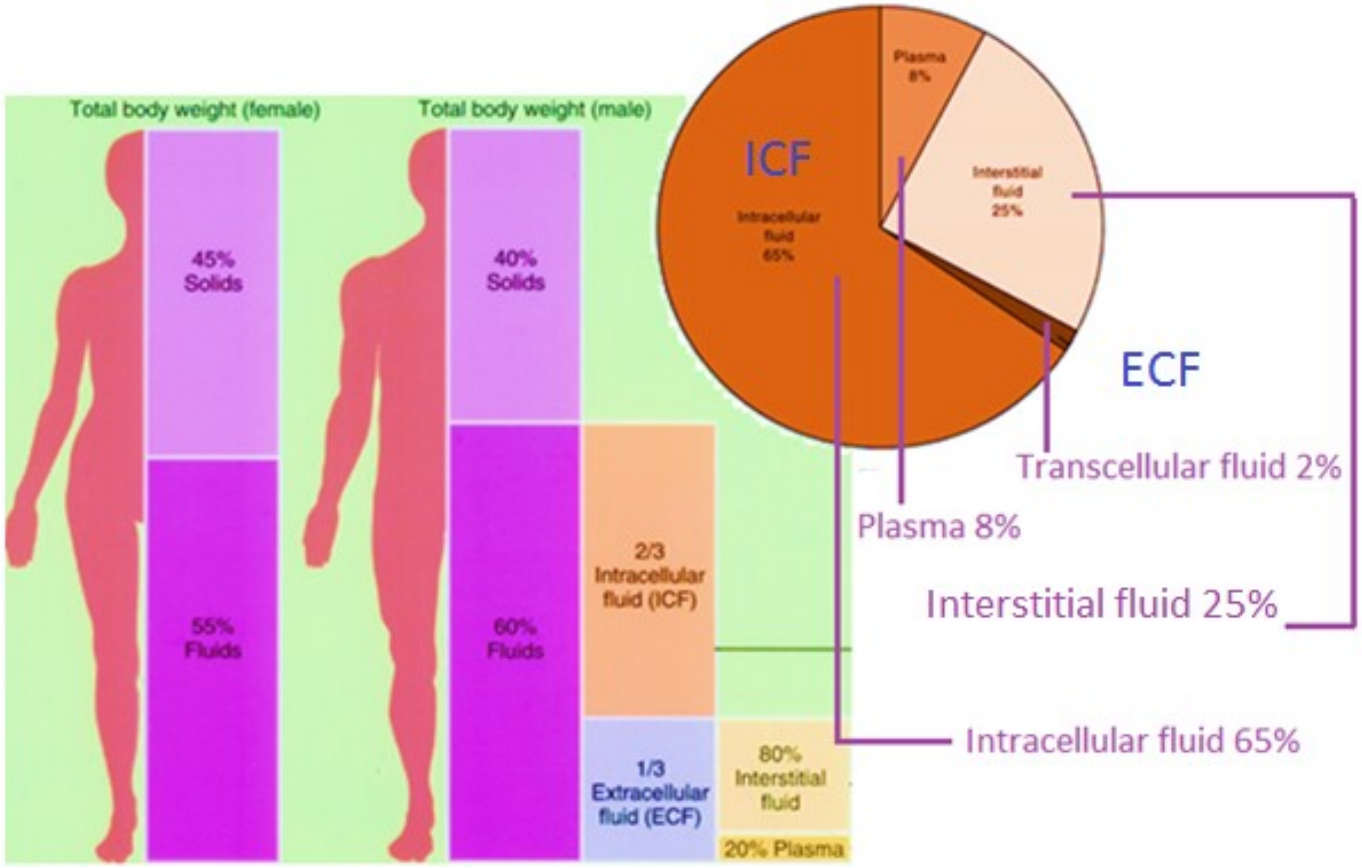
Varies é weight, age & sex; in early embryo it is (97%), in Newborn it is (77%), in Adult male it is (60%) & in Adult female (54%), while in the elderly (45%).

Function of body fluids: water is the most important nutrient for life, the primary body fluid. Act as medium for transport, needed for cellular metabolism, solvent for electrolytes & other constituents, helps to maintain body temperature, helps digestion & elimination& acts as a lubricant.

Mechanism of Gain & Loss of body fluids: the gain is through (for adult); fluid intake about 1500 ml, food intake about 1000 ml & Oxidation of nutrients 300 ml (10 ml of H_2O/100 Kcal). The losses are through the "Sensible", can be seen include; urine 1500 ml, sweat 100 ml. "Insensible", not visible, include; skin (evaporation) 500 ml, lungs 400 ml, faeces 200 ml. The loss of 10% body fluid (8% wt. loss) is serious, loss of 20% body fluid (15% wt loss) is fatal. The fluid gained each day should be equal to the fluid lost & each is equal to 2 -3 Litres/day on average.

Compartments of body fluids

- Interstitial (fluid around/between cells).
- Intravascular (plasma fluid in blood vessels).
- Transcellular (as in CSF, synovial fluid etc..).



HYPERKALAEMIA

- Hyperkalemia = plasma K^+ conc. > 5.0mmol/L
- Critical hyperkalemia = plasma K^+ conc. > 6.5 mmol/L

Causes: •Acute/chronic renal failure. •Metabolic acidosis •Hyperglycaemia. •Thrombocytosis. •Leucocytosis. •Trauma. •Burn. •Prolonged tourniquet (muscle cells release K as result of tissue anoxia). •Digoxin toxicity. •Succenyl Choline (anaesthesia). •Non selective ß-blockers as Propranolol, Labetalol •ACEIs • NSAIDs & •Lab error.

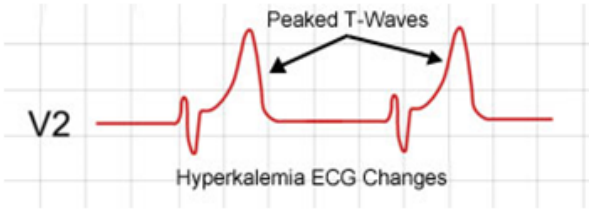
Clinical picture: •Vague •Weakness •Flaccid paralysis •Malaise •Lethargy.

ECG changes

*No P wave.

*Tall peaked T wave

* Widened QRS



Management

•Ca gluconate amp 10%, 10 ml over 2-5 min., or •Glucose 50%, 1 ml/Kg + Insulin 1 u/5 gm glucose, or

•$NaHco_3$ amp 20 ml (17.5 mEq), if pt is acidotic, 1 amp over 5 min, or 1-2 ml/Kg (1-2 meq/Kg) or

•Normal saline + Lasix 20-80 mg, or 1 mg/Kg IV.

HYPERCALCAEMIA

Mild: Ca^+ level is 10.5 - < 12 mg/dl. Moderate: 12-14 mg/dl (think in malignancy if serum Ca^+ >13 mg/dl). Severe: if serum Ca^+ is >14 mg/dl.

98% of the body calcium is in the skeleton, only 2% is in the circulation of ẃ 50% is free calcium (ionized Ca^{++}) ẃ is the physiologically active & the reminder 1% is bound to proteins. The calcium regulation is under control of:- **1-PTH:** inhibits osteoblasts, stimulate osteoclasts, thus stimulates bone resorption & renal tubular reabsorption of calcium, thus ⇧ blood calcium. **2-Calcitonin:** secreted by thyroid gland, inhibits

osteoclasts, stimulate osteoblasts & ⇧ urine calcium excretion by inhibiting renal calcium reabsorption, thus ⇩ blood calcium.

Causes

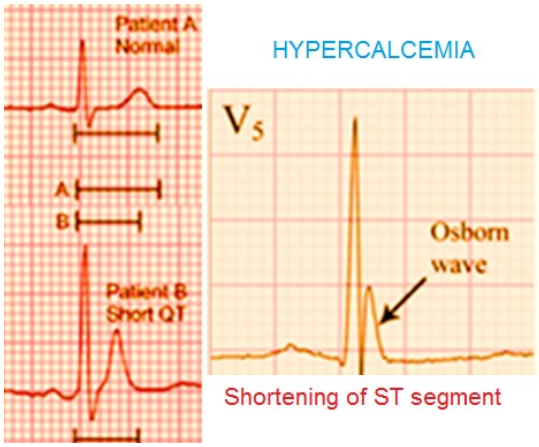
90% of hypercalcaemia are due to primary hyperparathyroidism & malignancies. The primary hyperparathyroidism include; parathyroid adenoma (90%), hyperplasia (5%) & parathyroid carcinoma (5%). Other causes include; iatrogenic from excess Vit D or excess dietary intake of calcium. May be caused by drugs as Thiazide diuretics, or Lithium or excess Vit A. Also é immobilization, hyperthyroidism, Milk alkali syndrome (result from use of more calcium for osteoporosis), Sarcoidosis, TB, Histoplasmosis, Paget`s disease of bone, Multiple myeloma & Bone metastasis.

Clinical picture

May range from non-existent to severe. Pt may present é stones (renal or biliary), bone or abdominal pain, polyuria, water depletion, dehydration, constipation, anorexia, nausea, weakness, lethargy, psychatric overtones (depression, anxiety, confusion) & ECG changes.

ECG changes

•Shortening of QT interval. •J waves (Osborn wave) as notching of the terminal QRS, best seen in lead V5 (as é severe hypothermia). •Elevation of ST segment. • Arrhythmia.



Investigations

⇧ **PTH:** in primary, secondary, or tertiary hyperparathyroidism or é familial hypocalciuric hypercalcaemia.

⇩ **PTH:** in malignancy, excess Vit.D, granulomatous disease, milk alkali sy.

Serum Ca^+ level: pt is hypercalcaemic if serum ioniz- ed Ca^+ **>** 5.6 mg/dl & total serum Ca^+ **>** 10.5 mg.

Urine Ca^+: if there is ⇧ of urine Ca think of hyperparathyroid, excess vit. D, or granulomatous disease. If urine Ca is <200 mg/day, think in familial hypocalciuric hypercalcaemia. If urine Ca is normal it is associated é milk alkali sy. In case of malignancy the urine Ca is variable (either ⇧, ⇩, or normal).

Urine phosphate: ⇧ in case of hyperparathyroidism, excess Vit D, or malignancy. It is normal in case of granulomatous disease, milk alkali sy or familial hypocalciuric hypercalcaemia.

Serum alkaline phosphatase: ⇧ in case of hyperparathyroidism, malignancy, granulomatous disease. ⇩ in case of excess Vit D. Normal in case of milk alkali sy & familial hypocalciuric hypercalcaemia.

Management

- Aggressive hydration: ½ normal saline or normal saline.
- Diuretic: no Thiazide diuretic to be given as it will ⇧ calcium level, loop diuretic as Furosemide to be given after rehydration.
- Calcitonin amp 50, 100u, 4u/Kg SC or IM.
- Bisphosphonates intravenous: act by reducing bone resorption.
- Steroids: useful in case of Vit D excess & granulomatous diseases.

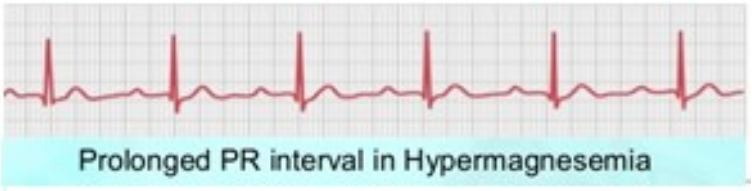
HYPERMAGNESAEMIA

Clinical picture

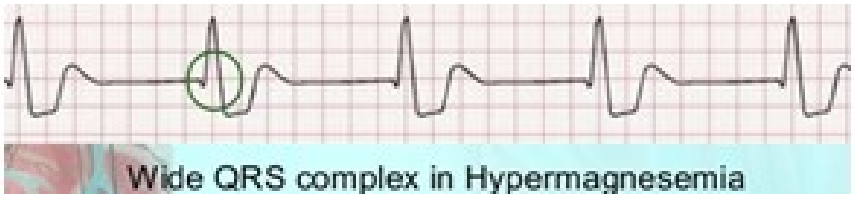
Mg^{++} is required to support the heart muscle`s normal contraction-relaxation actions. ⇧ of Mg^{++} level may cause delayed conduction of electrical impulse. Too much ⇧ of Mg^{++} depress the CNS, breathing & produces Hypotension, ⇩ of heart rate, diaphoresis, flushing, drowsiness, ⇩ of the mental status, hyporeflexia, weakness, paralysis, heart block & ECG changes.

ECG changes

Prolonged PR interval, widened QRS, ventricular dysrhythmias & heart block.



Prolonged PR interval in Hypermagnesemia



Wide QRS complex in Hypermagnesemia

Causes

•⇧ Mg^{++} intake •⇩ Renal excretion •Dehydration •Addison's & other adrenal diseases •Hyperparathyroidism •Hypothyroidism •Kidney failure •Acidosis.

Diagnosis

▲ Mg^{++} is < 2.0 mEq/L & ▲ The ECG changes.

Management

•Diet restrictions for Mg. •Circulatory & respiratory support. •Administer diuretic, IV Lasix to ⇧ Mg excretion (only when renal function is adequate). •1 gm Ca gluconate reverses cardiac effects. •Haemodialysis may be used in severe cases of hypermagnesaemia because approximately 70% of serum Mg is not protein bound & can be removed through dialysis.

HYPERNATREMIA

Hypernatremia is much less common than Hyponatraemia & it is often iatrogenic (e.g. excessive normal saline), seen in 1% of hospitalized pt & is more common among infants & old age pts, risk factors ⇧ é age > 65 yrs & é dementia, mental or physical disabilities. Hypernatremia is defined as Serum Na **>** 145 mmol/l.

Classified into; *Mild (Na 146-149) *Moderate (Na150-169) *Severe (Na ≥ 170).

⇧ Na^+ conc. in blood creates an osmotic gradient between the ECF (plasma, interstitial fluid) & ICF (cells fluid) causing movement of water into the extracellular space, in severe cases it affect brain cells causing shrinkage of brain cells, permanent brain damage & IC Hge.

Causes

•Excess water loss. •Excess solute intake. •Hyperosmolar feeding. •Inadequate fluid intake. •Excess insensible water loss. •Tachypnea. •Burns. •Nephrogenic diabetes insipidus (deficient response of kidney to the ADH). •Central diabetes insipidus (deficient ADH secretion by posterior pituitary). •Diarrhea •Hypertonic dehydration •Osmotic diuretics as Mannitol •Hyperosmolar hyperglycemic stat •Iatrogenic as excess intake of normal saline or $Na^+Hco_3^-$ or é TPN. •Primary hyperaldosteronism •Acute & Chronic renal failure. •Drugs as Lithium & Amphotericin B.

Types

■Hypovolemic hypernatremia: H_2o deficit is **>** Na^+ deficit.

■Hypervolemic hypernatremia: excess Na^+ gain.

■Euovolemic hypernatremia.

Clinical picture

•Fatigue. •Nausea. •Vomiting. •Headache. •Flushed skin. •Confusion. •Seizures. •Coma.& death. •⇧ Capillary refill time. •⇩ COP related to ⇩ of myocardial contractility.

Management

•Calculate water deficit: 0.6 X Wt X {(current Na ÷ 140) -1}

•Correction must be ve-very slowly & Na^+ should not be lowered by >2 meq/L/day, as over correction can lead to cerebral edema, seizures & death.

•The typical fluid is dextrose 5% in water.

HYPOKALAEMIA

As mentioned before, K^+ is vital for regulating the normal electrical activity of the heart. The ⇩ of the extracellular K^+ causes myocardial hyperexcitability é the potential to develop re-entrant arrhythmias. Nearly 98% of the body`s K^+ is intracellular. The normal serum level of k^+ is 3.5-5 meq/L. Hypokalaemia divided into;

- Mild: K^+ 3-3.5 meq/L
- Moderate: K^+ 2.5-3 meq/L
- Severe: K^+< 2.5 meq/L.

Causes:

•Diarrhoea/Laxative abuse.

•Vomiting / Metabolic alkalosis.

•Liver cirrhosis. DM. Primary Hyperaldosteronism.

•Steroids, Digitalis, ß-blockers, Thiazide, Loop diuretics.

•Renal tubular acidosis.

Clinical picture

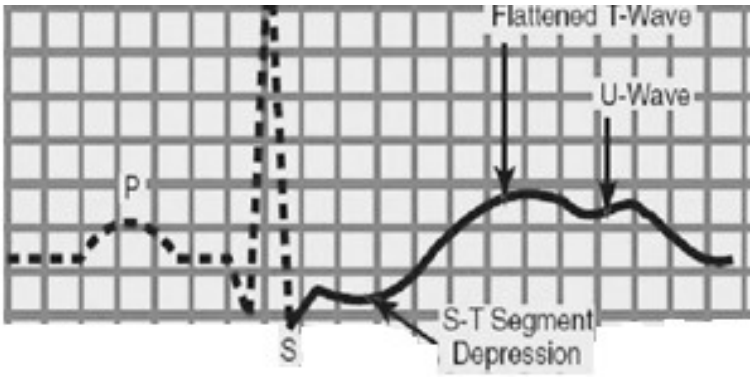
Symptoms depend upon the degree & duration of hypokalaemia.

*Mild hypokalaemia are often asymptomatic.

*Moderate/severe hypokalaemia present é; Cardiac arrhythmia or arrest. Paralytic ileus. Muscle weakness/cramps & Polyuria.

ECG changes

Hypokalemia
ECG tracing has ST-segment depression, flattened T-wave, and a U-wave.



•Prolonged P-R interval. •Widened QRS complex •QT interval usually indiscernible as T wave flattens. •Depressed S-T segment. •T wave amplitude is ⇩, inverted T wave & U wave may be seen.

Management

▲Mild hypokalemia treated by oral kcl tab maximum 20 meq (2 tab of 600 mg Kcl)

▲Severe form treated by Kcl 10 ml amp 15% (contain 1.5 gm Kcl), added to NS & infused over 12-24 hrs, maximum dose not more than 40 meq/L of NS. Repeat until all symptoms resolve.

HYPOCALCAEMIA

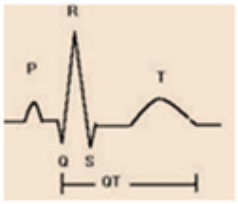
Ca is important in cardiac function; it exerts a +ve inotropic effect on heart. ⇩ in Ca levels may cause ⇩ myocardial contraction. Hypocalcaemia is defined as total serum Ca^+ < 8.5 mg/dL or ionized Ca^+ < 4.6 mg/dL. The total serum Ca^+ levels must be corrected for serum albumin levels. Ionized Ca^+ levels do not require such correction. Acute, severe hypocalcaemia is a medical emergency. Approximately 40% of serum Ca^+ is ionized (free), while the other 60% is complexes, primarily to albumin. Only the ionized Ca^+ is transported into cells & metabolically active. ⇩ in the ionized Ca^+ cause symptoms. Hypoalbuminemia alters total serum Ca^+ conc. éout affecting the ionized Ca^+. The serum total Ca^+ conc falls approximately 0.8 mg /dL for every 1 gm/dL reduction in the serum albumin conc.

Causes

Major factors that influence the serum Ca^{++} conc. are PTH, Vit D & serum phosph-orus level. Hypocalcaemia most commonly occur é Vit D deficiency, chronic renal failure, hypoparathyroidism (typically due to neck surgery, rarely from autoimmu-ne destruction or congenital abnormality) or may be idiopathic hypocalcaemia.

ECG changes

Prolonged QT Interval



- Prolonged Q-T interval.
- Prolonged S-T segment.
- May associated é flattening of T wave.

Clinical picture

A. Trousseous sign: finger taping over aathe course of facial nerve will result in twitching of muscles of the face

B. Convulsion- Carpopedal spasm

C. Chvosteck sign: keeping SBP for 3 min. will result in carpopedal spasm

Cardinal features are •Muscle spasm (Trousseous sign, Chvosteck sign, Carpopedal spasm) •Irritability •Tetany •Paraesthesia •Seizures & •Arrhythmias.

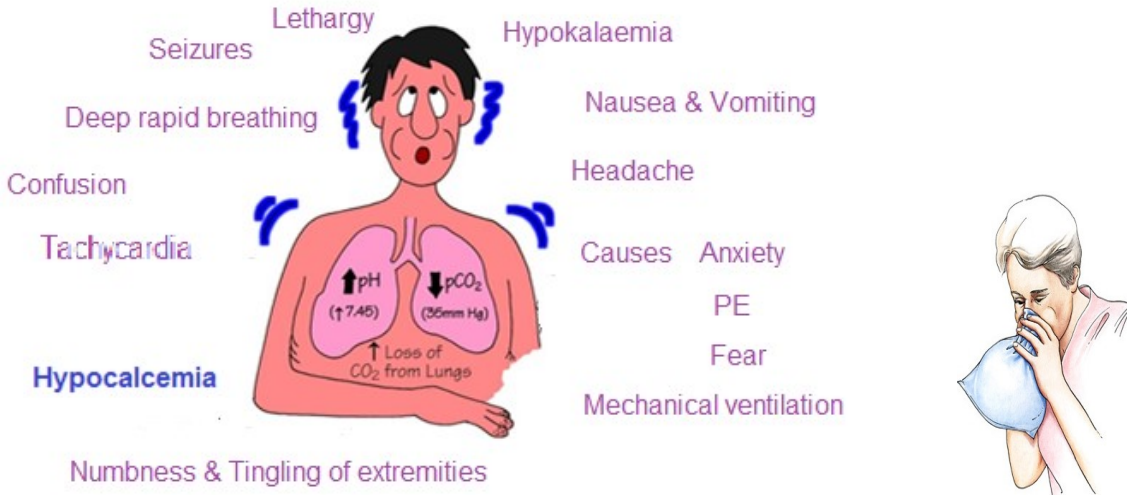
Investigations

- ⇧ PTH.
- ⇩ Ca & ⇧ Phosphorus levels in blood.
- Normal serum alkaline phosphatase.
- X Ray skull (basal ganglia calcification).

Management

Ca gluconate 10% ampule 10 ml=I gm=4.5 meq, 100 mg or 1 ml/Kg stat, slowly & strictly intravenous. Chronic hypocalcaemia often responds to Rx é vit. D derivatives & calcium.

HYPERVENTILATION SYNDROME



Over breathing, breathing is fast & deeper, result in inhalation of lot of O_2 & ⇩ of Co_2 in blood. Follow psychic trauma. More common in women, anxiety, fear, & mechanical ventilation.

Clinical picture

Tachypnea, irritability, carpopedal spasm, spasm of neck & jaw muscles, result from alkalosis &excess washing of CO_2 causing respiratory alkalosis & hypocalcemia.

Management

- Breathing through a Paper Bag.
- Valium 5, 10 mg amp, 0.25 mg/ Kg/dose IV/IM stat (suppository 5, 10 mg), then daily dose of 0.25 mg/Kg/ day ÷ 4
- Ca gluconate 10%, 10 ml ampule, strictly IV 1 ml/Kg =100 mg/Kg, after dilution é 5% Glucose in a ratio of 1: 4 é monitoring of heart rate.
- Treating alkalosis is thro-ugh giving normal saline & correction of hypokalaemia.

HYPOMAGNESAEMIA

(Magnesium ˂1.4 meq/L)

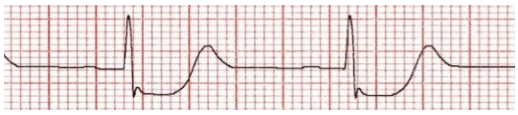
Causes

Mg^{++} deficiency is often associated é low blood Ca &/or K. Hypomagnesaemia may be caused by: •Irritable Bowel Sy. •Ulcerative Colitis - because Mg^{++} is absorbed in the intestines & then transported through the blood to cells & tissues. •Alcoholism or withdrawal from alcohol. •Malnutrition. •Starvation. •Inadequate intake of mineral •Kidney disease. •Pancreatitis. •Hyperglycemia. •Medications- as Diuretics (⇧ loss of Mg^{++} through urine), Digitalis, Cisplatin, Cyclosporine, Aminoglycoside antibiotics, ins-ulin administration. •Large amount of Mg^{++} can be lost by prolonged exercise. •Excessive sweating. •Chronic diarrhoea. •Hypoparathyroidism as PTH helps control Ca^{++}, Ph^{++}, Mg^{++} & Vit. D levels within the blood & bone, in such condition the blood Ca^{++} levels fall & Ph^{++} levels rise.

Clinical picture

▲Anorexia ▲Nausea ▲⇩ Intestinal motility ▲+ve Trousseau's & Chvostek's signs ▲Neuromuscular irritability & Hyperreflexia ▲Seizures ▲Shallow respiration ▲Laryngospasm ▲Hyperventilation ▲Cardiac arrhythmia ▲Apathy ▲ Mood cha-nes ▲Agitation ▲Confusion ▲Insomnia.

ECG changes



- Depressed ST segment.
- Tall T waves.
- Irregular ventricular rhythm.

Management

- Eliminate contributing drugs.
- Seizure precautions.

•IV $MgSO_4$, 25-50 mg/kg/dose for replacement & 30-60 mg/kg/day for maintenance, IV dose must be given over 120 min via IV pump (500 mg $MgSO_4$ = 49.3 mg elemental Mg = 4.06 meq Mg). Monitor hourly $MgSO_4$. •Diet Therapy.

HYPONATRAEMIA

(Serum Na^+ <135 meq/L)

Na^+ is the main electrolyte in the body & is important for many body functions, its normal value in blood is 135-145 meq/L. Hyponatraemia represent relative excess of water in relation to Na^+. Hyponatraemia is the most common electrolyte abno- rmali-ty in geriatric & hospitalized pt, seen in 30% of pts treated in the ICU & in 3% of hospi-talized pts, swelling of the body is the most danger effect of Hyponatraemia causing brain oedema, seizures, coma & respiratory arrest.

Causes

•⇧ Water retention. •Low salt intake. •Polydipsia. •Advanced renal failure. •Thiazide diuretics. •Adrenal insufficiency.

Types

✶***Hypovolemic hyponatraemia;*** ⇩ Na^+ & H_2O (signs of dehydration).

✶***Hypervolemic Hyponatraemia;*** ⇩ Na^+& ⇧ H_2O (oedema, liver cirrhosis, HF).

✶***Euvolumic Hyponatraemia;*** normal appearance.

Clinical picture

*Mild Hyponatraemia (Na^+ **<**130 meq/l); malaise, nausea, drowsiness.

*Moderate Hyponatraemia (Na^+ ﹤120 meq/l); vomiting, headache, confusion, muscle cramps, ⇩ reflexes. *Severe Hyponatraemia (Na^+ ﹤110 meq/l); seizures, coma.

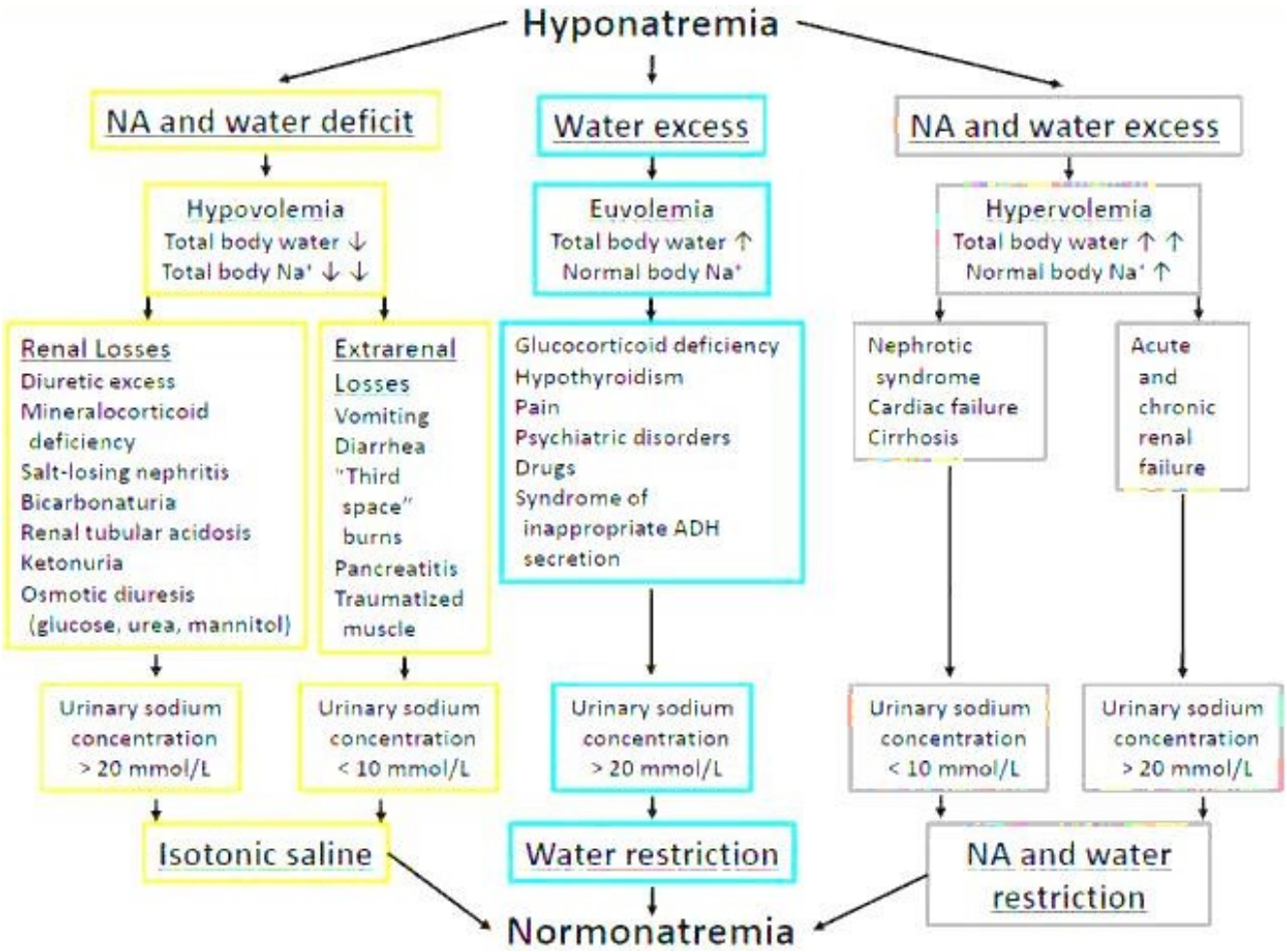
Management

*Serum & urine osmolality & urine Na^+ conc are initial tests to do.

*Mild or no symptoms: fluid restriction.

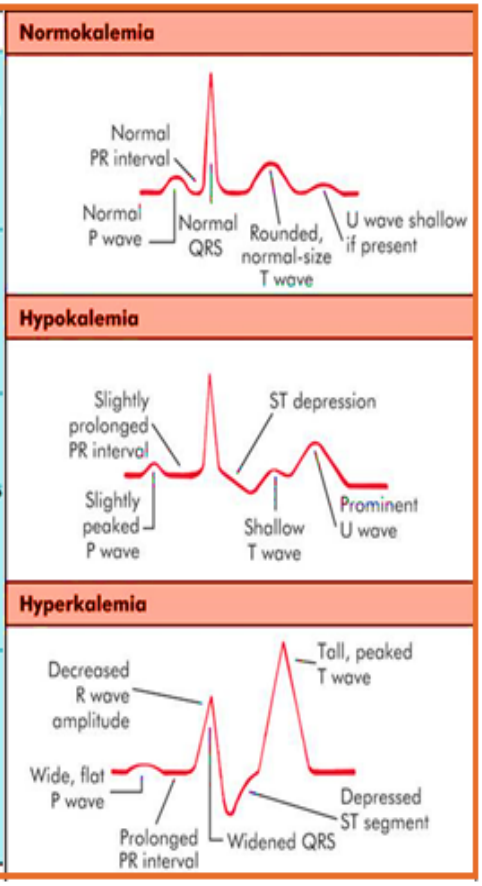
*Severe symptoms: give bolus of 3% saline, 100 ml (this raise Na^+ level 2-3 meq/l). Calculate Na^+ deficit (total body water X (Desired Na^+ - Pt Na^+). The total body water is equal to 60% of body weight in males & 50% in females). Correction should not exceed 10 meq/L during the 1st 24 hrs to avoid central pontine myelinolysis ẃ is a form of osmotic demyelination in ẃ the symptoms start to occur after 2-6 days from the rapid correction in the form of dysarthria, dysphagia, lethargy, quadriparesis, seizures & coma.

Example; 60 Kg female é serum Na^+ level 116 meq/l.? We need in the 1st 24 hrs to raise serum Na^+ level to 124 meq. ∴Na^+ deficit = 50% X 60 X (124 ÷ 116) =240 meq. ∴ Give 240 meq Na^+ during the next 24 hrs. ∵ 3% saline solution contains Na^+ 500 meq/l (hypertonic saline) & the 0.9 saline contain Na^+ 154 meq/l (normal saline). # Give 480 ml of the hypertonic saline or 1560 ml of the normal saline over the next 24 hrs & Repeat until all symptoms resolve.



SUMMARY

Electrolyte	Excess	Deficit
Sodium (Na)	Hypernatremia Thirst CNS deterioration Increased interstitial fluid	Hyponatremia CNS deterioration
Potassium (K)	Hyperkalemia Ventricular fibrillation ECG changes CNS changes	Hypokalemia Bradycardia ECG changes CNS changes
Calcium (Ca)	Hypercalcemia Thirst CNS deterioration Increased interstitial fluid	Hypocalcemia Tetany Chvostek's, Trousseau's signs Muscle twitching CNS changes ECG changes
Magnesium (Mg)	Hypermagnesemia Loss of deep tendon reflexes (DTRs) Depression of CNS Depression of neuromuscular function	Hypomagnesemia Hyperactive DTRs CNS changes



INTRAVENOUS FLUID COMPARISON

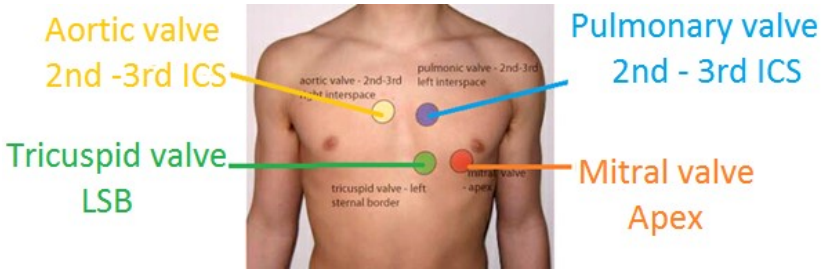
Type	Solution	Uses	Special Considerations
Isotonic	Dextrose 5% in water	Fluid loss. Dehydration. Hy-pernatremia	Use cautiously in renal & cardiac pt. Can cau-se fluid overload
Isotonic	0.9% NaCl	Shock. Hyponatraemia. Blo-od transfusion.R esuscita-tion. Fluid challenges. DKA	Can lead to overload. Use é caution in pt é HF or oedema
Isotonic	Ringer`s Lact.	Dehydration. Burns. Lower GI fluid loss Acute blood lo- ss. Hypovolemia	Contain K^+, Don`t use é renal failure. Don`t use é liver disease, can`t metabolise lactate
Hypotonic	0.45% NaCl	Water replacement DKA. Gastric fluid loss from NG tube or vomiting	Use é caution. May cause cardiov-ascular colla-pse or ⇧ IC pressure. Don't use é liver disease, or burns
Hypertonic	Dextrose 5% In ½ NS	Later in DKA Rx	Use only when blood sugar falls < 250 mg/ dl
Hypertonic	dextrose 5% in NS	Temporary Rx for shock if plasma expanders not avail-able. Addison's crises	Do not use in cardiac or renal pt
Hypertonic	Dextrose 10% in Water	Water replacement TPN	Monitor blood sugar level

COMPOSITION OF COMMON IVF (meq/L)

	Na (mEq/L)	K (mEq/L)	Cl (mEq/L)	HCO3 (mEq/L)	Dextrose (gm/L)	mOsm/L
D5W					50	278
½ NS	77		77			143
D5 1/2NS	77		77		50	350
NS	154		154			286
D5NS	154		154		50	564
Ringers Lactate (RL)	130	4	109	28	50	272

PRACTICAL POINTS

Sites of heart valves



Heart Sounds

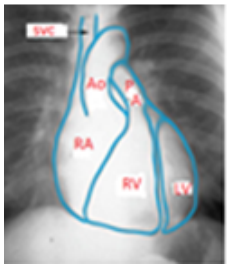
*First heart sound (S1): result from closure of mitral & tricuspid valves.

*Second heart sound (S2): may be soft, loud, widely split, or reversed split.

*Third heart sound (S3) : diastolic filling of the ventricle. It is normal persons < 30 yrs old. Characteristic of LV failure.

*Fourth heart sound (S4): Atrial contraction against a stiff ventricle. May be heard in AS, HOCM, hypertension.

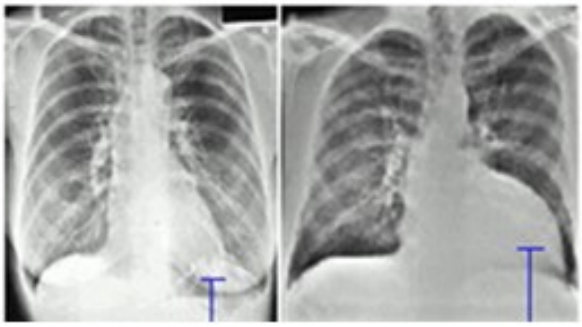
*Murmurs



opposite	Stenosis	Regurge
Aortic	Systolic	Diastolic
Pulmo	Systolic	Diastolic

- Ejection systolic murmur: AS or PS
- Soft systolic murmur: ASD, or VSD.
- Diastolic murmurs: AR or PR.

CXR



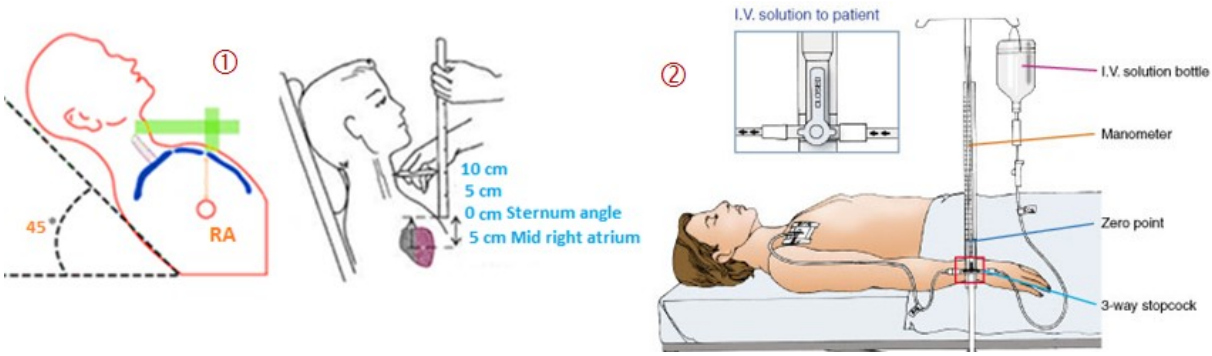
The X Ray on the left shows a normal heart, on the right, the heart is enlarged(Rt)

- RVH: cardiac shadow ⇧, no angle between apex & diaphragm.
- LVH: cardiac shadow ⇧, angle between apex & diaphragm.

Causes of wide pulse pressure

▲Anaemia ▲Thyrotoxicosis ▲AR ▲Liver disease ▲Systolic hypertension (old age)

Central Venous Pressure



CVP, also known as mean venous pressure' (MVP) is the pressure of blood in the thoracic vena cava, near the right atrium of the heart. CVP reflects the amount of blood returning to the heart & the ability of the heart to pump the blood into the arterial system. The normal range of CVP is 5-10 cmH_2o when taken from the mid axillary line at the 4^{th} ICS, & equal to 8-15 cmH_2o for pt on ventilators.

Method for measuring CVP

① Indirect assessment: inspection of jugular vein pulsation in neck.

② Direct assessment: fluid filled monitor connected to CVC, calibration transducer

③ Electronic transducers (in ICU).

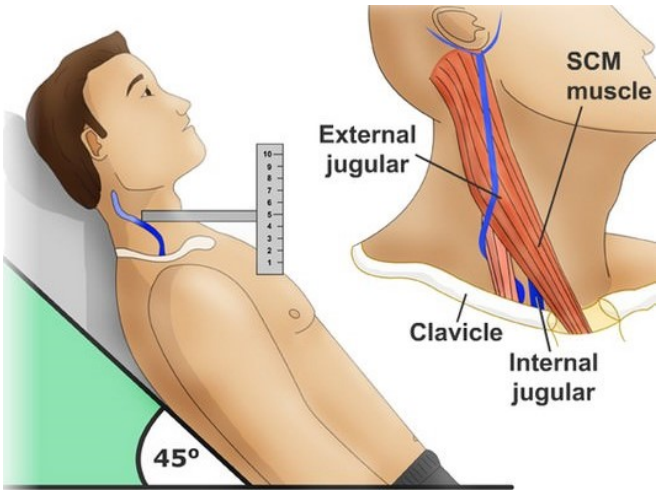
Position the pt at 45^0 angle on the examining table. Place ruler at the sternal angle

(the sternal angle is about 5 cm above the right atrium). Hold another ruler horizontally at the top of the venous pulse & note how many cm this is above the sternal angle. Add 5 cm to this total (accounting for the distance between the sternal angle & Rt atrium), the total is the JVP. Normal is < 9 cm. The normal range of CVP is 5-10 cmH_2o when taken from the mid axillary line at 4^{th} ICS & equal to 8-12 cmH_2o for pt on ventilators. indicator of volume overload, especially on the Rt side of the heart. Best combination of sensitivity & specificity in diagnosis of HF.

Indications for CVP monitoring

- Emergency fluid resuscitation.
- Hemodialysis.
- TPN.
- Administration of irritant drugs.
- Poor venous access.

Jugular Venous Pulse



Defined as the oscillating top of vertical column of blood in right internal jugular vein that reflects pressure changes in Right Atrium in cardiac cycle. Jugular venous pulse is defined as the oscillating top of vertical column of blood in the right Internal Jugular Vein (IJV) that reflects the pressure changes in the right atrium in cardiac cycle. Jugular venous pressure (JVP) is the vertical height of oscillating column of blood.

Why is Internal Jugular Vein preferred?

• IJV is anatomically closer to and has a direct course to right atrium while Extern- al Jugular vein does not directly drain into Superior vena cava.

•IJV is valveless & pulsations can be seen. Due to presence of valves in External ja- gular vein, pulsations cannot be seen.

•Vasoconstriction secondary to hypotension (as in CHF) can make EJV small & bar- ely visible. •EJV is superficial and prone to kinking.

Why is Right Internal Jugular Vein preferred?

•Right jugular veins extend in an almost straight line to superior vena cava, thus favoring transmission of the hemodynamic changes from the right atrium.

•The left innominate vein is not in a straight line & may be kinked or compressed between Aortic Arch & sternum, by a dilated aorta, or by an aneurysm.

Evaluation of JVP

•Level. •Waveform. •Respiratory variation in level and wave pattern. •Hepatojugular reflux. •Venous hum. •Liver size & pulsations

Technique of measuring JVP

1) Position: Semi-reclining position ē 45° angle between the trunk (not the neck) & the bed. then, turn the head slightly towards left shoulder, so that the neck muscles are relaxed. Not in sitting position: because the upper level of venous column is below the clavicle. Not in supine position: because the whole venous column moves beyond the angle of jaw into the intracranial cavity.

2) Identify Jugular venous pulsation

•Assure good lighting (can use tangential beam of light through torch).

•Look between the two heads of sternocleidomastoid muscle.

•Note the upper level of pulsation, waveform & respiratory variation.

Do not mistake the carotid pulsations for venous pulsations.

JUGULAR VEIN	CAROTID ARTERY
No pulsations palpable.	Palpable pulsations.
Pulsations obliterated by pressure above the clavicle	Pulsations not obliterated by pressure above the clavicle
Level of pulse wave decreased on inspiration; increased on expiration.	No effects of respiration on pulse.
Usually 2 pulsations per systole (x & y descents).	One pulsation per systole.
Prominent descents.	Descents not prominent.
Pulsations sometimes more prominent ē abdominal pressure.	No effect of abdominal pressure on Pulsations

3) Locate the sternal angle (Angle of Louis):

It can be felt as a transverse prominence, about 5cm below the suprasternal notch at the level of 2nd costal cartilage.

4) Measurement

Measure the vertical distance (cm) between the horizontal lines drawn from the upper level of venous pulsation & the sternal angle. This can be done by using 2 rulers – one placed horizontal to the upper level of pulsation & another taking the vertical distance of that ruler from the sternal angle.

5) Calculate the right atrial pressure

Normally, the centre of right atrium is 5 cm below the sternal angle. Hence, Add + 5 cm to the above measurement to obtain the right atrial pressure.

6) Conversion: 1.3 cm of H2O or blood = 1 mmHg

Interpretation

1) Normal level of JVP:•From sternal angle: <4 cm.•From centre of right atrium: <9cm •In mmHg: <7 mmHg

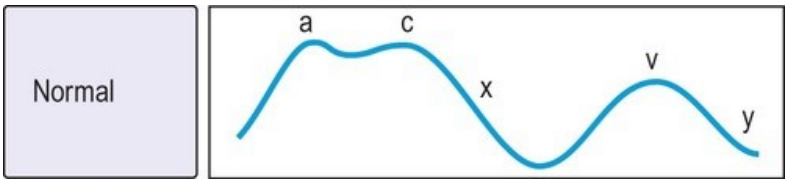
Causes of elevated JVP (Jugular venous distension):

1- RVF. 2- Pericardial compression (constriction/tamponade). 3- Tricuspid stenosis. 4- Superior vena cava obstruction- no pulsations. 5- Excessive fluid administration. 6- Renal failure. 7- ASD ē mitral valve disease.

Causes of lowered JVP : 1-Dehydration. 2-Hypovolemia.

2) Wave pattern & Abnormalities

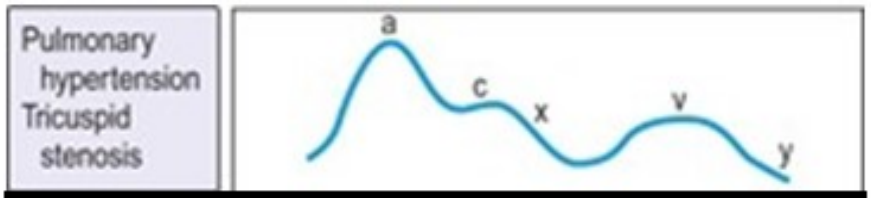
The normal JVP consists of 3 ascents or positive waves (a,c and v) &2 descents or negative waves (x, x' & y)



a wave is produced by atrial systole. x =atrial contraction finishes.

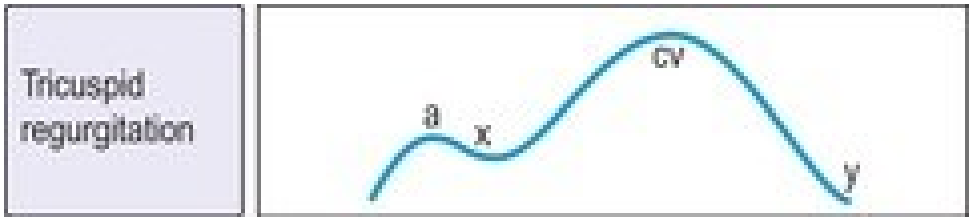
c wave occurs during the x descent & is due to transmission of right ventricular systolic pressure before the tricuspid valve closes. v wave = venous return filling the right atrium. The y descent follows the v wave when the tricuspid valve opens.

Increased a wave occurs in what conditions?



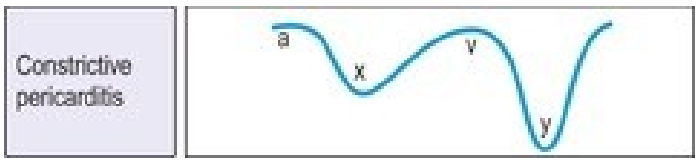
Right ventricular hypertrophy 2ry to pulm. hypertension or pulmonary valve stenosis. Giant cannon waves occur in complete heart block & ventricular tachycardia.

Giant v waves occur in?



Giant v waves occur in tricuspid regurgitation.

A steep y decent is seen in?



A steep y descent is seen in constrictive pericarditis & tricuspid incompetence.

3) Venous hum

Continuous bruit over neck veins (normally noiseless) due to ⇧ velocity of blood flow or ⇩ viscosity of blood. May be;

- Physiological: Children, Pregnancy.
- Pathological: Hyperkinetic states, Anaemia, Thyrotoxicosis, Beriberi, Intracranial AV fistula.

4) Respiratory variation

Normal: venous column rises during expiration & falls during inspiration.

Kussmaul's sign: Paradoxical rise in JVP during inspiration seen in case of; Constrictive pericarditis, Cardiac tamponade, Restrictive cardiomyopathy (because of ⇧ venous return in inspiration cannot be accommodated as increased pulmonary filling leading to inspiratory filling of neck veins.

5) Hepatojugular reflux (Provocative test)

When pressure is applied over the liver by pressing firmly below the right costal cartilage margin for 30 sec, the venous pressure gets exaggerated initially due to ⇧ venous return. Later the myocardium accomodates the extra venous return & the level falls. Positive test: rise in JVP for >10 sec. in case of:-

- Early HF.
- False positive: Valsalva (abdominal guarding), fluid overload.
- False negative: in case of:- SVC/IVC obstruction. Budd Chiari syndrome.

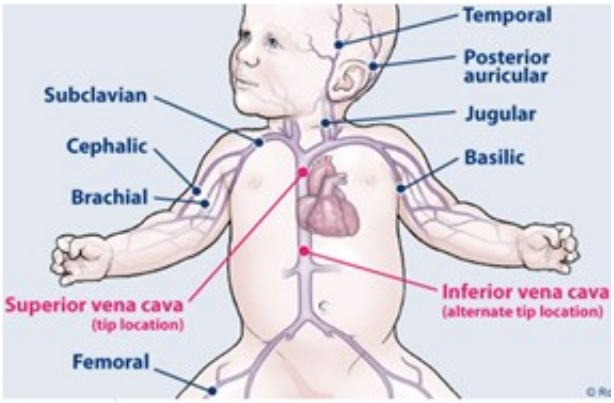
This test also helps to differentiate venous pulsation from the arterial pulsation.

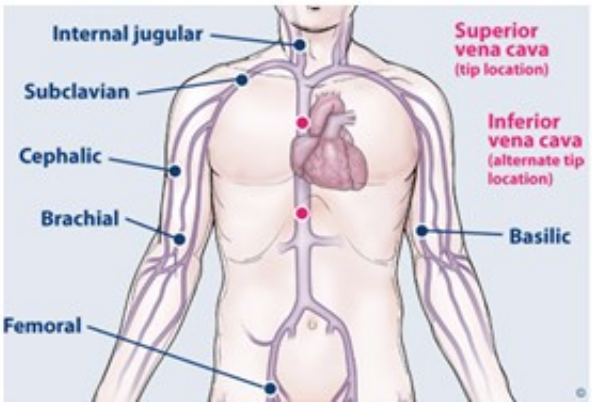
6) Liver pulsations

In an infant, the liver is the only guide to the recognition of elevated right atrial pressure as the JVP is difficult to delineate.

Central lines Canulation

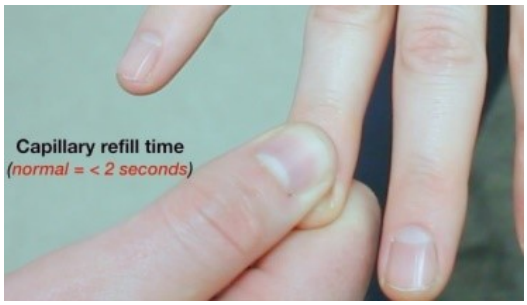
Ultra sound guide for CVC





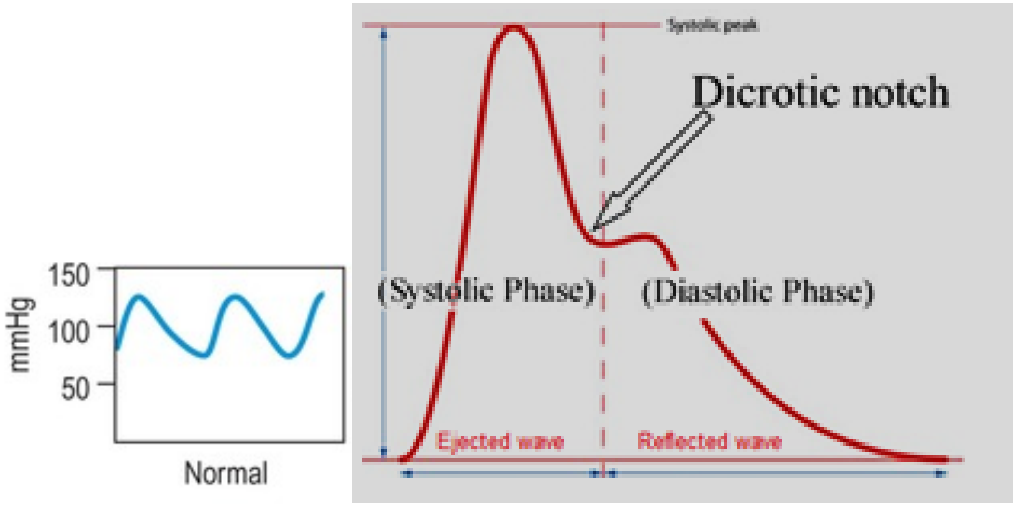
Capillary refilling test

Crude method of assessing blood circulation, in infants can tested by applying pressure over the sternum, or foot. In adults can be tested in finger nails while elevated above the level of the heart, or in middle of forehead. Restoration of time > 3 sec is considered sluggish circulation & means that pt need expansion of intravascular volume, seen in case of shock, dehydration, ⇩ COP, or hypothermia.



PULSE

One of the important vital signs, & may be the only available clew for diagnosis of serious illness ẃ is going on when other data not available? Pulse is the indirect measure of heart beat & activity of the heart. It is a wave of expansion & recall occurring in an artery in response to the pumping action of heart. The normal pulse has a small anacrotic wave on the upstroke ẃ is not felt. This is followed by a big tidal or percussion wave ẃ is felt by the palpating finger. On the following down stroke there is a notch (dicrotic notch) followed by a wave (dicrotic wave) both of ẃ are not normally palpable. In adults, the normal pulse appears at regular intervals & has a rate between 60-100 bpm. There may be a mild variation in the rate between the two phases of respiration ẃ is called sinus arrhythmia.



Procedure of taking pulse

Place tips of 2 fingers other than thumb lightly over pulse site. Thumb is not used in assessing pulse as it has its own ẃ can be mistaken for pt`s pulse. Do not press the artery ē more force. After getting the pulse regularly, count the pulse for one whole minute looking at the second hand on the wrist watch. Assess for rhythm, & volume of pulse & condition of blood vessel.

Characteristics of pulse

1. Pulse rate: number of beats per minute. Normally in adults it is 60-100 bpm.

2. Rhythm: is the time interval between pulse beats. Normally are equal & regular.

3. Tension: is the degree of compressibility & depends upon the resistance of the wall of the artery.

4. Volume: it is the fullness of artery. It is force of blood felt at each beat.

5. Delay: for both radial pulses, & radial & femoral pulses.

Purposses of taking pulse

-To establish base line data.

-To check abnormalities in rate, rhythm & volume.

-To monitor any changes in health status of the pt.

-To assess response of heart to cardiac medications, activity, blood volume.

-To check the peripheral circulation.

-To determine number of heart beat per minute.

Factors affecting the pulse

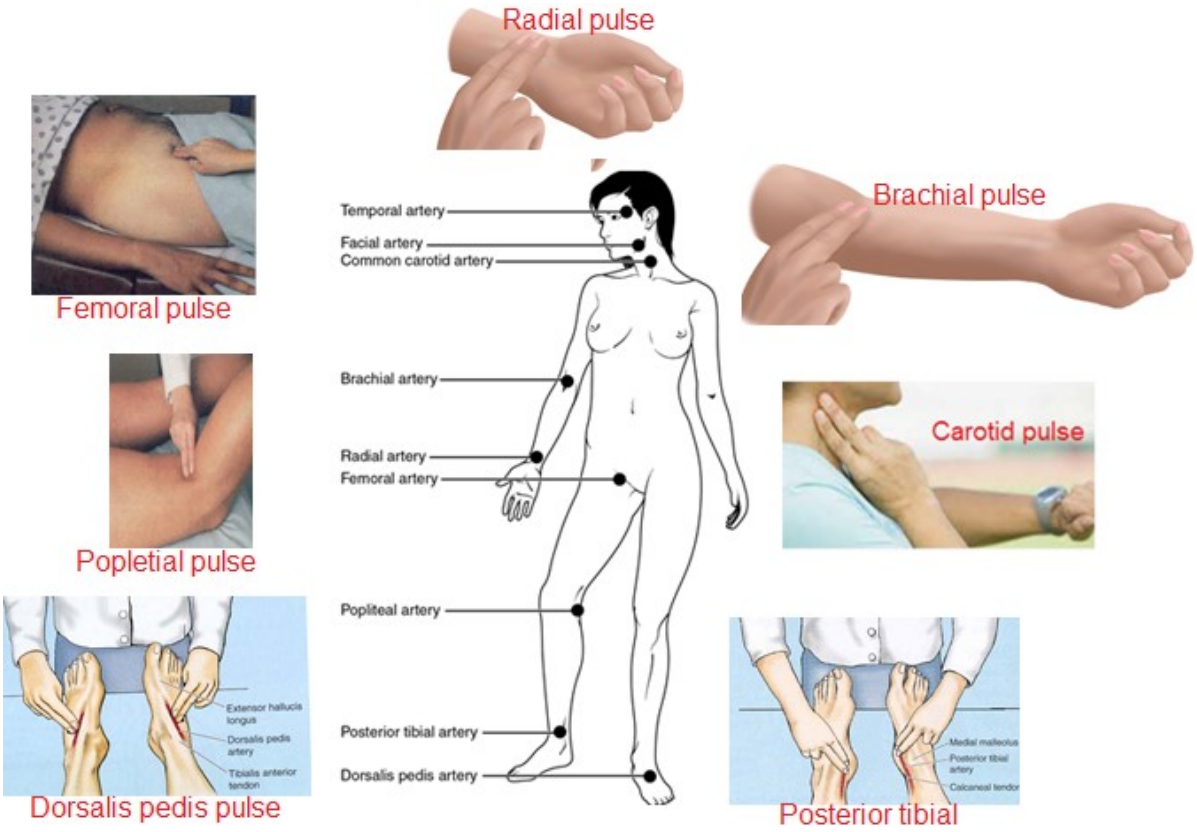
- Age: very old person have slow pulse rate & children will have faster beat.
- Sex: females have a slightly higher pulse rather than males.
- Exercise/activity: pulse rate is much faster during exercise.
- Stature: the short & thin persons have a more rapid pulse than tall & heavy.
- Emotions: anger or excitement ⇧ the pulse rate temporally.
- Fever: when body temp ⇧, the pulse rate usually ⇧ as well. Pulse ⇧ at a rate of about 10 bpm each degree rise of body temp.
- Blood pressure: when BP ⇩, the pulse may ⇧ to ⇧ the flow of blood. If BP ⇧, the pulse rate may ⇩ to correct the blood flow.
- Drugs: stimulant drugs ⇧ the pulse rate. Depressant drugs ⇩ the heart rate.
- Disease condition: heart disease, thyroid disease & other infections affect pulse.
- Acute pain & anxiety: ⇧ pulse rate.

- Sever & chronic pain: ⇩ pulse rate.
- Position: ⇩ while lying & ⇧ while standing.
- Hypovolemia/Hemorrhage: blood loss ⇧pulse rate because of demand of O_2.

Normal Pulse Rates

Age	Rate
Before birth	140–150
At birth	90–160
First year of life	115–130
Childhood years	80–115
Adult	60–80

Sites of checking pulse



❄ Radial: inner aspect of the wrist on thumb site.

❄Temporal: over the temporal bone or superior & lateral to the eye.

❄Carotid: at the side of the trachea where the carotid artery runs between the tr-achea & sternocleidomastoid muscle.

❄Apical: left side of the chest in the 4th, 5th, or 6th ICS in the MCL.

❄Brachial: medially in the antecubital space, above the elbow.

❄Femoral: below inguinal ligament, midway between symphysis pubis & ASIS .

❄Popliteal: medial or lateral to the popliteal fossa ē knees slightly flexed.

❄Posterior tibial: on the medial surface of the ankle behind the medial malleolus.

❄Dorsalis pedis:along dorsum of foot between extensor tendons of 1st & 2nd toe.

❄Facial: at the outer angle of the lower jaw.

Abnormal Pulses

Tachycardia: when the resting pulse rate ⇧ to > 100 bpm in adult.

*Sinus: •Exercise •Infants •Excitements •Anxiety •Fever •Hyperthyroidism.

*Medication: •Ca Ch BL (Nifedipine) •Sympathomimetics •Vasodilators.

*Arrhythmia: •Atrial Fibrillation •Atrial flutter •Ventricular tachycardia.

Bradycardia: a pulse rate < 60 bpm.

*Sinus rhythm: •Sleep •Athletic training •Hypothyroidism.

*Medication: •Beta-blockers •Digoxin •Verapamil, Diltiazem.

*Arrhythmia: •Carotid sinus hypersensitivity •Sick sinus syndrome •2nd degree heart block. Complete heart block.

Causes of irregular pulse

*Occassionaly Irregular pulse: Extrasystole.

*Regular irregularity: •Ectopic beat occurring at a regular interval •2nd degree heart block • Sinus arrhythmia.

*Irregular irregularity pulse: •Atrial fibrillation •Multiple ectopics.

Pulse apex deficit

Difference in heart rate & pulse rate;

• Atrial fibrillation(> 10/ min)

•Multiple ectopics (< 10/min)

High volume pulse

Physiological causes: •Exercise •Pregnancy •Advanced age •⇧ environment temp

Pathological: • Arteriosclerosis •Exercise •AR •PDA •Atriovenous fistula •Fever. •Thyrotoxicosis •Anaemia •Beri Beri •Complete heart block •Cirrhosis liver.

Low volume pulse

Causes: •LVF •Hypovolemia •Peripheral arterial disease •Shock •Severe aortic st-enosis •Pericardial effusion.

Varying volume

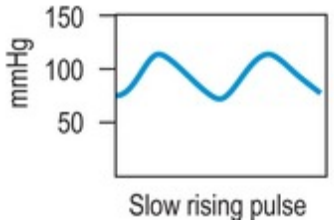
•Combination of low, normal or high volume pulse in varying manner.

•Seen in: Atrial fibrillation or Ventricular tachycardia.

Thready pulse

Pulsations are not easily felt & slight pressure causes it to disappear. The pulse ra-te is rapid & the pulse wave is small & disappears quickly. This is seen in shock esp- ecially cardiogenic.

Weak pulse / Pulsus Parvus

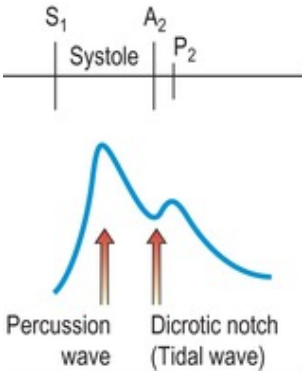


The pressure is diminished & the pulse feels weak & small, reflecting ⇩ stroke volume (e.g. HF), restrictive pericardial disease, hypovolemia, MS & ⇧ peripheral resistance (e.g. exposure to cold, severe CHF). Pulsus Parvus (weak & delayed) is seen in AS. The pulse is stronger than thready, light pressure causes the pulse to disappear.

Anacrotic Pulse

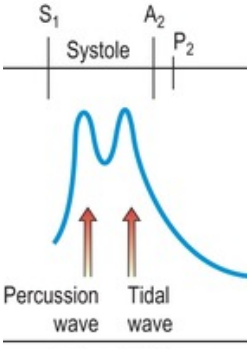
Is a slow rising, double beating pulse where both the waves are felt during systole. The waves that are felt are the anacrotic wave & the tidal wave. It is best felt in the carotids in aortic stenosis.

Dicrotic pulse



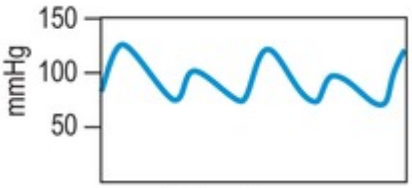
Description: Occurs in? results from an accentuated dicrotic wave. It occurs in sepsis, hypovolaemic shock & after aortic valve replacement.

Pulsus Bisferiens



Is a rapid rising, twice beating pulse (⇧arterial pulse ē a double systolic peak), where both the waves are felt during systole. Here the percussion wave is felt first followed by a small wave. It is seen in: •Idiopathic hypertrophic subaortic stenosis (HCM). & •Severe AR.

Pulsus Alternans

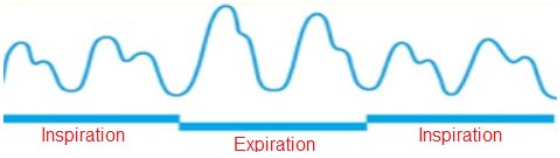


Variation in pulse amplitude occurring ē alternate beats due to changing systolic pressure (Change in ventricular contractility, causing changes in end-diastolic volume & pressure). When the cuff pressure is slowly released while taking BP, phase I Korot-koff sounds are initially heard only during the alternate strong beats; ē further release of cuff pressure, the softer sounds of the weak beat also appear. Degree of pulsus alt-

ernans can be quantitated by measuring the pressure difference betw-een the strong & the weak beat.

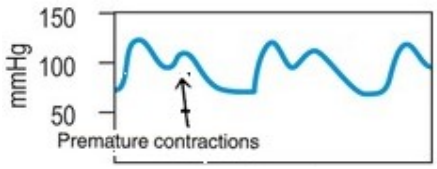
Causes: •LVF – usually accompanied by a left-sided S3 •May be seen in severe AR.

Pulsus Paradoxus



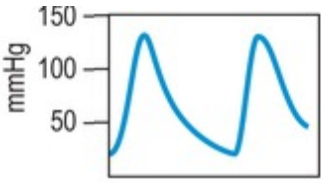
Pulse becomes smaller or disappear at end of deep inspiration (normally). It called Paradoxus pulse as heart sounds still be heard on auscultation over precordium, when no pulse is palbable at radial artery. SBP normally falls by 3-10 mm during inspiration. This is because though there is ⇧ venous return to the right side of the heart there is relative pooling of the blood in the pulmonary vasculature as a result of lung expansion & more negative intrathoracic pressure during inspiration. This ⇩ the venous return to the left atrium &ventricle & subsequently causes fall in left ventricular output decreasing the arterial pressure. When the SBP falls > 10 mmHg during inspiration, it is referred to as pulsus paradoxus. A reverse pulsus paradoxus may occur in pts receiving continuous airway pressure on a mechanical ventilator. Pulsus paradoxus is seen in superior vena cava obstruction, lung conditions like asthma, emphysema or airway obstruction, cardiac conditions like pericardial effusion, constrictive pericarditis & severe CHF.

Pulsus Bigeminus

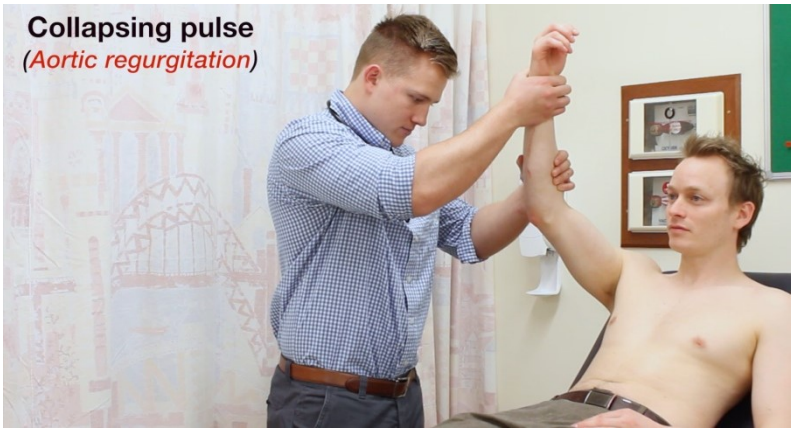


Normal beat alternating ē a premature contraction. May masquerade as pulsus alternans. Causes include; ⇩ BP (e.g. severe HF, hypovolemic shock, cardiac tamponade) & peripheral resistance (e.g.fever). Aortic valve replacement. Present in normal individuals after exercise.

Collapsing' or 'water hammer' pulse



A 'large-volume pulse characterized by a short duration ē a brisk rise & fall. This is best appreciated by palpating the radial artery ē the palmer aspect of four fingers while elevating the pt's arm above the level of the heart. Is associated ē ⇧ stroke volume of the left ventricle & ⇩ in the peripheral resistance, leading to a wide pulse pressure. The pulse strikes the palpating finger ē a rapid, forceful jerk & quickly disappears. It is caused by the artery suddenly emptying because some of the blood flows back from the aorta into the ventricle. It may be seen in fever, alcohol consumption & pregnancy It is also seen in high output states like anaemia, beri beri or cor pulmonale, liver cirrhosis, Paget's disease, AV fistula, thyrotoxicosis. Cardiac lesions like AR, rupture of sinus of Valsalva into the heart chambers, PDA, aortopulmonary window & systolic hypertension may show Water hammer pulse as well. A collapsing pulse is characteristic of aortic valvular regurgitation or a persistent ductus arteriosus.



CHAPTER V

DISEASES OF THE KIDNEYS

- Introduction
- Nephritic Syndrome
- Nephrotic Syndrome
- Renal Vein Thrombosis
- Acute Renal Failure
- Chronic Renal Failure
- Urinary Tract Infection
- Renal Stones

Introduction

Renal function

Based upon 4 sequential steps:-

1. Blood from the renal arteries is delivered to the glomeruli.

2. Glomeruli form an ultra-filtrate, ẃ subsequently flows into the renal tubules.

3. Tubules reabsorb & secrete solute &/or water from ultra-filtrate.

4. Final tubular fluid, the urine, leaves the kidney draining sequentially into the renal pelvis, ureter & bladder, from ẃ it is excreted through the urethra.

Causes of renal disease

Traditionally classified based on the anatomic portion affected as:-

1.Prerenal disease: ⇩ glomerular perfusion is most commonly caused by volume depletion &/or relative hypotension. This may result from: true hypoperfusion due to bleeding, or GIT, urinary, or cutaneous losses, or effective circulatory fluid volume depletion as in CHF, shock, or cirrhosis.

2.Vascular diseases: affecting the kidney from either acute & chronic disease. The major acute causes include; vasculitis, malignant hypertension, scleroderma & thromboembolic disease. Major chronic causes include; benign nephrosclerosis & bilateral renal artery stenosis.

3.Glomerular disease: include numerous idiopathic & secondary disorders. Two general patterns (é considerable overlap) are seen:-

•Nephritic pattern: associated é inflammation on histologic examination & produces an active urine sediment é RBCs, WBCs, granular & often cellular casts & variable proteinuria.

•Nephrotic pattern: associated é inflammation on histologic examination & is primarily manifested by proteinuria.

4.Tubulinterstitial diseases: divided into acute & chronic. The most common acute disorder is ATN, ẃ typically occurs in hospitalized pts. Acute interstitial nephritis, ẃ is often drug induced & cast nephropathy in multiple myeloma. The major chronic disorders for tubulinterstitial diseases include; polycystic kidney, vesicoureteral refl-ux, autoimmune disorders (as Sarcoidosis & Sjögren's syndrome) or analgesic abuse.

5.Obstructive uropathy: obstruction to the flow of urine can occur anywhere from the renal pelvis to the urethra. The development of renal insufficiency in pt éout intrinsic renal disease requires bilateral obstruction & is most commonly due to prostatic disease.

Renal diseases manifestations

Pts present é variety of manifestations:-

Signs & Symptoms resulting directly from alterations in kidney function, including; ⇩ or no urine output, flank pain, oedema, or urine discolouration, asymptomatic ⇧ of plasma creatinine, or abnormalities on urine analysis.

Signs & Symptoms of renal failure include; anorexia, vomiting, mental status changes (including seizures), oedema & hypertension.

Certain Symptoms/Signs may suggest an underlying diagnosis e.g. unilateral flank pain is most consistent é renal stone or infarction or infection or obstruction. The total absence of urine is primarily observed é bilateral ureteral obstruction or shock. A constellation of symptoms & signs may also favour a particular set of disorders e.g. pt é oedema + ⇧BP + red to brown coloured urine + rapid ⇧ of plasma creatinine almost certainly has glomerulonephritis or vasculitis. Other manifestations, are relatively nonspecific & can observed é wide variety of disorders.

Disease duration

Important aspect of evaluation of pt é renal disease is the determination of disease

duration. The differential diagnosis can frequently be narrowed if the disease duration is known. Comparing current urine analysis or plasma creatinine é previous results:- pt é current plasma creatinine 4mg/dl but plasma level of 1.0mg/dL one month previously has acute disease, while the same pt é prior plasma creatinine of 3 mg/dL 2 yrs ago has a slowly progressive CRF. When previous urine analysis or plasma creatinine is unavailable, certain clinical elements may suggest the duration of disease. These include: recent onset of symptoms or signs, such as:- fever & discoloured urine, suggests an acute process. The ⇧ of serum creatinine after the initial evaluation is indicative of at least an acute component to the disease, while a stable value of it is suggests a chronic disease. In addition, the rate of ⇧ of serum creatinine may help distinguish possible disorders.

Diagnostic work up

1. Assessment of renal function: once renal disease discovered, the presence or degree of renal dysfunction should be assessed & the underlying disorder is diagnosed. Glomerular filtration rate either through eGFR or serum creatinine & less often by creatinine clearance, used clinically to assess the degree of renal impairment & to follow the course of the disease. However, since all renal disorders variably affect renal function, eGFR has no diagnostic utility.

2. Urine analysis: since characteristic findings on microscopic examination of urine sediment strongly suggest certain diagnosis. e.g. finding RBCs casts is diagnostic of vasculitis or glomerulonephritis. The presence of muddy brown granular & epithelial cell casts in pt é ARF, suggestive of ATN. Even a normal urinalysis has diagnostic utility. The urine volume has little diagnostic value. Anuria may be due to shock or complete bilateral urinary tract obstruction, or renal cortical necrosis & bilateral vascular occlusion (as é TTP, or haemolytic uremic syndrome).

3. Radiologic/imaging studies: required to assess UT obstruction, stones, renal cyst or mass, disorders é characteristic radiographic findings, renal vascular diseases or Vesic-oureteral reflux.

4. Renal U/S: may show small kidneys ẃ is most consistent é chronic disease because of the progressive loss of renal parenchyma é time. However the presence of normal size kidneys does not R/O chronic disease. Obstructive uropathy: hydronephrosis, hy-droureter, stone & site of obstruction can be seen by U/S.

5. Other studies: may be ordered to make specific diagnosis; IVP (not commonly used now). Renal biopsy: has limited vlue.

ACUTE NEPHRITIC SYNDROME

Is the clinical correlate of acute glomerular inflammation. Characterized by sudden onset (i.e. over days to wks) of ARF & oliguria (**<** 400 ml of urine/day) associated é hy-pertension, oedema & presence of active urinary sediments.

Clinical features

ECFV expansion, oedema & ⇧ BP develop because of impaired GFR & enhanced tubu-lar reabsorption of salt & water. Pt may present é CHF & pulmonary oedema. Pictures of ARF may also occur. Evidence of underlying cause can detected (fever, skin lesions, or joint swelling).

Laboratory tests

- Urine analysis: as a result of injury to glomerular capillary wall, urine typically reveals RBCs casts, dysmorphic RBCs, leukocytes & subnephrotic proteinuria of **<**3.5 gm/24 hrs (nephritic urinary sediment). Haematuria is often macroscopic.
- Renal function test: ⇧ serum creatinine.
- Serology: immunologic assays suggesting the underlying disease.

Etiology

Acute nephritic syndrome can result from renal-limited primary glomerulopathy or secondary glomerulopathy complicating systemic disease. In general, rapid diagnosis & prompt Rx are critical to avoid the development of irreversible renal failure. Immunecomplex glomerulonephritis may result from:-

1. Idiopathic.

2.Represent response to known antigenic stimulus(post infectious glomerulonephritis

3. Part of multisystem immunecomplex disorder (lupus nephritis, Henoch-Schonlein purpura, cryoglobulinemia, bacterial endocarditis).

POST-STREPTOCOCCAL GLOMERULONEPHRITIS

Epidemiology

This is the prototypical post-infectious GN & leading cause of acute nephritic syndrome. Most cases are sporadic, though the disease can occur as an epidemic. GN develops, on average, 10 days after pharyngitis or 2 wks after a skin infection (impetigo) é a nephrogenic strain of *group A β-haemolytic streptococcus*. Immunity to these strains is type-specific, long-lasting. Repeated infection & nephritis are rare. Epidemic post-streptococcal GN is most commonly encountered in children of 2-6 yrs of age é pharyngitis during the winter months. This entity appears to be ⇩ in frequency, possibly due to more widespread & prompt use of antibiotics. Post-streptococcal GN in association é cutaneous infections usually occurs in a setting of poor personal hygiene or strept super-infection of another skin disease.

Clinical Picture

The classic presentation of post-streptococcal GN is full-blown nephritic syndrome é oliguric ARF; however, most pts have milder disease. Indeed, subclinical cases outnumber overt cases by 4-10 fold during epidemics. Pt é overt disease present é gross

haematuria (red or "smoky"), headache & generalized symptoms as anorexia,nausea, vomiting & malaise. Swelling of renal capsule can cause flank pain.

On examination: • Hypervolemia. • Oedema. • Hypertension.

Complications

•CHF & Pulm oedema • ARF • Sever hypertension é hypertensive encephalopathy.

Laboratory findings

Urinalysis: urinary sediment is nephritic é dysmorphic RBCs, RBCs casts, leukocytes, occasionally leukocyte casts & subnephrotic proteinuria & **<** 5% of pts develop nephrotic range proteinuria.

Renal function test: serum creatinine often mildly ⇧ at presentation.

Serology: most pts (**>**90%) have circulating antibodies against streptococcal exoenzymes such as ASO, DNAase.

Course/ Prognosis

Post-streptococcal GN is typically an acute disease é spontaneous recovery occurring in almost all pts, even those who develop renal insufficiency. Resolution is generally quite rapid, assuming concurrent resolution of infection. Diuresis typically begins within one wk & the serum creatinine returns to the previous baseline by 3-4 wks. Haematuria usually resolves within 3-6 months. Proteinuria also falls during recovery, but at much slower rate. Generally, long-term prognosis is good.

Treatment

1. Eliminating the strept infection: é antibiotics.

***2. Supportive* Rx:** until spontaneous resolution including:-

a) Bed rest. & Salt restriction. b) Diuretics to control ECFV.

c) Antihypertensive drugs to control high BP.

3. Dialysis: some pts may need it.

NEPHROTIC SYNDROME

Is clinical complex characterized by significant proteinuria of >3.5 gm/1.73 m^2/24 hrs (for practical purpose >3-3.5 gm/24 hrs).

Etiology

1. Multisystem diseases account for 50-70% of adult Nephrotic syndrome as seen é; DM, collagen vascular diseases & amyloidosis.

2. Neoplasms: including; leukaemia, lymphoma & solid tumours.

3. Infections: including; viral, bacterial, protozoal & helminthic.

4. Primary glomerulopathies (idiopathic): account for 30-50% of adult Nephrotic syndrome In children 90% of cases are primary glomerulopathies. The Nephrotic sy is temporary disturbance in kidney function, more in boys & in age group 2-5 yrs. The prognosis is poor in case of age ⟨1 yr, or é severe degree of hypoproteinaemia, or é marked ⇧ of serum creatinine & é prolongation of PT.

Clinical picture

1. Proteinuria & hypoalbuminemia: in general, the greater the proteinuria, the lower the serum albumin level. Hypoalbuminemia is compounded further by ⇧ renal catabolism & inadequate hepatic synthesis of albumin. The proteinuria is believed to be due to ⇧permeability of the glomerular basement membrane to protein.

2. Oedema: common sites include; feet, face, per orbital areas & scrotum. Hypoalbuminemia & primary water & salt retention by kidney are the postulated mechanisms for oedema formation.

3. Hyperlipidaemia: believed to be a consequence of ⇧ hepatic lipoprotein synthesis & ⇩ clearance. Hyperlipidaemia may accelerate atherosclerosis & progression of renal disease.

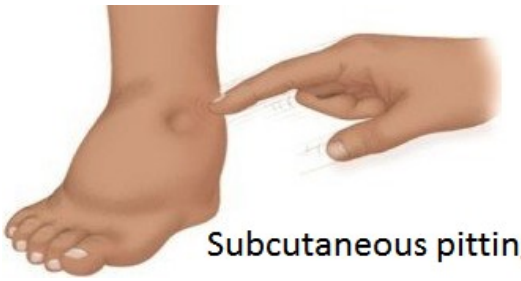
4. Hypercoagulability: is multifactorial, some of the mechanisms are loss of antithro-

mbin III in the urine, ⇧ fibrinogen production by the liver & ⇧ platelet aggregation. Spontaneous peripheral arterial or venous thrombosis, renal vein thrombosis & pulmonary embolism may occur. The clinical features that suggest acute renal vein thrombosis include:-

- Sudden onset of flank or abdominal pain, gross haematuria.
- Left sided varicocele (as the left testicular vein drains into the renal vein).
- ⇧ proteinuria & an acute decline in GFR.

5. Other complications

- Protein malnutrition.
- Iron-resistant microcytic hypochromic anaemia due to transferrin loss.
- Hypocalcaemia as consequence of Vit D deficiency due to enhanced urinary excretion of cholecalciferol-binding protein.
- ⇧ Susceptibility to infection from urinary loss & ⇧catabolism of immunoglobulin.



Subcutaneous pitting edema

Investigations

Confirming proteinuria: proteinuria 40mg/Kg/day, or >2 gm/day or measuring urinary protein by dipstick (+3: +4 diagnostic). Serum proteins: <2½ gm/dL. ⇩ Serum sodium. ⇧ Serum cholesterol. Urine analysis: microscopic haematuria. ⇧ Blood urea & creatinine. Prolonged PT. Immunoglobulins electrophoresis, complement (C3,C4) & autoantibodies (ANA, ANCA, anti-dsDNA & anti-GBM). Renal U/S. Renal biopsy to identify the underlying histopathologic anomaly: minimal change in 80% of cases in children <10yrs. Membranous glomerulopathy in 60-70% of cases in adults. Focal segmental glomerulosclerosis.

Treatment

Fluid Balance, Hypovolemia & BP. A 'no added salt' diet is appropriate measure. If hypovolemia is present it should be promptly corrected é administration of 10-20 ml/kg of 4.5% albumin. Diuretics used in some cases to help control oedema until remission begins, e.g. Furosemide at 2 mg/kg/24 hr. The use of diuretics should be reviewed on a daily basis & the pt's electrolytes should be checked regularly. 20% albumin in combination é diuretics is used in centers to relieve severe symptomatic edema: 0.5-1.0 gm/kg of 20% Albumin can be given slowly over 4-6 hrs & 0.5-1 mg/kg of Furosemide given at the end or midway through the infusion. Rapid administration should be avoided to prevent intravascular volume overload. 20% Albumin should never be used to correct low serum albumin.

Measures to control proteinuria/hypertension: ACEIs: ⇩ proteinuria by ⇩ GF presssure. Controlling hypertension by keeping BP < 130/80.

Infection: streptococcal pneumonia & G-ve organisms are the commonest pathogens causing possible peritonitis, septicemia, or cellulitis. Prophylactic oral Phenoxy Methyl Penicillin (12.5 mg/kg twice daily) is recommended while the pt is edematous & any suspected infection to be treated é broad spectrum antibiotics while awaiting culture.

Thromboembolism: anticoagulant indicated for pt é deep venous or arterial thrombosis or pulmonary embolism. Heparin may not be effective because of urinary loss of antithrombin III.

Hyperlipidaemia: may need lipid lowering agents.

Mobilization: bed rest may ⇧ the risk of venous thrombosis, so pt is encouraged to mobilize as normal.

Diet: 'no added salt', diet is advisable in view of the salt & water overload. No evidence for use of a high protein diet. Encouraged to have a normal healthy diet.

In case of no response: add Prednisolone orally 1 mg/Kg/day ÷ 3 (tab 5 mg) for 4 wks or until urine return to normal, then do weaning gradually over 2 wks + Aldactone 25mg tab (Spironolactone) 1mg/Kg/day + Lasix 40mg tab (1 mg/Kg/day). 90% respond to those regimes. 20% need further investigations as renal biopsy, may need course of cyclophosphamide.

RENAL VEIN THROMBOSIS

Pt é Nephrotic sy. is at ⇧ risk of developing venous & arterial thromboembolism. RVT in pt suffering from Nephrotic sy is rarely present é flank pain & most pts are asymptomatic & recover spontaneously. The Rx of RVT consists of handling the primary condition & treating the thrombosis itself by anticoagulant. In severe cases é grave prognosis, thrombolytic therapy is needed. The mechanism of thromboembo-lism in Nephrotic sy & optimal diagnostic & anticoagulant management strategies remain controversial. 70% of cases RVT seen in the neonatal period as result of; polycythaemia, dehydration, asphyxia, umbilical catheterization, DM, or CHD.

Clinical picture

RVT may be uni or bilateral & may extend to inferior vena cava. Most often has insidious onset & produces no symptoms referable to the kidney. Acute RVT is usually due to trauma, severe dehydration or a generalized hypercoagulable state, typically presents é symptoms of renal infarction, including flank pain, microscopic or gross hematuria, marked ⇧ in serum lactate dehydrogenase & ⇧ in renal size on radiographic study. The bilateral RVT may present é ARF.

Pathogenesis

⇧ Platelets aggregation: thrombocytosis,⇩ RBCs deformability & ⇧ VWF in Nephrotic sy favor platelet transport towards the vessel wall & ⇧ platelet adhesion. Hypoalbumilbuminemia results in ⇧ availability of normally albumin-bound arachidonic acid ⇨

leading to ⇧ formation of thromboxane A2 in platelets, another stimulus for platelet aggregation. ⇧ levels of LDL, cholesterol may ⇧ platelet aggregation.

Activation of coagulation system: Nephrotic pt demonstrat urinary loss of plasma proteins including factor IX, X, XII, prothrombin, antithrombin & α2-antiplasmin. In contrast, proteins of higher molecular weight, including factor V, VIII, VWF, fibrinogen & α 2-macroglobulin accumulate, presumably because of ⇧ synthesis. F VIII levels are typically ⇧ as much as 2-3-fold compared to controls & may be a risk factor for RVT. There is inverse correlation between serum albumin & fibrinogen levels in Nephrotic sy. Hyperfibrinogenemia may contribute to the procoagulant state by providing more substrate for fibrin formation & by promoting platelet hyperaggregability, ⇧ blood viscosity & RBC aggregation.

Endogenous anticoagulants: antithrombin deficiency occurs in 40-80% of pts é nephrotic sy. Antithrombin correlate negatively é proteinuria & positively é serum albumin level, presumably due to urinary loss of this factor. The association between antithrombin deficiency & venous thromboemolism is inconsistent among different studies.

Additional factors

•Intravascular volume depletion & exposure to steroids.

•Loss of fluid across glomerulus causing hemoconcentration in the postglomerular circulation ẃ is worsened by diuretic therapy.

Factors associated é RVT in the absence of Nephrotic sy.

•Trauma (or kidney biopsy) •Oral contraceptives •Hypovolemia.

Diagnosis

Estimated sensitivity & specificity of CT scan é contrast was 92.3% & 100 %, respectively. IV pyelography was found to have a sensitivity of 34.1% & a specificity of 87.2%. Selective renal venography is reference standard for diagnosis

Treatment

The risks associated é asymptomatic RVT have not been compared to the risks of long term anticoagulation, therefore prophylactic anticoagulation is not recommended. Pts é symptomatic RVT or thromboembolic event are treated é low molecular weight Heparin & then warfarin. Some pts are partially resistant to Heparin therapy due to severe antithrombin deficiency. Warfarin therapy given for minimum of 6-12 months & some physicians recommend continuing Rx for as long as the pt remains Nephrotic. Local thrombolytic therapy é/éout thrombectomy in pts who have signs of acute RVT has been successfully done in small number of pts.

ACUTE RENAL FAILURE

Is a syndrome characterized by:-

•Rapid decline in GFR (hours to days).

•Retention of nitrogenous wastes due to failure of excretion.

•Disturbance in ECFV. •Disturbance in electrolyte & acid base homeostasis.

Based on the amount of urine output. ARF may classified as:-

Anuric: urine volume is ˂100 ml/day, or

Oliguric: urine volume is ˂400 ml/day, or

Non-oliguric*:* urine volume is ≥400 ml/day.

Epidemiology

ARF complicates ~5% of hospital admissions & up to 30% of admissions to ICUs. It is usually asymptomatic & is diagnosed when biochemical screening of hospitalized pt reveals a recent ⇧ in plasma urea & creatinine. Most ARF is reversible, the kidney being relatively unique among major organs in its ability to recover from almost complete loss of function. Nevertheless, ARF is associated é major in-hospital morbidity & mortality, in large part due to the serious nature of illnesses that precipitate ARF &

may complicate a wide range of diseases, ẃ for purposes of diagnosis & management are conveniently divided into 3 categories includes:-

1. Prerenal ARF

Nearly in 55% of cases of ARF due to:-

I. Hypovolemia: as a result of Hge, burns, dehydration or GIT fluid loss (vomiting, surgical drainage, diarrhoea). Or as a result of renal fluid loss (diuretics, osmotic diuresis e.g. DM). Or from sequestration in extravascular space (pancreatitis, peritonitis, trauma, burns & severe hypoalbuminemia).

II. Low COP: diseases of myocardium, valves, pericardium or arrhythmias, pulmonary hypertension & massive pulmonary embolus.

III. Altered renal systemic vascular resistance ratio: systemic vasodilatation (as ē sepsis, anaphylaxis, renal hypoperfusion é impairment of renal autoregulatory responses). Drugs (as ē NSAIDs, ACEIs).

2. Renal ARF

Account for nearly 40% of all ARF due to:- Interstitial nephritis: e.g. AGN. or bilateral renovascular obstruction, unilateral in the setting of one functioning kidney. *Ischemic ATN* from hypovolemia, low COP, renal vasoconstriction, systemic vasodilatation, obstetric complications (abruption placenta, postpartum Hge). *ATN from **exogenous** toxins* as é Radiocontrast, Cyclosporine, Antibiotics as Aminoglycosides, Chemotherapy as é Cisplatin, organic solvents as é Ethylene Glycol, Acetaminophen. ATN from ***endogenous*** toxins as é Rhabdomyolysis, Haemolysis, Uric Acid, Oxalate, Plasma cell Dyspraxia (Myeloma).

3. Postrenal ARF

Account for ~5% of ARF as é ureteric calculi, blood clot, cancer, external compression (retroperitoneal fibrosis), or bladder neck obstruction (neurogenic bladder, prostatic hypertrophy, calculi, cancer, blood clot, stricture, cong urethral valve, or phimosis).

Diagnosis

Careful history is essential:

- Exposure to nephrotoxins & drugs.
- Anuria may indicate postrenal causes.
- Skin rash may indicate allergic nephritis.
- Evidence of volume depletion as diarrhoea or bleeding.
- Pelvic & PR examination & look for evidence of abortion.
- Ischemia or trauma to legs or arms may indicate rhabdomyolysis.
- Recent surgical or radiologic procedures.
- Past & present use of medicaion.
- Family history of renal diseases.

Physical examination

Prerenal ARF: suggested by clinical signs of; intravascular volume depletion (orthostatic hypotension, rapid pulse & poor skin turgor).

CHF suggested by (⇧ JVP, S3, dependent oedema, pulmonary rales).

Acute allergic nephritis: suggested by signs of allergy (peri-orbital oedema, maculopapular rash, wheezing, eosinophilia).

Lower Urinary tract obstruction: suggested by supra-pubic or flank mass or symptoms of bladder dysfunction (hesitancy, urgency).

Uraemia: from the adverse effect of renal failure on other organ systems.

Complications

Intravascular overload: weight gain, ⇧ BP, ⇧ JVP, pulmonary oedema.

Electrolyte disturbance:-

- Hyperkalaemia (>5.5 meq/l) result from ⇩ renal excretion combined é tissue necrosis or haemolysis.

•Hypercalcaemia (> 10.5 mg/dl) may occur during recovery phase following rhabdomyolysis induced ARF.

•Hypocalcaemia (<8.5 mg/dl) results from ⇩ active Vit D, hyperphosphatemia, or hypoalbuminemia.

•Hyponatraemia (<135 meq/l) results from excessive water intake in the face of excretory failure.

•Hyperphosphatemia (>5.5 mg/dl) results from failure of excretion or tissue necrosis.

Metabolic acidosis (PH < 7.35) is associated é sepsis or severe HF.

Hyperuricemia: due to ⇩ uric acid excretion.

Bleeding tendency: from platelet dysfunction, coagulopathy associated é sepsis (DIC).

Seizure**:** may occur related to uraemia.

CRF: a modest degree of decline in filtration may exist in 10% of pts for several months following ARF. In pts é underlying renal diseases who experience ARF, progression to CRF is relatively likely.

Diagnostic work up

1. Urine analysis: presence of few formed elements or hyaline casts is suggestive of prerenal or postrenal azotaemia. Many RBCs may suggest calculi, trauma, infection or tumour. Eosinophilia: occurs in 95% of pts é acute allergic nephritis. Brownish pigmented cellular casts & many renal epithelial cells are seen in pts é ATN. Pigmented casts éout RBCs in é +ve dipstick for occult blood indicate hemoglobinuria or myoglobinuria. The dipstick test may show trace or no proteinuria in case of prerenal or postrenal ARF. Mild to moderate proteinuria é ATN. Moderate to severe proteinuria é glomerular diseases. RBCs & RBC casts in GN.

2. Urine & blood chemistry: most of these tests help to differentiate prerenal azotaemia, in ẃ tubular reabsorption function is preserved, from ATN where tubular reabso-

rption is severely disturbed. Osmolality or specific gravity: ⇩ in ATN & post-renal ARF (urine is diluted), while they ⇧ in prerenal ARF (urine is concentrated).

The BUN/plasma creatinine ratio is normal at 10-15 : 1 in ATN, but may be **>** 20 : 1 in prerenal disease due to the ⇧ in the passive reabsorption of urea that follows the enhanced proximal transport of Na & H_2O. Thus, high ratio is highly suggestive of prerenal disease as long as other cause is not present. But this criterion not highly specific.

RF index: urine Na^+ to urine to plasma creatinine ratio ($\mathbf{U_{Na}/U_{cr}/P_{cr}}$), values **<**1% is consistent é prerenal ARF & **>**1% indicates ATN.

Fractional excretion of Na^+: is ration of urine-to-plasma Na^+ ratio/to urine-to-plasma creatinine expressed as % [($\mathbf{U_{Na}/P_{Na}}$)/($\mathbf{U_{cr}/P_{cr}}$) X 100], value ﹤1% suggest prerenal failure & values ﹥1% suggest ATN.

3. Radiography/imaging: •U/S: helps to see the presence of the two kidneys & evaluating kidney size & shape, detecting hydronephrosis or hydroureter, helps to see renal calculi & renal vein thrombosis. •Retrograde pyelography: when obstructive uropathy is suspected.

Management

1) Prevention: because there are no specific therapies for ischemic or nephrotoxic ARF, prevention is of paramount importance. Many cases of ischemic ARF can avoided by close attention to cardiovascular function & intravascular volume in high-risk pts, such as the elderly & those é pre-existing renal insufficiency. Indeed, aggressive restoration of intravascular volume has been shown to ⇩ the incidence of ischemic ARF dramatically after major surgery or trauma, burns, or cholera. The incidence of nephrotoxic ARF can be reduced by tailoring the dosage of potential nephrotoxins to body size & GFR; for example, reducing the dose or frequency of administration of drugs in pts é pre-existing renal impairment.

2) Preliminary measures: Exclusion of reversible causes: obstruction should be relived & infection should be treated. **Correction of prerenal factors**: intravascular volume & cardiac performance should be optimized. **Maintenance of urine output**: although the prognostic importance of oliguria is debated, management of non-oliguric pts is easier. Loop diuretics may be useful to convert oliguric form of ATN to non-oliguric form. High dose loop diuretic as Furosemide (up to 200-400mg IV may promote diuresis in pts who fail to respond to conventional doses.

3) Specific therapy: to date, there are no specific therapies for established intrinsic renal ARF due to ischemia or nephrotoxicity. Management of these disorders should focus on elimination of the causative hemodynamic abnormality or toxin, avoidance of additional insults, prevention & Rx of complications. Specific Rx of other causes of intrinsic renal ARF depends on the underlying pathology. The composition of replacement fluids for Rx of prerenal ARF due to hypovolemia must tailored according to the composition of the lost fluid. Severe hypovolemia due to Hge should be corrected é packed RBCs, whereas isotonic saline is usually appropriate replacement for mild Hge or plasma loss (e.g. burns). Urinary & GIT fluids can vary greatly in composition but are usually hypotonic. Hypotonic solutions (e.g. 0.45% saline) are usually recommended as initial replacement in pts é prerenal ARF due to ⇧ urinary or GIT fluid losses, although isotonic saline may be more appropriate in severe cases. Subsequent therapy should based on measurements of the volume e & ionic content of excreted or drained fluids. Serum K^+ & acid-base status should be monitored carefully. The postrenal ARF requires close collaboration between nephrologists, urologist & radiologist. Obstruction of urethra or bladder neck is usually managed initially by transurethral or suprapubic placement of bladder catheter, ẃ provides temporary relief while the obstructing lesion, is identified & treated definitively. Similarly, ureteric obstruction may be treated initially by percutaneous catheterization of dilated renal pelvis or ureter.

4) Conservative therapy

Diet: adequate calorie intake. Generally, sufficient calorie reflects a diet that provides 40-60 gm/day of protein & 35-50 kcal/kg/day (lean body weight). In some pts, severe catabolism occur & protein supplementation of 1.25 gm of protein/kg/ day is required to maintain nitrogen balance. Restricting dietary protein to approximately 0.6 gm/kg /day of protein of high biologic value (i.e. rich in essential amino acids) may be recommended in severe azotaemia.

Fluid & Electrolyte management: following correction of hypovolemia, total oral & IV fluid administration should be equal to daily sensible losses (via urine, stool & naso-gastric tube or surgical drainage) + estimated insensible loss (i.e. respiratory & dermal losses) ẃ usually equals 500 ml/day. Strict input/output monitoring.

Metabolic acidosis: not treated unless serum HCO_3 ⟨15 mmol/l or arterial pH ⟨7.2, the more severe acidosis is corrected by oral or IV $NaHCO_3$, initial rates of replacement are guided by estimates of bicarbonate deficit & adjusted thereafter according to serum levels. Pts are monitored for complications of bicarbonate ad-ministration as hypervolemia, metabolic alkalosis, hypocalcaemia & hypokalaemia. From a practical point of view, most pts requiring $NaHCO_3$ need emergency dialysis within days.

Hyperkalaemia: cardiac & neurologic complications may occur if serum K^+ > 6.5 meq /l, in such condition restrict dietary K^+ intake, give either Ca gluconate 10 ml of 10% solution over 5 min or glucose 50 ml of 50% sol. + insulin 10 units IV, or K^+ binding ion exchange resin or dialysis if medical therapy fails or the pt is very toxic.

Hyperphosphatemia: usually controlled by restriction of dietary phosphate & by oral aluminium hydroxide or Ca^{++} carbonate, ẃ ⇩ GIT absorption of Ph^{++}.

Hypocalcaemia: does not usually require Rx.

Anaemia: necessitate blood transfusion if severe or é delayed recovery.

GIT Bleeding: regular doses of antacids ⇩ the incidence of GIT Hge significantly & may be more effective in this regard than H2 antagonist, or proton pump inhibitors.

Infection: meticulous care of IV cannula, bladder catheters & other invasive devices is mandatory to avoid infections.

Dialysis: replaces renal function until regeneration. Haemodialysis & peritoneal dialysis appear equally effective for management of ARF.

Absolute indications for dialysis include:-

- Symptoms or signs of the uremic syndrome.
- Refractory hypervolemia.
- Sever hyperkalaemia.
- Metabolic acidosis (most pts requiring $NaHCO_3$ need emergency dialysis).

Prognosis

The initial azotemic stage is either oliguric or non-oliguric. Morbidity & mortality are affected by the presence of oliguria (GI bleeding, septicaemia, metabolic acidosis & neurologic abnormalities are common in oliguric than in non-oliguric pt). Mortality rate for oliguric pt is 50% where as that of non-oliguric pt is only 26%. It should be stressed, however, that pt usually die from the squeal of the primary illness that induced ARF & not from ARF itself. The mortality is affected by both severity of the underlying diseases & the clinical setting in ẃ ARF occurs, e.g. mortality of ATN is 60% when it results from surgery or trauma & 30% when it occurs as a complication of medical illnesses & 10-15% when pregnancy is involved. Ischemic ATN has 2 X the mortality risk of nephrotoxic ATN. In agreement é this interpretation, mortality rates vary greatly depending on the cause of ARF: ~15% in obstetric pts, ~30% in toxin related ARF, ~60% following trauma or major surgery. Oliguria (urine **<** 400 ml/D) at the time of presentation & a rise in serum creatinine of **>**3 mg/dl are associated é poor

prognosis & probably reflect the severity of renal injury & of the primary illness. Mortality rates are higher in older debilitated pts & in those é multiple organ failure. Pt é no complicating factors who survive an episode of ARF have a 90% chance of complete recovery.

CHRONIC RENAL FAILURE

Progressive & irreversible reduction of renal function, over a period of >6 months, to a level <20% of the normal, as a result of destruction of significant number of nephrons. End stage renal disease represent a clinical state or condition in ẃ there has been an irreversible loss of endogenous renal function, of a degree sufficient to render the pt permanently dependent upon renal replacement therapy (either dialysis or transplantation) in order to avoid life-threatening uraemia. Uraemia is the clinical & laboratory sy reflecting dysfunction of all organ systems as a result of untreated or undertreated ARF or CRF. Azotaemia refers to the retention of nitrogenous waste products as renal insufficiency develops.

Aetiologies

1. Prerenal causes

•Severe long standing renal artery stenosis.

•Bilateral renal artery embolism.

2. Renal causes

•Chronic glomerulonephritis either primary or secondary (represent 30% of cases).

•Chronic tubule-interstitial disease as Vesico-ureteral reflux or chronic pyelonephritis.

•Vascular disease as hypertensive nephrosclerosis.

•Diabetic nephropathy.

•Connective tissue diseases as SLE or scleroderma.

•Hereditary disease as polycystic kidney.

3. Post renal cause obstructive nephropathy

•Urolithiasis.

•Benign prostatic hypertrophy.

In general the commonest causes for end stage renal disease are chronic glomerulonephritis, hypertension & diabetic nephropathy.

Stages of CRF

1. Stage of ⇩ renal reserve: basal GFR either normal or even elevated (hyperfiltration), adaptation ⇧ the function of the remaining nephrons. Pts are symptom free. BUN & creatinine are normal or slightly ⇧.

2. Stage of renal insufficiency: GFR ⇩ by 70% (GFR will be 30% of normal). The pt may remain asymptomatic. Biochemical evidence of the decline in GFR, i.e. ⇧ in serum urea & creatinine. Early manifestations of renal insufficiency include; nocturia, mild anaemia, loss of energy, anorexia. Disturbances in nutritional status. Sudden stress such as infection, urinary tract obstruction, dehydration, administration of nephrotoxic drugs may induce signs & symptoms of uraemia.

3. Stage of renal failure: GFR falls to ‹30%. ⇧ Number & severity of uremic clinical manifestations. Biochemical abnormalities & raised BUN & creatinine.

4.End stage renal diseases: GFR falls ‹ 5-10% of normal. Continued survival éout renal replacement becomes impossible.

Pathophysiology

Uremic manifestations occur mainly due to accumulation of nitrogenous wastes & the reason for accumulation of these wastes is ⇩ renal excretion & ⇩ catabolizing capacity of the kidney. Most toxins in uraemia are byproducts of proteins & A.A. metabolism, because unlike CHO & fats (ẃ are metabolized to Co_2 & H_2o, ẃ can be excreted through the lungs & skin), the byproducts of proteins are non-volatile organic acids.

Clinical manifestations & Complications

1. Fluid, Electrolytes & Acid Base Disturbance

(a) Volume expansion & contraction (oedema, dehydration). As long as water intake does not exceed the capacity for free water clearance, the ECFV expansion will be isotonic & the pt will remain normonatremic. On the other hand, hyponatraemia will be the consequence of excessive water intake. Pt é CRF also have impaired renal mechanisms for conserving Na^+ & H_2o. When an extrarenal cause for fluid loss is present (e.g. vomiting, diarrhoea, sweating, fever), those pts are prone to volume depletion & dehydration. In the face of Na^+ intake, pt may retain Na^+ & H_2o ẃ may lead to CHF, peripheral oedema & ascites.

(b) Potassium Homeostasis: most commonly, clinically significant hyperkalaemia does not occur until the GFR falls to <10 mL/min. Factors that contribute to ⇧ serum K^+ level include; endogenous K^+ load (e.g. haemolysis, trauma, infection), exogenous K^+ (e.g. administration of stored blood, K^+ containing medications, K^+ containing dietary salt substitute), or acidosis: facilitates influx of K^+ form ICF to ECF, or drug: (e.g. K^+ sparing diuretics, ACEI).

(c) Metabolic acidosis*:*common disturbance during the advanced stages of CRF. In advanced renal failure, total urinary net daily acid excretion is usually reduced markedly.

2. Renal Osteodystrophy & Metabolic Bone Disease

Is due to disturbance in bone Ph^+ & Ca^+ metabolism. Hyperphosphatemia is a feature of advanced RF. Total plasma Ca^+ in pt é CRF often significantly lower than normal. Pt. é CRF tolerate hypocalcaemia quite well; rarely the pt is symptomatic from the ⇩ Ca^+. Note that the low serum Ca^+ is attributed to 2ry hyperparathyroid. The ⇩ Synthesis of 1, 25 Dihydroxy Vit D during CRD plays a key role in the pathogenesis of hyperparathyroidism, both directly & through hypocalcaemia. The abnormal Vit D metabolism

may be related to the renal disease itself (since the active Vit D metabolite is normally produced in the proximal tubule) & related to the hyperphosphatemia, ẃ has a suppressive effect on renal 1α-hydroxylase enzyme. Some of the resulting bony abnormalities are; ostitis fibrosa cystica is due to osteoclastic bone resorption of especially terminal phalanges, long bones & distal end of clavicle. Renal rickets (osteomalacia). Osteosclerosis; enhanced bone density in upper & lower margins of vertebrae.

3.Cardiovascular complications

(a) CHF &/or pulmonary oedema: may be due to volume overload, or ⇧ pulmonary capillary permeability.

(b) Hypertension is the most common complication of end stage renal disease. Results from fluid overload. Sometimes very severe form.

(c) Pericarditis: metabolic toxins are responsible for pericarditis. The finding of a multicomponent friction rub strongly supports the diagnosis. The pericardial effusion is often haemorrhagic.

4. Hematologic abnormalities

(a) Normocytic normochromic anaemia: may be severe (Hb 4-6 gm/dl). The cause is multifactorial including; ⇩ synthesis of erythropoietin (the most important factor), also toxins suppress the bone marrow, the blood loss (mainly GI) &⇩ RBCs life span.

(b) Bleeding tendency: attributed to platelet dysfunction: pt may manifest é bleeding & easily bruisability, GI bleeding, or ICHge.

(c) ⇧ Susceptibility to infection: due to change in leukocyte formation, function, Lymphocytopenia & atrophy of lymphoid tissue.

5. Neuromuscular abnormalities

In early stage include; irritability, drowsiness & insomnia. In the intermediate stage may present é mild behavioural change, poor judgment, irritability, hiccup, fasciculati-

on, twitching. In terminal stage pt present é asterixis, myoclonus, chorea, seizure, stupor ẃ may lead to coma, peripheral neuropathy (distal sensory polyneuropathy, restless leg syndrome (ill-defined sensation & leg discomfort).

6. Gastrointestinal abnormalities

Early symptoms include: anorexia, hiccup, nausea & vomiting. Uremic fetor: pt's breathe smells like urine. Mucosal ulceration leads to GI bleeding & peptic ulcer.

7. Endocrine & Metabolic abnormalities

Hypogonadism is common. In men ⇩ plasma testosterone level, impotence, oligospermia. In women amenorrhea, inability to carry pregnancy to term.

8. Dermatologic abnormalities

Pallor due to anaemia. Ecchymosis, hematoma. Pruritus & excoriation (Ca^{++} deposits). Yellowish colouration of skin: urochromes. Uremic frost is seen in advanced uraemia: it is due to high concentration of urea in sweat & after evaporation of sweat, a fine white powder can be found on the skin surface.

Differentiate ARF from CRF

The following findings characterize CRF:

•⇩ kidney size on U/S. •Long standing nocturia. •Pruritus. •Finding of broad tubular casts on urine analysis. •Anaemia (not always). •Renal osteodystrophy.

Identification of aggravating factors

• Hypovolemia/Hypotension. •Hypertension. •CHF. •Sepsis. •Nephrotoxin.

Evaluation of reversible underlying aetiology

•Malignant hypertension •Obstructive uropathy •Systemic lupus.

Establishing the underlying cause

•History of: hypertension, DM, systemic infectious or inflammatory diseases.•Metabolic diseases. •Exposure to drugs/toxins. •Family history of renal & urologic disease.

In evaluating the uremic syndrome, questions about appetite, diet, nausea, vomiting, hiccoughing, shortness of breath, oedema, Wt change, muscle cramps, bone pain, mental acuity & daily activities are especially helpful.

Physical Examination

Particular attention should be paid to:-

•Blood pressure. •Funduscopy. •Precordial examination. •Examination of the abdomen for bruits & palpable renal masses. •Extremity examination for oedema. •Neurological examination for asterixis, muscle weakness & neuropathy. •Evaluation of prostate size in men & potential pelvic masses in women should be undertaken by appropriate physical examination.

Diagnostic work up

These should focus on search for clues to an underlying disease process & its continued activity. Tests to determine severity & chronicity of the disease include:-

•Serial measurements of serum creatinine, BUN, Hb, electrolytes (Ca^{+}, Ph^{+}) & alkaline phosphates to assess bones.

•Urine analysis is helpful in assessing the presence of on-going activity of the underlying inflammatory or proteinuric disease process & when indicated should be supplemented by a 24 hrs urine collection for quantifying protein excretion. The presence of broad casts on examination of the urinary sediment is a nonspecific finding seen é all diverse aetiologies & reflects an advanced stage of CRF.

•U/S of kidneys; verifies the presence of two symmetric kidneys, provides an estimate of kidney size & R/O renal masses or obstructive uropathy. The documentation of presence of symmetric small kidneys supports diagnosis of progressive CRF é an irreversible component of scarring. The occurrence of normal kidney size suggests the possibility of acute rather than chronic process. However in some diseases, CRF may

be present é normal sized or even enlarged kidneys. e.g. Amyloidosis, Polycystic kidney & Diabetic Nephropathy.

Management

① *Treating reversible causes of renal dysfunction:* in addition to exacerbation of their original renal disease, pt é CRD & a recent ⇩ in renal function may be suffering from an underlying reversible process such as:- hypotension or dehydration, administration of nephrotoxic drugs, urinary tract obstruction, severe hypertension, or infection. Therefore correcting of these reversible causes can improve the renal function.

② *Slowing the rate of progression of renal diseases:* ACEI or ARBs slows the progression of CRF. The BP control ⇩ the progression of CRF. The target BP for pt é proteinuria is 125/75 mmHg & for pt éout proteinuria is 130/85 mmHg. The possible efficacy of dietary protein restriction, in slowing progression of renal diseases, is less clear.

③ *Treatment of the complications of renal dysfunction*

(a) Volume overload

- Dietary Na^+ restriction.
- Diuretic, usually é loop diuretic.

(b) Hyperkalaemia

- Low K^+ diet or concurrent use of a loop diuretic (to ⇧ urinary K^+ losses) often ameliorates the degree of hyperkalaemia.
- Glucose + Insulin. or
- Ca^+ gluconate; 10 ml of 10% solution over 5 min.
- Correction of acidosis ($NaHCO_3$ administration) or
- Using K^+ exchange resins: Kayaxalate.

(c) Metabolic acidosis: alkali therapy advocated to maintain plasma bicarbonate >22 meq /l., $NaHCO_3$ (in daily dose of 0.5-1 meq/kg/ day) is the agent of choice.

(d) Hyperphosphatemia: dietary phosphate restriction may limit the development of 2ry hyperparathyroidism in pts é CRF. Intake of about 800 mg/day may be desirable but can be accomplished only by limiting protein intake.

(e) Hypertension: salt restriction. Diuretics: loop diuretic recommended for Rx of hypertension & oedema in pt é CRF. Thiazide diuretics have additive effect when administered é loop diuretic for refractory oedema. Antihypertensive drugs (ACEI & ARBS).

(f) Anaemia: blood transfusion in selected pts, also recombinant erythropoietin.

(g) Malnutrition: it is probably reasonable to restrict intake to 0.8-1.0 gm/kg/day of high biologic value protein (plant source), this level of restriction avoids protein malnutrition & may slow progressive disease. Overall, the diet for most pts é CRF should provide approximately 30-35 kcal/kg/day.

④ *Renal replacement therapy:* identification, adequate preparation of the pt in whom renal replacement therapy will be required. Education. Informed choice of renal replacement therapy either chronic haemodialysis or Kidney transplantation.

Acute UTI subdivided into 2 general anatomic categories:-

1) Lower UTI including; urethritis & cystitis.

2) Upper UTI; acute pyelonephritis, prostatitis, intrarenal & perinephric abscesses.

From a microbiologic perspective

UTI exists when pathogenic microorganisms detected in urine, urethra, bladder, kidney, or prostate. In most instances, growth of $>10^5$ organisms/ml from a properly collected midstream "clean-catch" urine sample indicates infection. Especially in symptomatic pt, a smaller number of bacteria (10^2-10^4/mL) may signify infection. In urine specimens obtained by suprapubic aspiration or "in & out" catheterization & in samples from a pt é an indwelling catheter, colony counts of 10^2-10^4/ ml indicate infection.

Recurrence of UTI after Rx

Infections that recur after antibiotic Rx can be due to the persistence of the originally infecting strain that become evident within 2 wks of cessation of treatment, termed relapse, or due to reinfection é new strain that become evident after 2 wks of drug cessation.

Epidemiology

•Non-catheter-infection ẃ is rare in men < 50 yrs but common among women between 20-50 yrs. Asymptomatic bacteriuria is more common among elderly men & women (community acquired).

•Catheter associated (nosocomial) infections. The vast majority of acute symptomatic UTIs involve young women. It is unusual in men < 50 yrs old. Development of asymptomatic bacteriuria parallels that of symptomatic as high as 40-50% in some studies.

Etiology

1. Community acquired: commonest causes are E. coli (80%). Staphyococcus saprophyticus is a G+ve, coagulase -ve bacterium belonging to the staphylococcus gen- us (10%). Klebsiella pneumonia (5%). Others (5%). In acute uretheral sy (sexually transmitted organisms: N. Gonorrhoea, Chlamydia Trachomitis, Trichomonas, Can-dida & Herpes Simplex) may cause lower UTI. In elderly Enterococcus Fecalis may be a cause for UTI. Bacteraemia is often due to Staphylococcus Aurous.

2. Hospital acquired/catheter associated: Escolar (30%). Enterococci (15%). Pseudomonas (10%). Staph Aurous, Yeasts & other Enterobacteriacea.

Routs of inoculation

Urethral inoculation: the urinary tract should be viewed as a single anatomic unit that is united by a continuous column of urine extending from the urethra to the kidney. In the vast majority of cases bacteria gain access to the bladder via the urethra. Ascent of bacteria from the bladder may follow & is probably the pathway for most UTIs. Whether bladder infection ensues depends on interacting effects of the pathogenicity of the strain, inoculum size & the local & systemic host defence mechanisms.

Haematogenous spread: pyelonephritis occurs most often in debilitated pts who are either chronically ill or receiving immunosuppressive therapy. Metastatic staphylococcal or candidal infections may follow bacteraemia or fungemia, spreading from distant foci of infection in the bone, skin, vasculature, or elsewhere.

Rrisk factors for UTI

1.Gender & Sexual activity: the female urethra appears to be particularly prone to colonization é colonic G-ve bacilli because of its proximity to anus, its short length (about 4cm) & its termination beneath the labia. Sexual intercourse may cause the introduction of bacteria into the bladder & is temporally associated é the onset of

cystitis; it thus appears to be important in the pathogenesis of UTIs in younger women. In males who are ˂50 yrs old & who have no history of heterosexual or homosexual rectal intercourse, UTI is exceedingly uncommon & this diagnosis should be questioned in the absence of clear documentation. An important factor predisposing to bacteriuria in men is urethral obstruction due to prostatic hypertrophy. Men (& women) who are infected é HIV & who have CD4 counts of ˂200/µL are at ⇧ risk of both bacteriuria & UTI. Finally, lack of circumcision has been identified as risk factor for UTI in both NN & young men.

2. Pregnancy: is clearly associated é altered uretheral smooth muscle function & higher incidence of asymptomatic bacteriuria & 20-30% of pregnant women é asymptomatic bacteriuria subsequently develop pyelonephritis. UTIs are detected in 2-8% of pregnant women. Symptomatic upper UTI, in particular, are unusually common during pregnancy. Bladder catheterization during or after delivery causes additional infections. ⇧ incidence of LBW infants, premature delivery & NN mortality result from UTIs during pregnancy, particularly those infections involving the upper urinary tract.

3. ***Vesicoureteral reflux:*** defined as reflux of urine from the bladder cavity up into the ureters & sometimes into the renal pelvis. Vesicoureteral reflux occurs during voiding or é elevation of pressure int he bladder. It is common among children é anatomic abnormalities of the UT as well as among children é anatomically normal but infected UT. In the latter group, reflux disappears é advancing age & is probably attributable to factors other than UTI. It may promote ascending infection in several ways, including ⇧ delivery of bacteria, ⇧ size of inoculum & incomplete bladder emptying.

4. Obstruction: any impediment to the free flow of urine caused by; tumour, stricture, stone, or prostatic hypertrophy result in hydronephrosis. This results in urinary stasis & impairs host defence, ẃ greatly ⇧ the frequency of UTI.

5. Neurogenic bladder dysfunction: interference é the nerve supply to the bladder, as in spinal cord injury, tabes dorsalis, multiple sclerosis, DM & other diseases, may be associated é UTI.

6. DM: associated é high rate of infection. Part of the risk is mediated through neurogenic bladder disturbance & partly due to other immune disorders in diabetes.

7. Immune deficiency: congenital, acquired or drug induced immunodeficiency are associated é ⇧ susceptibility to infection.

8. Bacterial virulence factors: not all strains of E. coli are equally capable of infecting the intact UT. Bacterial virulence factors markedly influence the likelihood that a given strain, once introduced into the bladder, will cause UTI.

9. Genetic factors: increasing evidence suggests that host genetic factors influence susceptibility to UTI. Maternal history of UTI is more often found among women who have experienced recurrent UTIs than among controls.

Clinical presentation

Cystitis

Pts é cystitis usually report dysuria, frequency, urgency & supra pubic pain. The urine often becomes grossly cloudy & malodorous & it is bloody in about 30% of cases. If a genital lesion or a vaginal discharge is evident, then pathogens that may cause urethritis, vaginitis, or cervicitis, such as C. Trachomatis, N. Gonorrhoeae, Trichomonas, Candida & Herpes Simplex Virus, should be considered.

Acute pyelonephritis

Symptoms generally develop rapidly over few hours or a day & include; fever, shaking chills, nausea, vomiting & diarrhoea. But the symptoms may or may be not present. Physical exam show; fever, tachycardia, generalized muscle tenderness, marked tenderness on deep pressure in one or both costovertebral angles or é deep abdominal

palpation. In some pts signs & symptoms of G-ve sepsis are predominate.

Urethritis

Approximately 30% of women é acute dysuria, frequency & pyuria have midstream urine cultures that show either no growth or insignificant bacterial growth. Clinically, these women cannot always be readily distinguished from those é cystitis. In this situation, a distinction should made between women infected é sexually transmitted pathogens, such as C. Trachomatis, N. Gonorrhoeae, or Herpes Simpl- ex & those é low count E. Coli or Staph infection of the urethra & bladder. Chlamy- dial or Gonococcal infection should be suspected in women é gradual onset of illn- ess, no haematuria, no suprapubic pain & >7 days of symptoms. The additional history of recent sex-partner change, especially if the pt's partner has recently had Chlamydial or Gonococcal Urethritis, should heighten the suspicion of a sexually transmitted infection, as should the finding of mucopurulent cervicitis. Gross hae-maturia, suprapubic pain, abrupt onset of illness & duration of illness of < 3 days & history of UTI favour the diagnosis of E. Coli.

Catheter-associated UTIs

Bacteriuria develops in at least 10-15% of hospitalized pts é indwelling urethral catheters. Risk of infection is 3-5%/day of catheterization. Clinically, most catheter-associated infections cause minimal symptoms & no fever & often resolve after withdrawal of catheter. G-ve bacteraemia, ẃ follows catheter-associated bacteriuria in 1-2% of cases, is the most significant recognized complication of catheter-induced UTI. The catheterized UT has repeatedly been demonstrated as the most common source of G-ve bacteraemia in hospitalized pts, generally accounting for about 30% of cases.

Diagnostic work up

1. Urine analysis: urinary sediment: leukocytes >5 WBCs/high power field in centri

fuged urine or >10 WBCs/HPF in unspun urine suggests UTI. Microscopic bacteriuria: single microorganism per oil immersion field of unspun urine is indicative of a colony growth on culture of $>10^5$ colonies/ml. Gram stain of urethral discharge may be helpful in pts suspected of having STDs.

2. Urine culture: is definitive mean for diagnosis. A clean catch, mid-stream urine specimen should be collected. The growth of $>10^5$ colonies/ml in the presence of symptoms signifies infection.

3. Blood: ⇧ WBCs in the blood.

4. Radiologic & U/S evaluation: helpful in identification of some predisposing conditions such as urolithiasis, prostate hypertrophy, or vesicoureteral reflux.

Treatment

1. Except in acute uncomplicated cystitis in women, a quantitative urine culture, rapid diagnostic test should be performed to confirm infection before Rx is begun.

2. Factors predisposing to infection, such as obstruction & calculi, should be identified & corrected if possible.

3. Relief of clinical symptoms not always indicate bacteriologic cure.

4. In general, uncomplicated infections confined to lower UT respond to short courses of Rx, while upper UT infections require longer Rx. The anatomic location of UTI greatly influences the success or failure of Rx regimen.

Treatment of pyelonephritis

Decision to hospitalization: indications for admission to hospital include:-

1. Inability to maintain oral hydration or take medications.
2. Concerns about pt compliance.
3. Uncertainty about the diagnosis.
4. Severe illness é high fevers, pain & marked debility.

Empiric antibiotic choices: the initial antibiotic Rx is selected on the basis of urine analysis & an understanding of epidemiology & bacteriology of infection. Knowledge of the antimicrobial susceptibility profile of uropathogens in the community helps to guide Rx decisions. Ampicillin & Sulphonamides should not be used for empiric Rx because of high rate of resistance among causative uropathogens. In comparison resistance to the Fluor quinolones & Aminoglycosides is very low in uncomplicated UTIs, achieving higher tissue levels. So these drugs are preferred for empiric Rx. All pregnant women should be screened for bacteriuria in the 1st TM & should be treated if bacteriuria detected.

Acute uncomplicated pyelonephritis in women: E. Coli, P. Mirabilis, Staph. Saprophyticus are the common causes. Norfloxacin 400 PO BID or Ciprofloxacin 500 mg PO BID for 7-14 day, or single dose of Ceftriaxone 1 gm or Gentamicin 80 mg IV followed by TMP-SMX 480 mg 2 tabs PO BID for 14 day.

Acute uncomplicated lower UTI in women: treated é TMP-SMX: 480 mg 2 tabs PO BID for 3-5 days or Norfloxacin 400mg or Ciprofloxacin 500 mg PO BID for 5-days.

Complicated UTI in men & women: E. coli, Proteus, klebsiella, Pseudomonas, Serratia, Enterococci, Staph, are the common aetiologies. In case of mild-moderate illness, no nausea or vomiting: outpatient Rx include; Norfloxacin 400 mg PO BID or Ciprofloxacin 500 mg PO BID for 10-14 days.

Severe illness or possible urosepsis: hospitalization is required**.** Ceftriaxone 1gm IV daily or BID or Gentamicin 80 mg IV TID or IV Quinolones as Ciprofloxacin 200-400 mg IV BID. If Enterococcus is suspected based upon the Gram stain, Ampicillin 1-2 gm IV Q6 hrs + Gentamicin 1.0 mg/kg IV Q8 hrs or adjusted for renal function).

Note: IV medication should be changed to PO as soon as the pt became afebrile & then give PO TMP-SMX or Ciprofloxacin or Norfloxacin for 10-21 days.

Parenteral therapy: for hospitalized pts, Aminoglycosides 3-5 mg/kg given once daily are cost effective, associated é low toxicity when used for short duration & adequate dosage. They provide a therapeutic advantage compared é beta-lactams, because of their marked & sustained concentration in renal tissue.

Urologic evaluation: routine urologic investigation of young healthy women é acu- te uncomplicated pyelonephritis is generally not recommended. Urologic consultation & evaluation of the upper UT é U/S should be considered if the pt remains febrile or has not shown signs of demonstrable clinical improvement after 72 hrs of Rx to R/O the presence of obstruction, renal or peri-nephric abscesses, or other complications of pyelonephritis. It is reasonable to perform a urologic evaluation, starting é U/S to R/O nephrolithiasis or obstructive uropathy, after 2 recurrences of pyelonephritis or if any complicating factor identified.

Prognosis

In pts é uncomplicated cystitis or pyelonephritis, Rx ordinarily results in complete res- olution of symptoms. When repeated episodes occur, they are always reinfections, not relapses. Acute uncomplicated pyelonephritis in adults rarely progresses to renal functional impairment & CRD. Repeated upper UT infection often represent relapse rather than reinfection & a vigorous search for renal calculi or underlying urologic ab- normality should be undertaken. If neither is found, 6 wks of chemotherapy may be useful in eradicating an unresolved focus of infection. Repeated symptomatic UTIs in children & in adults é obstructive uropathy, neurogenic bladder, structural renal dis- ease, or DM may progress to CRD é unusual frequency. Asymptomatic bacteriuria in these groups as well as in adults éout urologic disease or obstruction, predisposes to ⇧ numbers of episodes of symptomatic infection but does not result in renal impair- ment in most instances.

RENAL STONES

Renal stones are common, 10% of all people will have a renal stone in their life, it is commoner in males (male: female ratio 3:1). Peak of urinary calculi is between 3rd-4th decades of life. There is seasonal variants é stones, occurring more often in the summer months suspecting the role of dehydration in this process. The stones are composed of metabolic products present in glomerular filtrates & typically classified by their location into; Nephrolithiasis refers to kidney stone. Uretrolithiasis refers to the presence of stones in ureter & Cystolithiasiss refers to the presence of stones in bladder.

Pathophysiology

Slow urine flow resulting in super saturation of urine é particular element that 1st become crystallized & later become stone. Damage to the lining of urinary tract.

Etiology

Metabolic: ⇧ urinary level of calcium, oxalic acid, uric acid, citric acid or cysteine, hyperparathyroidism (cause hypercalcinuria) & renal tubular acidosis.

Stasis/slow urine flow: due to obstruction to urine flow (stricture).

Warm climate: cause ⇧ fluid loss, ⇩ urine volume &⇧ solute concentration.

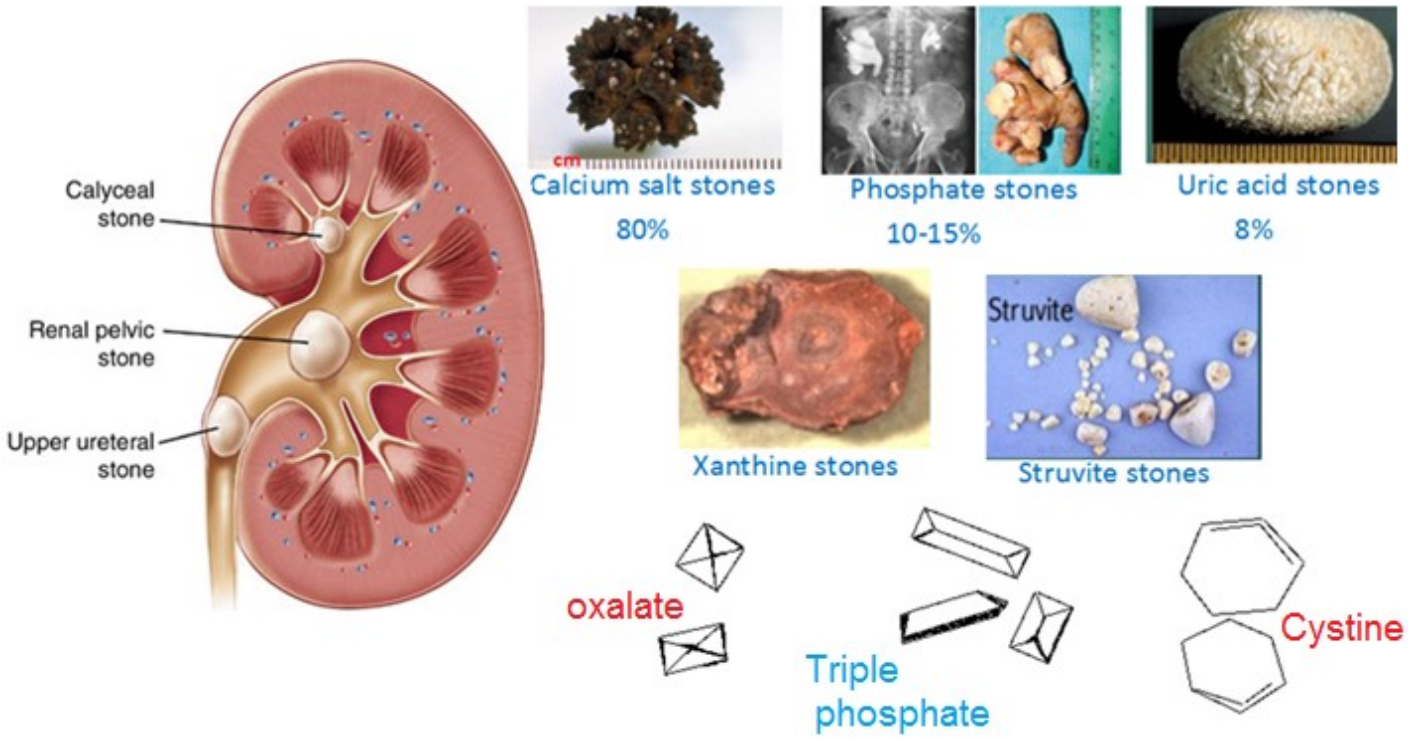
Diet: large intake of protein diet (⇧ uric acid excretion), excess tea & fruit juices (⇧of urinary excretion of oxalate), large intake of calcium & oxalate, low fluid intake, excess intake of Vit D or C, or é deficiency of Vit. A ẃ cause desquamation of epithelium ẃ act as a nidus for stone.

Genetic factor: +ve family history of stones.

Life style : sedentary occupation or immobility.

Presence of UTI: urea splitting organisms (E. Coli, Staph, Proteus, Klebs).

Types



Calcium salt stones: 80% of renal stones. Calcium oxalate stones are small white/brown, sharp projections, hard, radiopaque, lodge in ureter.

Phosphate stones: 10-15% of renal stones. Either calcium, magnesium or ammonium phosphate stones, deposited in alkaline urine, occur é infection (nidus), enlarge rapidly forming stag horn calculus, are large, smooth, white colour, lodge in renal pelvis (filling renal calyces), taken its shape & are radio opaque.

Uric acid stones: 8% of renal stones. Associated é hyperuricemia é or éout gout. The stones are small, friable & yellow in colour, deposited in acidic urine, radiotranslucent & may form stag horn calculus.

Cysteine stones: occur in cystinuria (metabolic disorder of cysteine "AA", inherited as AR, runs in the family, typically appear during child hood & adolescence, the defect is in the resorption of cysteine from renal tubules, deposited in acidic urine, the stone is soft, yellow & radio opaque.

Struvite stones: called also triple phosphate stone, composed of magnesium, am

monium phosphate mixed é carbonate, associated é UTI, formed in the presence of urea splitting organisms in urine (E. Coli, Staph, Proteus, klebsiella), on top of nidus of bacterial cells. The stones are hard, white, may form stag horn calculus & are radio opaque.

Xanthine stones: rare, result from deficiency of xanthine oxidase enzyme. The stone is smooth & red in colour.

Clinical picture

- Severe abdominal pain.
- Flank pain.
- Frequency.
- Dysuria.
- Oliguria or Anuria.
- Obstructive Uropathy (haematuria, Nausea & Hydronephrosis).

Investigations

Urine analysis: volume, cells, type of crystals. PH **>**8 suggest UTI-triple phosphate. ***Bacterial cell count & urine culture.***

X Ray UT: 90% of calculi are visible on X-ray. Will miss radiolucent uric acid stones or small stones & stones é overlying bony structures.

IVP: no longer fevered (low sensitivity & higher radiation exposure).

Sonar UT: for pts needing avoidance of radiation (e.g. pregnancy or childbearing).

Non contrast C-T scan: has significantly better sensitivity, specificity, can detect st-ones not visible by plain UT, or IVP.

24 hrs urine for Calcium, Phosphate, Magnesium, Uric acid.

Complications

✶Obstructive uropathy. ✶Hydronephrosis. ✶Gross haematuria.

Management

- Stones <5 mm mostly pass spontaneously.
- Those > 5 mm, 20% pass spontaneously, the remaining will need.
- urological intervention.
- Excess water intake- water is considered the best diuretic-(3 L/day).
- Lasix 40 mg tab. 1 mg/Kg every other day, or Aldactone 25 mg, 1X1.
- Symptomatic Rx include; Voltarin 75 mg IM, or Tramal ½ IM & ½ IV, or Glucolyamine IV in the running drip.

Specific treatment

Oxalate crystals

Change urine PH to alkaline, Citrocid Magnesium plus or, Epimag sachets, 1 sachet + ½ cup water X 3 after meals. The types of foods ẃ ⇧ alkalinity of urine include; Milk, Milk products, Fruits & Vegetables.

Phosphate calcium

Change urine PH to acidic, Vit C capsule 1 X 3. Types of foods ẃ ⇧ acidity of urine include; Cereals, Tea, Coffee, Chocolate, Nuts, Tomato, Fish, Meat & Strawberry.

Uric acid crystals

Change urine PH to alkaline. Urosolvin sachets 1 sachet + ½ cup of water X 3 after meals. Colchicine tab 1 X3. The types of foods ẃ ⇧ alkalinity of urine.

DISEASE OF THE GASTROINTESTINAL SYSTEM

- Approach to pts é GI disorders
- Gastritis
- Peptic ulcer
- Dyspepsia
- Malabsorption
- Hepatitis
- Chronic liver diseases
- Hepatocellular Carcinoma
- Diarrheal diseases

APPROACH to PATIENT é GI DISORDERS

Pts é GI disorders may present é variety of symptoms that are specific to the GIT &/or to general systemic symptoms. Disorders of the GIT also give a variety of signs. Commonly include:- •Abdominal pain, abdominal distension. •Dyspepsia. •Diarrhoea or constipation. •GIT bleeding. •Jaundice. •Change in weight & change in appetite. •Nausea, vomiting. •Change in stool colour.

During history taking, detailed analysis of the above symptoms should be done & history of medications should also be elicited. The usual techniques & steps of physical examination of GI system should be followed, that include: inspection, palpation, percussion & auscultation.

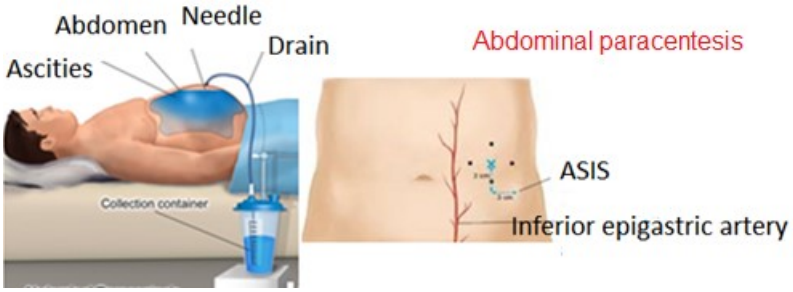
Diagnostic work up

(1) Stool microscopy: for intestinal parasite; ova, cyst or trophozoites, pus or RBCs.

(2) Stool culture: indicated in certain cases of infectious diarrhoea.

(3) Chemical analysis of stool: for faecal fat & occult blood.

(4) Abdominal paracentesis: is simple bed side or clinic procedure in ẃ a needle is inserted into the peritoneal cavity &ascetic fluid is removed. Diagnostic paracentesis refers to removal of small quantity of fluid for testing of clinically evident ascites. Therapeutic paracentesis refers to remove fluid in refractory ascites é resp embarrassment.



Technique

- Empty the urinary bladder.
- Pt lying flat or slightly probed up.

o Give local anaesthetics.

o Site of aspiration is the right or left iliac fossa, 4-5 cm superior & medial to the ASIS, or 2 cm below the umbilicus in the midline.

o For diagnostic purpose 10 cc syringe used & for therapeutic purpose trocar & flanged cannula are used, if this is not available IV set é needle may be used.

o Fluid is analysed Biochemically (protein, glucose, Lactate dehydrogenase), Bacteriologically (gram staining, AFB staining & culture), Cytologically (cell count & differential & specfic gravity). Ascites is classified into; exudative & transudative.

The main differences are:

	Exudative	Transudative
Specific gravity	> 1.018	< 1.018
Protein	> 2.5 gm/dl	< 2.5 gm/dl
Serum ascetic albumin gradient	< 1.1	> 1.1
Causes	Bact. peritonitis, Malignancy	CHF, Cirrhosis,Nephrotic sy.

(5) **Plain X-ray:** no contrast is used & can be taken erect (for air fluid level) or supine.

Contrast X-rays: barium used to outline the lumen of the GIT. include;

o Barium swallow (for oesophagus). o Barium meal (for stomach).

o Barium meal & follow through (for intestine. o Barium enema (for rectum).

(6) Endoscopy: is visualization of the lumen of the GIT é endoscope. Include 2 types depending their flexibility:- Rigid endoscope used for removal of foreign body & Fibro-optic endoscope is flexible, used for visualization of the GIT. Divided into:-

(a) Upper GI endoscopy; used to visualize structures up to the 2nd part of duodenum. Can be used for diagnostic & therapeutic purposes (to stop bleeding varices, ulcers, or to dilate oesophageal strictures).

(b) Lower GI endoscopy: include 3 different types:- 1-Colonoscopy for diagnosis/management of colonic polyps or ulcers. 2- Sigmoidoscopy to visualize the sigmoid colon.

3- Proctoscopy to visualize the rectum & anus.

Diagnostic work up for diseases of hepatobiliary system

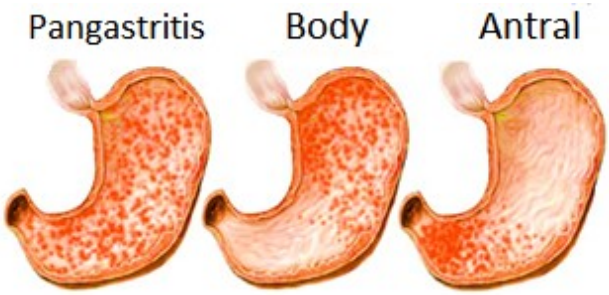
① ***Biochemical tests:*** tests for the detoxification capacity of the liver:- serum ammonia & bilirubin & urine bilirubin. Tests for synthetic function of the liver: serum albumin & PT. Tests indicating liver damage:- serum transaminases; SGOT & SGPT. Tests ẃ show cholestasis: alkaline phosphatase & direct SB.

② ***U/S:*** non-invasive procedure helpful in diagnosing the following:- cirrhosis, metastasis, cholelithiasis, cysts, or abscesses.

③ ***Biopsy:*** either; Open biopsy, done during laparotomy, allows taking adequate tissue samples, or Needle biopsy, done percutaneously.

④ ***Cholangiography:*** is contrast study of biliary tree. Contrast can be given orally, percutaneously, IV, or by using endoscope; the last is known as endoscopic retrograde cholangiopancreaticography (ERCP).

GASTRITIS



Gastritis refers to histologically confirmed inflammation of gastric mucosa. It is not synonymous é dyspepsia or gastric erythema seen during endoscopy. Classified into acute & chronic. May affect the whole stomach (pangastritis), or affecting body or antrum of stomach.

Acute gastritis

Commonly caused by:- Helicobacter pylori. Other causes include: Drugs (ASA, NSAID. Alcohol in high doses. Severe stress. Other infections such as viruses (CMV, Herpes si-

implex), mycobacterium & syphilis. The pt usually asymptomatic but at times he may present é sudden onset of epigastric pain é neutrophilic infiltration, oedema & hyper-aemia of the gastric mucosa. If not treated, Helicobacter pylori gastritis may progress to chronic gastritis. Removal of the offending agents may be adequate treatment.

Chronic gastritis

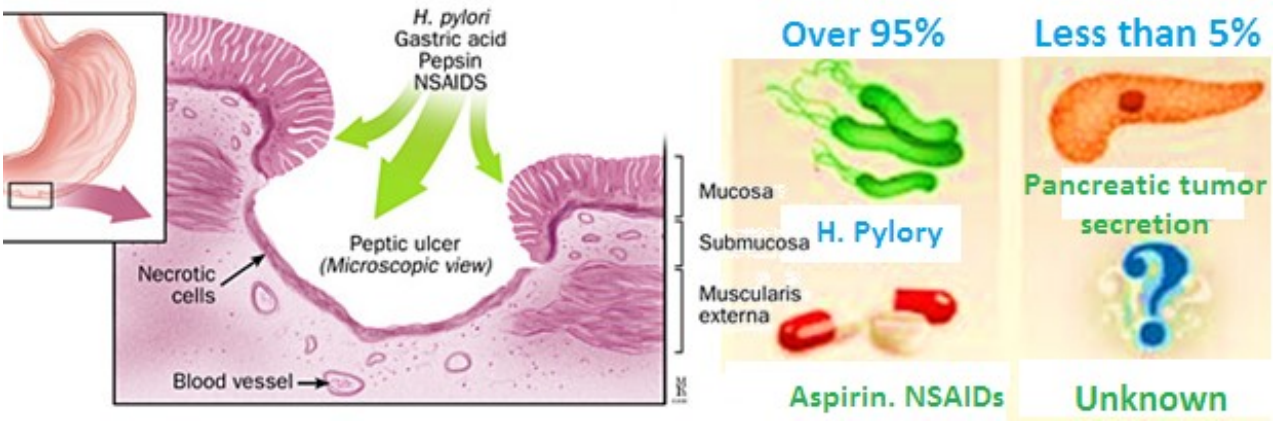
Defined as a histological demonstration of lymphocytic & plasma cell infiltration of gastric mucosa. Superficial gastritis is followed by atrophic gastritis (characterized by distortion & destruction of gastric glands), progressing to gastric atrophy (é loss of gastric glands), ẃ then undergo intestinal metaplasia (replacement of gastric mucosal cells by intestinal epithelial cells) & finally progressing to gastric carcinoma. Chronic gastritis classified into 2 groups:-

1. Chronic fundal gastritis: Inflammation limited to gastric fundus &body é antral spa-ring. Associated é pernicious anaemia, é circulating autoantibodies to parietal cells (autoimmune).

2. Chronic antral gastritis: is more common involves the antrum & mostly associated é Helicobacter pylori infection. However, the inflammation may progress to involve the gastric fundus & body causing pan gastritis usually after 15-20 yrs. Histology im-proves é eradication of Helicobacter pylori.

Treatment

- Aimed at controlling the squeal, not the inflammatory process.
- Life-long parenteral Vit B_{12} is recommended for pts é pernicious anaemia.
- No need for treatment of Helicobacter pylori, unless there is ulcer or MALT Lymphoma.



An ulcer is a break in the mucosal surface **>** 5 mm in size é depth to submucosa. Peptic ulcer caused by discrete tissue destruction caused by acid & pepsin. Ulcers occur most commonly in stomach & proximal duodenum & less commonly in oesophagus & rarely on other portions of small intestine.

Incidence

Duodenal ulcers occur more frequently than gastric ulcers. This is probably due to the likelihood of gastric ulcers being silent & presenting only after complications. Autopsy studies suggest similar incidence of gastric ulcers & duodenal ulcers. Peptic ulcer disease occurs more commonly in males than females. Gastric ulcers occ-ur later in life than duodenal ulcers (peak in the 6^{th} decade of life). 90-100% of duodenal ulcers & 75-85% of gastric ulcers are associated é *H. pylori* infection. About 15-20% of pts have both gastric & duodenal ulcers. Pts é gastric ulcers have a 33% chance of developing subsequent duodenal ulcers.

Risk factors

① ***Helicobacter Pylori infection:*** H. Pylori is a G-ve microaerophilic rod bacteria found attached to gastric epithelium, éout invading the gastric epithelium. The bacterium produces lots of factors, ẃ enable its existence in the acidic environment that include;

o Urease: ẃ splits urea to Co_2 + ammonia & alkalinize the acidic environment.

o Catalase, adhesins, lipase, & platelet activating factor.

The prevalence of H. pylori infection varies throughout the world & depends to a great extent on the overall standard of living. 80% of population in developing countries may infected by age 20. Transmission of H. pylori occurs from person to person following an oral-oral or faecal-oral route. The pathophysiology of H. pylori infection is virtually associated é chronic active gastritis, but only 10% of the infected individuals develop frank peptic ulcer. The basis for this difference is unknown. The end result is dependent upon the interplay between bacteria & host factors. H. pylori infection is present in 90-100% of duodenal ulcers & 75-85% of gastric ulcers. The end result of H. pylori infection are:-

o Gastritis. **o** Peptic ulcer diseases. **o** Gastric cancer. **o** MALT lymphoma.

② ***Non-steroidal anti-inflammatory drugs:*** are among the commonly used over-the-counter & prescription drugs. The spectrum of morbidity ranges from nausea & dyspepsia (50-60%) to serious GIT complications, as frank peptic ulceration complic-ated by perforations or bleeding in as many as 3-4% of users/yr. These drugs inhibit prostaglandin synthesis, ẃ maintains gastro duodenal mucosal integrity & repair. Gastric ulcers occur at higher frequency than duodenal ulcers é the use of NSAIDs. Prostaglandins & related molecules are called eicosanoids as class. Discovered in the 1X300 by Alfven Euler. They are produced in small amounts in almost all tissues, act locally & have an extremely short half-life & are not stored. The function of Prostaglandin are:-

(1) Activation of the inflammatory response, production of pain & fever when tissues are damaged, WBCs are mobilized to the site to minimize tissue destruction.

(2) Blood clots form when a blood vessel is damaged. Closely related molecules called thromboxanes stimulate constriction & clotting of platelets. Conversely, PGI 2 is produced to have opposite effect on blood vessels walls where clots should not formed.

(3) Certain prostaglandins (i.e. PGE 2) are involved é induction of labor by inducing uterine contractions.

(4) Prostaglandins are involved in several other organs, it regulate salt & fluid balance in body, ⇧ Blood flow in kidneys, ⇧ secretion of protective mucus in GI tract, inhibit acid synthesis in GI tract, leukotrienes, related molecules, promote constriction of bronchi associated é asthma.

③ Miscellaneous factors

•Cigarette smoking; carries higher incidence of peptic ulcer & its complications é delayed ulcer healing.

•Generic factors, personality & diet may be associated é PUD; however the mechanisms are not yet established.

•Corticosteroids alone do not predispose to ulcers; but they ⇧ the risk of ulcer development if given é $NSAID_S$ •Aspirin: as it inhibit both COX-1&2.

•Unknown factor.

Pathophysiology

Peptic ulcers develop as a result of an imbalance between protective mucosal defensive factors & aggressive factors.

The defensive factors include: -

o Prostaglandins. o Mucous. o Bicarbonates. o Mucosal blood flow.

The aggressive factors include:-

o Pepsin. o Hydrochloric Acid.

Whereas acid-peptic injury is necessary for ulcer to develop, acid secretion is normal in almost all pts é gastric ulcers &⇧ in approximately 30% of pts é duod ulcers.

Clinical presentations

Dependent on ulcer location & pt age. Course is usually chronic, recurrent. Pain is the

most common symptom & described as burning, or felt as hunger, often localized to epigastrium & relieved by food or antacids.

Gastric ulcer: symptoms often not follow consistent pattern, especially when ulcer located in pyloric channel, where symptoms of obstruction may predominate (bloating, vomiting from oedema & scarring).

Duodenal ulcer: pain is consistent, usually absent when pt wakes up but appears in midmorning, relieved by food but reoccurs again 2-3 hrs after meal & may be severe to awaken the pt at night.

Differences in clinical manifestations

Change in pain character may herald development of complications. For example; duodenal ulcer pain that becomes constant & no longer relieved by food or antacids, or radiates to the back or to either upper quadrant, may signal the penetration to pancreas. Pain ẃ is accentuated rather than relieved by food &/or accompanied by vomiting often indicates gastric outlet obstruction. Abrupt, sever or generalized abdominal pain is characteristic of free ulcer perforation into the peritoneal cavity.

	Duodenal ulcer	Gastric ulcer
Age	Uncommon before age 15 yrs	Peak incidence is later than DU.
Food & Antacids	Pain relieved	Pain aggravated
Pain & Food	90 min-3 hrs after food (hunger pain)	Within 30 minutes after food
Nausea & Vomit	Not common	Common
Weight Loss	Uncommon.	Common (Fear to eat)
Perforation	More common	Less common
Bleeding	Less common	More common

Physical finding

- Epigastric tenderness is most frequent finding.
- Signs of peritonitis may be found in ulcer perforation.

Diagnosis

1) Barium examination of upper GIT: sensitivity of this investigation to detect ul cers ranges from 70-90%.

2) *Endoscopy:* is most sensitive & specific method for diagnosis for the following:-

- Direct visualization & photographic documentation of PUD.
- Permits mucosal biopsy for detection of H. pylori infection.
- Provides baseline reference for the assessment of ulcer healing.

3) *Tests for H. pylori:* there are 2 categories of tests for the diagnosis:-

i) Invasive tests (Endoscopy); rapid urease test, histology & culture.

ii) Non-invasive tests ẃ include:-

- Urea breath test: simple, rapid, useful for early follow up. Is false -ve é recent Rx.
- *Serology*: inexpensive, convenient, not useful for early follow up.

Treatment

Objectives: relief of symptoms, eradication of H. pylori & to promote ulcer healing.

1) Antibiotics Rx of H. pylori indicated in case of documented H. pylori infection associated é PUD or MALT lymphoma. No single agent is effective for eradication of H. pylori; hence a combination of multiple drugs is essential. Proton pump inhibitors (Omeprazole) are added to antibiotics or H_2 blockers (Ranitidine) can be used alternatively.

2) Acid Neutralizing/Inhibitory drugs, include:-

a) Antacids: are the most frequently used drugs before the advent of antihistamines (H_2 blockers). They are now rarely, if ever, used as the primary therapeutic agent, however are often used by pt for symptomatic relief of dyspepsia. A combination of Mg & Aluminium Hydroxide (marketed as Maalox or other brands) are widely used at a dose of 15-30 ml at 1 hr & 3 hrs after meals & at bedtime.

b) H_2 receptor antagonists: include Cimetidine is the most commonly used drug, the

dose is 800 mg at bedtime or 400 mg twice a day for 4-6 wks. Ranitidine used at a dose of 150 mg PO twice a day or 300 mg at bedtime for 4-6 wks.

c) Proton pump inhibitors: they inhibit H^+ pump, ẃ is important for synthesis of hydrochloric acid. Omeprazole 20mg PO/D for 4-8wks. When these drugs are used for anti-H. pylori treatment, it has direct antimicrobial effect on the organism.

d) Dietary advice: there is no specific diet recommended. They are generally advis- ed to avoid smoking, coffee & foods that cause or aggravate symptoms.

	Dose	Duration
Triple therapy		
Bismuth subsalicylate plus	2 tabs QID	2 wks
Metronidazole plus	250 mg QID	
Tetracycline	500 mg QID	
Or Omeprazole plus	20 mg, BID	2 wks
Clarithromycin plus	250 or 500 mg BID	
Metronidazole or Amoxicillin	500 mg BID 1 gm BID	
Quadruple therapy		
Omeprazole plus	20 mg, BID	2 wks
Bismuth subsalicylate plus	2 tabs QID	
Metronidazole plus	250 mg QID	
Tetracycline	500 mg QID	

Surgical Treatment: indicated for:-

•Perforation: immediate surgery recommended. If this not possible, admit the pt to ICU & put him on continuous NG suction & broad spectrum antibiotics.

•Obstruction not responding to medical Rx.

•Uncontrolled/recurrent bleeding or Suspected malignancy.

Complications

All pts é the following complications need special hospital care:-

***Hge:** the most common complication, pt present é hematemesis, passage of tarry stools, weakness, hypotension, syncope, thirst & sweating resulting from associated blood loss. Immediate treatment can be given via endoscopy (electro cautery, alcohol injection/sclerosant) or surgery.

***Penetration:** is entering of adjacent confined space (e.g. lesser sac) or organ (e.g. pancreas, liver). Adhesions prevent leakage into peritoneal cavity. Radiographic evaluation é contrast study usually needed to confirm the diagnosis & surgery is usually recommended.

***Perforation:** presents as acute abdomen é sudden, intense, steady epigastric pain. Confirmed é upright or lateral decubitus X ray abdomen.

***Obstruction:** gastric outlet obstruction may be caused by scarring, spasm, or inflammation. Symptoms include recurrent large volume vomiting, persistent bloating, fullness after eating, loss of appetite; Wt loss, dehydration & alkalosis due to prolonged vomiting. Succession splash for over 6 hrs after a meal, gastric aspiration or X rays may help in the diagnosis. Treat such pt é nasogastric tube aspiration & acid suppression if causes are temporary. But if the pyloric canal scarred, do endoscopic pyloric balloon dilatation or surgical treatment.

***Cancer:** stomach cancer is intestinal type adenocarcinoma of gastric body & antrum, commonly associated é H. pylori infection. Moreover, there is ⇧ incidence of MALT lymphoma. Treating H. pylori might cure lymphoma, but chemotherapy or radical surgery must be used when such treatment fails. For adenocarcinoma, surgery is always treatment of choice.

DYSPEPSIA

Pain centred in the upper abdomen or discomfort characterized by fullness, bloating, distension or nausea. Is the classic symptom of PUD. It is a common clinical problem & may be seen in 25-40% of adults. Only 15-25% pts é dyspepsia are found to have either gastric or duodenal ulcers.

Causes

•Gastritis. • Gastroesophageal reflux disease. •Gastric cancer. •Gastroparesis.

In 60% of dyspeptic pts no cause is identified (functional or non-ulcer dyspepsia) condition most likely related to abnormal perception of events in the stomach caused by afferent visceral hypersensitivity.

Aetiology of non-gastritis mucosal injury

1. NSAIDs: acute ingestion of NSAIDs cause ⇧ mucosal permeability & back diffusion of H^+ leading to hyperaemia, sub epithelial Hge & superficial erosions, while chronic ingestion of NSAIDs cause inhibition of gastro duodenal mucosal prostaglandin leading to ⇩ mucus, bicarbonate production, mucosal blood flow & finally ulceration.

2. Stress related mucosal damage, as a result of mucosal ischemia caused by ⇩ in blood flow (from shock, catecholamine release), impairs mucosal resistance to acid back diffusion. Hyperaemia of the mucosa evolves & erosions & then frank ulceration in the stomach & duodenum that go into bleed.

Clinical features

•May be absent.

•Epigastric pain.

•Hge (hematemesis, melena).

Diagnosis: •History of drug ingestion. •Endoscopy.

Treatment: •Removal of offending agent. •Antacids. •H_2-blocker. •Surface acting agents (sacralfate). •In pt é Hge: volume replacement, endoscopic control of bleeding.

MALABSORPTION SYNDROMES

Syndromes resulting from impaired absorption of one or more dietary nutrients from the small bowel. Many diseases or their consequences can cause malabsorption. The mechanism may be direct impairment of absorption or abnormalities of digestion that finally leads to impaired absorption. Malabsorption may occur for specific nutrients as CHO, fats, micronutrients or affect many nutrients together.

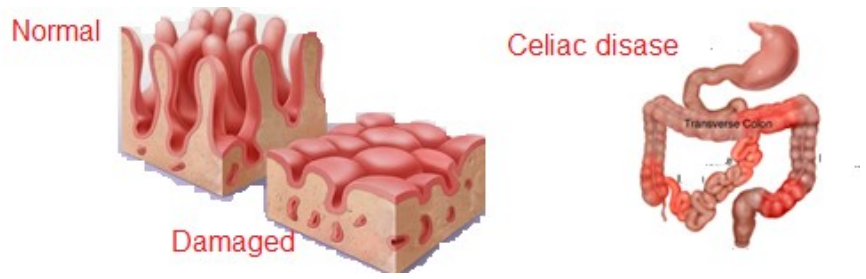
Aetiologies

(1) Mal-Digestion: refers to a defect either in the intraluminal hydrolysis of triglycerides or in micelle formation, ẃ results from the following conditions:-

- Pancreatic insufficiency from chronic pancreatitis or carcinoma.
- Deficiency of conjugated bile salts due to cholestatic or obstructive liver diseases.
- Bile salt deconjugation due to bacterial overgrowth in blind loop (after Billroth II-gastrectomy) or jejunal diverticulitis.
- Inadequate mixing of gastric contents é bile salts &pancreatic enzymes as a result of previous gastric surgery.

(2) Intrinsic bowel diseases

- Celiac or Whipple`s disease ẃ cause damage to absorptive surface of intestine. Celiac disease cause flattening of the intestinal villa & inflammatory cell infiltration.
- Crohn's disease: inflammatory bowel diseases, result in intestinal mucosal damage.



- Whipple's disease is a systemic disease that may cause intestinal mucosal damage & lymphatic obstruction.
- Collagenous sprue: deposition of collagen substance in lamina propia of intestine.

•Non granulomatous ulcerative ileojejunitis ẃ is rare & of unknown aetiology present ē fever, weight loss & malabsorption.

•Eosinophilic gastroenteritis: characterized by infiltration of the wall of stomach & small intestine or colon by eosinophils, many pts present é specific food allergy.

•Amyloidosis: amyloid infiltration of submucosa of small intestine.

(3) Inadequate absorptive surface: from extensive small bowel resection. Resection of 50% of small intestine is well tolerated, if the remaining bowel is normal.

(4) Lymphatic obstruction: Intestinal lymphangiectasia or lymphoma.

(5) Multiple defects: after gastrectomy ẃ may result in poor mixing of gastric contents é pancreatic enzymes & stasis in the afferent loops é bacterial overgrowth. Radiation enteritis, ẃ may interferes é intestinal blood supply & Bacterial overgrowth may occur secondary to radiation stricture, also lymphatic obstruction may occur due to oedema or fibrosis. DM may alter gut motility (diabetic neuropathy), bacterial overgrowth & exocrine pancreatic insufficiency may lead to malabsorption.

(6) Other causes

•In HIV infected pts malabsorption may be caused by cryptosporidiosis, isosporiosis or intestinal mucosal atrophy due to HIV virus itself (HIV enteropathy).

•Tropical sprue is endemic malabsorption disorder occurring in the tropics & believed to have an infectious cause.

•Parasitic causes such as Hookworm, Tapeworm & Strongyloidosis.

•Other causes include; hypoparathyroidism, or drugs as Neomycin, kanamycin may cause malabsorption, Phenytoin causes Folic A. malabsorption.

Clinical features

Signs & symptoms are caused either by the effects of osmotically active substances within the GIT or from nutritional deficiencies. Pt may present é the following:-

Steatorrhoea: passage of abnormal stools, ẃ are greasy soft, bulky & foul smelling & may float in the toilet because of their ⇧ gas content (greasy or oily film of droplets may be seen on the surface of water). This is often associated é abdominal distension, bloating, or discomfort & flatulence resulting from ⇧ intestinal bulk & gas production.

Weight loss: ẃ may be severe & involve marked muscle wasting.

Secondary nutritional deficiencies: deficiency of Iron, Folic Acid, or Vit. B_{12} leading to anaemia. Deficiency of calcium (common) partly due to lack of Vit D causing rickets, osteomalacia, paraesthesia**,** tetany & carpopedal spasms. Thiamine (B_1) & B_{12} deficiency may cause neuropathy. Malabsorption of Vit K (mainly fat-soluble) can lead to hypoprothrombinemia é bruising & bleeding tendency. Protein malabsorption may lead to hypoproteinemic oedema. Dehydration, K^+ loss & muscle weakness from profuse diarrhoea. Secondary endocrine deficiencies may result from malnutrition.

Some specific clinical features of malabsorption

- Lactase deficiency manifests é explosive diarrhoea, abdominal bloating & gas after milk ingestion.
- Pancreatic lipase deficiency manifests é greasy stools é undigested fat.
- Dermatitis herpetiformis often associated é mild degree celiac like Enteropathy.
- Biliary cirrhosis & pancreatic cancer may cause jaundice.
- Mesenteric ischemia may cause abdominal angina.
- Chronic pancreatitis may cause boring central abdominal pain.
- Zolinger Elson sy frequently manifest é severe persistent ulcerative dyspepsia.

Diagnostic workup

Symptoms & signs may point to the diagnostic impression of malabsorption. Any combination of weight loss, diarrhoea & anaemia should raise the suspicion of malabsorption. Laboratory studies are essential to confirm the diagnosis include:-

(1) Direct measurement of faecal fat: 3-4 days stool collection required for this measurement. Faecal fat **>** 6 gm/day is abnormal.

(2) Stool inspection, microscopic examination: look for undigested food fragments & do direct microscopy for ova & parasites. Sudan III staining for the presence of fat.

(3) Absorption tests help to define the site of the lesion: D-xylose absorption testis specific for proximal small-bowel (jejunal) absorption. 5 gm of D-xylose given PO to the fasting pt & urine to be collect for the next 5 hrs, the presence of ⟨1.2 gm of D-xylose in the 5 hrs urine collection considered abnormal.

(4) Iron malabsorption: low serum ferritin & iron levels. In case of pt é adequate diet intake & lack of blood loss, iron malabsorption is suspected. Diminished iron storage on bone marrow examination may also found.

(5) Folic acid absorption: is suggested by low serum Folate.

(6) Schilling test: used to diagnose Vit B_{12} malabsorption.

(7) X-ray abdomen: using small-bowel follow-through, X ray may show pancreatic calcification as a sign of chronic pancreatitis.

(8) Small-bowel biopsy: during endoscopy to show mucosal changes.

Treatment

Individualised according to underlying cause.

However, if the underlying cause is not treatable as in short bowel syndrome, adequate substitution of missing nutrients must be ensured.

HEPATITIS

Hepatitis is a broad category of clinic-pathologic conditions resulting from viral, toxic, pharmacologic or immune mediated damage to the liver. Hepatocellular necrosis & inflammatory cell infiltration of the liver are common pathologic features.

There are 2 types of hepatitis, defined based on duration:-

- *Acute hepatitis:* lasts for <6 months.
- *Chronic hepatitis:* sustained inflammatory response >6 months

Aetiologies

Viral: hepatitis A, B, C, D, E, G, & other viruses such as EBV, CMV, herpes virus etc.

Toxins: amanita phylloides (mushroom), carbon tetrarchloride.

Drugs: acetaminophen, INH, chlorpromazine, erythromycin, heavy Alcohol intake.

Others causes: autoimmune hepatitis, Wilsons disease & fatty liver.

ACUTE VIRAL HEPATITIS

Is the most common form of acute hepatitis; caused by hepatitis viruses (designat- ed as HV) HAV, HBV, HCV, HDV, HEV, HGV, all of ẃ are RNA viruses except HBV ẃ is a DNA virus. 350 million people over the world are chronically infected é HBV. Chrono- logically arranged according to date of discovery are:-

- Hepatitis B Hepadnavirdae (1970).
- Hepatitis F (1970) - not separate entity -mutant of B virus.
- Hepatitis A Picornairidae (1973).
- Hepatitis D ? (1977).
- Hepatitis E Caliciviridae (1983).
- Hepatitis C Flavivridae (1988).
- Hepatitis G Flaviviridae (1995).

	A	B	C	D	E
Virus source	Faeces	Blood, Blood derived Body fluids	Blood Blood derived Body fluids	Blood , Blood derived Body fluids	Faeces
Transmis-sion	Fecal-oral	Per-cutaneous Per-mucosal	Percutaneous Per mucosal	Percutaneous Per mucosal	Fecal-oral
Ch infection	No	Yes	Yes	Yes	No
Prevention	Pre/post ex-posure imm-unization	Pre/post exposure immunization. do-nner screening	Blood donner Screening	Pre/ post exp-osure immun-ization	Ensure sa-ve drinki-ng water

HEPATITIS A

HAV & HEV transmission is faecal-oral. Both viruses are implicated in most instances of water borne & food transmitted infection & in epidemics of viral hepatitis.

Clinical picture

Incubation period average 30 days, range 15-50 days. For those **<** 6 yrs clinical illness (jaundice) appear in **<** 0%. For those aged 6-14 yrs jaundice appear in 40- 50% & for those **>**14 yrs 70-80 % will have jaundice.

Prodromal phase lasts for several days & characterized by malaise, fatigue, anorexia, vomiting, myalgia & headache. Pt will have aversion to smell of food & cigarette é mild fever & flue like symptoms. Arthritis & Urticaria may be present.

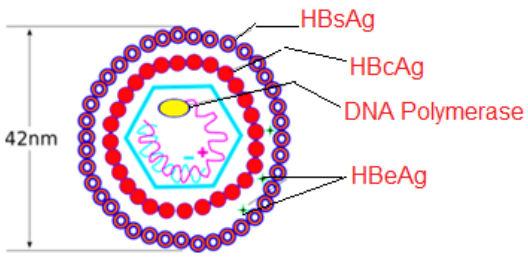
Jaundice appears late usually when pt start to improve in their sense of wellbeing. It may be absent (non-icteric hepatitis) in some pts. Dark urine & pale stool is common in cholestasis. Liver usually tender &enlarged. Splenomegaly seen in 20% cases. No chronic squally.

Diagnosis: can be made by detection of anti HAV antibody, ẃ is IgM initially & IgG later on. The IgG antibody confers life-long immunity.

Management: mainly supportive: rest to limit fatigue, maintain hydration, adequate dietary intake, vitamin supplementation has no proven value, Vit. K can be given if there is prolonged cholestasis, repeat investigations after 10 days, alcohol should be avoided until serum transaminases normalize, Metochlopromide for nausea. Admit pt é severe vomiting or é deteriorating LFTs, especially those é encephalopathy or prolonged PT. In general HAV may be regarded as non-infectious after 2-3 wks.

Prevention: for both HAV & HEV include; general measures as hand washing after toilet use, careful handling of disposal, sterilization of contaminated clothing & utensils. For close contacts to HAV infected pt: Immune serum globulin (IgG) as soon as possible but no later than 6 wks after exposure. Active immunization to travellers to endemic areas, health care workers, workers in restaurant, food dealers to be given vaccine for hepatitis A in 2 doses é 12 months apart. The first dose give 90% immunity & second dose gives 100% immunity.

HEPATITIS B



Is a kind of hepadna virus. The virus consists of an outer protein shell (envelope, contain HBsAg) & an inner body (core, contain HBcAg, HBe Ag, HBV-DNA & DNAP).

Transmission

HBV is DNA virus, mainly transmitted by parenteral (via blood/blood products, contaminated needles), sexual contacts & perinatal route. The virus was found in all body fluids & excreta. It is DNA virus (large virus), not crossing placenta, but infection occurs during labour, most cases (95%) occur during delivery from abrasions in infant`s skin or mucosa, small maternofetal bleeds across placenta, or in case of threatened

abortion. Trans placental transmission occurs in 5% of cases. If pregnant woman is carrier, the baby has 90% chance to be infected & become a carrier, 25% of those babies will die later during adult hood from chronic liver disease or cancer, HDV can occur in top of HBV. the HBV is the only sexually transmitted disease to have a protective vaccine.

Clinical features: IP average 60-90 days, for children <5 yrs age jaundice appear in <10% of cases. Those >5 yrs, jaundice appear in 30-50%. 70% of cases are asymptomatic (called silent disease), or presented é flu-like symptoms, 25% develop severe symptoms (preicteric, icteric & post icteric phases), fever, malaise, anorexia, nausea, vomiting, jaundice, black discolouration of urine. 5% develop chronic hepatitis B carrier. Neonatal infections mostly asymptomatic & 90% become chronic carriers. Slowly resolving HBV infection may persist for 6-12 months é eventual complete resolution. Persistent of HBsAg éout evidence of liver damage resulting in asymptomatic or "healthy" HBV carriers). Acute case-fatality rate is 0.5-1%. Chronic infection for those <5 yrs is 30-90% & for those >5 yrs is 2-10%. Premature mortality from chronic liver disease: is 15-25%.

Diagnosis: battery of seriological tests are used for diagnosis of acute & chronic hepatitis B. The complete HBV (Dane particle) consists of several antigenetically distinct components, including surface coat antigen (HBsAg), core antigen (HBc Ag) & E antigen (HBe Ag). They help in diagnosis, monitoring progress & infectivity. The **HBsAg** usually cleared within 3 months. It may persist in some pts for 6 months to 1 yr éout complications. Its clearance from blood precedes the appearance of HBsAB é time gap in between (called window period), during ẃ the only evidence of HBV infection may be HBc AB. The **HBeAg** indicates HBV replication & therefore infectiveness to others. Used mainly for monitoring response to therapy. The **Anti-HBs** document rec-

overy &/or immunity. The **Anti-HBc IgM** is a marker of acute infection. The **Anti-HBc IgG** is a marker of past or chronic infection. The **Anti HBe** indicates that the virus is no longer replicating. The **HBV-DNA** indicates active replication.

Hepatitis B markers

Anti.HBc(IgM)	Anti.HBc(IgG)	HBsAg	Anti.HBs	Interpretation
+ve	-ve	+ve	-ve	Acute HBV infection
-ve	-ve	+ve	-ve	Early acute HBV infection
-ve	+ve	-ve	+ve	Resolved acute HBV infection
-ve	-ve	-ve	+ve	Not infected-Prior vaccination
-ve	-ve	-ve	-ve	Not infected
-ve	+ve	+ve	-ve	Ch. HBV infection

Treatment: HBV is potentially infectious to contacts throughout its course, although the risk is low once HBsAg has cleared. **Interferon** for HBeAg +ve carriers é chronic active hepatitis, has response rate is 30 to 40%. **Lamivudine** is a nucleoside analogue reverse transcriptase inhibitor, is well tolerated & most pts will respond favorably. However, tendency to relapse on cessation of Rx. Another problem is the rapid emergence of drug resistance. Successful response to Rx will result in the disappearance of HBsAg, HBV-DNA.

Prevention: meticulous disposal of contaminated needles & other blood contaminated utensils. For close contacts to HBV infected pt, give HBIG within 7 days & subseqently HBV vaccine. Screening all pregnant women for HBSAg, if +ve she should be given HBIG, no antiviral approved for use in pregnancy. Baby of infected mother shou-

ld be given HBIG at birth, followed by HB vaccine ½ ml IM, 3 doses, 1st after birth, 2nd at 1 month age & the 3rd at 6 month age. This regime is 95% effectiveness in prevention perinatal transmission of hepatitis. The breast feeding not contraindicated.

HEPATITIS C

HCV largely transmitted parentally & is the main cause of post transfusion hepatitis, especially before discovery of anti-HCV antibodies. Virus is transmitted less frequently through sexual & perinatal routes. The IP is 6-7 wks. Jaundice seen in 40% of cases. Chronic hepatitis stat occurs in 70% of cases. Persistent infection occurs in 85-100%. There is no protective antibody response identified. 70% of cases will develop chronic hepatitis, 20% of them in 20 yrs will develop liver cirrhosis, 5% will develop hepatoma, 15% of pts will clear the virus spontaneously but will maintain the virus antibody in their bodies for the rest of their life. HCV has 6 genotypes. The most common genotype in Egypt & Middle East is genotype 4, the SVR (sustained virological response) for genotype 4 é Rx is 50%- by mean that no virus detected after the course of 6 months Rx. The spectrum of chronic hepatitis C infection is essentially the same as chronic hepatitis B infection. All the manifestations of chronic hepatitis B infection may be seen, albeit é a lower frequency i.e. chronic persistent hepatitis, chronic active hepatitis, cirrhosis & hep-atocellular carcinoma.

Diagnosis

Anti HCV: generally used to diagnose hepatitis C infection. Not useful in the acute phase as it takes at least 4 wks after infection before antibody appears. HCV-RNA-various techniques are available e.g. PCR & branched DNA, may be used to diagnose HCV infection in the acute phase. However, its main use is in monitoring the response to antiviral therapy. HCV Ag: used in the same capacity as HCV-RNA tests but is much easier to carry out.

Comparisons of some features of hepatitis A, B & C

	A	B	C
IP	15-45 days	30-180 days	15-160 days
Onset	Acute	Insidious	Insidious
Age	Children & young adult	Any age	Any age
Transmission			
*Fecal oral	+++	-	Unknown
*Per-cutaneous	±	+++	+++
*Non Per-cutaneous	±	++	++
Severity	Mild	Often severe	Variable
Prognosis	Generally good	Worse é age	Moderate
Chronicity	Non	5-10%	65-85%
Prophylaxis	Immunoglobulin HA vaccine	HBIG HB vaccine	Non
Carrier	None	0.1-30%	Exist

Treatment

HCV Genotype	Therapy	Duration	SVR Rate
Genotype 1	Interferon Ribavirin Protease inhibitor	24-48 weeks	67-75%
Genotype 2	Interferon Ribavirin	24 weeks	74%
Genotype 3	Interferon Ribavirin	24 weeks	69%
Genotype 4	Interferon Ribavirin	48 weeks	60%
Genotype 5	No guidelines	Not applicable	N/A
Genotype 6	No guidelines	Not applicable	N/A

Interferon: is effective for HCV infection. New protocol for HCV according to genotype include: Sofosbuvir + Ribavirin + α Peginterferon X 12 wks. Interferon may be considered for pts é chronic active hepatitis. The response rate is around 50% but 50% of responders will relapse upon withdrawal of Rx.

Ribavirin: there is less experience é Ribavirin than Interferon. However, recent studies suggest that a combination of Interferon & Ribavirin is more effective than interferon alone.

HDV INFECTION

HDV is an incomplete RNA virus & requires presence of HBV to cause infection. Thus, it causes hepatitis when HDV infection occurs at the same time as HBV infection (HDV coinfection) or in pts é chronic HBV infection (super infection). The HDV infection can be diagnosed by detection of HDV antibodies.

HEV INFECTION

IP 15-60 days. Illness severity ⇧ é age. No chronicity. Case-fatality: overall 1-3%.

Investigations for Viral Hepatitis

Liver enzymes: damage to hepatocytes causes release of intracellular enzymes like alanine transaminase (ALT) & aspartate transaminase (AST). The normal levels are 0-35 u/L. In acute hepatitis, liver enzymes often ⇧ to 20 fold or more.

Serum bilirubin: normal level is 0.3-1 mg/dl, when levels go **>** 2.5-3 mg/dl, jaundice appears, while in neonates, jaundice become apparent at a level of 5 mg/dl.

Serum alkaline phosphatase: normal range is 44-147 u/L, it may vary slightly from lab to lab. They also can vary é age & gender. High levels of ALP are normally seen in children undergoing growth spurts & pregnant women. In hepatitis ALP ⇧ by about 3 fold except in cholestatic hepatitis, in ẃ the ⇧ is very much higher.

Serum proteins & PT: are good indicators for liver affection & prognosis.

CBC: leucopenia é atypical lymphocytes (relative lymphocytosis) is common & thrombocytopenia.

Hepatitis markers: involves antigen & antibody detection. Allows the identification of etiologic agents. It helps in planning of preventive & other public health measures for

close contacts of infected people. It helps in evaluating prognosis. **PCR:** for viral load.

Fibroscan: include 5 grades:-

F0: where there is no liver fibrosis.

F1: where there is

minimal fibrosis.

F2: mild fibrosis.

F3: moderate fibrosis.

F4: where there is advanced liver cirrhosis.

Geno type for HCV.

Complications

Cholestatic hepatitis: occurs most commonly during HAV & HEV infection. Self-limited. Pruritus is a common symptom. Marked conjugated hyperbilirubinemia, dark urine, pale stool & ⇧ serum alkaline phosphatase.

Fulminant hepatitis: occur in about 1% of cases. Defined as the onset of encephalopathy, occur within 8 wks in pt é acute liver disease, associated é massive hepatocellular necrosis & commonly follows HAV, HBV (usually super infection of HBV infection by HDV), HCV & HEV (in pregnancy).

Chronic hepatitis: occurs in HBV & HCV infection. Manifest é persistently ⇧ AST & ALT for > 6 months.

Portal hypertension: pt present é varicose veins, piles, ascites, hepatic encephalopathy, hepatic-renal sy., RF, DM, & secondary bacterial infection.

ALCOHOLIC FATTY LIVER & HEPATITIS

Alcoholic fatty liver: characterized by right upper quadrant pain. Incidentally discovered tender hepatomegaly. Jaundice is rare, liver transaminases mildly elevated (< 5 X normal). It is completely reversible on cessation of alcohol.

Alcoholic hepatitis: is severe & prognosticaly ominous lesion, characterized by the following pathologic triads: •Mallory bodies (intracellular eosinophilic aggregates of cytokeratin) usually seen near or around nuclei. •Infiltration by polymorph nuclear leukocytes. •A network of interlobular connective tissues surrounding hepatocytes & central veins (spider fibrosis).

Clinical manifestations

Wt loss, anorexia, nausea, vomiting & abdominal pain are common presenting symptoms. Hepatomegaly in 80% of cases, splenomegaly is often present, fever, jaundice, spider angioma, palmar erythema, gynecomastia, ascites, encephalopathy may present ẃ indicate severe disease, CBC strikingly elevated, transaminases modestly ⇧ (200-400 u/l), the ratio of ASAT to ALIT frequently exceeds one in cotrust to viral hepatitis in ẃ the ratio is approximately one, prolonged PT, hypoalbuminemia & hyperglobulinemia.

Complications & prognosis

Can reverse é cessation of alcohol.

Commonly progresses to liver cirrhosis.

CHRONIC HEPATITIS

Hepatic inflammatory process that fails to resolve after 6 months of Rx.

Etiologies

Except HAV & HEV, all hepatitis viruses can cause chronic hepatitis. Other causes include; autoimmune disorders, drugs like methyldopa & idiopathic.

Pathological classification

Chronic Persistent Hepatitis: inflammatory activity confined to portal areas.

Chronic Lobular Hepatitis: inflammatory activity & necrosis are scattered throughout the lobule. No periportal fibrosis.

Chronic Active Hepatitis: inflammatory activity in portal areas, spills out into lobule (periportal hepatitis, piecemeal necrosis) in association é necrosis & fibrosis. Thought to have significant risk for progression to cirrhosis.

Chronic Viral Hepatitis: complicates about 1% of acute HBV (young, immuno-competent) & 85-90% of acute HCV will develop chronic hepatitis. About 20% of the later will develop cirrhosis in 10-20 yrs. Subjects é either HBV or HCV infection have greater risk of hepatocellular carcinoma.

Treatment

Can suppress hepatic inflammatory activity in 30-40%. HB-therapy is indicated for pts whom are +ve for HBsAg & HBcAg (high replicative phase). Treat é Interferon α &Lamivudine. Hepatitis C can be treated é Interferon α & Ribavirin.

LIVER CIRRHOSIS

It is the end result of fibrous scarring & hepatocellular regeneration that constitute the major responses of the liver, to a variety of long standing inflammatory, toxic, metabolic & congestive insults. The normal hepatic lobular architecture replaced by interconnecting bands of fibrous tissue surrounding nodules derived from foci of re-generating hepatocytes. The following pathologic changes are the cause of the clinical manifestations & complications of liver cirrhosis:-

- Fibrous scarring & disruption of hepatic architecture distort vascular bed leading to portal hypertension & intrahepatic shunting.
- Disturbed hepatocellular function.

Causes of liver cirrhosis

- Alcohol & HCV are major causes in developed countries.
- HBV is the commonest cause in developing countries.
- Other causes: biliary obstruction (intrahepatic, extra hepatic) & autoimmune.

Clinical/laboratory features

•Hypoalbuminemia. •⇩Coagulation factors resulting in prolonged PT. •Hyperbilirubinemia. •⇧Blood ammonia level. •Hepatic encephalopathy. •Ascites. •Portal hypertension: ascites, varices, splenomegaly causing thrombocytopenia & leucopenia & hepatic encephalopathy.

Complications & Management

(1) Portal Hypertension: normal portal pressure gradient 10-15 cm of saline. Portal hypertension said to exist when portal pressure gradient is >30 cm of saline. Portal hypertension leads to formation of venous collateral vessels between portal & systemic circulation. Collateral vessels may form at several sites, the most important clinically being those connecting portal vein to the azygous vein that form dilated, tortuous veins in the sub-mucosa of the gastric fundus & oesophagus.

Types of portal hypertension include:-

•Pre-sinusoidal: ⇧ resistance to portal blood flow into liver e.g. schistosomiasis causes periportal fibrosis & pre-sinusoidal portal hypertension.

•Sinusoidal: the commonest, the resistance is in the liver sinusoids.

•Post-sinusoidal: ⇧ resistance to the hepatic venous outflow from the liver, causes include hepatic vein thrombosis or CHF.

(2) Variceal Hge: oesophageal varices have mortality 30-60% if it bleeds. May present é hematemesis, melena & hematochezia.

Management: the Rx depends on the speed & volume of bleeding. Acutely bleeding pt should be referred to ICU. Resuscitation & medical therapy include; Somatostatin reduces splanchnic BP when given IV, Vasopressin é Nitroglycerine help to ⇩ systemic vasoconstriction. Endoscopic therapy: injection of sclerosing agent &/or ligation. Balloon tamponade (compressing bleeding varices temporarily). Portosystemic shunt.

Prevention: the following drugs can be given for pts diagnosed to have chronic liver disease, but not given during active variceal bleeding:- Non selective β-blockers (Propranolol & Nadolol). Mon nitrates (Isosorbide mononitrate) ⇩ portal BP.

3) Ascites: transudative, the serum to ascetic albumin gradient is ›1.1, clinically detectable when ›500 ml is present. The most sensitive clinical sign is shifting dullness. Subclinical ascites can be detected by U/S.

Management: •Salt restriction to ‹2 gm/day •Fluid restriction if serum Na^+ level is ‹120 meq /l. Spironolactone is an aldosterone antagonist, often effective when given é loop diuretics. Diuresis should be monitored because vigorous diuresis leads to hypovolemia & hypokalaemia & ppt hepatic encephalopathy. The goal of diuresis should be dependent on the extent of oedema & be monitored by daily body wt. measurement to ensure gradual loss of wt i.e. ⇩ wt by 0.5 kg/day if no peripheral oedema present, or ⇩ wt by 1 kg/day if peripheral oedema is present. Refractory ascites is defined as persistent tense ascites despite maximal diuretic Rx (Spironolactone 400 mg/day, Furosemide 160 mg/day) or if azotaemia develops (creatinine ›2 mg/dl) while the pt is receiving submaximal doses. It occurs in 10% of ascites of chronic liver disease, such pts should referred to hospitals for Rx ẃ include; repeated large volume paracentesis (é IV albumin replacement) & Surgical Rx including; Porto systemic shunt & Liver transplant.

Complications

a) Spontaneous bacterial peritonitis: usually due to enterobacteriacae or pneumococci. Characterized by fever, abdominal pain & tenderness. Hepatic encephalopathy may be ppt by the infection. Diagnosis of infection is suspected when ascetic polymorph nuclear cell count is >250/µl & confirmed by asci-etic fluid culture & treated é 3^{rd} gen Cephalosporin for 5-7 days. The indications of

prophylactic Rx include previous history of spontaneous bacterial peritonitis, or pt é GIT Hge, or ascetic protein <1 gm/dl, or candidates of liver transplantation. Drugs; Norfloxacin 400 mg/day, Ciprofloxacin 750 mg once weekly, or Cotrimoxazole 960 mg/day for 5 days (Monday-Friday).

b) Hepato-pulmonary sy.: characterized by abnormal arterial oxygenation in a pt é cirrhosis & or portal hypertension. Thought to be from intrapulmonary vasodilatation leading to impaired O_2 transfer that improves é 100% O_2. Clinical features range from subclinical abnormalities in gas exchange to profound hypoxemia causing dyspnoea at rest. It is a functional disorder that reverses é liver transplant.

c) Hepato-renal sy.: is functional RF in the presence of hepatic cirrhosis. Occurs when there is significant hepatic synthetic dysfunction & severe ascites. Vigorous diuresis, paracentesis & sepsis may predispose to hepatorenal sy. Typically the ki-dneys are histologically normal é capacity of regaining normal function in the event of recovery of liver function. There is severe cortical vasoconstriction. Hepatorenal sy. characterized by ⇩ GFR, oliguria,⇩ urine Na^+ (<10 mg/l), normal urinary sediment & azotaemia often é disproportionately high levels of BUN & creatinine. Hepatorenal sy. is diagnosed after prerenal causes of RF is excluded. Mortality rate of hepatorenal sy. is 95%. Management: volume expansion to R/O volume depletion. Low dose Vasopressin or Norepinephrine may be given. Liver transplantation is accepted management.

d) Hepatic encephalopathy

hepatic coma or porto-systemic encephalopathy- complex neuropsychiatric syndrome

may complicate advanced chronic liver diseases & or extensive porto-systemic shunt. Include 2 major forms:-

•Acute hepatic encephalopathy; occurs in the setting of fulminant hepatitis. Cerebral oedema plays a more important role. Mortality rate is very high.

•Chronic hepatic encephalopathy; occurs in chronic liver disease & is often reversible.

Pathogenesis: the hepatocellular dysfunction & porto-systemic shunt lead to inadequate removal of nitrogenous compounds &toxins ingested or produced in the GIT, getting access to the brain & causing hepatic encephalopathy. The compounds commonly incriminated in causing hepatic encephalopathy include:- Ammonia is very well known & studied. GABA. Short chain fatty acids. Mercaptans cause of fetor hepaticas.

Clinical features & Stages of hepatic encephalopathy

- Disturbance of higher neurologic function.
- Intellectual & personality disorder.
- Dementia, inability to copy simple diagrams (constructional apraxia).
- Disturbance of consciousness.
- Disturbance of neuromuscular function (asterixis), hyperreflexia & myoclonus. The findings are usually asymmetrical, but may be symmetrical.

Manifestations depend upon hepatic encephalopathy stage:-

	Hepatic encephalopathy stages
I	Apathy, restlessness, reversal of sleep rhythm, slowed intellect, impaired computing ability, impaired hand writing
II	Lethargy, disorientation, drowsiness, asterixis
II	Stupor (arousable), hyperactive reflexes, extensor plantar reflex
IV	Coma

Management of chronic hepatic failure

(1) Identify & treat ppt factors including:-

•GI bleeding. •⇧ dietary protein constipation. •Alkalosis •Hypovolemia. •Infection. •Azotaemia. •Hypokalaemia from over diuresis. •CNS depressant drugs.

(2) Reduce & Eliminate substrates for the generation of nitrogenous compounds: -

•Restrict dietary protein: for pt in coma no protein should given, for noncomatose pt restriction of protein to 40-60 gm/day.

•Cleanse the bowel é enema in pt é GIT Hge.

(3) Reduce colonic bacteria that generate ammonia using oral preparations of neomycin or metronidazole.

(4) Prevent diffusion of ammonia from bowel lumen to blood by administering oral lactulose, or lactose , all of ẃ are fermented by colonic bacteria to organic acids & reduce stool PH. The hydrogen ion produced traps ammonia in colon & changes it to non-diffusable NH_4^+.

Supportive measures

•IV Fluid: 2 litre/day of glucose & ringers solution. (no saline because of the secondary hyperaldosteronism).

•Antibiotic: Claforan as it is not excreted by liver 1 gm/12 hrs.

•Liver support; Heapmarine tab/Heapmerz amp IV.

•Laxatives: Lactulose syrup or Enema/6 hrs (using 1000 ml warm water + Lactulose syrup 2 spoon).

•Brain stimulant; Neurobion/Becoztm: amp IM every other day.

GIT Haemorrhage

•Dicynone: 2 amp/day (⇧ capillary resistance). •Konakion 2 amp/day (Vit K essential for formation of factors 2, 7, 9, 10). •CyKlokapron: 2 amp/day (inhibit plasminogen).

HEPATO CELLULAR CARCINOMA

One of the most frequent malignancies & important cause of mortality particularly in middle aged men in developing countries. The incidence is less in developed countries. Arises in cirrhotic liver & closely associated é chronic HBV or HCV. The HB DNA has been shown to integrate into the host cell genome, where it may disrupt the tumour suppressor genes &/or activate oncogenes. Vaccination prevent HB infection & ⇩ the incidence of hepatoma. Hepatocellular carcinoma is more common in males (male to female ratio 4:1 to 8:1). The median survival rate is ˂6 months from the time of diagnosis.

Clinical & Laboratory findings

- Abdominal pain, wt loss, abdominal mass.
- Derangement of liver function.
- Unusual manifestations ẃ include; bloody ascites, tumour emboli, jaundice, gynecomastia, Hepatic bruit or friction rub.
- Metabolic effect including; erythrocytosis, hypercholesterolemia, hypoglycaemia, hypercalcemia & acquired porphyria.
- ⇧ serum α fetoprotein (>400 mg/dl).
- U/S; mass lesion é varying echogenicities.
- Biopsy is confirmative.

Treatment

Usually unsatisfactory but some options include:-

- Chemotherapy.
- Radiotherapy.
- Liver transplantation.

DIARRHEAL DISEASES

⇧ In stool frequency & volume. Stool is usually liquid & the 24 hrs output is usually **>**250 gm/day. Normal stool weight is about 100-200 gm/day for people in develo-ped countries who usually consume diets containing less fibre. Stool weight is affected by fibre contents of diet, affected also by gender (higher in males), affected by medica-tions, & possibly by exercise & stress. Normal bowel habit ranges from 3 times/day to 3 times/wk. Thus, one has to know the normal bowel habit of the individual & the na-ture of the current symptoms before diagnosis of diarrhoea. About 9 litres of fluid is presented to the GIT daily (7 litres from the secretion & 2 litres from diet). Of this 100-200 ml of fluid is excreted é faeces & the rest will be reabsorbed. Fluid absorp-tion follows Na^+ absorption, ẃ is co-transported é chloride ion, glucose & amino acids & through Na^+ channels. Na-Glucose co-transport is unaffected by many diarrheal diseases.

Classification of diarrhoea

*Based on the duration: ***Acute diarrheal disease:*** lasts 2-4 wks, usually infectious in origin, resolves é/éout Rx. ***Chronic diarrheal diseases:*** lasts for **>** 4 wks. The common causes include; malabsorption, inflammatory bowel diseases (ulcerative colitis, irrita-ble bowel sy., colonic cancer & HIV/ AIDS. Infectious causes are not common causes of chronic diarrhoea.

*Based on the nature of diarrheal stool: ***Non-inflammatory diarrhoea:*** is watery, non bloody, associated é periumblical cramps, nausea & vomiting. It is small intestinal in origin. ***Inflammatory diarrhoea:*** dysentery is bloody diarrhoea.

*Pathophysiologic classification: most diarrheal states are caused either by inadequa-te absorption of ions, solutes & water or by ⇧ secretion of electrolytes that result in accumulation of water in the lumen. Based on this concept diarrhoea can be classified as the following:-

*__Secretory diarrhoea:__ occurs when the secretion of fluid & electrolytes ⇧ or when the normal absorptive capacity of the bowel ⇩. It usually follows stimulation by mediators like enteric hormones, bacterial enterotoxins (e.g. cholera, heat labile E. coli toxin, salmonella enterotoxin), vasoactive intestinal peptides or laxative. These agents activate the adenylcyclase -cAMP system. These mediators block $Na^{+}CL^{-}$ absorption & induce chloride secretion. These events can result in massive diarrhoea éout evidence of cell injury, as shown by the ability of the cell to absorb Na^{+} if cou-pled to nutrients (Na^{+} to glucose or Na^{+} to amino acids). That is why cholera &other forms of secretary diarrhoea can be treated é oral solutions containing Na^{+} & glucose. Diarrhoea of secretary origin persists even if the pt fasts.

*__Osmotic diarrhoea:__ result from the presence of poorly absorbed or non-absorba ble substance in the intestine ẃ is osmotically active, resulting in secondary accumulation of fluid & electrolytes. Such non-absorb substances include lactose in pts é lactase deficiency. This type of diarrhoea is usually caused by malabsorption.

*__Abnormal intestinal motility:__ causes or contributes to diarrhoea, seen in DM, irritable bowel syndrome, post-vagotomy states, carcinoid syndrome & hyperthyroidism. The mechanism of abnormal intestinal motility includes the following; if small bowel peristalsis is too rapid, an abnormal large amount of fluid & partially digested food stuffs may delivered to the colon. Extremely slow peristalsis may allow bacterial overgrowth & bile salts deconjugation to cause 2ry malabsorp ti on. Rapid colonic motility may not allow adequate time for colon to absorb fluid delivered to the caecum (normally 90% of fluid absorbed from colon).

__*Exudation:__ inflammatory or infectious conditions that result in damage to intestinal mucosa can cause diarrhoea by a number of mechanisms. There is loss of blood, mucous proteins & serum proteins. Mucosal damage can interfere é absorption. induce

secretion & affect motility, all of ẃ contribute to diarrhoea.

Infectious diarrhoea: microbes cause diarrhoea either directly by invasion of gut mucosa or indirectly through elaboration of different types of toxins as enterotoxins, cytotoxins & inflammatory mediators.

Secretory toxin induced diarrhoea: pts seldom have fever or major systemic symptoms. Little or no inflammatory response. The organisms colonize the intestinal mucosa but don't invade the intestinal wall, for examples:-

(a) Vibrio cholera produces enterotoxins ẃ stimulate adenylatecyclase ẃ results in massive intestinal secretion.

(b) Enterotoxigenic E.Coli is the major cause of traveller diarrhoea.

(c) Non-typhoidal salmonella like S. typhimarium.

(d) Shigella dysentery may initially cause secretary diarrhoea.

Cytotoxins induced diarrhoea: cytotoxins are soluble factors that directly destroy mucosal epithelial cells. Examples:-

(a) Shigella dysentery produces toxin causing destructive colitis.

(b) Enterohemorrhagic E. coli.

(c) Clostridium perifringens, Vibrio parahemolyticus.

(d) Clostridium defficile causes pseudomembranous colitis in pt treated é antibiotics.

Diarrhoea caused by invasive pathogens: characterized by fever & other systemic symptoms like headache & myalgia. The diarrhoea is frequent but small in volume. associated é crampy abdominal pain & tenesmus. These pathogens induce marked inflammatory response, stool usually contains pus cells, proteins & often gross blood. Common invasive pathogens include:-

Acute shigellosis: faeco-orally transmitted, as few as 10-100 bacteria are enough to cause diarrhoea. Bacteria initially multiplies in the small intestine causing secretary

diarrhoea, later on it invades the colonic epithelium causing bloody diarrhoea. Resolves spontaneously in 3-6 days.

Acute Salmonellosis: transmitted by ingestion of contaminated meat, poultry products. The non-typhoidal salmonellae invade primarily the distal ileum. Causes short lived (2-3 days) illness characterized by fever, nausea, vomiting & diarrhoea. This is in marked contrast to the 3-4 wks febrile illness caused by salmonella typhi & paratyphi, ẃ are not usually associated é diarrhoea.

Campylobacter jejuni: may be responsible for up to 10 % of acute diarrhoea worldwide. It invades both the small & large intestines.

Enterohaemorrhagic E.coli: produces bloody diarrhoea éout evidence of mucosal inflammation (grossly bloody stool é few or no WBCs).

Viral causes: as Norwalk & Rota viruses. Rota viral infection is the commonest cau- se of diarrhoea in infants & children, preceded by URTI or otitis media in 50% of cases, vomiting start first & stop then watery stool lasts for 3-5 days, can spread as epidemic in paediatric word. Invade & damage villous epithelial cells. Cause diarrhoea by interfering é absorption through selective destruction of absorptive villous tip cells & sparing secretory crypts. Stool is usually watery, its content resembles those of non-invasive diarrhoea é few inflammatory cells.

Protozoal causes: a) Giardia Labia: few organisms are necessary for infection. Multiplies in small intestine, attach to & occasionally invade the mucosal cells. Its clinical features span from an acute diarrheal illness to chronic diarrhoea associated é malabsorption & Wt loss. Diagnosis based on identification of the organism either in stool or duodenal mucous or by small intestine biopsy. Cysts or trophozoites can identified in the stool & Rx should be given in both cases.

b) Entamoeba histolytica: cause syndromes ranging from mild diarrhoea to fulminant

amoebic colitis é multiple bloody stools, fever & severe abdominal pain.

c) Cryptosporidium parvum & Isospora belli: occasionally cause self-limited acute diarrheal illness in otherwise healthy individual. May cause voluminous life threatening diarrheal diseases in pt é AIDS. Modified acid fast staining of stool will identify both organisms.

Summary of classification

Acute diarrhoea	Presence of three or more loose stools within 24 hrs
Dysentery	Bloody diarrhoea, visible blood & mucous present
Persistent diarrhoea	Episodes of diarrhoea lasting > 14 days

Evaluation of pt é diarrhoea

Careful interview of pt é diarrhoea contributes in etiologic diagnosis, the history should include:-

*Duration of illness: if the diarrhoea lasts for 2-4 wks, acute diarrheal diseases are said to exist. These are usually infectious in origin. However, if it lasts for **>** 4 wks consider chronic diarrheal diseases while the infectious causes are unlikely. In such cases the common causes include; malabsorption, inflammatory bowel diseases (ulcerative colitis), irritable bowel sy., colonic cancer & immunosuppression like AIDS.

*Diurnal variation? Is there is any relation to any part of the day? Nocturnal ⇨ organic causes. Non nocturnal ⇨ functional causes like irritable bowel syndrome.

*Is the diarrhoea watery or bloody? Bloody diarrhoea usually inflammatory or ischemic in origin, caused by invasive organisms, ulcerative colitis, or neoplasms.

*Volume of diarrhoea? Large volume diarrhoea indicates small bowel or proximal colonic diseases. Scanty, frequent stools associated é urgency suggest left colon or rectal diseases.

*Any association é specific meal intake ? Fat ⇨ it is due to fatty intolerance.

Sweet diet ⇨ it is due to osmotic diarrhoea.

Milk & milk products ⇨ it is due to lactase deficiency.

*Is there is history of drug intake ? Penicillin may be associated é pseudomembranous colitis. Intake of laxatives or chemotherapy.

*Presence of underlying disease? D.M., or systemic symptoms….

Physical examination: assess severity of dehydration, wt loss & other associated signs in pt é chronic diarrhoea. In infants signs of dehydration as; sunken eyes, depressed fontanels, dry tongue, loss of skin turgor & poor peripheral circulation. It is divided into mild, moderate & severe according to % of fluid loss (2-5%, 5-7%, or 7-10%).

Diagnosis

1) ***Culture & Sensitivity testing:*** to detect pathogenic bacteria strains. A+ve stool culture is found for 40% of pts who have WBCs in the stool associated é fever.

2) ***Microscopic exam of stool:*** to identify ova & parasites.

3) ***Guaiac:*** to detect occult blood.

4) ***Sudan staining:*** to detect fat droplets.

5) ***Proctosigmoidoscopy:*** to exclude diagnosis of inflammatory bowel disease.

Management

1. Rehydration: pt é massive diarrhoea & vomiting é hypotension, IV fluids like ringer's lactate/normal saline should be given in adequate amount. Pt éout hypotension oral fluid containing Na^+, glucose, K^+ & Cl^- ions (ORS) are preferred.

2. Antimicrobial therapy: antibiotics: most acute infectious diarrheal diseases do not require antibiotic because majority of them are self-limited & are viral in nature. Of the noninvasive bacterial diarrhoea, antibiotics ⇩ the volume of diarrhoea only in cholera, Doxycycline 300 mg single dose is the drug of choice. For invasive bacterial diarrhoea caused by E.coli & shigella, Ciprofloxacin 500 mg or Norfloxacin 400 mg X 2

daily for 3-5 days is indicated. Antiprotozoal for Entamoeba Histolytica, Metronidazole 500 mg PO TID, 7 days. For Giardia lamblia: Metronidazole 250 mg TID for 5 days. For Isospora belli: Cotrimoxazole 960 mg QID for 10 days then 960 mg BID for additional 3 wks. In immunocompromised pt continue maintenance dose of the same drug 3 times a wk. When no specific therapy is available or no cause identified, it's appropriate to give empirical Rx e.g. antibiotics for possible bacteria overgrowth, Flagyl for Giardia, Cholestyramine for bile acid malabsorption.

CHOLERA

Caused by bacteria Vibrio Cholera. Mode of infection is through contaminated water, food, poor hygiene & poor sanitation of environment. The IP is 1-2 days.

Clinical Picture: effortless, painless, severe watery diarrhea (rice water stool) up to the loss of 1 Liter/hr. Vomiting in severe cases. Rapid development of marked dehydration, metabolic acidosis, hypokalemia & hypotension. Electrolyte imbalance. The condition may be fatal within few hrs.

Investigations: ▲Serum electrolytes. ▲Stool culture. ▲Agglutination. ▲BABGs.

Management: rapid correction of dehydration, electrolyte imbalance, using normal saline or ringer lactate, Kcl 15%, & $NaHco_3$ in case of metabolic acidosis, saline éout alkali leads to pulmonary oedema especially if pt is oliguric & excess fluids given.

Septrin syrup 40 mg TMS + 200 mg SMZ, tab 80 + 400 mg, double strength tab 160 mg + 800 mg, dose TMS 4-8 mg/Kg ÷ 2 for 3 days or Erythromycin syrup 200 mg, tab 500 mg, dose 30 mg/Kg/day ÷ 3 X 3 days, or Quinolone group: Ciprofloxacine tab 500 mg, 1 X 2 X 5 days for adults, or amp 200 mg/100 ml for IV infusion.

In addition to isolation & notification of authorities for protective measures.

Chapter VII

DISEASE OF METABOLISM & ENDOCRINE SYSTEM

- Introduction
- Diabetes Mellitus
- Thyroid Diseases
- Adrenal Gland Diseases
- Pituitary Gland Diseases

INTRODUCTION

Like the nervous & the immune systems the endocrine system main function is being a media of intercellular communication for a proper function of the body. This is achieved by organic compounds (hormones). Hormones are directly released into the blood therefore are said to be produced by “ductless glands”. Some hormones are bound to carrier proteins for transport but it is the free form that is physiologically active. These hormones first bind to plasma membrane of the target cells receptors. Then a series of cascade reactions (biochemical reactions that initiate & accelerate themselves ẃ are mediated by cyclic AMP) or by direct enzyme induction on the nucleus should occur before the nucleus of the cells is influenced to send a command for an action. The release of hormones is controlled by feedback of serum level but also the physiologic, morphologic & biochemical effects of hormones could play a role. These hormones are finally inactivated in target tissues é the exception of thyroid & insulin ẃ are degraded in the liver & kidneys as well. The state of endocrine function is evaluated by level of hormone or the metabolic effects of the hormone. With few rare exceptions both high & low levels of hormone result in disease, e.g. High level of thyroid hormone results in hyperthyroidism while a low level of hormone results in hypothyroidism. The endocrine functional assessment is very important in clinical practice but é serious challenge for resource limited nations like ours. Hormone levels are too low making routine laboratory determination difficult & as a result very sensitive assay are needed ẃ are not routinely available due to expense & special expertise needed. The other challenge result from the very nature of pattern of hormone secretion during the day making it necessary to take samples at specific times of the day or doing interventions to suppress or stimulate hormone production when the levels are borderline for decision making.

Homeostasis: feed back control (-ve & +ve) is a fundamental features of endocrine system. Each of the major hypothalamic-pituitary hormone axes is governed by a negative feedback (a process that maintains hormonal levels within normal range).

Hypothalamus: produces releasing hormones that stimulate the pituitary gland:-

- TRH stimulate the production of TSH.
- CRH stimulate the production ACTH.
- GnTH stimulate the production LH/FSH.
- GHRH stimulate the production GH.

The hypothalamus is affected by -ve feedback from the pituitary gland as well as from serum level of different hormones or their metabolic effect. The hypothalamus produces Antidiuretic hormone ẃ participates in control of fluid, electrolyte & Oxytocin ẃ participate in uterine contraction after delivery. These 2 hormones are released from the posterior part of pituitary gland.

Pituitary gland: release trophic hormones, stimulate the peripheral endocrine glands.

- TSH stimulates thyroid gland to produce T3 & T4.
- ACTH stimulates the adrenal cortex to produce cortisol.
- LH/FSH stimulate the ovaries or the testis.
- GH produced by the anterior pituitary & influence body growth.
- Prolactin is also produced by anterior pituitary & influence lactation in females.

Thyroid gland: produce T3 & T4).

Adrenal glands: produce cortisol, mineralocorticoids & androgens.

Ovary/Testes: produce hormones that control sexual activity & reproduction.

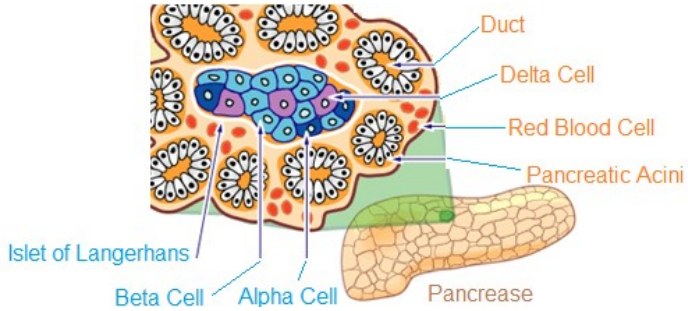
Pancreas: produces insulin & glucagon. ***Stomach:*** produce gastrin.

Liver: produces somatostatin.

Kidneys: produce: renin, angiotensin, erythropoietin & Vit D.

DIABETES MELLITUS

Metabolic disorder characterized by hyperglycemia due to an absolute or relative lack of insulin or due to a cellular resistance to insulin.



Insulin is produced by the β-cells in the islets of Langerhans in the pancreas. Its secretion is stimulated by amino acids & parasympathetic nerves. It is inhibited by glucagon. The Biochemical actions of insulin include:-

- Switching off hepatic glucose production (inhibits gluconeogenesis).
- ⇧ Uptake & utilization of glucose by muscle.
- Inhibits lipolysis.

By doing so insulin prevents ketogenesis, also enhances uptake of A.A. into muscle for protein synthesis & inhibition of breakdown of proteins.

Epidemiology

The number of people suffering DM around the world is about 360 million & expected to ⇧ to 500 million by yr. 2030, of ẃ 97% are type 2 DM. The rates of DM in Egypt has significantly ⇧ exceeding international rates, Egypt is now ranked 8th highest in the world in terms of the disease. The Incidence in Egypt rose to 16.5 million people, 50% of them do not know they suffer from DM.

Impact on health: ▲DM is the 6th leading cause of death due to cardiovascular effects resulting in atherosclerosis, CAD, stroke. ▲Increasing prevalence of type II DM in older adult population (65–74 yrs). ▲D.M. is a leading cause of end stage renal failure. ▲Major cause of blindness ▲Frequent cause of non-traumatic amputation.

Type 1 DM

Formerly known as insulin-dependent DM, or Juvenile-onset DM accounts for 10% of cases of DM. is due to β-cell destruction é absolute deficiency of insulin. The β-cells of pancreas no longer produce insulin, the α cells of pancreas produce excess glucagons causing hyperglycemia. Believed to be due to autoimmune destruction of β-cells. The triggering agent (viral infection) will expose these cryptic (hidden) self-antigens to ẃ the immune system has not developed tolerance. Therefore an autoimmune process is set-up destroying its self-tissue, in this case the β-cells of the islets of Langerhans. The other mechanism of injury is molecular mimicry between trigger antigen (virus) & β-cell antigen, or instance coxsackie virus antigen & that of glutamic acid decarb-oxylase found within the β-cells has similar chemical structure, so that the antibodies produced to fight the foreign antigen of the virus also cross react é antigens of self-tissue bearing glutamic acid decarboxylase hence destroying it. The disease is pro-gressive going through phases of antibody production, then phase of impaired GTT followed by an abnormal FBS & finally culminating in an abnormal fasting blood sugar é Ketonemia. Type 1 characterized by hyperglycemia, breakdown of body fats & pro-tein & development of ketosis. It has also genetic predisposition, it may be idiopathic. Pt require insulin for survival & develop ketoacidosis when is not on adequate insulin RX. Oral hypoglycaemic agents will not be effective to lower the BG level. Usually oc-curs in childhood or early adult hood. Pt is usually thin.

Honeymoon period: in young people who are diagnosed for the first time to have ov-ert DM, the DM may have been ppt by acute metabolic stressful conditions (such as infection or pregnancy), in such circumstances, the ⇧ metabolic demand for insulin, may lead to a relative insulin deficiency & pt become symptomatic & may need exog-enous insulin to control their symptoms é the return to baseline metabolic demands,

when the stressful event abates, the pancreatic reserve may be adequate to maintain normal or near-normal BS level. Such pt. may undergo a period of transient "cure" during ẃ they may not require exogenous insulin to control their BS level. Because of this, such pt is said to be in "***honeymoon***" period. This is unfortunately is transient & the pt will be needing insulin again when progressive destruction of β-cells leads to absolute insulin deficiency.

Diagnosis of type 1 DM: pt is symptomatic plus: ☆RBS is ≥ 200 mg/dl or ☆FBS ≥ 126 mg/dl or ☆ 2 HPPBS ≥ 200 mg/dl during an GTT.

Diabetic Ketoacidosis: was formerly considered as hallmark of type 1 DM. However currently it is known that some type II DM pts who are being treated by oral hypoglycaemic agent may also develop DKA. It is acute metabolic crisis in pt é DM characterized by:-

- Hyperglycaemia (BG 250-600 mg/dl).
- Metabolic acidosis (ketosis).
- Hypotension & features of dehydration.
- Results from breakdown of fat & over production of ketones by the liver & loss of bicarbonate.
- Occurs when Diabetes type 1 is undiagnosed or known diabetic has increased energy needs, when under physical or emotional stress or fails to take insulin.
- Mortality as high as 14%.

Pathogenesis

Any event that ⇩ insulin availability or cause stress that ⇧ the insulin demand, lead to sever insulin deficiency & the effect of counter regulatory hormones such as glucagon, cortisol, epinephrine & GH becomes overwhelming. This biochemical changes cause:- ⇧ glucose production by liver, ⇧ glycogen degradation to glucose, ⇩ glucose

uptake & utilization by muscles, lipolysis (enhanced break down of free fatty acids & subsequent ketogenesis). This ⇧ in blood levels of ketone bodies as acetoacetic acid, β-hydroxybutyric acid & acetone, resulting in metabolic acidosis. The above biochemical processes results in significant hyperglycaemia & DKA.

Precipitating factors: DKA may occur after several days of worsening DM control, or may appear suddenly within few hrs. Some of the precipitating factors are:-

- Intercurrent infection.
- Dehydration.
- Poor compliance é insulin or discontinuation.
- Stressful conditions as tra-uma, surgery or emotional crisis.
- Excessive alcohol intake.

Signs & symptoms: volume depletion: dehydration -dry tongue & buccal mucosa, poor skin turgor & hypotension. Kussmaul respiration (deep, fast breathing resulting from metabolic acidosis). Acetone "fruity" odour of breath: due to acetone. Nausea & vomiting & frequent complaint of abdominal pain. Mental status changes: lethargy & confusion ẃ may evolve into coma é severe DKA. Cerebral oedema is extremely serious complication, seen most frequently in children. Signs of infection, ẃ may be precipitate DKA, should be looked for & a history of DM for comatose pt.

Laboratory diagnosis

1. RBG: usually high (averaging 500 mg/dl, may range from 600-1200 mg/dl).

2. Urine dipstick for ketones: this test is 97% sensitive. Serum ketone level can also be measured to confirm hyperketonemia.

3. ABG analysis: can diagnose metabolic acidosis as indicated by ⇩ serum bicarbonate (usually <10 meq/L) & ⇩ PH to <7.35

4. Additional laboratory evaluation: ●Electrolytes: serum K^+: look for hyper or hypo-

kalaemia. Na^+ tends to ⇩ because of dilution as the osmotic effect of hyperglycaemia ⇧the ECF volume. Serum osmolality is high 〉350mosm (normal 280-300).

- BUN, creatinine.
- Urine culture/sensitivity.
- Blood cultures: should be done to identify any infectious process ẃ may ppt DKA.

Treatment DKA

Acute management: requires immediate attention & hospital admission.

① **Supportive Rx:** airway maintenance, supplemental O_2 as needed & Rx of shock.

② **Fluid replacement:** to correct dehydration caused by glucose induced osmotic diuresis. The fluid deficit in pt é DKA averages 3-5 L, ẃ should promptly replaced. Hence give 5-6 L of fluid in the first 24 hrs. Initially one litre of 0.9 % Na^+Cl^- is given over ½ an hr. Continue é one litre NS every hr. for the first 2-3 hrs. Then ½ NS (0.45% Na^+Cl^-) at slower rate till pt well hydrated. Ensure adequate renal renal perfusion. Hourly monitoring of BG, When the BG level falls to 200-300 mg/dl, change the IVF to 5-10% DW to prevent hypoglycaemia & carefully monitor urine output.

③ **Insulin:** administered to ⇧ glucose use in the tissues, to inhibit ketogenesis & to counter balance the effect of counter regulatory hormones. 20 u of regular insulin, 10 u IV & 10 u IM is given é the initial fluid resuscitation. Then 5-10 u of is given per hour till BG level drops to 250-300 mg/dl. BG determination is done every hr. The expected rate of fall in BG is 75-100 mg/dl/hr. When BG reaches a range of 250-300 mg/dl, 5-10 % glucose sol should be infused to prevent hypoglycaemia. Insulin infusion should not be stopped until Ketonemia clears. It is preferable to give 5 or 10% DW é insulin injection (5u/25 gm glucose), rather than stop the insulin, because insulin is still required to clear the acidosis & ketotic state. Shift to sliding scale when ketone clears. Shift to intermediate insulin when pt's BG &precipitating factor (s) is under complete control.

④**Potassium replacement:** serum K+ level may be ⇧ initially because of K^+ ion movement from ICF to ECF in metabolic acidosis. Later, é Rx, the serum K^+ becomes low because of both renal loss of K^+ & the movement of K^+ ions back to ICF as the acidosis is corrected. Pt é DKA is expected to have a K^+ deficit of 300-400 meq, ẃ should promptly replaced. Start replacing K^+ as soon as pt has adequate urine output. K^+CL^- is infused at a rate of 20-40 meq/hr. Monitor serum K^+ levels hourly & the infusion must be stopped if the K^+ level is >5 meq /l. The monitoring of serum K^+ must continue even after K^+ infusion is stopped in the case of (expected) recurrence of hypokalaemia. Oral K^+ can be given if IV K^+ is not available. Encourage pt to eat K^+ rich fruits (such as banana). Monitor cardiac rhythm since hypokalemia puts client at risk for dysrhythmias.

⑤ **Close follow-up of pt:** monitor BG & K^+ as well as urine output hourly. Maintenance fluids should consist of (½ strength NS) é additives as indicated; 150-200 ml/hr adjusted according to urine output. Evaluate for potential ppt factors including infection, pregnancy, MI, or inappropriate use of insulin. Oral intake resume when pt mental status improves & nausea & vomiting are controlled. Initial diet should consist of fluids & solid diet resume when ketoacidosis is corrected.

Hyperglycaemic coma (hyperosmolar, non-Ketotic)

Usually occurs in elderly type II pt that do not develop ketosis. Often ppt by serious intercurrent illnesses (MI, stroke, pneumonia, sepsis).

Symptoms

Such pt present é several wks history of polyuria, wt. loss & diminished fluid intake that is followed by confusion, lethargy or coma.

Physical examination

Pt have extreme dehydration, hypotension, tachycardia & altered state of consciousness or coma. Dehydration is caused by a hyperglycaemia induced osmotic diuresis,

when not matched by adequate fluid intake.

Laboratory studies: very high BG, may range from 600- 1200 mg/dl.

Management: fluid replacement: administration of IVF & bringing down BG by using rapidly acting insulin preparation, taking all the precautions as mentioned before during rehydration & using insulin. In addition to identification & Rx of any ppt factor.

Type II DM

95% of DM pts are type II. Condition of fasting hyperglycemia occurring despite availability of body's own insulin. Was known as non-insulin dependent DM or adult onset DM. Both are misnomers, it can be found in children & type II DM may require insulin. Type II DM, occurs é intact β-islet cell function but there is peripheral tissue resistance to insulin. There may be some ⇩ in insulin production or hyper-insulin state. Insulin resistance play central role in pathogenesis. In obesity, there is ⇧ production of non-esterified fatty acids, leads to resistant of peripheral organs to insulin ẃ leads to ⇧ gluconeogenesis in the liver & ⇩ peripheral uptake & utilization of glucose by muscles. Initially there is hyper secretion of insulin by β-cells, to overcome the insulin resistance. But later on β-cells fail to respond to the level resistance. Then β-cell number ⇩ & amyloid is deposited in islets. Pt do not require insulin for survival at least in the earlier phase of diagnosis & are not prone to develop ketoacidosis but may develop it under conditions of stress. BG level can corrected by oral hypoglycaemic agents. Usually occurs in people ›40 yrs of age, mostly in obese pt. The pancreas produce also; Glucagon & Somatostatin.

Glucagon: is a peptide hormone, produced by α cells of the pancreas, that raises the conc. of BG. Its effect is opposite that of insulin. The pancreas releases glucagon when the conc. of glucose in the blood stream falls too low. Glucagon causes the liver to convert stored glycogen into glucose, ẃ is released into the blood stream. Thus, gluc-

agon & insulin are part of a feedback system that keeps blood glucose levels at a stable level.

Somatostatin: produced by Delta cells of the pancreas, inhibits the secretion of other pancreatic hormones such as insulin & glucagon. In addition this hormone is produced by the hypothalamus (known as GHIH) act by inhibiting the anterior pit-uitary from secretion of GH, & also inhibit the pituitary secretion of TSH.

Pathophysiology of type II DM

(1) Sufficient insulin production to prevent DKA, but insufficient to lower BG through uptake of glucose by muscle & fat cells.

(2) Cellular resistance to insulin ⇧ by obesity, inactivity, illness, age.

Risk factors for type II DM

- History of diabetes in parents or siblings.
- Obesity (especially of upper body).
- Physical inactivity.
- Race/ethnicity: African, Indian, American, Hispanic origin.
- Women: history of gestational DM or delivered baby BW > 4 kg, polycystic ovary.
- Pts é hypertension; HDL <35 mg/dl &/or triglyceride level >250 mg/dl.

Manifestations of type II DM

1. Pt usually unaware of DM. Discovers DM when seeking health care for another concern. Most cases are not diagnosed for 5-6 yrs after the development of the disease. Usually does not experience wt loss.

2. Possible symptoms or concerns: hyperglycemia, polyuria, polydipsia, blurred vision, fatigue, numbness in extremities & skin Infections.

Diagnosis

Is made incidentally during routine medical check-up. Therefore it is advisable to scre-

en pt for DM, é any of the following risk factors:-

- Obesity (BMI > 25 kg/m^2)
- First-degree relative é DM.
- History of GDM or delivery of a baby é BW > 4 kg.
- Hypertensive pt.
- Hyperlipidaemia: HDL <35 mg/dl or trigl- yceride >250 mg/dl.
- History of impaired FBS or glucose tolerance on prior testing.

Other specific types of DM

A) Genetic defects of β-cell function: MODY 1, MODY 2, MODY 3 etc.

B) Genetic defects in insulin action: type A insulin resistance, Lipodystrophy sy.

C) Diseases of the exocrine pancreas: chronic pancreatitis, pancreatectomy.

D) Endocrinopathies: Cushing sy, Pheochromocytoma, Acromegaly.

E) Drug/Chemical: ß-blockers, oral contraceptives, steroids.

F) Gestational onset DM: first presents during pregnancy. Occurs in 2-10% of pregnancies. 30-60% chance of developing Type II DM.

Investigations of DM

- FBS & 2 HPPBS.
- Glycolated Hb (A1c) for level of glucose in last 6 months.
- Lipid profile.

Criteria for diagnosis of DM

- Symptoms of DM.
- RBG ≥ 200 mg/dL. or
- FBS >126 mg/dl. or
- 2-HPPBS >200 mg/dl after a glucose load of 75 gm.

These criteria should be confirmed by repeat tests on a different day.

RBS defined as blood sample éout regard to time since the last meal.

FBS defined as no caloric intake for the last 8 hrs.

GTT: BG measured after ingestion of 75 gm of anhydrous glucose dissolved in water. Pt is said to have impaired glucose tolerance if the FBS is **>** 110 mg/dl.

Somogyi phenomenon: refers to hyperglycemia 2ry to a period of drug-induced hypoglycaemia é metabolic compensation (⇧ gluconeogenesis & sympathetic out flow). If controlling high glucose becomes a problem (especially morning glucose), consider checking for hypoglycaemia in the time leading up to high readings.

Comparison Type I & Type II

Characteristic	Type 1	Type 2
Age of onset	Childhood	>age 40
Rate of onset	Abrupt	Gradual
Family Hx	⇧ prevalence é +ve F/H type 1	⇧ prevalence é +ve F/H type 2
Islet cell ABs	Yes	No
Body weight	Thin, undernourished	Overweight, obese
Insulin	Insulin Rx is mandatory	Insulin not necessary initially
Symptoms	Wt loss,⇧ thirst,⇧ urination	May be asymptomatic

Management

Target Goals

Glycolated Hb (AIC)	≤ 7%
FBS	70-130 mg/dl
2HPPBS	< 180 mg/dl
Blood pressure	< 130/80
Lipids	LDL < 100 mg/Dl

Criteria for control

- No symptoms.
- Normal growth.
- 2 HPPBS < 200 mg/dl.
- One urine sample/day is negative for sugar.
- Insulin dose reduced to 50% of starting dose.

Non pharmacologic therapy

Diet therapy: pt should be given proper advice about his diet. Maintenance of a normal BMI should be the prime target through recommending calories intake according to age, sex & activity. Alcohol ingestion should be limited. Diet should include 60-65% CHO, 25-35% fat & 10-20% protein. Pts are advised to significantly ⇩ cholesterol intake. Avoid simple sugars (e.g. sugar, soft drinks, honey & other sweets). High fibre diet as vegetables slow the absorption of digested food in the form of simple sugars. Fresh fruit as water melon & lemon can be freely taken as opposed to oranges bananas that must be taken é caution. Dividing meal into 4-6 equal parts may help in achieving stability in some cases.

Exercise: has multiple +ve benefits to diabetic pt including:- ⇩ cardiovascular risk, ⇩ BP, maintain muscle mass, ⇩ body fat & helps in losing wt. Exercise is beneficial for both types of DM (I & II). Regular exercise 20-30 min., aerobic exercise such jogging, walking, swimming etc. 3-4 days/wk is recommended. NB: pts on insulin should be cautious to avoid hypoglycaemia during exercise & certain precautions as as; early recognition of hypoglycaemic symptoms, avoidance of strenuous exercise ,availability of sugary drink or candy in case of feeling hypoglycaemic.

Weight reduction: maintain normal BMI of 20-25. Wt loss ⇧ sensitivity to insulin & may lead to ⇩ the demand of exogenous insulin or oral hypoglycaemic agents.

Education: involving pts in their own Rx plan is essential. Pt can be involved in his care through regular health education to achieve the ideal knowledge, attitude ẃ is crucial to proper management of DM. The areas of pt education include; Pt should understand that DM needs life-long Rx & follow up. Goal of Rx should be set together é the pt. To avoid excess alcohol intake & smoking. The benefit of wt reduction, diet & regular exercise. Proper foot care. Hypoglycaemia causes & symptoms & the simple first aid measures to be taken ē feeling such symptoms. The complications of DM. Insulin injection technique & self glucose monitoring. All must be clarified to pt.

Pharmacologic therapy

Insulin: beef, pork & recombinant human insulin are available. Humulin is generally preferable & tends to be less immunogenic than beef or pork insulin & therefore there is less insulin resistance secondary to anti-insulin antibodies.

Type 1 DM: pt must be started on insulin at time of diagnosis, the average daily insulin requirement is approximately 0.3 u/Kg/day for such pt.

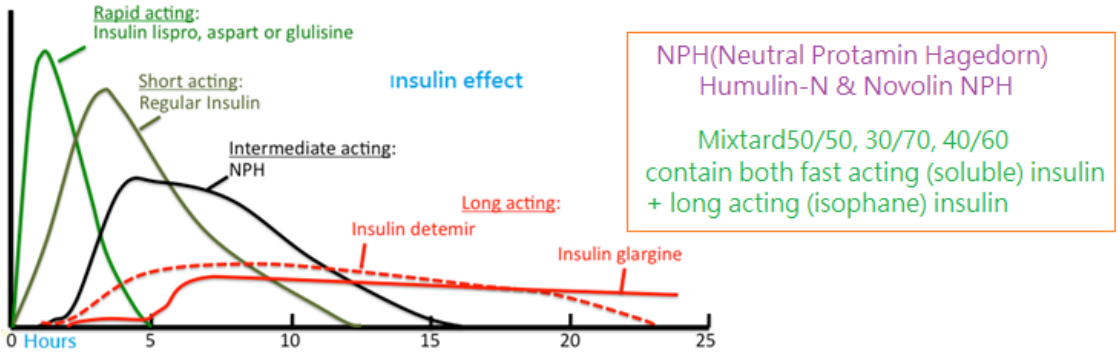
Insulin side effects: the most serious complication of insulin is hypoglycaemia. Hypersensitivity, atrophy or hypertrophy of injection sites may also occur.

Diabetic pt presenting é Ketoacidosis

Glucose control initially obtained é sliding scale using regular insulin. Measure BG /6 hrs & give SC regular insulin depending on the RBS measurement. Once glucose stabilized é regular insulin 6 hourly injections, 2/3 of the last 24 hrs insulin requirement is given, in the form of intermediate acting insulin, as SC injection/day. If the total daily requirement of insulin is ›40 u, 2/3 of the total insulin requirement is given as morning dose & 1/3 as evening dose. If the intermediate acting agent does not give adequate control of daytime BG, a short acting agent may added according to the pt dietary habits, to the morning or evening intermediate dose.

Insulin preparations

Preparation	Onset	Peak & Duration	Use & Rout
Short acting (Crystalline/Regular)	30-60 min	P: 1-4 hrs D: 4-6 hrs	ketoacidosis, rapid control of high sugar & acidosis. IV, IM, SC
Intermediate-acting (NPH or Lente)	1-3 Hrs	P: 6-12 hrs D: 18-26 hrs	Long term control of sugar, given twice/ day. SC.
Long-acting (Ultralente PZI,NPH)	4-8 Hrs	P: 14-24 hrs D: 28-36 hrs	Long term control of sugar given once/ day . SC.



Other option of Rx for pt before acute complications: start é 20-25 u of intermediate insulin (equivalent to daily insulin production by islets of Langerhans) S.C, daily. Gradually ⇧ the dose by 3-5 u every 4-5 days till acceptable level of BG is achieved.

Insulin pump: administers continuous SC insulin infusion é meal time boluses.

Multiple daily insulin injection é frequent BS determinations.

long-acting insulin (as Ultra-lente) to provide a base of insulin delivery augmented by regular insulin at meal times. This type of Rx approach needs lot of commitment from the pt & physician. It helps to achieve near normal BG level & thus delays the development of chronic complications.

Hospitalized diabetic pt for something else or post-operative or diabetic pt in ICU

- If blood sugar before meal = 225-275 ⇨ give 5 U crystalline insulin.
- If blood sugar before meal = 275-325 ⇨ give 10 U.
- If blood sugar before meal = 325-375 ⇨ give 15 U.

Oral hypoglycaemic agents

These groups of drugs widely used in type II pts whose hyperglycaemia has failed to be controlled é conservative measures (diet, exercise, wt reduction).

Sulfonylureas: stimulate pancreatic ß cells to secrete insulin.

Sulfonylureas	Dose (mg)	Duration (hr)
First Generation		
Tolbutamide (Orinase)	1000-1500	6-8
Chloropropamide (Diabinese)	250-375	24-60
Tolazamide (Tolinase)	250-375	12-24
Second Generation		
Glipizide (Glucotrol)	5-20	10-24
Glyburide (Micronase)	2.5-20	16-24
Third Generation		
Glimepiride (Amaryl)	1-2	24

Glyburide is more likely to result in glycaemic control when used once a day than is Glipizide. It should used in a twice-daily dosing if 20 mg/day is required (maximum daily dose). N.B. the effectiveness of sulfonylureas declines up to 10% annually as the failure of ß cell function progresses.

Metformin: reduces BS levels by improving hepatic & peripheral tissue sensitivity to insulin éout affecting the secretion of insulin. Metformin (Cidophage, Glucophage tab 500, 850 & 1000 mg) used as monotherapy or in combination é Sulfonylureas or Insulin for type II DM. It is especially useful in overweight pt because it does not cause wt gain, appears to improve plasma lipid & fibrinolytic profiles associated é type II DM, also hypoglycaemia is not a problem é Metformin. The Initial dose 500 mg daily until initial nausea & anorexia are tolerated & then ⇧ to 500 mg BID. Dose can ⇧ by 500 mg weekly to maximum of 2500 mg if reasonable glycaemic control couldn't be achieved. Using Metformine é or after food may lessen the GI side effects (nausea & anorexia). Lactic acidosis is rare side effect of Metformin & the risk is minimized if Metformin is avoided in pt é renal disease, or CHF.

α-glycosidase inhibitors: ***Acarbose & Miglitol***: are oral agents that ⇩ the absorption of CHO, thus reduce postprandial hyperglycaemia. Can be used as monotherapy or in-combination é insulin or sulfonylureas. Start é Acarbose 25 mg é evening meal, may be ⇧ to maximum of 50-100 mg gradually in wks. In general, this group is less effective than other classes. Only effective in mild hyperglycemia, contraindicated in case of kidney disease or ulcerative colitis.

Thazolidinediones: ⇩ insulin resistance & ⇧ peripheral glucose utilization. ***Pioglitazone***: 15-45mg/day as single daily dose. Side effects; ⇧ of LDL, ⇧ B.Wt., Oedema.

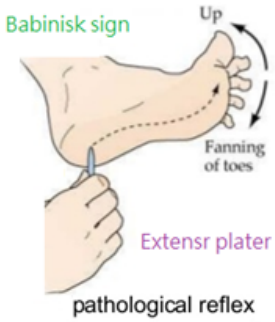
Use of Insulin in type 2 DM: Insulin usually added to an oral agent when glycaemic control is suboptimal at maximal doses of oral medications. An intermediate acting agent is used starting é low dose &⇧ as needed for glycaemic control (such as 5-10 u of NPH ⇧ as needed). Adding Intermediate-acting insulin (NPH or Lente) at bedtime is generally more efficacious than using it during the day. If using only insulin, start é morning injection & dose can be ⇧ by 5 units every 3-7 days until adequate control achieved. If early morning hyperglycaemia is a problem, intermediate acting insulin can be given twice daily as a split dose.

Follow up: since this is life-long disease, regular follow up is crucial. Points to give emphasis include; symptoms of hyper or hypoglycaemia, body wt, BP, visual acuity, oral cavity examination, examination of the feet, examination of the injection site, blood or urine sugar & urine for microalbumin or protein.

Acute Complications

Hypoglycemia

Feeling shaky and irritable
Sweating
Tingling lips
Feeling weak
Hunger
Nausea (feeling sick)



Hypoglycaemia In diabetic pt is caused by:-

- Overdose of insulin or hypoglycemic agents.
- Missing of meal or.
- Strenuous exercise.

Clinical manifestations

Early: one may feel the effects of sympathetic stimulation as cold sweat, irritability, abnormal behavior, hypertension, palpitation, ⇧ pulse volume, tremor, pupillary dilatation, exaggerated reflexes, +ve Babiniski (extensor planter) & hunger.

Later: if early symptoms are neglected then symptoms of the effect of hypoglycaemia on the brain (neurogenic manifestations) as disoriented, confused, dizziness, blurring, headache, nightmares & coma may occur.

Management

Hypoglycaemia is more dangerous than hyperglycaemia because it may cause irreversible brain damage. Any pt é DM losing consciousness should always be considered hypoglycaemic until proven otherwise by BS determination & should be managed by rapid IV administration of glucose or PO or NG tube administration of any concentrated sugar solution if he can swallow. Prolonged unconsciousness requires continuous 10% IV glucose.

Chronic Complications

Affect many organs & are responsible for majority of morbidity & mortality. Prevention of such complications is one of the major goals of care of diabetic pt. This is attempted by achieving as near normal BG level as possible. Several studies shown that é tight BG control, the occurrence of chronic complications can delayed several yrs.

1. Retinopathy: is one of the commonest chronic complications & one of the leading causes of blindness in developed countries. Symptoms may include difficulty of read

ing, blurring, shadowing ẃ may later on progress to total blindness.

Classification

a) Background retinopathy: early changes, often asymptomatic. Microaneurysm: occlusion of capillaries gives rise to distension & eventual rupture of vessels. Dot Hge: ⇧ permeability of capillaries & ruptured aneurysms. Hard exudates: proteins & lipids leak from capillaries.

b) Maculopathy: manifests é impairment of central vision & visual loss.

c) Proliferative retinopathy: asymptomatic unless complicated by Hge, new vessels formation ẃ is stimulated by ischemia.

d) Advanced diabetic disease: visual loss to the extent of complete blindness. Extensive fibrovascular proliferation develops following ischemia & necrosis. Retinal detachment created by extensive fibrosis.

Management

•Laser therapy. •ASA 100 mg/day may prevent further occlusion of small capillaries.

•Surgery: viterotomy removes clots & fibrosis that obstruct vision.

2. Neuropathy

Symptoms: Burning sensation, numbness, constipation or nocturnal diarrhoea, impotence & foot ulcer.

Classification

a) Polyneuropathy; the commonest neuropathy, characterized by distal symmetrical, manifests é tingling sensation, numbness & burning sensation. It is often progressive & may lead to total loss of sensation & absence of deep tendon reflexes.

b) Radiculopathy: neurogenic pain, is often self-limiting.

c) Amyotropy: atrophy of proximal muscles mainly hip girdle.

d) Autonomic neuropathy: may manifest é: -Postural hypotension -GIT: gustatory

sweating, gastroparesis & nocturnal diarrhoea. -Genitourinary: neuropathic bladder, erectile dysfunction.

e) Mon neuropathy: paralysis of a specific nerve or nerves e.g. diplopia, squint due to 3rd & 6th cranial nerves palsies.

Management: Symptomatic control of pain, diarrhoea, impotence.

3. Nephropathy

Is a common complication in DM. Start é the appearance of microalbumin in urine.

Clinical features: periorbital, pedal oedema & anasarca. Anaemia, uraemia & osteo-dystrophy in pts é end stage RF.

Laboratory: progression from micro to ⇨ macro albuminuria.

Management: tight BP control. ACEIs: ⇩ progression of renal diseases. Renal trans-plantation or dialysis in end stage RF.

4. Diabetic foot ulcer

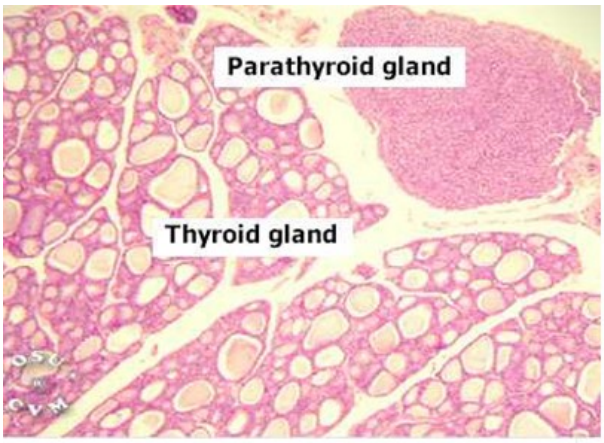
The following are underlying mechanism for diabetic foot ulcers:-

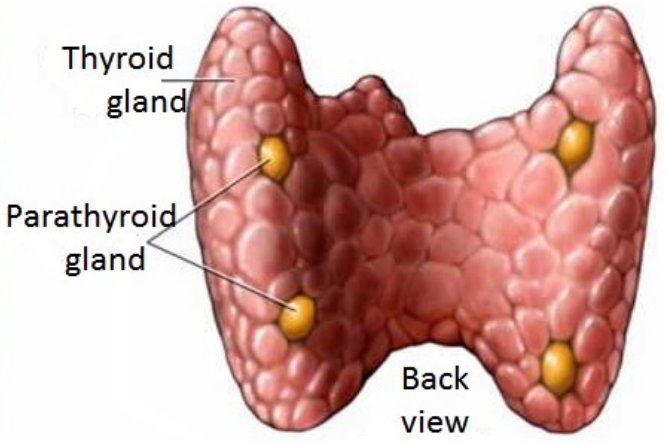
- Neuropathy: loss of pain sensation exposes to injury.
- Loss of sweating results dry skin that is susceptible to injury.
- Vascular: poor blood supply to the foot causes ⇩ healing of wound & poor recovery from 2ry infections.
- Abnormal pressure loading: due to neuropathy (Charcot's joints) or anatomical de-formity of the feet. Since foot is not in a normal anatomic position it is exposed to ab-normal load & pressure sores.

Symptoms & signs: numbness & burning, aching pain, swelling, darkening, abscess & cold extremity.

Foot care: advice the pt to put foot on comfortable shoes, to check for pebbles in shoe, to examine the foot daily, wash, dry & oil the feet, & to stop smoking.

THYROID DISORDER





Thyroid gland normally weighs 20gm & is visible in thin women. The basic unit of thyroid structure is a follicle which is spherical in shape, filled é colloid & encompassed by single epithelial cell layer. The colloid consists of thyroglobulins in ẃ thyroid hormones are stored. About 40 follicles form a lobule & group of lobules form a gland. The hormones produced by the thyroid gland are referred to as triiodothyronine & thyroxin. Thyroid disorders manifest é qualitative or quantitative alteration of thyroid hormone secretion, enlargement of thyroid, or both. Diminished production of these hormones leads to hypothyroidism, ẃ results in state of ⇩ metabolic activity. ⇧ production on the other hand leads to hyperthyroidism, ẃ in turn results in a state of ⇧ metabolic activity. Enlargement of thyroid- Goitre- is diffuse or focal enlargement of thyroid gland that may be metabolically hyperactive, hypoactive, or normoactive.

Transport & metabolism of thyroid hormones: of the total thyroid hormones in the blood, 80% is found in the form of T4 & 20% in the form of T3.. 99% of hormones is bound to carrier proteins (thyroglobulin) & is not physiologically active & it is only the remaining 1% ẃ is found free in the serum, ẃ is physiologically active. The advantages of carrier proteins are:- •They are reservoir to replenish free hormone level.

•They buffer any fluctuation in gland secretion.

•They protect against hepatic degradation & its renal excretion.

Regulation of hormone production

Hypothalamic TRH stimulates pituitary production of TSH, ẃ in turn stimulates thyroid hormone synthesis & secretion. The presence of adequate thyroid hormone sends a negative feedback signal that inhibit TRH & TSH production. When the level of thyroid hormone in blood ⇩ the production & release of TRH &TSH is enhanced. The TSH, secreted by thyrotrope cells of the anterior pituitary, plays a pivotal role in control of pituitary-thyroid axis & serves as the most useful physiologic marker of thyroid hormone function.

Thyroid function tests

Serum T3 & T4 level: measures the total bound (99%) & free (1%) hormone level. This gives some clue about serum level of thyroid hormone, but has limitation since serum level of the hormone is influenced by conditions affecting the level of carrier proteins. T3 & T4 levels ⇧ in hyperthyroidism & ⇩ in hypothyroidism.

Serum TSH level: is the most important test to asses thyroid function. In hypothyroidism the TSH level ⇧, as a result of feedback effects of low thyroid hormone level. It is a very sensitive test & because it usually becomes elevated even before thyroid hormones decline below normal. In hyperthyroidism the TSH level ⇩ because of the elevated thyroid hormones conc., leads to suppression of TSH release through a -ve feedback mechanism. It is very sensitive, because TSH may be suppressed even when thyroid hormone level are not elevated above normal range.

Radioactive iodine uptake: 24 hrs after administration of Iodine (I^{131}) isotope, assesses the rate of iodine uptake by thyroid gland ẃ demonstrates the degree of glandular activity. ⇧ uptake in hyperthyroidism & ⇩ uptake in hypothyroidism. The test is especially useful in diagnosing ectopic hormone production.

Thyroid antibodies: against T3 &T4 is evidence for autoimmune disease of thyroid.

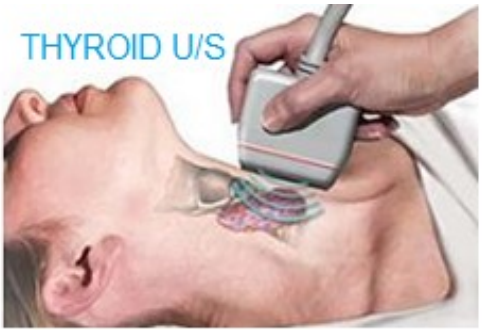
SICK EUTHYROID SYNDROME

State in ẃ serum level of thyroid hormones is abnormally low or high but pts are not symptomatic. Such clinical condition often results from severe illness, physical trauma, or stress during ẃ the thyroid hormone level may be low. In elderly pt taking drugs containing iodine, serum level of thyroid hormones may be abnormally high. Pt remains asymptomatic probably due to ⇩ impact on peripheral tissue.

HYPERTHYROIDISM

Hypermetabloic state, resulting from excessive thyroid hormone function. Thyrotoxicosis defined as state of thyroid hormone excess.

Examination of thyroid



Aetiology

Graves' Disease: is the most common cause of hyperthyroidism in the 3rd& 4th decades of life. Common in women. Is autoimmune disease caused by abnormal thyroid stimulating immunoglobulin of IgG class ẃ has long acting thyroid gland stimulating effect. Causes diffuse symmetrically enlarged thyroid gland é normal to slightly soft consistency. Associated é ophthalmopathy & dermatopathy.

Toxic Multinodular Goitre: usually develops insidiously in pt who has had a nontoxic nodular goitre for yrs. Thyroid gland is irregular, asymmetric & nodular in nature. This clinical condition may occur when a nontoxic multi nodular goitre has been exposed to excess iodine intake or when one of the nodules become autonomous (fails to fall under control of TSH -T3, T4) feedback axis.

Solitary Hyper functioning Adenomas: the thyroid gland contains a smooth, well-defined, soft-firm nodule that shows intense radioactive iodine uptake on scan é absence of uptake in the rest of the gland. Most pts é solitary adenomas do not become thyrotoxic. When they do, they are usually less toxic than Graves' disease.

Autoimmune or Hashimoto's Thyroiditis: normal size or enlarged non tender thyroid gland. Thyroid antibodies, when present, are high in titre. Improves spontaneously but frequently recurs.

Excess Exogenous Thyroid Hormone Administration: may occur because of dosage errors or occasionally in individuals taking large doses of thyroid hormones to lose weight or to ⇧ their energy. The thyroid gland is normal or small in size.

Subacute & Viral Thyroiditis: tender, diffusely enlarged thyroid gland é normal or ⇧ T4 & ⇧ ESR. Probably of viral origin & may manifest as a sore throat.

Rare Causes: radiation thyroiditis, thyroid carcinoma, excessive TSH stimulation, excessive iodine intake, struma ovarii.

Clinical features

- ***Metabolic changes:*** ⇧ BMR, wt loss é ⇧appetite, heat intolerance & sweating.
- ***Cardiovascular effects:*** weakness, dyspnoea on exertion, sinus tachycardia, AF in the elderly. Systolic hypertension, high output failure é wide pulse pressure.
- ***Gastro Intestinal Symptoms:*** lose stool or diarrhoea (may be the 1st sign).
- ***Skin & Hair Changes:*** warm & moist skin because of peripheral vasodilatation & fine silky hair is characteristic finding.
- ***CNS & Neuromuscular effects:*** nervousness, hyperactivity, dysphoria, emotional liability, poor concentration, fine tremors, muscle weakness, fatigue.
- ***Genitourinary Manifestations:*** polyuria, dysmenorrhea, oligo/ or amenorrhea.
- ***Ophthalmopathy:*** wide stare and lid lag: slow closing of the upper lid when the eye

moves downward, revealing sclera between the lid &cornea may occur in any form of hyperthyroidism. Exophthalmos: true thyroid exophthalmos is seen only in Graves' diseases, occurring in approximately 50% of cases. The eyes are pushed forward because of mucinous & cellular infiltration of extra ocular muscles. There is inflammation of conjunctiva & surrounding tissue. The pt may complain tearing, eye irritation, pain & double vision.

- ***Other Findings:*** Goitre. Gynecomastia.
- ***Features Specific to Grave`s Disease:*** thyroid gland is diffusely enlarged, smooth in consistency, bruit/thrill may be heard over it. Ophthalmopathy: exophthalmos. Thyroid acropathy: clubbing.

Diagnosis

- TSH is ⇧ in 98% of pts. It is the best screening test.
- Serum T3 & T4 level (free & total) may ⇧.
- Thyroid antibodies: antimicrosomal, antifollicular cell, antithyroglobulin ABs, thyroid-stimulating ABs, elevated especially in autoimmune thyroiditis.

Treatment

Graves' disease

***(*1) Anti-Thyroid Drugs:** inhibit the oxidation of iodine & coupling of iodotyrosines, thus ⇩ the synthesis of thyroid hormone. Propylthiouracil in addition ⇩ the conversion of T4 ⇨ T3 in peripheral tissues, dose 100-150 mg every 8 hrs or Methimazole: 15-60mg divided every 12hrs depending on severity. Although blockade of hormones synthesis is rapid, clinical improvement occurs after few wks or months, because a large pool of stored hormone continues to be released from thyroid. Pt becomes euthyroid 2-3 months after beginning of Rx. Propylthiouracil may achieve results faster because it prevents the peripheral conversion of T4 ⇨ active T3. After clinical improv-

ement, the dose of medication is tapered to the lowest dose to maintain euthyroid state & drug continued for 1½ yrs. The free T4 level should be checked after 1 month of Rx & then every 2-3 months. Advantages of Antithyroid drugs include; avoidance of hospitalization, surgery & anaesthesia. The occurrence of post Rx hypothyroidism is less likely. Disadvantages includes; permanent remission occurs in ⟨50% of pts. The Rx success depends on pt compliance to Rx. Side effects of anti-thyroid drugs includes; skin rash or joint pain & agranulocytosis.

(2) Radioactive Iodine: Iodine^{131}, 5-15 mCi, a single dose causes a ⇩ in function & size of the thyroid gland in 6-12 wks. Approximately 75% of pts é graves' disease are made euthyroid by single dose. Those who are still thyrotoxic after 12 wks are given a 2nd dose & additional dose can be given if needed. Eventually, almost all pts are cured in this way. ^{131}I Rx may be preceded & followed by antithyroid drug. Advantages: hospitalization, surgery & anaesthesia are avoided. The rate of cure is almost 100%. Little pt compliance is required. Disadvantages: there is risk of Rx induced hypothyroidism. Pregnancy is absolute contraindication to use it.

(3) Inorganic Iodine: rapidly controls hyperthyroidism by inhibiting hormone synthesis & release from the gland. One drop of saturated potassium iodide solution in juice is taken daily. Should not be used as a sole form of Rx. May be used alone for 7-10 days before surgery to ⇩ the vascularity of the thyroid gland.

(4) Surgery: subtotal thyroidectomy usually reserved for those unable to take antithyroid medications. Operation on thyrotoxic pt produces the risk of thyroid storm; therefore, Rx should be initiated é antithyroid drugs, long enough in advance for pt to return to a euthyroid state before surgery. Inorganic iodine may be given to ⇩ vascularisation of the gland.

Advantages of sugery: cure of hyperthyroidism is rapid. Success rate is high & most

pts are cured. Pt compliance required for shorter period.

Disadvantages of surgery: pt must hospitalized, surgical & anaesthetic risks are in-curred, surgical complications (hypothyroidism, recurrent laryngeal nerve palsy).

(5) ***Other Symptomatic Treatments:*** Propranolol: 80-200 mg/day in divided doses every 6 hourly, will reduce symptoms of tachycardia, palpitations, heat intolerance & nervousness but will not normalize metabolic rate & should not be used alone except in the case of transient hyperthyroidism secondary to autoimmune (viral) thyroiditis. Ophthalmopathy: smoking can worsen ophthalmopathy, also may be worsen (usually transiently) é radioactive iodine, this can be prevented by using Prednisone 0.5 mg/kg PO for 3 months starting 2-3 days after radioactive iodine. However this carries the risk of prednisone exposure. Symptomatic Rx includes; artificial tears or methylcellu-lose drops for the discomfort, patching or prisms for diplopia, diuretics & raising the head of the bed for the circumorbital oedema.

Treatment of other causes of hyperthyroidism

Toxic multi-nodular goitre: treated é surgery or I^{-131}.

Solitary hyper functioning adenomas: treated é I^{131} or surgery.

Autoimmune thyroiditis: is transient & does not require definitive Rx except in th-ose pts é recurrent hyperthyroidism. Propranolol may be used alone if symptoms are mild. Antithyroid drugs may be needed for a short time in some pts.

Subacute thyroiditis &viral thyroiditis: generally self-limited, treated é aspirin 650 mg QID & in severe cases, prednisone may be used at 40 mg PO/day, tapering to 10 mg/day over 2 wks, then continued for 1 month after pt becomes asymptomatic. Resolution usually occurs in 1-6 month & relapse is common.

THYROID STORM

A severe life-threatening form of hyperthyroidism. ⇧ stress associated é trauma or illness may cause this in a previously mildly hyperthyroid pt.

Signs & symptoms

Consistent é thyrotoxicosis; tachycardia, heat intolerance, Wt loss, fever, confusion, agitation, weakness, dyspnoea, diarrhoea & shock.

Treatment

When suspected, Rx should be instituted immediately.

Supportive Rx

•Control fever**:** Acetaminophen & cooling blanket. If fever is not controlled within hrs, concurrent infection should be suspected.

•Propranolol 20-40mg QID to control tachycardia, tremor.

•Fluid & electrolytes should be replaced.

Antithyroid Rx

•Propylthiouracil 250 mg PO QID (or Methimazole 20-40 mg PO or NG Q 6-8 hrs). Alternative is 0.5 gm of Na iodide in 1 litre of normal saline over 12 hrs.

•Give steroids equivalent to 300 mg of hydrocortisone/day (100 mg IV TID Q 8 hrs). Dexamethasone has some theoretical advantage because it prevents conversion of T4 ⇨ T3 peripherally.

Avoid aspirin because it may ⇧circulating active T3 & T4.

HYPOTHYROIDISM

Primary: refers to thyroid hormone deficiency as a result of thyroid gland disease.

Secondary: refers to TSH deficiency (pituitary).

Tertiary: refers to TRH deficiency, is commoner in females > 45 yrs.

Aetiology

Without thyroid enlargement: frequently develops following Rx of Graves' disease é

I^{131} or thyroidectomy. Idiopathic atrophy of thyroid gland is one of the commonest causes of hypothyroidism. May result from developmental defects or TSH or TRH deficiencies ẃ are less common.

With thyroid enlargement: chronic or Hashimoto's thyroiditis is one of the most common causes. Drugs, iodine deficiency & inherited defects in thyroid hormone synthesis are rare causes.

Thyroid State	TSH	Free T4
Normal	0.4 to 4.0 mIU/L	0.8 to 2.7 ng/dL
Primary hypothyroidism	>4.0 mIU/L	Decreased
Subclinical hypothyroidism	>5.0 to 10.0 mIU/L	Normal

Signs & Symptoms

Fatigue, weakness, lethargy, exhaustion, slow movement, cold intolerance. Slight or moderate Wt gain, but appetite tends to be diminished. Cold calmly dry skin. Brittle nails. Slow monotonous voice. Bradycardia. Carpal tunnel sy, oedema of the face & extremities. Hearing loss, hoarseness of voice. Hair loss, sparse eyebrows é loss of the lateral half. Pericardial effusion & ascites occasionally occur. Constipation. Menorrhagia. Memory impairment. Psychosis may develop é long standing cases & may be ppt by thyroid hormone replacement.

Physical examination

Thickened, puffy features is due to accumulation of mucinous mucoplysaccharide rich material in tissues. known as myxoedema. Yellowish dry skin. Non-pitting oedema. Hypothermia. Bradycardia. Delay in return phase of Achilles & other deep tendon reflexes is a specific finding. Loss of the lateral portion of the eyebrows (madarosis). Effect of hypothyroidism on organ systems as follow:-

CVS system: ⇩ COP, pericardial effusion. **Respiratory system:** hypoventilation, pleural effusion. **GIT:** constipation. **CNS:** ⇩ mental function, psychosis, depression. **Blood:** normocytic normochromic anaemia.

Management

Slow initiation: pts é severe hypothyroidism, older pt & pt é CVS disease, may have an ⇧ sensitivity to thyroid hormone & are at risk of acute CVS & other complications, if hypothyroidism is corrected too quickly. Therefore, these pts should be given very small dose of thyroid hormone, initially (25 *µg* L-thyroxin) ẃ is gradually ⇧ (every 2-4 wks) to a full maintenance dose during 6-12 wks.

Rapid initiation: younger pt & pt é less sever hypothyroidism, may be started on slightly higher dose (50µg L-thyroxin) & advanced to a full replacement dose more quickly (e.g. dose may be ⇧ to 100 µg two wks & 125 -150 µg in another 2 wks*).*

Check the TSH 2-3 months after changing the L-thyroxin dose (Eltroxin 50,100µg).

Maintenance therapy: most pts require 75-100*µg* of L-thyroxin daily. When symptoms of hypothyroidism have resolved, the dosage should be further adjusted so that serum TSH & thyroid hormones are maintained within the normal ranges. ***Cautions:*** elective surgery should avoided in hypothyroid pt because respiratory depression commonly occurs, in addition to ⇧ sensitivity to narcotics & hypnotics is also common in the hypothyroid pt.

MYXOEDEMA COMA

Severe chronic hypothyroidism ẃ is left untreated. Its life threatening clinical condition. May occur gradually (over yrs) or more acutely in response to a ppt factor as exposure to cold, infection, hypoglycaemia, respiratory depressants, or allergy.

Clinical picture

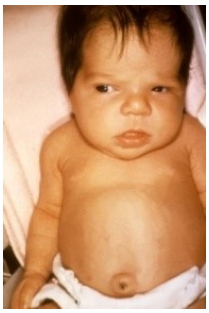
- Hypothermia.
- Hypoglycaemia.
- Shock.
- Hypoventilation.
- Paralytic ileus.
- Severely impaired conscious Level. The mortality rate is 50%.

Treatment: must be start rapidly, despite the risk associated é sudden hormone replacement. L-thyroxin 500 µg is given as IV bolus injection, followed by oral L-thyroxin

100 µg QID. Ancillary Rx include; temporary use of glucocorticosteriods, respiratory support, hypothermia & heat loss should be avoided.

CONGENITAL HYPOTHYROIDISM

Severe hypothyroidism beginning in infancy. Incidence 1/3000 live births. Many countries do screening program for congenital hypothyroidism on 7^{th}-10^{th} day of life, if TSH is high, confirmatory test by T_3,T_4 to be done.



Clinical picture: neonate usually present é unconjugated hyperbilirubinemia, but it may be conjugated & associated é NN hepatitis sy. Baby presented é prolonged jaundice, lethargic, inactive, reluctant to feed, constipation (baby physically & mentally constipated), big tongue, cold skin. Infants may have: hypotonia, umbilical hernia, delayed milestones, short limbs & large head, é a broad flat nose, widely set eyes & large tongue characterize this form of dwarfism. Other signs & symptoms typical of adult pt may be seen. Mental retardation may result if hypothyroidism goes untreated in the first few yrs of life.

Diagnostic workup

Thyroid function tests: ⇧ Ser. level of TSH is the earliest & most sensitive indicator of primary hypothyroidism. ⇩ TSH value indicates 2ry (pituitary) or tertiary (hypothalamic) hypothyroidism & both are rare causes. ⇩ Serum T3 & T4 level.

Delayed bone age.

Other laboratory tests; ⇧ AST, ⇧ CPK & ⇧ cholesterol, ⇧triglycerides, ⇩ Na & ⇩BS. Mild normocytic normochromic anaemia. ⇧ Prolactin levels secondary to ⇧ TRH levels. ECG: flat or inverted T waves é minor ST- segment depression & low amplitude.

Treatment

Thyroid hormone replacement: L-Thyroxin 'Eltroxin' 50, 100 mg tab, 4 ug/Kg/day, it is a synthetic agent & is the treatment of choice. The goal of treatment is to normalize TSH. For neonate, the calculated dose to be dissolved in water,given é feed.

THYROID ENLARGEMENT

GOITRE

Goitre is a simple enlargement of the thyroid gland. Commoner in females, highest incidence in the 2^{nd} - 6^{th} decades of life. Diffusely enlarged goitre is caused by; Iodine deficiency or excess, congenital defects in thyroid hormone synthesis, or é drugs (e.g. Lithium Carbonate) & dietary causes as cabbage, soybean, cassava etc. Most cases are asymptomatic. It is unusual to have pain & rare to have hoarseness or tracheal obstruction. Thyroid function tests should performed to all pts because it can be associated é hypo/hyper/or euthyroid.

MULTINODULAR GOITRE

Aetiology: most often caused by iodine deficiency.

Symptoms

Thyromegaly, occasionally é rapid enlargement & tenderness, secondary to Hge into a cyst. Rarely, tracheal compression occur, causing coughing or choking. Pt may complain of feeling a lump in the throat.

Physical examination: many nodules of varying sizes usually palpable, occasionally may be difficult to distinguish from the typically lobulated, Hashimoto's gland.

Diagnosis

Thyroid function tests: performed to R/O hypo or hyperthyroidism. The malignant transformation is rare, but should be considered if the gland is enlarging rapidly or hoarseness of voice develops.

Treatment

The main indications for Rx are compression of the trachea or oesophagus & venous outflow obstruction. Rx include:-

For Nontoxic multi-nodular goitre:- •surgery •Radioactive iodine •L-Thyroxin cause ⇩ TSH level & help to ⇩ the size of the goitre. Such Rx should not be given to pt é angina or other known heart disease unless the pt is hypothyroid & if the thyroid enlargement persists despite adequate TSH suppression, needle biopsy or subtotal thyroidectomy should considered.

For Toxic multi-nodular goitre;- options are:- •Antithyroid agent •Surgery •Radioactive iodine •Recently percutaneous injection of ethanol into toxic nodule.

SOLITARY THYROID NODULE

They are usually benign. One should suspect malignancy in case of:-

✶Pt é history of radiation exposure, or

✶Rapid enlargement of the nodule, or

✶Development of hoarseness or obstruction, or

✶Detection of a solid nodule that is cold on scan.

Diagnosis: history & radioiodine thyroid scan should be done on every pt é a solitary nodule. Hot nodules that take up the radioisotope are generally benign but fine needle aspiration of a solitary nodule is prudent.

Treatment

Indicated é signs of compression of trachea or oesophagus, or é the recurrence of a cystic nodule after aspiration. Rx is similar to that for multi-nodular goitre.

SUBACUTE or GRANULOMATOUS THYROIDITIS

Aetiology

Generally considered as viral. Mumps, coxackie virus are suspected as causes.

Clinical features

Early symptoms: prodromal phase of malaise, upper respiratory symptoms & fever that lasts 1-2 wks, then the thyroid gland becomes enlarged, firm & tender é pain radiating to ears, neck, or arms.

Hyperthyroidism: may occur due to thyroid hormone leaking from damaged follicles into circulation. The Thyroid pain & hyperthyroidism subside in few wks to months & the gland usually return to normal size. If enlargement persists, chronic thyroiditis should be suspected.

Diagnosis

Acutely swollen, tender & painful thyroid gland associated é symptoms of hyperthyroidism. ***Radioactive uptake:*** low radioactive iodine uptake in the face of high serum T3 &T4 level. This is because the follicles are damaged &unable to trap iodine.

Management

Is symptomatic, because the diseases are self-limited. ASA, NSAID & Steroids (in severe cases) to relive pain & tenderness. β-blockers can be used to relive symptoms of hyperthyroidism.

HASHIMOTO THYROIDITIS

Aetiology

It is an autoimmune disorder that mainly affects women. Antithyroid antibodies are present in most pts.

Clinical features

Thyroid gland enlargement is the main clinical manifestation, is the result of autoimmune damage that leads to lymphocytic infiltration, fibrosis & weakens ability of the thyroid to produce hormone. Pain & tenderness of the gland in sub-acute thyroiditis. Hypothyroidism is present in approximately 20% of pts.

Diagnosis

Suspected in any pt é firm, nontoxic goitre.

Serology: high titre of anti-thyroglobulin/antimicrosomal antibodies.

Thyroid function tests: often normal unless pt has hypothyroidism.

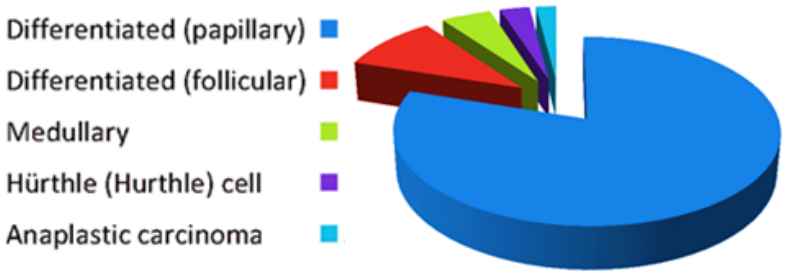
Therapy

L-thyroxin often ⇩ the size of goitre, useful even in pts é normal thyroid function.

Comparison of Hyper & Hypothyroidism

Hyperthyroidism	Hypothyroidism
Weight Loss	Weight Gain
Rapid Heart Beats	Exhaustion
Oily Skin	Dry Skin
Rapid Nail Growth	Brittle Nails
Infrequent Periods	Heavy Periods

MALIGNANCIES OF THE THYROID



Epidemiology

Thyroid cancer is common; found at autopsy in about 5% of pts é no known thyroid diseases. Usually slowly progressing), tends to remain localized to the thyroid for many yrs, ẃ is the reason for the low morality rate.

Aetiology

Genetic factors: medullary carcinoma of thyroid has familial tendency.

Radiation exposure: ⇧ the incidence of thyroid cancer.

Types & Classification

Papillary carcinoma: accounts for 70% of all thyroid cancers. Affects younger age group, 50% of pts are ˂40 yrs. It metastasize through lymphatic system.

Follicular carcinoma: accounts for 15% of all thyroid cancers. Histologically resembles normal thyroid tissue. It metastasizes haematogenously.

Medullary carcinoma: accounts for 5% of all thyroid cancers. Arises from Para follicular cells, produce Calcitonin, pts may have diarrhoea, may associated é multiple endocrine neoplasia syndrome, 20% of these carcinoma are familial.

Anaplastic carcinoma: account for 5% of thyroid cancers, usually affects pts ˃50 yrs of age & is highly malignant.

Other rare malignancies; include lymphoma, sarcoma, or secondary's from other malignant tumour.

Signs & Symptoms

Hard nodule in the thyroid is usually the 1st sign. Late signs include; hard, immobile thyroid, attached to skin é cervical or supraclavicular LNs enlargement, hoarsene-ss of voice, Horner`s sy., throat/ear/head pain, stridor, dysphagia.

Diagnosis

•U/S: nodules. •CT/MRI of neck.

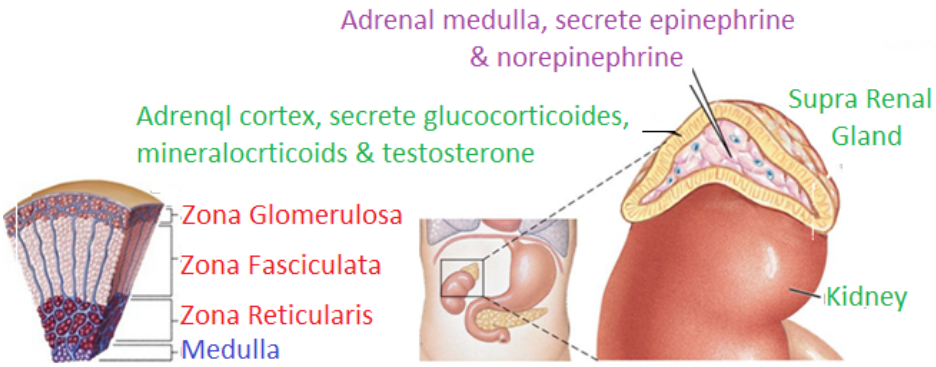
•Scintigraphy/radioiodine uptake: cold nodule éout or little uptake.

•FNA é cytology or biopsy. •Serum calcitonin level.

Treatment

Always combine: surgery; total thyroidectomy & neck dissection. Radiotherapy; external radiation in anaplastic carcinoma. Nuclear medicine: Iodine ^{131} ablative radiotherapy. Give T4 (L-Thyroxin), as high a dose as possible, to suppress the TSH effect on remaining metastases.

DISEASES OF THE ADRENAL GLAND



Adrenal gland located on top of both kidneys, the adrenal glands are triangular shaped, measure about ½" in height & 3" in length. It is composed of cortex & medulla. The medulla (inner part) constitutes 20% of the gland while the cortex (outer part) constitutes 80%. The cortex consists of 3 zones. The medulla & each of the 3 zones of the cortex each produce different hormones that serve a variety of functions in the body & are going to be illustrated as follow:-

Adrenal Cortex

Mineralocorticoids (Aldosterone) from Zona Glomerulosa, regulates electrolyte & fluid homeostasis.

Glucocorticoids (Cortisol & Hydrocortisone) from Zona Fasciculate, stimulate gluconeogenesis &⇧ BG in addition to its anti-inflammatory, anti-immunity & anti-allergic effect.

Sex hormones from Zona Reticularis, ancillary portion of sex hormone (secondary source), produces male hormones in women & female hormones in men to keep the effects of the dominant sex hormones in balance.

Adrenal Medulla

Adrenaline, Noradrenaline & Dopamine, there functions is to prolong & ⇧ sympathetic nervous system response to stress, ⇧ COP, affect BP & HR, ⇧ RR & Metabolic rate, cause vasoconstriction.

Common adrenal gland diseases

Disease of the adrenal cortex

(a) Excess production: Cushing sy (⇧cortisol). Conn's sy (⇧ aldosterone). Cancer.

(b) Inadequate production: Addison's disease (inadequate cortisol & aldosterone).

Disease of the adrenal medulla

Pheochromocytoma (⇧ catecholamine).

CUSHING'S SYNDROME

Caused by excessive concentration of cortisol (hypercortisolism) or other glucocorticoid hormones in the circulation.

Aetiology

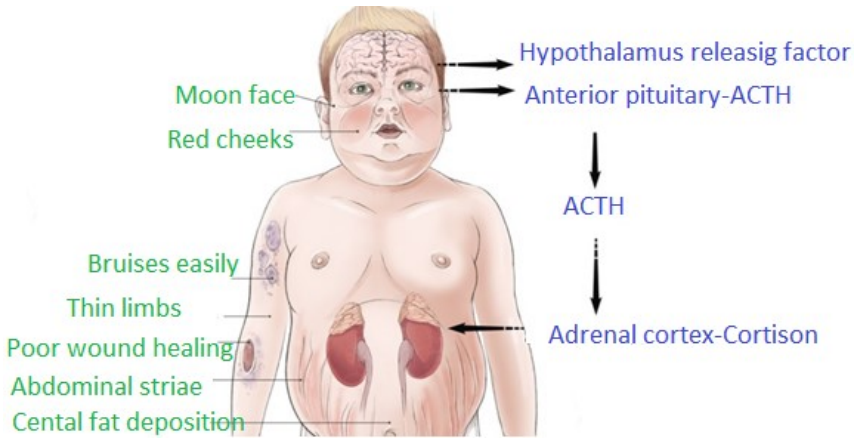
(a) Bilateral adrenal hyperplasia is the commonest cause. Caused by ⇧ pituitary secretion of ACTH. The pituitary tumour is large enough to be seen by skull X ray present in >10% of these pts & smaller basophilic adenomas found in >50% of pts.

(b) Adrenal adenomas & adrenal carcinoma produce excess cortisol.

(c) Ectopic ACTH production by tumour as oat cell carcinoma of lung, pancreas or bronchial carcinoid tumour, causing adrenal hyperplasia.

(d) Iatrogenic Cushing is expected complication in pt receiving long term glucocorticoid Rx for asthma, arthritis & other conditions.

Clinical features



Central obesity: caused by the effect of excess cortisol on fat distribution. Fat acc-

umulation in the face, neck & trunk, while the limbs remain thin. "Moon face" & "buffalo hump" (cervical fat pad) & supraclavicular fat pads contribute to the cushingoid appearance.

Hypertension: from the vascular effects of cortisol & Na^+ retention.

⇩ ***Glucose tolerance:*** is common, 20% of pts have overt DM as a result of hepatic gluconeogenesis &⇩ peripheral glucose utilization.

Symptoms of androgen excess: in adults, oligomenorrhea, hirsutism & acne may occur in women é Cushing, because of stimulation by the ACTH of adrenal andro- gen production.

Purple striae: linear marks on abdomen, where the thin, wasted skin is stretched by underlying fat. Atrophic skin é senile purpura.

Muscle wasting & weakness: reflects the catabolic effect of cortisol on muscle proteins.

Osteoporosis: is caused by ⇧ bone catabolism.

Susceptibility to bruising: caused by enhanced capillary fragility.

Psychiatric disturbance: especially depression, frequently seen.

Poor wound healing: due to impaired immune function.

Growth retardation: in children.

Diagnosis

Dexamethasone suppression test: in normal subjects, administration of a supra physiological dose of glucocorticoid results in suppression of ACTH & hence of cortisol secretion. This is the basis of Dexamethasone suppression tests, of ẃ there are several types. Administer dexamethasone 1 mg PO at 11 pm & measure serum cortisol at 8 am the following day. ˂5µg/dl in most individuals ẃ indicate normal.

The 48 hrs low dose test, ẃ is the most sensitive & specific screening test, entails the

administration of 0.5 mg Dexamethasone at intervals of exactly 6 hrs from 9 am on day 1 for 8 doses & measurement of serum conc. of Cortisol at 9 am on day 3 exactly 6 hrs after the last dose of Dexamethasone. A negative result is indicated when the serum concentration of cortisol at 9 am on day 3 is suppressed to ⟨50 nmol/l. Over 98% of pts é Cushing sy fail to "suppress" serum cortisol on the low dose test.

ACTH measurement

Help to differentiate the cause of Cushing syndrome.

(a) High normal or slight ⇧ of ACTH (Cushing syndrome).

(b) Marked ⇧ of ACTH (Ectopic ACTH production).

(c) Extreme ⇩ of ACTH (Functioning adrenal tumour).

Serum cortisol level- diurnal variation

Normally cortisol is highest in early morning & ⇩ throughout the day, reaching a low point at about midnight. Although the morning level may be ⇧ in pt é Cushing, a loss of normal diurnal variation & ⇧ in the evening level are characteristics.

Insulin tolerance test

In normal subjects & those é pseudo-cushing, insulin induced hypoglycaemia results in ⇧ ACTH & cortisol concentration. This response to hypoglycaemia is lost in most cases of cushing (90%). The test is contraindicated in any one é history of ep-ilepsy or cardiac disease & hypothyroidism or hypoadrenalism.

The 24 Hrs urine for cortisol: ⇧ in most pts.

CBC: leucocytosis é relatively low % of lymphocytes & eosinophils.

Skull X-Ray: sella turcica enlargement in 10% of pts é Cushing (macro-adenoma).

CT Scan Pituitary é contrast medium: detect 50% of pituitary adenomas.

CT scan Adrenals: reveal most adrenal tumours. Uniform enlargement of both adrenals suggests ACTH dependent Cushing either Cushing or ectopic ACTH.

Management

Adrenal Adenoma

Complete surgical resection of the adenoma cures the disease, but pts may need cortisol replacement post operatively for months.

Ectopic ACTH

Treating or removal of the tumour ẃ produce the ectopic ACTH.

Cushing disease

Pituitary radiation is effective in children but for adults it cures <1/3 of cases. Bilateral adrenalectomy cures Cushing disease. The disadvantages of bilateral adrenalectomy is the development of Addison's disease & the pt need life long cortisol replacement, also Nelson's syndrome in ẃ pituitary adenomas undergo rapid growth, perhaps because it is no longer inhibited by above normal level of cortisol.

Trans-Sphenoidal Pituitary Surgery

Is the treatment of choice for removal of pituitary adenoma, even when tumour can not be seen on CT or MRI. Trans-spheniodal exploration may disclose micro adenoma. Surgery is successful in 50-95% of cases & is followed by normal pituitary & adrenal function as well as cure of Cushing's disease.

HYPERALDOSTERONISM

Hyper secretion of mineralocorticoid, aldosterone.

Aetiology

Primary Aldosteronism: as é aldosterone producing adrenal adenoma (Conn's sy), in most cases it is unilateral small adenoma occur on either side. Adrenal carcinoma is rare. Bilateral cortical nodular hyperplasia is another cause.

Secondary Aldosteronism: the stimulus is outside the adrenal gland. Refers to ⇧ of production of aldosterone in response to activation of the renin-angiotensin system

as é accelerated phase of hypertension, pregnancy, CHF & other oedema states as é Nephrotic syndrome, CLD etc.

Pathophysiology: the excess aldosterone ⇧ the reabsorption of Na^+, + excretion of K^+ & hydrogen ions, in the distal renal tubules, ẃ result in progressive depletion of K^+.

Signs & symptoms: most pts have diastolic hypertension from Na^+ retention. Pt may complain heada- che & symptoms of other organ damage. Hypokalaemia & associated symptoms as muscle weakness, fatigue, impairment of urinary concentrating ability, polyuria, polydipsia, metabolic alkalosis, paraesthesia & tetany.

Investigations

***ECG:** evidences of LVH, evidences of hypokalaemia & arrhythmias.

***Hypokalaemia in hypertensive pts & Metabolic alkalosis:** is often the clue that triggers the search for primary aldosteronism.

***Serum aldosterone level:** elevated & its metabolites in 24 hrs urine.

***Plasma renin activity:** is useful indicator of whether elevated aldosterone is primary or secondary. ⇧ Plasma renin activity favours the diagnosis of 2ry type. While ⇩ in plasma renin activity é ⇧ aldosterone level suggests 1ry type.

***CT scan & MRI:** may detect secreting adenomas.

Treatment

***Surgery:** removal of solitary adenoma results cure of hypertension in 60% of cases & improvement in another 25%. In contrast only 20-50% of pts é bilateral hyperplasia are improved é surgery, even if bilateral adrenalectomy done. Adrenalectomy is done after 4 wks Rx é spironolactone (in case of adenoma, hyperplasia).

***Medical Treatment:** Spironolactone inhibits the effects of aldosterone on renal tubule (tab 50 mg/day) & é antihypertensive medication, high BP can be controlled.

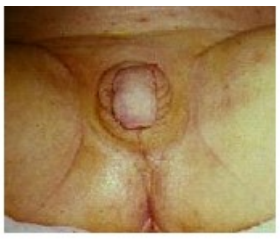
CONGENITAL ADRENAL HYPERPLASIA

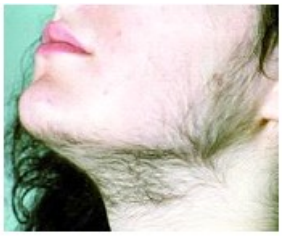
CAH is AR disorder of adrenal steroid biosynthesis. The defect is expressed as adrenal enzyme deficiency. 5 major enzyme deficiencies are clinically important: 21 Hydroxylase, 11-b-Hydroxylase, 17-a-Hydroxylase, 3-b-Hsteroid Hydrogenese & 20, 22 Desmolase deficiency. The enzyme deficiency causes reduction in end-products & accumulation of hormone precursors & ⇧ ACTH. The clinical picture reflects the effects of inadequate production of cortisol & aldosterone & the ⇧ production of androgens & steroid metabolites.

21 Hydroxylase deficiency

Most common type, accounts >80% of cases.

⇧ androgen production results in Ambiguous genitala in newborn Girl-classic form.





Women ē excess hair growth. non classic form

DIFFERENT FORMS OF 21-HYDROXYLASE DEFICIENCY			
Phenotype	**Classical Salt Wasting**	**Simple Virilizing**	**Non-classical**
Age at diagnosis	Newborn to 6 M.	Newborn to 2 Ys (♀) 2 to 4 Ys (♂)	Child to adult
Genitalia	♂ normal; ♀ ambiguous	♂ normal; ♀ambiguous	♂ normal; ♀virilized
21-Hydroxylase activity	**0%**	**1%**	**20% to 50%**
Hormones:			
Aldosterone	Reduced	Normal	Normal
Renin	Increased	Normal or increased	Normal
Cortisol	Reduced	Reduced	Normal
17 (OH) progesterone (nmol/L)	>5000	2500 to 5000	500 to 2500 (ACTH stimul.)
Testosterone	Increased	Increased	Variable, increased

Seen in 1: 5000-15000 live births. It is characterised by ⇩ production of cortisol & aldosterone & ⇧ production of progesterone; 17-OH-progesterone & sex steroids. The

urinary steroid metabolites (17-ketosteroids & pregnanetriol) ⇧ above normal levels. ⇩ secretion of aldosterone results in salt loss ē hyponatraemia & hyperkalaemia; plasma renin activity is therefore ⇧. In partial enzyme deficiencies, the aldosterone deficiency is not expressed, pt remain normonatremic & normokalemic. The ⇧ androgens causes virilisation of girls, or ambiguous genitalia & dark scrotum in boys. There are 2 forms, the early onset virilisation type ē /ēout salt-losing crisis & the late onset virilisation. Male babies ē late onset virilisation remains asymptomatic till childhood when showing sexual precocity signs.

Clinical Picture

- Ambiguous genitalia, labial fusion, clitromegaly, or penile, testicular enlargement & will developed muscles in boys, early appearance of pubic, armpit hair, hyperpigmentation of genitalia.
- Advanced bone age.
- Poor feeding.
- Diarrhoea, dehydration.
- Electrolyte disturbances.
- Arrhythmia.

Investigations

- Chromosomal studies: a Karyotype is essential in the evaluation of infant ē ambiguous genitalia in order to establish the chromosomal sex.
- Neonatal screening: done by measuring 17-OH-progesterone from heel blood samples collected on filter paper. This approach allow early identification of newborns ē CAH & prevent salt wasting crisis in boys who are unrecognized at birth. It also identifies the completely virilised girls ē ambiguous genitalia who may be mistaken for boys ē cryptorchidism.

- Prenatal diagnosis is possible through biochemical & genetic tests.
- ⇧ ACTH.
- ⇧ 17-OH-progesterone, 11 β Hydroxy progesterone in blood & urine ⇧20 times.
- Advanced bone age (from excess androgen).

Management

- Replacement therapy (4S): Steroids, Sugar, Salt & Sodium bicarbonate for metabolic acidosis.
- Correction of dehydration, acidosis & electrolyte imbalances.
- Prednisolone (5 time potent than hydrocortisone) 1 mg/Kg/day.
- Florinef (9 α Fludrocortisone) 0.1 mg tab daily in case of Aldosterone deficiency.

11- B-Hdroxylase Deficiency

Accounts for 5-10 % of cases of CAH. Gene is located on the long arm of chromosome 8. Characterized by ⇩ plasma renin activity & high serum 11-deoxycorticos terone & 11-deoxycortisol concentration ē ⇧ of its urinary metabolities (compound -S). Because of the strong mineralocorticoid activity of deoxycorticosterone, the condition is characterized by salt retention, ⇧ BP & hypokalaemia alkalosis. ⇧Plasma androgens may cause virilisation of female foetus.

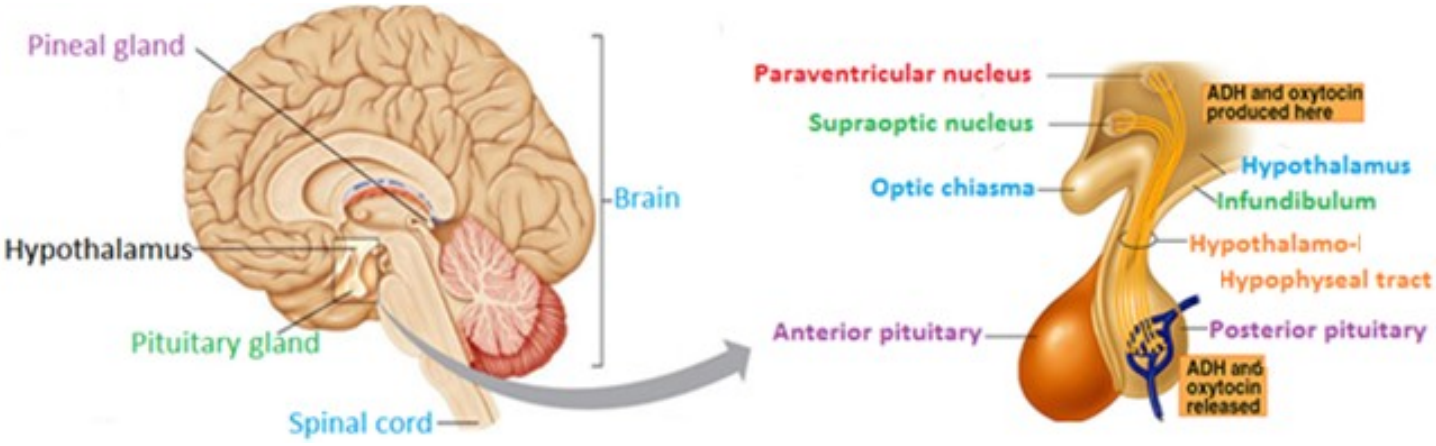
17- α – Hydroxylase deficiency:

Genetic defect is on chromosome 10. Presents ē similar features of those of 11-Hydroxylase deficiency except that androgens are low, so no virilisation in girls & genitalia is ambiguous in boys.

3- B- Hydroxysteroid dehydrogenase deficiency

A very rare disorder that result in accumulation of DHEA, ẃ is converted to testosterone in peripheral tissues. It can cause virilisation of female foetus & leads to ambiguous genitalia in the new-born.

DISEASES OF THE PITUITARY GLAND



The hypothalamus-pituitary unit is the most dominant portion of the entire endocrine system. The output of the hypothalamus-pituitary unit regulates the function of the thyroid, adrenal & reproductive glands & also controls somatic growth, lactation, milk secretion & water metabolism. Pituitary function depends on the hypothalamus & the anatomical organization of the hypothalamus-pituitary unit reflects this relationship. The pituitary gland lies in a pocket of bone at the base of the brain, just below the hypothalamus to ẃ it is connected by a stalk containing nerve fibres & blood vessels. The pituitary is composed of 2 lobes.

The anterior pituitary is connected to the hypothalamus by hypothalmoanterior pituitary portal vessels, it produces 6 hormones:-

•Prolactin H. •Growth H. •Thyroid stimulating H. •Adrenocorticotropic H.

•Follicle stimulating H. •Luteinizing H.

The posterior pituitary, secrete the following two hormones:-

Post pituitary hormones	Target	Effect
1- ADH	Collecting duct	H_2O retention
2- Oxytocin	Breast & Uterus	Milk let down & Smooth muscle contraction

HYPOPITUITARISM

Insufficient production of anterior pituitary Hormones. May be generalized or caused by the selective loss of 1 or more of pituitary Hormones.

GENERALIZED HYPOPITUITARISM

Partial or complete loss of anterior lobe pituitary function

Aetiology

Pituitary tumour: chromophobic adenoma or craniopharyngioamas.

Infarction/ischemic necrosis of the pituitary: shock, especially postpartum (She- eh-an's syndrome) or in DM, or sickle cell anaemia. Vascular thrombosis or aneurysm of the anterior cerebral artery.

Inflammatory/infectious: meningitis or pituitary abscess.

Infiltrative diseases: sarcoidosis or hemochromatosis.

Iatrogenic: irradiation or surgical removal of pituitary tumours or during operation for other brain tumours.

Clinical features

Onset is usually insidious &may not be recognized as abnormal by the pt, but occasionally it may be sudden or dramatic.

With slow progressive destruction of pituitary tissue

Failure of GH & gonadotrophin secretion occurs early. TSH failure comes next. ACTH level falls finally.

1) GH deficiency: in children cause growth failure. In adults cause ⇧ of the adipose tissue & ⇩ lean body mass, leading to ⇩ strength & exercise capacity.

2) LH & FSH deficiency: in women cause, amenorrhea, genital atrophy & infertility. If there is associated loss of adrenal androgens (because of concomitant ACTH deficiency), the pubic & axillary hair may be lost. In men deficiency cause loss of potency, &

libido, also testicular atrophy, regression of secondary sexual characteristics, ⇩ spermatogenesis & infertility.

3) TSH deficiency: symptom & signs of hypothyroidism.

4) ACTH deficiency: leads to secondary type of adrenal insufficiency ẃ differs from primary type in that: there is no hyperpigmentation of skin & mucous membrane. Hyponatremia & hypokalaemia are minimal, since aldosterone production, ẃ controls the balance of these electrolytes, mainly depends on the renin-angiotensin system.

5) Prolactin deficiency: postpartum failure of lactation.

Pituitary apoplexy

Is a symptom complex caused by haemorrhagic infarction of either a normal pituitary gland or, more commonly, a tumour. The acute symptoms may include severe headache, stiff neck, fever & visual disturbances. Varying degrees of hypopituitarism may develop suddenly & pt may present in vascular collapse because of deficient ACTH & cortisol secretion. Often the CSF is haemorrhagic.

Diagnosis

1) **Evaluation of target organ function:** often the 1st step in diagnosis.

- ***Evaluation of Thyroid Function: T4, T3, TSH.***
- ***Evaluation of ACTH***
- ***Evaluation of Prolactin***: prolactin not regularly depressed.
- ***Evaluation of Serum LH & FSH***: helpful in postmenopausal women.
- ***Evaluation of GH:*** may be undetectable under baseline condition, provocative manoeuvres are needed to prove inadequacy of hormone production; insulin-induced hypoglycaemia is the most consistent effective test; regular insulin at a dose of 0.1 U/kg BW, is given IV over 15-30 sec & venous blood samples are obtained to determine GH, cortisol, BG before insulin administration & 30, 60 & 90 min later after the

insulin dose. The fall in BG level is maximal at 30 min, is followed by ⇧in GH to a level > 8-10 ng/ml in normal individuals. Blood cortisol level is also ⇧. Failure of rise may suggest hypopituitarism.

2) Imaging studies: skull X ray of sella tursica (detects macroadenomas >10 mm). High-resolution CT or MRI.

3) Formal visual field testing.

Differential diagnosis

- Anorexia nervosa.
- Chronic liver disease (alcohol, hemochromatosis).
- Polyglandular autoimmune disease.

Therapy

1) Treatment of the underlying cause.

Surgery: if hypopituitarism is due to tumour & tumour is small & not secreting prolactin, most favour transphenoidal removal of tumour. Most endocrinologists consider Bomocriptine the initial Rx of prolactinomas, regardless of size of tumour, but é larger tumours associated ē suprasellar extension, resection of the entire neoplasm, either trans-sphenoidally or trans-frontally, may not be possible & adjunctive irradiation may be needed. After surgical or radiation Rx, other hormones may be lost as well & replacement may be needed accordingly. In pituitary apoplexy, trans-sphenoidal decompression of the often haemorrhagic tumour should be undertaken promptly.

2) Hormonal therapy (replacement)

Rx directed toward replacing the hormones of the hypo functioning target glands.

- **GH replacement:** given for children é growth failure.
- **Thyroid hormone replacement;** given in usual replacement dose.
- **Cortisol:** given in the usual replacement dose.

•**Oestrogens & Progesterone combination:** given to women to restore menstrual function & Testosterone may be given to men to restore libido & potency.

SELECTIVE PITUITARY HORMONE DEFICIENCIES

A clinical condition in ẃ one or more of the pituitary hormones are deficient; may represent an early stage in the development of more generalized hypopituitarism so evaluate pt regularly.

Types

***Isolated GH deficiency;** responsible for many cases of dwarfism.

***Isolated Gonadotropin deficiency:** occurs in both men & women & must be distinguished from 1ry hypogonadism.

***Isolated ACTH deficiency:** rare clinical entity. Symptoms of weakness, hypoglycaemia, wt loss & ⇩ axillary & pubic hair suggest the diagnosis. Plasma & urinary steroid levels are low & ⇧ to normal after ACTH therapy. No clinical or laboratory evidence of other hormonal deficiencies.

***Isolated TSH deficiency:** is likely when clinical features of hypothyroidism exist, plasma TSH levels are not elevated & no other pituitary hormone deficiencies exist. Plasma TSH levels are not always lower than normal, suggesting that the TSH secreted is biologically inactive.

***Isolated Prolactin deficiency:** has been noted rarely in women who fail to lactate after delivery.

HYPER SECRETION OF ANTERIOR PITUITARY

The most commonly secreted in excess are:-

*GH (Acromegaly or Gigantism).

*ACTH (pituitary type of Cushing syndrome).

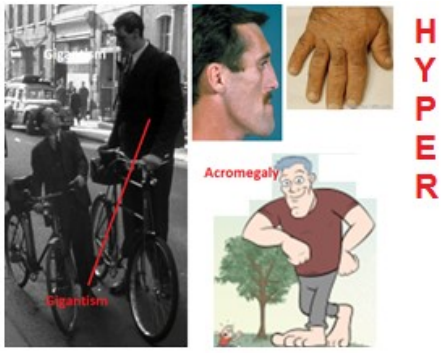
*Prolactin (results in Hyperprolactinemia).

GIGANTISM & ACROMEGALY

Excessive secretion of GH due to a pituitary adenoma of the somatotrophs.

Clinical features

⇧ GH may cause changes in bone, soft tissue & metabolism.



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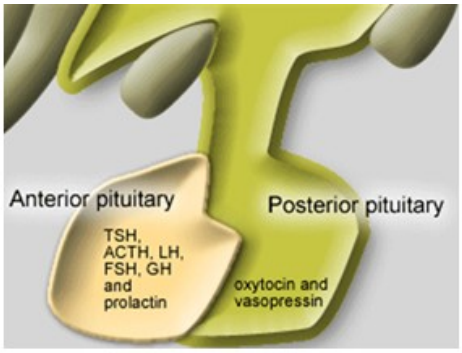

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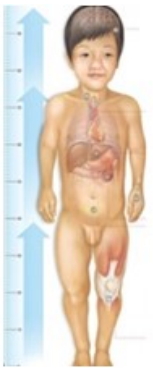


Gigantism

GH hypersecretion beginning in childhood before closure of epiphyses, may cause ⇧ linear growth of long bones resulting in gigantism. There is little bony deformity, soft tissue swelling or enlargement of peripheral nerves. Delayed puberty or hypogonadotropic hypogonadism may be present.

Acromegaly

GH hypersecretion beginning after epiphyseal closure in adults, cause soft tissue growth & bony enlargement, especially in accrual areas of the skeleton, ẃ may affect the pt's appearance. Enlargement of hands (especially fingertips) & feet: ⇧ ring, gloves & shoe size. Coarsening of facial features: thick skin folds, brows & nasolabial folds, enlargement of nose. Enlargement of mandible: proganthism & spreading of teeth. Body hair ⇧, the skin thickens & becomes darker. Excessive perspiration, offensive body odour may be noted. The voice becomes husky. The tongue enlarged & furrowed. Barrel chest deformity may be noted. Joint symptoms are common; crippling degenerative osteoarthritis. Galactorrhea in women & menstrual irregularities/amenorrhea. Impotence is common in men. Peripheral neuropathies are common, as are

headaches. Bitemporal hemianopia (visual field defect) may develop due to the pressure effect of pituitary adenoma. Enlargement of internal organs; heart, liver, kidneys, spleen, etc. Metabolic changes; poor glucose tolerance, from the anti-insulin actions of GH, is common. Overt DM occurs in only 10% of cases.

Diagnosis

***GH level**: should be measured in the morning under basal condition. A level **>**10 ng/dl favours the diagnosis of acromegaly.

***Glucose tolerance test:** to diagnose for possible DM.

***Skull X ray:** in most cases the pituitary adenoma is large enough to distort the sella tursica & can be seen on lateral skull X ray.

***CT or MRI:** will help to visualize the tumour.

***Other X ray changes**: enlargement of sinuses, tufting of distal phalanges.

Treatment

Ablative therapy: transpheniodal pituitary adenomectomey: results prompt normalizaton of GH in majority of pts.

Irradiation Rx: is generally indicated, but be aware of danger of hypopituitarism.

Medical therapy: indicated if surgery & radiotherapy are contraindicated or failed, give Bromocriptine up to 15 mg/d PO in divided doses.

HYPERPROLACTINEMIA/GALACTORRHEA

Clinical condition resulting from excess secretion of prolactin in men, or in women who are not breast feeding.

Aetiology

Prolactin secreting pituitary adenomas (Prolactinoma): more common in women than men, usually appearing during reproductive yrs. Majority are microadenomas (<10 mm in size). Men tend to have larger tumours (macroadenomas), ẃ usually are suspected because of neurologic impairment & hypogonadism.

Damage to hypothalamus or pituitary stalk: by tumours, granulomas & other process may prevent the normal regulatory effect of hypothalamic dopamine on lactotrope activity, resulting in ⇧ of prolactin.

Drugs: those inhibiting dopamine activity & thus interfere é its regulatory activity on prolactin secretion, e.g. Phenothiazines, Anti-depressants, Anti-hypertensives (Methyldopa, Reserpine), Opioids, Cimetidine, Metoclopramide, Contraceptives.

Other rare causes: 1ry hypothyroidism, chronic liver disease, RF.

Clinical feature

In women

•**Galactorrhea:** is direct result of prolactin excess.

•**Amenorrhea or menstrual irregularity** is due to inhibition of hypothalamic GnRH production by prolactin as well as the direct effect of prolactin on the ovaries •**Signs of oestrogen deficiency,** as hot flushes & dyspareunia.

In men

•**Loss of libido & potency.** •**Hypogonadism**

•**Headaches &visual difficulties:** result from the compression effect of the tumour ẃ are often larger in men, on the optic nerves.

Diagnosis

Prolactin levels: ⇧ serum prolactin level **>**300 ng/ml strongly suggests the presence of prolactinoma. Functional causes such as drugs seldom elevate the prolactin level **>**100-200 ng/ml.

***Skull XR,* CT/MRI:** are used to visualize the adenoma.

Visual field examination: for detection of bi-temporal hemianopia.

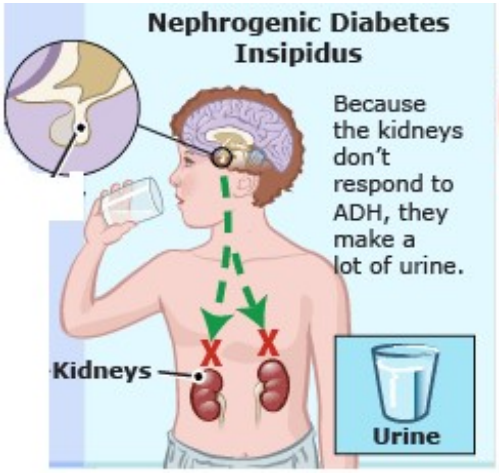
Therapy: depends on tumour size & its manifestation.

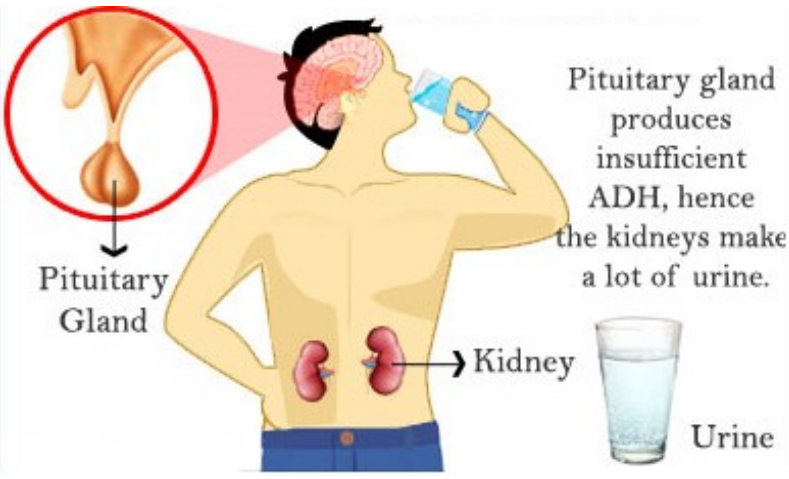
Surgical Rx: Trans-Sphenoidal surgery: cures most of small adenomas.

Medical Rx: Bomocriptine remarkably effective in ⇩ prolactin level to normal. It also ⇩ tumour size. The initial dose is 1.25 mg once or twice daily may need to be ⇧to 10-20mg daily for full effect. Side effects include; headache, dizziness, fatigue. The larger tumours é suprasellar extension are not cured by surgery. Such macroadenomas may be initially treated é Bomocriptine. If the tumour shrinks, there is greater chance for successful surgery.

Radiotherapy: reserved for therapy-resistant cases. May used in conjunction é surgery & Bomocriptine to further reduce tumour size.

CENTRAL DIABETES INSIPIDUS





Temporary or chronic disorder of the neurohypophyseal system due to deficiency of vasopressin (ADH) & characterized by excretion of excessive quantities of very dilute

(but otherwise normal) urine & by excessive thirst. ADH is produced by cells in the supraoptic & paraventricular nuclei of the hypothalamus, travels down through the pituitary stalk & stored in posterior lobe of pituitary.

Aetiology

Primary

- Genetic: DIDMOAD (Wolfram) syndrome, AD, AR.
- Developmental/Idiopathic: Septo-optic dysplasia.

Secondary/Acquired

- Trauma: Head injury, Post surgical.
- Tumour: Craniopharyngioma, Pituitary tumours, Metastases.
- Inflammatory; Sarcoidosis, Histocytosis, Meningitis, Encephalitis, GBS, Autoimm.
- Vascular: Aneurysm, Infarction.
- *Primary/Idiopathic:* account for about 50% of cases.
- *Injury to hypothalamus*-pituitary *area:* may result from head trauma, neurosurgical procedures such as hypophysectomy.
- *Less common causes:* neoplasms, histiocytosis, vascular lesions & infections.

Clinical features

The onset insidious or abrupt, occur at any age, presented é the following:-

Polyuria

Urine volume 3-15 Litre daily, result from the inability to reabsorb free water & concentrate urine. Nocturia is almost present, ẃ may disturb sleep & cause mild day fatigue or somnolence.

Thirst (polydipsia)

leads to ⇧ fluid intake. A conscious pt é normal thirst mechanism & free access to water will maintain hydration. However rapid & life threatening dehydration & hypovo-

lemia may develop rapidly, if urinary losses are not continuously replaced, ẃ may occur in unconscious pts or infants. In primary DI, only polydipsia & polyuria are present. In acquired DI, signs & symptoms of associated lesions are also found.

Diagnosis

Measurement of plasma osmolality

In untreated pts helps to distinguish the cause of polyuria. In DI, the loss of water leads to high osmolality (280-310 mOsm /kg). In psychogenic polydipsia excess fluid intake is primary & plasma osmolality is low (255-280 mOsm/kg).

Water deprivation test

Started in the morning by weighing the pt, obtaining venous blood to determine electrolyte conc. & osmolality & measuring urinary osmolality. Fluid intake is with- held & voided urine is collected hourly & its osmolality is measured. Dehydration is continued until; orthostatic hypotension & postural tachycardia appear, or 5% or more of the initial BW has been lost, or the urinary conc. does not ⇧ by >30 mOsm /L in sequentially voided specimens for 3 hrs. At this point, serum electrolytes & osmolality are again determined & 5 units of aqueous vasopressin or 2 µg of Desmopressin is then injected SC & urine osmolality is measured after one hour.

Disorder	Urinary osmol in response to H_2O deprivation	Urinary osmol in response to Vasoprssin injection
Normal	⇧ > 280 mOsm/kg	No ⇧
Central DI	NO ⇧	⇧
Nephro.DI	NO ⇧	No ⇧

Measuring circulating ADH concentrations by radioimmunoassay.

Differential diagnosis:

- Compulsive water drinking.
- Nephrogenic DI.

Treatment

***Hormonal Rx**

Aqueous vasopressin SC/IM in doses of 5-10 units. Since its effect lasts for 6 hrs or less, its use in chronic Rx is limited. Desmopresin (synthetic vasopressin) 0.05-0.2 ml applied to the upper respiratory mm twice daily by nasal cannula or nasal spray. The effect lasts 12-24 hrs, it can be given, SC or IV & it is a preparation of choice for both adults & children.

***Non-hormonal Rx**

To reduce polyuria; Chlorpropamide (oral hypoglycaemic) may ⇧ the endogenous ADH in pt who have partial deficiency of ADH. 250-500 mg PO makes pt asymptomatic (3-5mg/kg). Thiazide diuretics: have paradoxical effect on ⇩ urine output in DI. They are the preferred drugs for Rx of nephrogenic DI. Thiazides are only partially effective, they ⇩ the urine volume by about 30-50%.

****Restricting salt intake.***

****Prostaglandin inhibitors*** (indomethacin (1-3 mg/kg/D PO ÷ 2) may be effective.

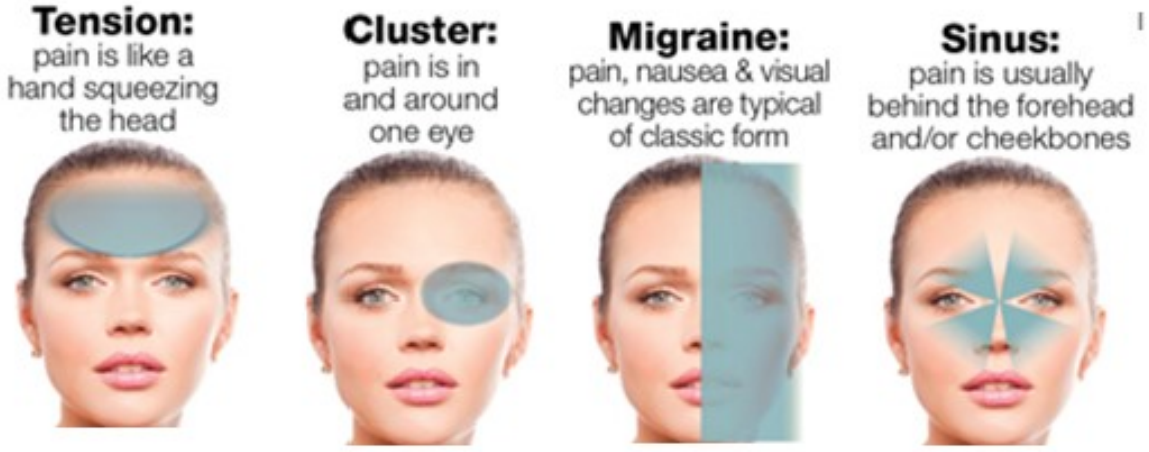
****Rx of treatable underlying cause.***

CHAPTER VIII

DISEASE OF THE NERVOUS SYSTEM

- Headache
- Stroke
- Coma
- Faints
- Seizures
- Parkinson's Diseases
- Movement Disorders
- Neuropathy
- Guillain-Barré Syndrome
- Spinal Cord Diseases
- Multiple Sclerosis
- Cranial Nerves Examination

HEADACHE



One of the commonest complaints in medical practice. As many as 90% of individuals have at least one episode of headache per year. Severe disabling headache is reported to occur at least annually by 40% of individuals worldwide.

Types

1- Tension headache

The most common type of headache. Is episodic or chronic in nature. Episodic headaches are usually the result of stress or fatigue. The pain of tension headache is usually diffuse across the entire head not sharp or local to one area, is often related to TMJD, trigeminal nerves & jaw function as well as poor (forward) head posture. Tension headache can last anywhere from 30 min to several days .Dull aching pain is characteristic of referred muscle pain & tightness across forehead. Sore muscles: of the head & neck are one of the hallmark signs of TMJD. Tension headache is common in women than men. Occur at any age, but onset during adolescence is common.

Classification

Episodic: if the headache occurs <5 days per month, it is considered episodic, even if it is very frequent or long lasting.

Chronic: headaches that occur> 15 days out of one month, often called chronic daily headaches.

Causes

Many doctors now believe that tension headaches are caused by fluctuations in the certain chemicals in the brain including serotonin & endorphins. The underlying reasons for the changes in the chemical levels, however, remain a partially understood mystery. There are several other factors that trigger tension headaches:-

- Stress, often precipitating grinding of the teeth & clenching of jaw muscles &/or tightening neck & shoulder muscles.
- Depression.
- Hard work - type "A" personalities tend to get headaches when work levels drop or they are on vacation?
- Bruxism-grinding of the teeth or clenching of the jaw often done unconsciously or during sleep.
- Poor posture & Sleep disturbances.

Clinical features

Tension headache is characterized by mild/moderate, bilateral pain. Is a constant, tight, pressing or band like sensation in the frontal, temporal, occipital or parietal area. Usually lasts **<**24 hrs but can persist for days or wks. Prodromal symptoms are absent, some pts have neck, jaw or TMJD. On examination some pts may have tender spots in the peri-cranial or cervical muscles.

Treatment

Although in many cases, tension headaches resolve spontaneously after a relatively short period of time, lifestyle changes can also help alleviate some of the underlying causes of headaches in most instances.

Medications may be used to reduce pain & minimize duration. **ASA, Acetaminophen, Ibuprofen or Diclofenac**. If Rx is unsatisfactory, addition of Caffeine or anal gesic may be used.

Physical Rx: different techniques used including:-*Hot or cold application. *Positioning. *Massage. *Stretching & Traction exercise.

Psychological *Rx:* includes reassurance, counselling, relaxation, stress management programs & biofeedback techniques reduce both the frequency & severity of chronic headache.

2. Cluster Headache

Is one of the most painful & debilitating headaches. Usually come éout any sort of warning & prevent any type of activity until it abates. These headaches recur periodically or in clusters, cycling through periods of pain & periods where the pain disappears. They tend to disappear as frequently as they come & tend to come in groups or cycles. Many pts suffer from 1-4 cluster headaches in a cycle, ẃ may last for several days. It's a vascular headache, common in men than women. The male: female ratio is 8:1, usually begins in the 3^{rd}-6^{th} decade of life. It is periorbital & less commonly temporal& has rapid onset éout warning. It is severe & explosive in quality lasting 30 min. up to 2 hrs & subsiding abruptly as they come. Characteristically occur in the spring & fall, occurs several times a day particularly at night & stay for 3-8 wks. During the attack the pt often have associated nasal stiffness, lacrimation & redness of the eye ipsilateral to the headache. Alcohol provokes attacks in about 70% of pts.

Classification

Episodic: present themselves from one wk to a yr. é long periods of remission.

Chronic: clusters occur for ›a yr., or é very short remission periods.

Causes: studies have linked changes in the following chemical levels of the brain to cluster headaches to:- •Hormones & •Neurotransmitters.

No triggers: there are typically no triggers that bring about or start cluster periods, but attacks may occur in specific period each yr. & pt may expect it.

Symptoms

Headaches occur every day & possibly many times per day. Attacks lasting from 15 min to up to 3 hrs. Recurring attacks at approximately the same time each day. Attacks usually occur at night. Pain typically ends as abruptly as it begins. Other symptoms that differentiate cluster headaches from other types of headache are:- drooping eyelids, runny nose, watery eyes & eye redness. These symptoms represent autonomic nervous system responses to headache.

Treatment

Acute attack/abortive Rx: inhalation of 100% oxygen & Sumatriptin 6 mg S.C. said to be helpful & Ergotamine or other Analgesics may also be used. Nasal triptan (Zomig). Sphenopalatine blocks can sometimes abort the attacks.

Preventions/prophylactic Rx: attacks can be prevented effectively by: Prednisolone, Lithium, Methysergide, Ergotamine, Sodium Valproate & Verapamil.

3. Migraine headache

A benign, episodic disease, characterized by, nausea, vomiting &/or other sympto-ms of neurological dysfunction. Is the most common cause of vascular headache & it affects 17% of women & 6% of men. Usually begins in childhood or young adult.

Aetiology

The cause is often unknown, but several common precipitants observed include:-

1) Family history of migraine present in nearly 2/3 of pts.

2)Psychological, Dietary & Environmental factors; emotional stress, depression, altered sleep pattern or sleep deprivation, menses, oral contraceptives, alcohol intake especially red wine, caffeine withdrawal, various food staffs (e.g. chocolates, nuts, aged, cheese, meals containing nitrates), perfumes.

3) It may develop after seemingly minor head injury.

Pathogenesis

Different hypothesis are proposed including:-

*1)**Vascular theory:*** said that migraine & neurological symptoms are results of extra-cranial vasodilatation & intracranial vasoconstriction.

*2)**Neuronal theory:*** slowly spreading neuronal depolarization is considered a cause

*3)**Trigeminovascular system abnormality:*** says, dysfunction of trigeminal nucleus caudalis leads to release of vasoactive neuropeptides resulting in migraine.

Clinical feature

Attacks may be ppt by some of the factors mentioned above. It is relieved by sleep & exhilaration & pregnancy. Classical migraine include:-

1. Prodromal phase: lassitude, irritability, difficulty in concentrating.

2. Aura phase: pt often report visual complaints, vertigo, aphasia or other neurological deficit before onset of headache.

3. Headache phase: characteristic migraine headache.

4. Headache termination: usually occurs within 24 hrs.

5. Post headache phase: feeling of fatigue, sleepiness & irritability.

Characteristics

Moderate to severe head pain, pulsating quality, often unilateral, exacerbated by physical activity &relived by sleeping, it is often associated é nausea &/or vomiting, photophobia, phonophobia/sonophobia (dislike & voidance of laud sounds or noi ses). Multiple attacks may occur, each lasting 4-72 hrs.

Types

Common migraine: the commonest variation of migraine headache. No focal neurological disturbance precedes the recurrent headache.

Classic migraine: associated é characteristic premonitory sensory, motor or visual

symptoms. Commonly associated é visual symptoms as scotomas or hallucinations

Complicated migraine: associated é dramatic transient neurological deficit, or attack that leaves a persisting residual neurological deficit.

Treatment

Should first involve removal of inciting agents when possible.

1. Acute/abortive Rx of migraine: these are lists of effective drugs:-

(a) NSAIDs as Aspirin, Paracetamol, Ibuprofen, Diclofenac may reduce the severity & duration of migraine attack. These drugs are effective for mild to moderate attacks & are most effective when taken early. Side effects; dyspepsia & GI irritation are common side effects.

(b) 5-Hydroxy tryptophan-1-agonists: is a serotonin agonist that ⇩ substance release at the trigeminovascular junction & include:-

i. Non selective (ergot preparations): widely used, has oral, sublingual, rectal, nasal & parenteral preparation & the parenteral form used for rapid relief of an attack. Usually prepared combined é caffeine ẃ potentiates the effect by improving absorption. Initial dose: 1-2 mg repeated every hr. if there is no relief of headache up to a maximum of 6-8 mg over 24 hrs. Side effects are nausea, vomiting, myalgias, chest discomfort, peripheral ischemia & even angina. Excess use may lead to rebound headache & dependency. Contraindicated in CHD.

ii. Selective-Triptans : Sumatriptan single 6 mg SC dose is effective in 70-80% of cases.

(c) Dopamine agonists: are used as adjunctive therapy.

2. Prophylactic Rx: includes drug regimens & changes in pts behaviour. Drugs that have capacity to stabilize migraine, indicated if the pt has 3 or more attacks/month, include β-blockers, tricyclic antidepressants & Ca Ch BLs, start é low dose & gradually ⇧ if there is no adequate response.

4. Secondary headaches

Headache associated é Brain Tumour

Dull headache, worse é exertion & change in position, accompanied by nausea & vomiting. Often, pt will have nausea & vomiting for wks before headache start. 30% of pts é brain tumour present é headache. Brain tumour can affect all ages & both sexes. Headache is usually intermittent dull aching; of moderate intensity ẃ worsens é time. It disturbs sleep in about 10% of pts, exacerbated by exertion & postural changes & é time pt can develop nausea & vomiting. Upon examination focal neurological deficit may be detected.

Temporal Arteritis Headache

Inflammatory disease of carotid artery & its branches, also called giant cell arteritis, common in elderly (average age 70), women account for 65% of cases. Associated é fever. Headache is located to temporal or occipital area, described as dull & boring. Usually worse at night & is often aggravated by exposure to cold, associated é wt loss, jaw claudication, tender vessels by the temples, polymyalgia rheumatica. 50% of untreated cases develop blindness due to involvement of ophthalmic artery & its branchs

Diagnosis: ESR is often elevated. Biopsy of temporal artery confirms the diagnosis.

Treatment: Prednisolone 80 mg/day for 4-6 wks.

Acute closed angle glaucoma

⇧ Pressure in eye ball, headache that starts é eye pain, blurry vision associated é nausea & vomiting. On physical exam, pt will have a red eye & a fixed mildly dilated pupil.

Sinus headaches

Congestion of the sinuses due to sinusitis, infection of one or more sinus cavities, colds, allergies, fungal or bacterial infection. Pain & pressure in cheeks & forehead,

pain ⇧ on lying down, associated é sore throat, thick yellow nasal discharge, fatigue, fever & cough.

Hypertension headaches

Pain surrounds the head in a band, worse in the morning & diminishes as the day goes on, cramps, dizziness, heart palpitation & fatigue may be associated.

Hypotension headaches

Called orthostatic, occur when changes in BP of the head occur dramatically, as é standing up from sleeping position or pt bend over & suddenly move upright. May associated é diplopia or double vision, blurred vision & dizziness.

Lumbar puncture headache

Occurs in 10-30% of cases of LP, usually begins within 1-2 days & persists for 3-4 days, pain is bifrontal or occipital, dull aching in nature, aggravated by sitting, stan-ding, head shaking, or jugular vein compression & disappears in prone or supine position. Treated by simple analgesics & lie pt supine.

Meningitis: inflammation of the meninges, presents é fever & meningismus, or stiff neck.

SAHge: acute, severe headache, stiff neck éout fever.

Medication overuse headache: in those using excessive pain killers for headaches.

Evaluation of a pt é headache

When evaluating a pt é headache, the goal is to:-

Distinguish serious from benign headache.

Pt. History: subjective evaluation. When & How the headaches present themselves , family history of headache, medical history, previous investigations, drugs intake, dosage, length of time taken & presence of +ve or -ve side effects.

History of present illness: How long does the pain last? Is it mild, moderate or sev-ere

pain? When does it occur? What is the 1st symptom of pain? Where it is located ? Is there any nausea or vomit? What medications taken & how did they affect? Duration? The conditions that produce, exacerbate or relieve it?

Physical examination: search for underlying serious illnesses. Vital signs: BP, pulse & temperature. Head & neck examination: scalp or sinus tenderness, examination of oral cavity & tempromandibular joint. Ophthalmologic evaluation: include; funduscopic examination, pupillary size, corneal clouding. Systematic evaluation of other systems: glands, chest, CVS, abdomen. Neurological examination include; change in mental status, focal neurological deficit, neck stiffness & other meningeal signs.

Differences between the common 3 types of headaches

	Migraine	Cluster headache	Tension headache
Severity	Moderate to severe	Severe	Mild to moderate
Duration	4 hours to 3 days	30 min. to 3 hrs	30 min - several hrs
Frequency	Several/month or/ yr	Multiple per day or per month	Persist days or wks
Site	One/both sides of the head	One side, focused at eye / Temple	Across head tightenss or pressure
+Features	Nausea &/or Vomite	Running nose, drooping eyelid	Sore muscles, TMJD
Aura	Yes	No	No
Sensitivity	Movement,light,noise	No	Uncommon

Investigation

Diagnosis of common 1ry headache is clinical. No specific test is available. Occasionally investigations including neuroimaging studies are important if the head-ache is atypical or associated é abnormalities on physical examination. The following clinical features should considered as indicators of serious underlying disease:-

1) First severe headache ever described as the worst type of headache in the pt's life may suggest SA Hge.

2) Subacute worsening over days or wks, or disturbs sleep or present immediately upon awakening may suggest tumour.

3) Abnormal neurological examination may suggest space occupying lesions.

4) Fever or other unexplained systemic signs may suggest meningitis.

5) Vomiting precedes headache.

6) Headache induced by bending, lifting or cough.

7) Known systemic illness.

8) Onset of headache in pts older than 55 yrs.

Summary of management of headaches

1- General pain relievers

	Aspirin	Paracetamol	Ibuprofen	Codeine	Tramadol
Fast?	✔✔		✔		✔
Safe?		✔✔			
OK for long term?	✖	✔✔	✖	✖✖✖	

2- Cluster specific treatment

Oxygen.

Triptans.

3- Migraine-specific treatments:

Triptans & Ergots. Imigran (Sumatriptin) 100 mg tab.

Migranil (Ergotamine 1mg + Caffine 50 mg + Phenobarbitone 200 mg+ Mepropamate 150 mg), 1-2 tab during the attack, can be repeated up to 3 times/day.

VERTIGO

Loss of equilibrium, we keep our equilibrium centrally through our cerebellum & peripherally through our eyes, vestibular apparatus of internal ears (cochlea, semicircular canals).

Investigations

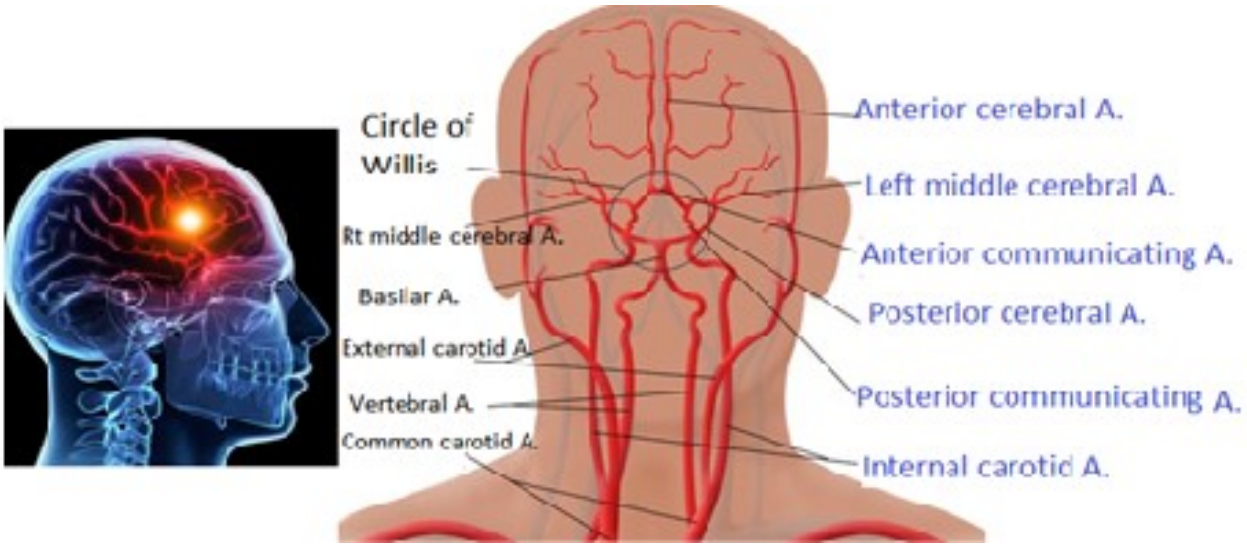
- Ear examination.
- ECG, EEG.
- Blood sugar.
- X ray of cervical spine.

Causes

- TIAs. - IC Hge. - Migraine. - Epilepsy. - Labrynthitis. - Acoustic neuroma.
- Cervical spondylitis. - SLE. - Antihypertensive drugs.

STROKE

Abrupt onset of non-convulsive, focal neurologic deficit resulting from sudden interruption of blood supply to parts of the brain, lasting 24 hrs or longer.



Brain Blood Supply

The brain is a very selfish organ. Requires constant supply of O_2 & glucose. Requires 2% of the total blood pumped by the heart. No storage in the brain for either fuel or

oxygen. Strokes occur in the brain & affect the opposite side of the body.

Blood supply of Brain

Carotid arteries: present in anterior neck, are large, frequently congested é plaque can be cleaned out surgically. Pairs of internal carotid artery: branch off from common carotid artery, splits into middle & anterior cerebral arteries. Before splitting it gives the following branches:-

1) Hypophysial arteries: further splits into anterior hypophysial ẃ supply hypothalmus & breaks into capillaries forming the hypophyseal portal veins ẃ convey hormones from hypothalamus into anterior pituitary. The posterior hypophysial artery supply neural lobe of the pituitary.

2) Ophthalmic artery: supply eyes, Para nasal sinuses & parts of nose.

3) Posterior communicating artery: runs backward to join the posterior cerebral A.

4) Anterior choroidal artery: supply choroid plexus of temporal horn of lateral ventricles, optic tract, uncus, hippocampus, & lateral geniculate nucleus.

Vertebral arteries: pass through cervical vertebrae, well protected, not accessible for surgical cleaning. The Circle of Willis (after English neuroanatomist Thomas Willis) is a confluence of vessels that gives rise to all major cerebral arteries. It shows many variations among individuals.

Etiologic Classification

Ischaemic stroke: accounts for 80-90% of cases, either embolic or thrombotic, the thrombotics include; Large vessel disease resulting from narrowing of cerebral arteries due to atherosclerosis or small vessel disease (lacunar infarct) or miscellaneous e.g. vasculitis resulting thrombus formation.

Haemorrhagic stroke: accounts for 10-20% of stroke cases, mainly associated é unrecognized or poorly controlled hypertension. Include primary IC Hge or SA Hge.

Classification based on stroke duration

Transient Ischemic attack: a stroke-like event lasting minutes, or hrs, that occurs when the brain is deprived of O_2 rich blood temporarily, but in ẃ the effects wear off completely after the blood-flow returns. Temporary disruption of blood flow to the brain-Like the unstable angina of the brain. TIA's do not result in permanent brain damage. Associated é focal neurologic deficit lasting **<**24 hrs confined to an area of brain perfused by specific artery. TIA is serious & too often ignored. TIA's should not be ignored as **>**1/3 of people will go on to have an actual stroke. 5% of strokes will occur within 1 month of the TIA or first stroke, 12% will occur within 1 year, 20% will occur within 2 years & 25% will occur within 3 yrs.

Reversible ischemic neurologic deficit: sudden onset of focal neurologic deficit ẃ lasts for **>**24 hrs, but these deficits recovers.

Stroke in evolution: focal neurologic deficit, the degree of ẃ is progressing over a couple of hrs or days.

Complete stroke: focal neurologic deficit, in ẃ the deficit neither improves nor gets worse over time. Often associated é infarction of part of the brain.

Epidemiology & Risk factor

Stroke is prevalent all over the worldwide. It is the 3rd commonest cause of death in developed world following CHD & cancer. It is a leading cause of disability. The prevalence & incidence of stroke is also on the rise in developing countries. The incidence is higher in men & old age. Man **>**45 yrs & woman **>**55 yrs of age?. Hypertension is the most common cause of ICHge, AF is important factor for recurrence, other causes includes; MI, CHF, asymptomatic carotid stenosis, hyperlipidaemia, smoking or exposure to tobacco?, DM, sickle cell disease, postmenopausal hormonal treatment, obesity, family history of stroke?, physical activity **<** a total of 30 min on most days ?

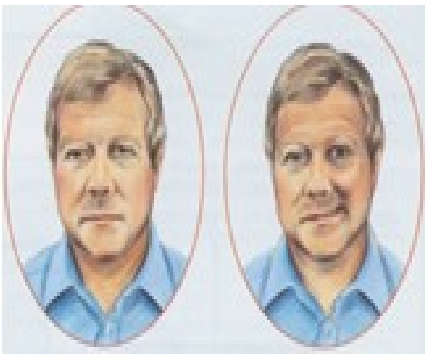
Signs & symptoms

Haemorrhagic stroke: sudden &dramatic: violent explosive headache, can present like a migraine headache, "pt usually say; worst headache of my life". Visual disturbance, sudden trouble seeing in one or both eyes, flashing of lights, aura, sensitivity to light. Nausea & vomiting. Neck & back pain due to blood in subarachnoid space. Weakness on one side, sudden trouble of walking, dizziness, loss of balance or coordi nation.

Ischemic stroke: harder to detect. sudden confusion, trouble speaking or understanding. Sudden trouble seeing in one or both eyes. Sudden numbness or weakness, of face, arm, or leg, especially on side of the body. Sudden trouble walking, dizziness, loss of balance or coordination & facial drooping.

Approach to a pt. é stroke

"fast" assessment": Face . Arm. Speech. Time of onset.



Face: look for facial drop, ask pt to smile or show his/her teeth (normally both si-des of face move equally & it is abnormal if one side of pt`s face droops.

Arms: motor weakness: look for arm drift by asking the pt to close eyes & lift arms (normally arms remain extended equally or drift downward equally & it is abnormal if one arm drifts down), also problem é gripping hands (NB: many elderly have arthritis in hands ẃ hurts to grip hands. May mimic weakness).

Speech: ask pt to say "You can't teach an old dog new tricks" (normally phrase repeated clearly & plainly but it is abnormal if the words slurred, contain lots of t's, k's &

c's, or abnormal or unable to speak, or unable to think of words, or inappropriate words. Expressive aphasia (unable to speak words- the area of brain where words are created is damaged). Receptive aphasia (unable to understand words -area where words are interpreted is damaged).

Time of onset: the window of opportunity to effectively treat stroke is 3 hrs, may be extended to 4½ hrs in some cases. Need to know "last known well". Is difficult when pt lives alone or woke up é the symptoms.

Characteristic features of different types of stroke

	Embolic	ICHge	Thrombosis	Lacunar infarct	SA He
Onset	Sudden. Max-imum deficit at onset	Sudden (deficit progresses over minutes to hrs)	Sudden, Gradu-al, step wise, or stuttering	Sudden, Gradual, Stepwise, or Stut-tering	Sudden, usually few or no focal signs
Time	Pt awake	Awake & active	Asleep, inactive	Asleep, inactive	Awake, active
TIA	None	None	Usually	May occur	None
Headac/Vomit	Sometimes	Usually	Sometimes	No	Stiff neck
CT scan	⇩ Density	⇧ Density	⇩ Density	Normal	Abnormal
LP	Clear	Bloody	Clear	Clear	Invariably

Differential diagnosis

•Unrecognized seizures. •Confusional states. •Syncope. •Toxic/ metabolic disease. •Hypoglycaemia. •Brain tumours. •Subdural hematoma.

Management

1) Assessment & maintenance of vital functions

Stroke should be considered as medical emergency, as it affects vital functions of an individual. For this reason the initial step in management of pt é acute stroke should be rapid assessment & maintenance of vital functions. This includes:-

a) Maintenance of air way & ventilation.

b) Control of BP: acute stroke alters auto-regulation of cerebral blood flow, comprom-

ising the blood supply to an already damaged brain. Close monitoring of BP & correction of both hypo or hypertension ⇩ this risk. If pt is hypertensive, treatment is recommend only if the DBP ≥ 120 & SBP ≥200 mmHg. Short acting antihypertensive are preferred. If pt is hypotensive, it should be corrected by fluid administration & treatment of the underlying cause for it.

c) Control of body temp.: fever occurs in 44% of pts é acute stroke. Fever may be due to stoke or infections. Because fever worsens the prognosis of stroke, body temperature should be controlled appropriately.

d) Fluid management: maintenance of euvolumic state, establishment of IV access using normal saline (rather than glucose sol.) is also important. Glucose is said to be neurotoxic & it is better avoided in pt é stroke. N.B.: exclude causes of brain dysfunction, ẃ mimic stroke like states like syncope, migraine, hysteria & trauma.

2) Determine presumptive diagnosis of stroke subtype

Numbers of clinical features are useful in determining the type of stroke. A good history taking & proper. physical examination may suggest the possible cause of stroke. Important historical information include the followings:-

Mode of onset & pattern of progression:- embolisms usually occur suddenly when the pt is awake, most often early in the morning, giving maximum deficit at onset. Haemorrhagic stokes also occur suddenly while pt is awake & may be physically active or straining & progresses within minutes to hrs. Thrombosis often occurs during the sleeping hrs or present upon arising from bed & progressing in a stepwise fashion.

Prior history of TIA: often associated é thrombotic (atherosclerotic).

Associated symptoms: headache, vomiting, reduced alertness suggest haemorrhagic stroke than ischemic stroke.

Very severe headache é altered consciousness éoutmajor neurologic deficit may sug-

gest SAHge. If pt having fever raises suspicion of infective endocarditis. Seizure is common in embolic stroke. Looking for other medical conditions/risk factors associated é stroke as ⇧ BP, DM, AF, CHF, MI, smoking, use of drugs like OCP may suggest the diagnosis.

Physical examination

May give clue to the type of stroke the pt. is suffering from. Absent or ⇩ peripheral pulses suggest atherosclerosis or embolism. Presence of neck bruit suggests extracranial occlusion of carotid A. Cardiac abnormalities as AF, murmurs or cardiac enlargement may suggest embolic stroke (embolus originating from the heart). Fever raises concern for infectious aetiologies. Ophthalmoscopic examination- papilloedema or retinal Hge may suggest SAHge or ⇧ ICP.

3) Confirmation of diagnosis

Different investigations are needed to confirm the diagnosis:-

Imaging studies (CT/MRI)

Are the most important initial diagnostic tests in pt é str-oke. CT can identify or excludes haemorrhagic stroke & other conditions ẃ simulate stroke (like neoplasm & abscesses). Detects acute SAHge in 95% of cases. Detects signs of ischemia as early as 2 hrs after stroke onset. Complete infarction usually seen after 24 hrs. The MRI is more sensitive than CT for early diagnosis of brain infarction.

Other tests

Lumbar puncture may needed for diagnosis of small SAHge ẃ may missed by CT/MRI.

Carotid doppler studies to look for carotid artery narrowing. Duplex sonar in neck vessels (if stenosis is **>** 80% or atheroma **>**I cm, surgical intervention is recommended (stent or end arterectomy).

CT scan or MR angiography to identify the exact location & the blocked artery.

ECHO cardiography to look for cardiac sources of embolization.

ECG: to look for arrhythmias such as AF.

CBC . ESR. VDRL .

Tests for HIV infection: stroke associated é vasculitis is common in HIV +ve pts.

FBS & Lipid profile to look for DM & hyperlipidaemia (risk factors for stroke).

Coagulation profile to look bleeding tendencies.

4) Management of specific stroke

Time is tissue. The longer the brain is éout O_2 & glucose the more the brain cells die. The goal of Rx is interruption of further brain damage & prevention & management of complication.

General measures: admit the pt where close follow up can be given. Continue follow up. Maintenance of vital functions: Airway & ventilation. Controlling of BP. Controlling of body temperat- ure. Fluid administration& hydration. If pt is comatose or has impaired mental status; changing the pt position every 2 hrs to avoid bed sores. Bladder/Bowel care; if pt has incontinence-catheterize. Infections as aspiration pneumonia should treated é antibiotics.

Atherosclerotic stroke (thrombotic)

i) Thrombolytic therapy: in developed countries thrombolytic therapy é medications such as rt-PA, within 3 hrs of onset of stroke, helps to lyse the thrombus & restore perfusion to the affected brain. Anticoagulants & fibrinolytic agents should be withheld until CT has R/O brain Hge. IV rt-PA represents the 1st FDA-approved Rx for ischemic stroke. Pt. treated é tPA within 3 hrs of onset of symptoms (the 3 hrs window) were at least 30% more likely to have minimal or no disability at 3 months compared é those treated é placebo. However, there were 10-fold ⇧ in the risk of fatal ICHge in the treated group (3% vs 0.3%) & frequency of all symptomatic Hge (6.4% vs 0.6%).

The use of fibrinolytic agents carries real risk of major bleeding. Whenever possible, the risks & potential benefits of tPA should be discussed é the pt & the pt's family before Rx is initiated. Use caution when treating people é severe stroke or early CT changes of recent major cerebral infarction (e.g. sulcal effacement, mass effect or edema) because these findings are associated é an ⇧ risk of Hge. rtPA is given IV at a dose of 0.9 mg/kg (maximum dose 90mg) is recommended if pt can be treated within 3 hrs of symptom onset & if BP can be lowered é antihypertensives to ˂185/110 mmHg. rtPA is appropriate in pt who have also suffered a seizure, provided residual symptoms are stroke related & not postictal. Recommended in eligible pt in the 3-4.5 hrs window. Eligibility criteria are similar to those for the 3 hrs window except for the exclusion of pt ˃80 yrs old, those on oral anticoagulants, those é a baseline NIHSS score ˃25, those é imaging evidence of ischemic damage to ˃1/3 of the middle cerebral artery territory & those é history of both stroke & DM. Physicians should be prepared to manage potential side effects as bleeding & angioedema. Streptokinase is not recommended for acute stroke, nor are other fibrinolytic or defibrinogenating agents. Contraindications for Thrombolytic therapy include:-

- Extensive infarct on CT. - Recent surgery. - Head trauma.
- GI or urinary Hge. - Bleeding disorders.
- Anticoagulation é prolonged PT/PT. - Seizure at stroke onset.
- Severe uncontrolled hypertension.

ii) Anticoagulants: use of heparin & warfarin is controversial. Low dose heparin can be given for prevention of thromboembolism.

iii) Antiplatelet aggregation agents: Aspirin ⇩ the incidence of stroke & vascular mortality. General recommendation is to give 325 mg of Aspirin daily. It may not help to resolve the already formed thrombus but prevents recurrence.

Embolic stroke (cardiogenic)

Anticoagulation is indicated to prevent recurrent embolic stroke. Heparin should be initiated when acute phase of stroke is over. Care should be taken to avoid haemorrhagic transformation of infarction. Warfarin used for chronic anticoagulation.

Intra Cranial Haemorrhage

Hge into the brain can be devastating condition, causing collapse or sudden development of a focal neurological deficit. Death may occur because of compression or distortion of vital, deep brain structures or ⇧ ICP. Optimal management relies on the prevention of continued Hge, appropriate Rx of ⇧ ICP. Continue supportive measures. Control very high BP. Surgical consultation for removing hematoma.

Sub Arachnoid Haemorrhage

(a) Supportive measures bed rest, sedatives, analgesic, laxative. (b) Control of BP. (c) Nimodipin (Ca Ch. Bls.) is given to prevent neurologic deterioration due to vasospasm. (d) Saccular aneurysms are treated surgically.

Prevention of further stroke

- Control of blood pressure. Control of blood sugar in diabetic pt. Cessation of smoking. Physical activity & Weight reduction.
- Anticoagulation for AF. ASA 75 mg PO daily in individuals >50 yrs é history of TIA.
- Surgery (endarterioactomy): if a narrowed carotid artery (> 80%) is detected by Doppler of neck veins.

Rehabilitation

To start early, include:-

- Physiotherapy.
- Occupational.
- Speech therapy.

COMA

Maintenance of conscious state requires proper functioning of cerebral hemispheres, reticular activating system found in brain stem & corticothalamic connections. If there is structural, metabolic or toxic insult to these structures, it results in alteration of conscious level of different levels.

Conscious state: awareness of self & surroundings require intact reticular active-ating system in brain stem & intact cerebral hemispheres & subcortical structures.

Coma: state of deep sleep like appearance, pt lies é the eyes closed, total absence of awareness of self & environment even é vigorous stimuli.

Stupor: sleep like unarousability, from ẃ the pt can awakened by vigorous stimuli.

Drowsiness: state of reduced consciousness characterized by easy arousal that can be maintained only for brief period of time. sleepiness & difficulty in remaining alert but easy arousal by stimuli. Persistence of alertness for a brief period (simulate light sleep). May caused by lack of sleep, medications, substance abuse, or cerebral disorders.

Confusion: person is uncertain about what to do or unable to understand something clearly.

Permanent Vegetative state: is a permanent condition that emerges after severe brain injury. Pt unawareness of self or external stimuli. The autonomic functions are relatively well maintained. Breathing, circulation & internal organ functions are intact & sleep-awake cycle exists & pt may be awake but he is totally unresponsive. No cognitive function (mental functions including thinking, feeling, sensing & intuition). Can`t localize pain, or follow verbal commands. BP & respiration maintained.

Pt can survive é medical & nursing support. Very slim chances that the individual might recover. Condition may last for yrs.

Brain death: is differ from coma & PVS. This is a state in ẃ there has been cessation of cerebral blood flow; as a result there is global loss of brain function. Complete lack of activity anywhere in the brain. Pt kept alive through artificial means, he is clinically & legally dead. Confirmatory EEG for legal purposes: isoelectric "flat line". Other tests: shine a light into eyes, corneal reflex, pain sensation, caloric tests, gag or cough reflex tested & removal from ventilator for short period to see if it stimulates respiration. Organs for transplantation if there is consent.

Causes

"Big 3" (STD); Stroke. Trauma. Drug Overdose.

Remember AEIOU-TIPS; •A Alcohol. •E Epilepsy/Exposure to heat or cold. •I Insulin (diabetic). •O Over dose/Oxygen deficiency. •U Uraemia (kidney failure). •T Trauma (shock or head injury). •I Infection/Iatrogenic. •P Psychogenic/Poisoning. •S Strokes.

(1) Diseases é no focal neurologic signs

No focal neurological signs, pupils are reactive & normal IC pressure. The loss of consciousness in such pt is diffuse bilateral hemispheric impairment, pt have normal brain stem function. Causes include:-

Metabolic disturbances: hepatic or uremic encephalopathy, diabetes emergencies, myxoedema, hyperthyroidism, hyponatremia, osmotic demyelination syndrome (central pontine myelinolysis) from rapid correction of hyponatremia, hypernatre- mia, hypocalcaemia, hyperkalaemia, hypoxia, hypercapnia.

Drug Overdose: Benzodiazepines, Barbiturates, Opioids, Antidepressant drugs.

Medication side effects: Reye`s syndrome & Aspirin poisoning.

Deficiency states: Thiamine -in alcoholics-, Niacin deficiency.

Intoxications: alcohol, sedative drugs, opiates, carbon monoxide poisoning, alcoholism, acetaminophen.

Severe infection: Septicaemia,Meningitis, Encephalitis,Cerebral Malaria or abscess.

Sever hypo or hyperthermia.

Hypertensive encephalopathy or eclampsia.

Status epilepticus.

(2) Diseases é focal neurologic signs

The focal neurological signs include, dilated pupils not reactive & ⇧ ICP. These disorders cause coma by affecting the RAS. They are classified into 2 depending on lesion location:-

1) Supratentorial (hemispheric) lesions: epidural or subdural hematoma. Large ischemic infarction. Intra-parenchymal Hge. Tumour or abscess or trauma.

2) Infra-tentorial lesions: as é pontine or cerebellar hematoma. Basilar artery thrombosis or ischemic cerebellar infarction or tumour or abscess. So this group incl- ude; head injuries, brain contusions, SAHge or ICHge, ischemic stroke, or in case of diffuse microvascular abnormality disease**:** as é TTP, cerebral malaria, rocky mo-ntain spotted fever, also é primary brain tumour or metastasis.

Pathophysiology

Either diffuse insult to both cerebral hemispheres or focal lesion in the RAS in the upper pons, mid brain or diencephalon.

Coma approach

Complete & rapid assessment is critical for optimal care, this include; History from third parties. Clinical examination: quick & precise Glasgow coma scale. Rapid & appropriate investigation to find cause & institute appropriate treatment.

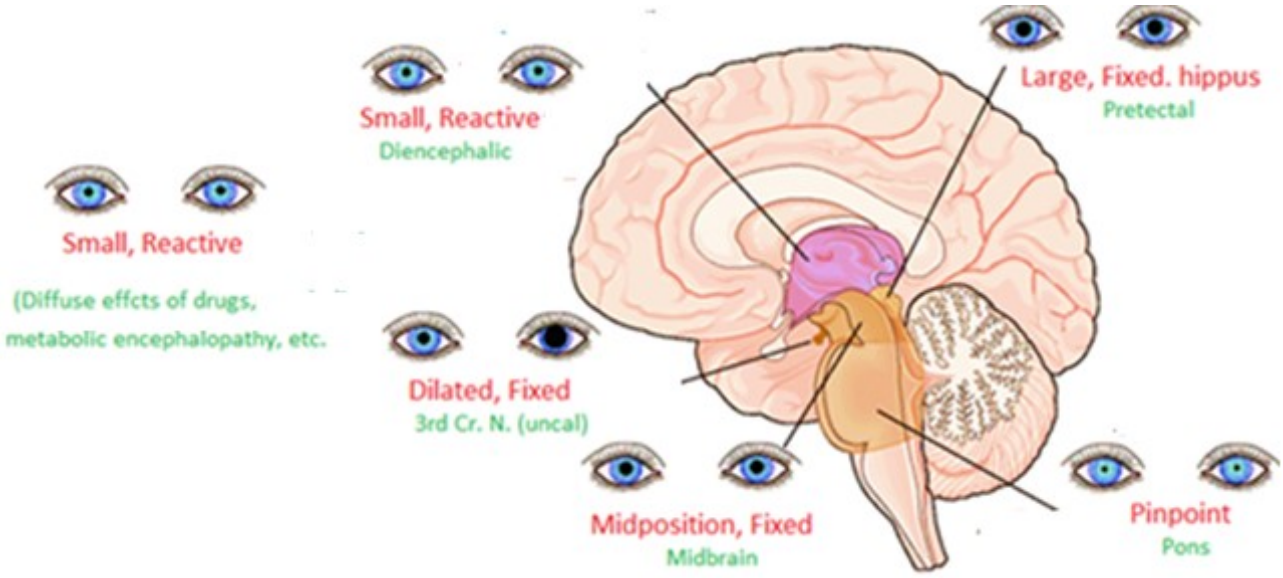
Glasgow coma scale

Eyes response	Verbal response	Motor response
4 Eyes opening spontaneously	5 Oriented	6 Obeys commands
3 Eyes opening to speech	4 Confused	5 Localizes to pain
2 Eyes opening in response to pain	3 Inappropriate words	4 Withdraw from pain
1 No eye opening	2 Incomprehensible sounds	3 Flexion as pain response
	1 None	2 Extension to pain 1 No motor response

Coma is classified according to –GCS- into:-

Severe: score 3-7, Moderate: score 8-12, Mild: score 13-15

Eye Movements

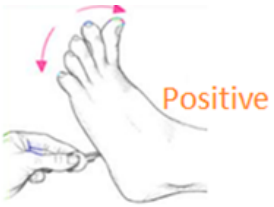


- Roving, slow, conjugate, lateral to & fro movements: metabolic encephalopathies or bilateral lesions above brainstem
- Ocular dipping: slow downward dipping followed by brisk return: diffuse cerebral damage.
- Skew deviation in horizontal plane: cerebellar or pontine lesion.
- Doll`s eye reflex: normally when the head is turned in a lateral plane the eyes move in the opposite direction. Absence of this response indicates brainstem lesion.
- Caloric testing: 40-60 mL of ice cold water in the ears will cause the eyes to move towards the irrigated ear. Absence indicates brainstem damage.

Signs of lateralization

Unequal pupils. Weakness one side of body, or one limb. +ve Babiniski sign.

Stroke lateral aspect of the sole using your thumb nail or sharp object. Normally, this elicts flexion of all toes, this considered - ve sign.



In +ve sign, the great toe dorsiflex & other toes fan out

Establishment of the cause

By taking careful history, doing rapid physical examination & investigations:-

•Past medical history**:** looking for disease like DM, hypertension, liver cirrhosis, CRD, malignancies. History of medications: legal or illicit drugs (sedative, hypnotic) & history of drug abuse.

•Circumstances & rapidity é ẃ change in mental status developed: sudden onset indicating vascular causes, gradual onset indicating metabolic or infectious causes, or fluctuations suggesting subdural hematoma.

•Recent pt complaints preceding loss of consciousness: medical & or neurologic symptoms: fever suggesting infections. Polyuria & polydipsia indicating DKA.

•Details regarding the site where the pt. was found (e.g. presence of empty drug vials or evidence of fall or trauma).

Physical examination

Vital signs**:** BP, pulse, temp., abnormal breathing pattern. Hypertension-suggest hypertensive encephalopathy. Fever-suggests systemic/CNS infections. Tachypnea suggest pulmonary infections or acidosis.

Head & neck examination: evidence of trauma, presence of meningismus.

General systemic exam: looking for evidences of systemic illnesses like liver cirrhosis, CRD, meningococcemia. Signs of trauma or injections (drug abuse).

Neurologic exam: is the corner stone of assessment of comatosed pt, it should be descriptive & systematic, including:-

Level of consciousness: GCS: points for GCS are given for best response in each category & are added •Severe coma: score 3-7 •Moderate coma: score 8-12 •Mild coma: score 13-15. NB: if pt trachealy intubated: best score is 10 & the worst is 2.

Brain stem reflexes: assessment of brainstem functions helps to localize the cause. Can be done using brain stem reflexes including; pupillary light response, ocular movements, corneal reflex & respiratory pattern.

Pupillary light response: pupillary reactions are examined é bright, diffuse light. During examination the size, shape, symmetry & reaction to light should be noted on both eyes.

- Normally reactive & round pupils of size (2.5-5 mm) exclude midbrain damage.
- Bilaterally small (1-2.5 mm) & reactive pupils are seen in metabolic encephalopathies or deep bilateral hemispherical lesions.
- Unilateral dilatation (>6 mm) & unreactive pupil signifies a compression or stretching of 3rd cranial nerve from effects of a mass above.
- Bilaterally dilatation of unreactive pupils, indicates severe midbrain damage, usually from compression by a mass, such as hydrocephalus or thalamic Hge.
- Pinpoint pupils (<1 mm) & reactive, characterize narcotic or barbiturate overdose but also occur é severe pontine Hge.

Ocular Movements: before manoeuvres, eyes are observed by elevating the lids & noting the resting position & spontaneous movements of eyeballs:-

- The lid tone tested by lifting the eyelids & noting their resistance to opening & the speed of closure& movement of eye balls. Resistance to opening eye lids may suggest hysteric conversion.

•Easy eyelid opening é slow closure indicates sever coma.

•Midline deviation of eye balls suggests frontal/pontine damage.

•Dysconiugate gaze (abduction or adduction) suggests cranial nerve lesions.

•Spontaneous eye movements roving, dipping, bobbing suggest damages being at different sites.

Occulocephalic reflex: elicited by moving the head from side to side while eyes held open; If eyeballs move to opposite direction of head movement, this indicate intact brainstem function (+ve Doll's eyes"). If eyeballs move to the same direction of head movement, this suggest brainstem dysfunction.

Occulovestibular reflex: test performed by irrigating the ear é cold water to stimulate the vestibular apparatus. In pt é intact brain stem the eyes move to the irrigated ear. No movement é brain stem damage.

Corneal reflex: this test assesses the integrity of dorsal midbrain & pontine. It is lost if the reflex connections between 5^{th} (aff) & 7^{th} (eff) cranial nerves within the pons are damaged.

Respiration: abnormalities of respiratory pattern can help in diagnosis but are of less localizing value in comparison to other brainstem signs:-

-Shallow, slow & regular breathing: suggests metabolic or drugs.

-Cheyne-Stokes: signifies Bi-hemispherical damage or metabolic suppression & commonly accompanies light coma.

-Rapid & deep (Kussmaul): usually implies metabolic acidosis, pontomesenephalic lesions & severe pneumonia.

-Agonal gasps: reflect bilateral lower brain stem damage, it indicate severe brain damage & near death state.

Motor function/response: Posture & Tone & Reflexes

-Quadriparesis/flaccidity: suggest pontine or medullary damage.

-Decorticate posturing: flexion of elbows & wrists é supination of arms & extension of legs, suggests severe bilateral or unilateral hemispheric or diencephalic lesion (damage above midbrain).

-Decerebrate posturing: extension of elbows & wrist é pronation of forearm & extension of legs, indicates damage to the brainstem (mid brain).

-Spontaneous activities: if the pt is yawning, swallowing, coughing or moaning the coma is not deep.

-Abnormal body movements: seizure, myoclonus may suggest status epilepticus, or uraemia.

-Assess tone, response to painful stimuli & presence of asterixes.

-Asymmetric motor responses have localizing value, associated é structural/surg-ical but not é metabolic or medical coma.

-The signs of lateralization include:- unequal pupils, weakness one side of body, weakness one limb, +ve Babiniski sign.

Differential diagnosis

Psychogenic coma: pt often has history of psychiatric illness. Resistance to having the eyelids opened (pt resists eye-lid opening when the examiner tries to open it). Failure of the pt's arm, when held by the examiner over the pt's face, to fall up on the face when released by the examiner. Nystagmus when the ear is irrigated é cold water. Adversive head & eye movements.

Diagnosis: history from third parties: history of acute/chronic liver disease, hepatitis C, Bilharziasis. Clinical examination: quick & precise (GCS). Rapid & appropriate investigation to find cause & institute appropriate treatment.

Investigations

- CBC & Biochemistry (Electrolytes, Sugar, LFTs, KFTs) & blood slides (for Malaria).
- ABGs: (O_2, Co_2, pH, HCo_3).
- Blood cultures.
- Drug screen & Toxicological analysis (urine, blood), alcohol levels.
- LP for CSF examination: should be done as soon as possible unless ⇧ ICP is suspected to exclude infections & SA Hge.
- MRIs where possible or CT Scans (in case of trauma, bleeds, Hge).
- U/S abdomen.
- Thyroid function tests (rarely).
- EEG, ECG & CXR

Management

Immediate management in hospital

- Never forget ABC: airway, breathing, circulation. Maintaining an adequate airway, optimal ventilation & adequate perfusion (BP).
- With the possibility of cervical fracture immobilization of neck is essential.
- ETT often indicated.
- Coma cocktail: 50 mL of 50% dextrose + thiamine 100 mg + Naloxone 0.4 mg (adults). IV fluids, 2 liters daily as glucose 5% 8 hourly & ringer lactate 24 hourly, no saline to pt é hepatic coma because of having secondary hyperaldosteronism ẃ lead to Na^+ & H_2O retention. This treatment is given if hypoglycaemia is even remote possibility & thiamine is given é glucose to avoid Wernicke disease in malnourished pt. Ryle tube for nasogastric tube feeding to be inserted.
- Fluid chart & urine catheter.
- Close monitoring.

In case of GIT Hge/or hepatic coma

Liver diseases are commonly seen in Egypt, either 2ry to viral hepatitis (C & B), or Bilharziasis. Anorexia, malaise, foeter hepaticas, right epigastric pain, gastro intestinal Hge, hematemesis, melena, hallucination, coma.

- NPO.
- Dicynone amp 250 mg, 2 amp 8 hourly (⇧ resistance of capillary wall).
- Konakion amp 10 mg (for formation of Vit K dependent factors), 2 amp 8 hourly.
- CyKlokapron amp 500 mg, 2 amp 12 hourly as infusion or slowly IV (inhibit conversion of plasmonigen into plasmin).
- Antibiotic (not excreted through liver); Claforan 1 gm/12 hrs.
- Rectal enema 6 hourly, using 1000 ml warm H_2O + 5 measures of Lactulose, or 4 tab Neomycin, alternatively.
- Vit B_x, Neurobion amp IM every 2 days.
- Liver support, Hepamarin tab. 1X3, or hepamerz amp IV daily.
- Brain support; Nootropil 1000 mg IV.

Specific management

Further Rx depends on the cause always. Manage the primary cause of coma, e.g. Stroke. Seizures. Diabetic coma. Myxoedamtous coma. Uremic coma. Meningitis, Electrolyte imbalances. Trauma; neurosurgery. Raised ICP. Each of them discussed separately in the book.

Long-term Management

- Intensive nursing care.
- Vital & Neurological signs monitoring.
- Recovery position
- Mechanical ventilation.
- Pressure sores prevention.
- Care of the eyes.
- Airway clearance by bronchial toilet.
- Fluid & Nutrition management.
- Catheterization of bladder.
- Bowel care ± disposable diapers.
- Physiotherapy to protect muscles & joints.
- Deep venous thrombosis prophylaxis (see alphabetical index).

Prognosis

Criteria for prognosis

⊙ Depth of coma as by GCS. ⊙ Pupillary reflexes.

⊙ Eye movements. ⊙ Motor responses. ⊙ Age.

Worst prognosis

- Structural damage.
- SA Hge.
- Cerebrovascular causes.
- No corneal reflex.
- No pupillary reflex.
- Decerebrate posture.

Good Prognosis: metabolic causes.

FAINTING ATTACK

Fainting attack (syncope) in Greek; syncope = cut off. Syncope is a symptom & not a diagnosis, its sudden brief loss of consciousness associated é loss of postural tone, from ẃ recovery is spontaneous. The underlying mechanism of syncope is sudden global hypo perfusion of cerebral cortices or focal hypo perfusion of RAS in mid brain.

Incidence

Seen in 15% of individuals **<**8 yrs & 20% of individuals 40-59 yrs & 25% of individuals **>**70 yrs. Fainting attack represent 6% of hospital admission.

Causes

- ***Neurally mediated:*** in 60% of cases.

Vasovagal attack: when the body over react to triggers as fear, sudden anxiety, stress, unpleasant sight, unpleasant experience, hearing unpleasant news, excitement, trauma, painful stimuli, hunger, dehydration, lack of sleep, standing for long periods, seeing or exposure to medical procedures as venepuncture, injection of medicine, lumbar puncture, pleural or ascetic tap, digital rectal disimpaction, rectal enema, exposure to high temperature, seeing blood, pressing upon certain pla-ces in the throat, sinuses & eyes (also known as vagal reflex), severe menstrual cramps, violent coughing as a result of sudden rise of intrathoracic pressure ẃ cause ⇩ in venous return to the heart, ⇩ in COP & BP, or during micturition or defecation. The vasovagal attack result from corresponding

malfunction in the parts of the nervous system that regulate HR & BP, activation of

nucleus tractues solitarii of brainstem (vagus nerve) enhance the parasympathetic (vagal) tone & withdrawal of sympathetic tone causing cardio inhibitory response characterized by a drop of HR (-ve chronotropic effect) & in contractility (-ve inotroopic) & vasodepressor effect resulting in vasodilatation & hypotension.

Carotid sinus hypersensitivity: changes in carotid sinus pressure as a result of digital pressure, or tight collar

- **Orthostatic:** 15% of cases. In some people while suddenly standing up, commonly in elderly people due to impaired autonomic functions & in cases of Addison`s disease & on people on hypotensive drugs like Levodopa, Phenothiazine. Vertebrobasilar artery insufficiency when blood supply to brain is affected by sudden movement of neck.
- **Cardiac arrhythmia:** 10% of cases. Sinus bradycardia. Supraventricular/Ventricular tachycardia. Atrioventricular block. Long Q-T syndrome.
- **Structural:** 5% of cases. AS/Aortic dissection. Acute myocardial ischemia. Hypertrophic myopathy. Pulmonary hypertension.
- ***Psychatric:*** commoner in young females; Hysterical or Panic attack or Generalized anxiety disease. Major depression. Hyperventilation syndrome.
- ***Unexplained:*** in 10%.

Clinical picture

1) Prodromal phase: of tingling/numbness in limbs, light headache, nausea, sweating, sudden darkness before eyes.

2) Sudden loss of consciousness: lasts hardly for ›2 min, pt is cold, sweaty é slow pulse, sighing respiration, sluggish reaction of pupils, diminished deep reflexes & may fall to the ground, sometimes pt may show convulsive movements though it is not a typical epileptic attack.

3) Rapid recovery: pt regains consciousness shortly, complain of exhaustion & weak

ness. ***The clinical examination may not be helpful unless there is CVD, as cardiac murmur or arrhythmia, cyanosis, or ⇩ carotid pulse.***

Diagnosis

- History & physical examination.
- Orthostatic BP: diagnostic, ⇩ in the SBP by ≥ 20 mmHg.
- ECG: to look for arrhythmia, prolonged Q-T interval, AV Block, sinus bradycardia (< 50 bpm), SVT, IHD, hypertrophic cardiomyopathy.
- Exercise test ECG: for those é unexplained syncope or those é syncope during or shortly after exercise.
- ECHO/Doppler: is diagnostic for AS, aortic dissection, hypertrophic cardiomyopathy, CHD, also to determine the EF for CHF.
- Carotid sinus massage: is diagnostic for carotid sinus syndrome, start carotid massage on the right side for 5-10 sec, wait for 2 min & repeat in the left side é monitoring pulse & BP. It is contraindicated in pt é CVA, or recent AMI. Drugs causing syncope: Nitrates, Antihypertensives, Antiarrhytmics, Psychotherapy drugs, Hypoglycaemic agents, Illicit drugs.

Tilt test

Very useful in confirming diagnosis. vasovagal syncope. Pt is supine in the pre- tilt

phase & then placed at 60-70 degrees for 20-45 min. if no event is reproduced & vital signs remains normal, then testing is replaced é pharmacologic provocation, the most common protocol is infusion of Isoprenaline or sublingual Nitroglycerine, test considered +ve if the pt has a symptomatic ⇩ BP or ⇩ HR.

Management

Based upon the underlying cause of syncope. In simple vasovagal attack, pt is advised to avoid ppt factors as long period of standing, starvation, dehydration, heat exposure or alcohol intake, to avoid exciting situations, to ⇧ his fluid & salt intake. If pt feel like he might faint, to lie down & left his legs above level of heart, this allows gravity to keep flowing to the brain, if he can`t lie down to set down & to put his head between his knees until he feel better.

SEIZURE & EPILEPSY

Seizure: is a paroxysmal event due to abnormal excessive discharge of cerebral neurons. The paroxysmal event may be subtle or dramatic. Depending on the distribution of the discharge, manifestations may be; motor, sensory, autonomic, or psychiatric manifestation.

Epilepsy: is a syndrome characterized by recurrent (two or more) unprovoked seizure attacks, due to a chronic, underlying process in the brain. This definition implies that a person é a single seizure, or recurrent seizures due to correctable or avoidable circumstances, does not necessarily have epilepsy.

Classification

Epileptic seizures can be classified in many different ways. Commonly used classification is developed by International League against epilepsy:

(1) Partial seizures

a- Simple partial seizure é motor, somatosensory, or psychiatric symptoms.

b- Complex partial seizure.

c- Partial seizure é secondarily generalization.

(2) Generalized seizures

a. Absence seizure (petit mal).

b. Tonic-colonic seizure (grand mal).

c. Myoclonic seizure. d. Colonic seizure.

(3) Unclassified seizures

a) Neonatal seizure.

b) Infantile spasm

The basis for this classification is manifestations during seizure attack & the EEG features between attacks. It is useful in understanding the underlying aetiology,

selecting appropriate Rx & understanding the prognosis of seizure type.

Epidemiology

Epilepsy affect 0.5-4% of population around the world. The prevalence is said to be higher in developing countries. Grand mal seizure account for 40-80% of epileptic seizures. It is estimated that 5-10% of the population will have at least one seizure attack in their life time, é highest incidence occurring in early childhood & late adulthood.

Aetiology/Risk factor

Causes of epilepsy/seizure are vary greatly in different age groups & across different regions of the world:-

- ***Idiopathic or cryptogenic:*** unknown cause, in majority of cases.
- ***Genetic factor:***+ve family history.
- ***Perinatal causes:*** perinatal asphyxia or infection, birth trauma.
- ***CNS infections:*** encephalitis, toxoplasmosis, cerebral malaria.
- ***Head trauma:*** penetrating head injury, depressed skull fracture, ICHge & prolonged post traumatic coma (⇧ the risk of seizures).
- ***Neoplasms:*** metastatic or primary brain tumour.
- ***Vascular causes:*** infarction, stroke or vascular malformations.
- ***Metabolic:*** hyponatraemia, hyo or hyperglycaemia, uraemia.
- ***Inflammatory causes:*** SLE.
- ***Degenerative diseases:*** Alzheimer disease.
- ***Drugs:*** Theophylline, Cocaine, Lidocaine.

Clinical features

(1) Partial Seizures

(a) Simple partial/focal seizures: these are seizure activities in ẃ consciousness not

impaired. Manifestation can be motor, sensory, autonomic or psychiatric. Motor manifestation is usually focal colonic or tonic movement of angle of mouth, finger or thumbs. This seizure activity may spread over one side of the body to involve larger body parts (e.g. the convulsive activity can start in the face, move to ipsilateral arm then to the leg). The rest of manifestations include transient sensory abnormalities, flushing & sweating or odd feelings.

(b)Complex partial seizure: these are focal seizure activities accompanied by impairment of the pt ability to maintain normal contact é the environment. Pt is unable to respond appropriately to visual or verbal commands during the seizure attack & has impaired recollection or awareness of ictal phase. The seizure frequently begins é aura, ẃ may manifest é hallucination (e.g. olfactory, visual, auditory or gustatory) & complex illusions (e.g. having experienced a new event). The start of the ictal phase is often a sudden behavioural arrest or motionless stare, ẃ is often accom panied by automatism, ẃ is involuntary automatic behaviour (repeated complex activities like chewing, lip smoking, "picking movement" of the hands & display of emotions). They have also postictal confusion & transition to full recovery may take minutes to hrs.

(c) Partial seizure é secondary generalization: these are focal seizure ẃ evolves into generalized seizure. Usually of tonic-colonic type, difficult to differentiate from 1ry generalized tonic-colonic seizures.

(2) Generalized seizures

These are seizure disorders ẃ arise from both cerebral hemispheres simultaneously éout any detectable focal onset.

(a) Absence seizure: characterized by sudden & brief lapses of consciousness éout loss of postural control. The seizure typically lasts for few seconds, consciousness returns as sudden as it was lost. Usually manifest é blank staring, may have also subtle

motor manifestations as blinking of eyes, chewing movements. No postictal confusion. Seizures may occur as many as hundreds of times/day. Usually detected by unexplained day dreaming & decline in school performance. Usually begins in childhood (4-8 yrs) & often has a good prognosis, 70% of pts develop spontaneous remission during adolescence.

(b) Generalized tonic colonic seizures (Grand mal): the most common seizure type. Usually begins abruptly éout warning (no aura or focal manifestations) include:- The ictal phase is begins é tonic contraction of muscles throughout the body, ẃ is responsible for loud moan/cry (due to tonic contraction of muscles of respiration & larynx), tonic posturing, impaired respiration & pt falls to the ground. There may be tongue biting due to tonic contraction of the jaw muscles. After 10-20 sec. the tonic phase evolves to colonic phase characterized by bilateral jerking colonic movement involving the whole body ẃ lasts for 1 min. The postictal phase characterized by unresponsiveness, muscle flaccidity, excessive salivation & frothing of saliva ẃ may cause stridorous breathing & partial airway obstruction. Bladder or bowel incontinence may occur. Pt gradually regain consciousness over minutes to hrs & during this transition there is typically a period of postictal confusion, headache, muscle ache & fatigue that can last for many hrs.

(c) Atonic seizures: sudden loss of postural muscle tone, lasting 1-2 sec. Consciousness is briefly impaired. It usually manifest as a head drop or nodding movement, while a longer seizures may cause the pt to collapse.

(d) Myoclonic seizures: sudden & brief muscle contraction involve one part of the body or the entire body. Sudden jerking movement observed while falling asleep. Commonly seen é metabolic disorders, degenerative or anoxic brain injury.

Complications

•Status epilepticus. •Accidents. •Hypoxic brain damage. •MR & Impairment of intellectual functions. •Sudden death. •Psychosocial (social stigma).

Diagnostic approach/evaluation

Pt's history & physical examination can aid in the determination of whether or not a seizure or some other transient event was responsible for the pt's symptoms.

History of the event; presence of any prodromal symptoms, description of seizure by reliable observer. Postictal symptoms. Urinary incontinence, myalgia, tongue bit/oral lacerations.

History of suggesting cause &risk factors; febrile convulsion (H/O of high fever), CNS infections (current/previous), head injury, stroke, developmental abnormality, family history, alcohol abuse.

Physical examination

Complete neurological examination. Look for; skin for evidence of neurofibromatosis, organomegally (metabolic storage diseases), & CVS/carotid artery.

Investigations

EEG: the most useful test for diagnosis. Should be performed while the pt is asleep & awake. Abnormal EEG supports the diagnosis of seizure & may give information about its type. However normal EEG can be found in epileptics.

MRI: may help to see any space occupying lesion in the brain.

Laboratory assessment: may be required including; CBC, urine analysis, BG, liver & renal function tests, electrolytes & toxicological screening.

Differential Diagnosis

- Syncope. • TIA. • Migraine.
- Psychogenic seizure (hysterical).

Management

Goal of therapy: complete control of seizure, prevention of development of complications & socioeconomic consequences.

Treatment of underlying condition

•Metabolic disorders such as hypoglycaemia, hyponatremia or drug intoxication should be corrected.

•Structural CNS lesion like tumours may be removed surgically.

Avoidance of ppt factors

•Maintain normal sleep schedule •Avoid taking excess alcohol •Reduce stresses using; physical exercise, meditation, & counselling.

Suppression or control of recurrent seizure

The goal of antiepileptic therapy is to achieve complete control of seizure é no or minimal side effects, preferably using single agent & easy dosing schedule.

When do we start antiepileptic drugs?

Used é recurrent seizures of known or unk-nown cause & can`t reversed or é single seizure due to; identified CNS lesion (tumour, infection, trauma), or pt é abnormal neurological examination, or pt. presenting as status epilepticus, postictal todd's paralysis, or pt é strong family history of seizure disorder, or pt é abnormal EEG. The anticonvulsant therapy not often initiated in pts é single unprovoked convulsion é normal neurologic examination, normal neuroimaging study & EEG unless they experience a secondary seizure.

General principles

Attempt usually made to prevent subsequent seizure using a single agent, in order to limit side effects. The drugs should be administered in a progressive dose until seizure control has been achieved or until drug toxicity occurs. Only if monothera-

py fails should a second drug be added to the pt regimen. If control is achieved, then the first agent might be carefully withdrawn. A number of drugs are available for treatment of epilepsy & the choice is based on the seizure type.

Selection of antiepileptic drugs

	Tonic-Colonic Seizures	Partial Seizures	Absence Seizures	Atypical. Absence. Myoclonic. Atonic Seizures
1st Line	Valproic acid Lamotrigine	Carbamazepine Phenytoin Valproic acid	Valproic acid Ethusuximid	Valproic acid
2nd Line	Phenytoin Carbamazepine Phenobarb	Topiramate Phenobarb	Lamotrigin Clonazepam	Lamotrigin Clonazepam Topiramate

i) Phenobarbitone: in developing countries, it is the drug of choice for the control of partial & GTC seizures, due to the wide availability & cheaper cost of the drug. Its efficacy is quite acceptable in comparison to most of the AEDs but it has some side effects that might interfere é compliance. These side effects have to be explained to the pt & his family. This drug is available in the following dosage forms; 15, 30, 60 & 1500 mg tab. The usual starting dose for adults is 60 mg PO daily. If seizure is not controlled the dosage may be ⇧ gradually at intervals of not less than 2wks to a maximum dose of 200mg PO BID. The common side effects of phe-nobarbitone ne are; fatigue, listlessness, depression, insomnia (especially in childr- en), distractibility, short attention span (especially in children), hyperkinesia, irrita- bility, poor memory & ⇩ libido. In cases of RX failure or poor control é maximum tolerable doses of drug, a second AEDT often added to the regimen. Addition of a second drug is associated é worsening of adverse effects; hence care should be taken, before adding second drug.

ii) Phenytoin: usually prescribed as a second line drug in resource limited settings. 100 mg PO BID or TID ẃ may be gradually ⇧ to a maximum of 200 mg PO TID (i.e. 600 mg daily). Side effects include; nystagmus, ataxia, gingival hyperplasia, coarse-

ning of facial feature, & toxic hepatitis & liver damage.

iii) Carbamazepine: often given for Rx of partial seizure, as a low initial dose is advised, 200 mg PO BID & gradually ⇧ the dosage by 200 mg every week until the best response is achieved or maximum dose of 1600 mg/day. Side effects include; aplastic anaemia, dizziness, drowsiness, skin rash & transient diplopia.

When to stop antiepileptic drugs?

It is common practice to continue Rx until the pt has been seizure free for at least 3 yrs. Thereafter, consideration of drug withdrawal is based on the following:-

- The ease é ẃ control was achieved starting from time of AED initiation.
- The type of seizure.
- The presence of other neurological comorbidity e.g. MR or focal neurological deficit.

The probability of relapse after stopping Rx is somewhere around 10-40%. It is not known whether remissions for 3 or more yrs consist of "cure" or "control" & so drug withdrawals have to be gradual, over a period of months to minimize the risks of relapse. Most relapses occur within a year of discontinuing medications. The more severe & long lasting a pt's active epilepsy before remission, the greater the risk of relapse.

When to refer pt. to a Neurologist?

Failure to respond to drugs, or development of side effects of it, or recurrence of previously controlled seizure, or occurrence of changes in the pattern of seizure, or é appearance of previously absent symptoms.

Managing psychosocial issues

- Social stigma: health education to avoid misconceptions in the public.
- Psychiatric problems: depression, psychosis, anxiety should treated.
- Social problems: encourage pt to go school/work, to marry & establish family.
- Educate pts & families about the disease & precautions pt should take.

•Advice pt to avoid alcohol & drugs, advice to avoid heights, to avoid cooking é open fire, or machineries, to avoid swimming/diving.

What should families or attendants do during active seizure?

No traditional Rx is beneficial, to be calm, turn head to side, loosen pt's clothing, Keep from injury, do not insert anything into mouth.

STATUS EPILEPTICUS

Medical emergency, characterized by continuous or repetitive discrete seizures é impairment of consciousness during interictal period ẃ lasts for 〉30 minutes.

Causes or precipitating factors

•Non-compliance é AEDs.

•Refractory epilepsy.

•CNS infections.

•Metabolic derangement.

•Tumours.

•Trauma.

•Stroke.

Clinical features

Generalized status epilepticus is obvious when the pt is having over convulsion, however after 30-35 min of uninterrupted seizure, the signs may become increasingly subtle. Pt may have mild colonic movement of only the fingers, or fine, rapid movement of eyes.

Complications

•Aspiration. •Hypoxia. •Metabolic acidosis. •Hypotension. •Hyperthermia. •Rhabdomyolysis & associated myoglobinuria. •Multiple physical injures including vertebral bone fracture, irreversible neuronal injury.

Management

1. Emergency supportive measures: Keep airway patent & maintain breathing. Se cure IV line & take blood for laboratory investigation. Give glucose IV é thiamine.

2. Control the seizure

1st step: Lorazepam 0.1 mg/kg IV 2 mg/min. or Diazepam.

2nd step: if seizure continues, Phenytoin 20 mg/kg IV, 50 mg/min.

3rd step: if seizure continues, Phenobarbital 20 mg/kg IV 50 mg/min.

4th step: if seizure continues, general anaesthesia é Medazolam, Propofol or Phenobarbital, if seizure becomes refractory in resource limited setting Diazepam 5-1500 mg IV is given 2-3 times & if the seizure is not controlled Phenytoin 1000 mg PO is given through NG tube. Phenobarb can also be used.

3. Treat precipitating cause: metabolic abnormalities/infections.

4. Give maintenance antiepileptic drug: after condition controlled.

PARKINSONISM

Clinical syndrome characterized by:- Resting tremors, Bradykinesia, & Rigidity.

Aetiologies

1. Parkinson's diseases is sporadic & idiopathic é unknown aetiology. Is the commonest cause of parkinsonism, 75% of all cases?. Characterized by degeneration of cells in substantia nigra, ẃ causes deficiency of dopamine (neurotransmitter) in CNS, leading to a series of changes in motor control pathways. These changes are believed to be due to accumulation of the presynaptic protein α-synuclien.

2. Other known causes: account for 25 % of all cases include:-

a) Familial (primary Parkinson's diseases).

b) Other neurodegenerative diseases:- Shy-Drager sy., motor neuron disease é PD features, dementia é Lewy bodies, progressive supranuclear palsy, Wilson's disease

& Huntington's disease.

c) Miscellaneous acquired conditions include:- •Vascular parkinsonism (stroke affecting extrapyramidal structure). •Normal pressure hydrocephalus. •Cerebral palsy. •Repeated trauma: "dementia pugilistic" é Parkisonian features (e.g. seen in professional boxers like Mohamed Ali). •Infectious: post encephalitis, neurosyphilis .•Hypothyroidism/pseudo-hypoparathyroidism. •Drugs: as neuroleptics; antipsychotics as Haloperidol or Chlorpromazine. Methyldopa, Valproic Acid, antiemetics as Metoclopramide. •Toxins: as Cyanide, Methanol, Carbon Monoxide.

Epidemiology

PD affect >1 million people in US (of those >55 yrs). In Egypt no statistics available. The peak age of onset is the 60s (range is 35-85 yrs). Familial PD tend to have an earlier age of onset (< of 50 yrs).

Risk factors for Parkinsonism

- Positive family history.
- Male gender.
- Head injury.
- Exposure to pesticides.
- Consumption of well water.
- Rural living.

Clinical Features

Diagnosis of PD can made é some confidence in pt who present é at least 2 of the following 3 cardinal signs:-

1. Resting tremor: in 85% of pt é true PD, the diagnosis of PD is difficult when tremor is absent. Tremors starts unilaterally &has gradual onset, affecting 1st distally involving the digits & wrist where it may present é "pill-rolling" character. Usually spreads

proximally, ipsilaterally & to the leg, before crossing to other side after a year or two. May appear later in the lips, tongue, jaw but spears the head.

2. Bradykinesia/akinesia: is the most disabling feature ẃ interferes é all aspects of daily living. Pt have trouble in walking, rising from seated position, turning over in bed, dressing etc. Fine motor movement is also impaired as evidenced by ⇩ manual dexterity & hand writing (micrographia). Soft speech (hypophonia) is the other form of bradykinesia. Masked face & ⇩ eye blinking.

3. Rigidity: felt as a uniform resistance to a passive movement about a joint throughout the full range of motion. Brief regular interruption of resistance during passive movement "cogwheels rigidity".

Gait disturbance: pt have shuffling short steps.

Festinating gait: typical feature of parkinsonism, result from combination of flex- ed posture & loss of postural reflex, ẃ causes the pt to accelerate in an effort to catch up é the body's centre of gravity.

Freezing of gait: feature of more advanced PD, occurs commonly at the onset of locomotion, when attempting to change direction to turn around & upon entering narrow space such as a doorway. Abnormalities of balance & posturing tends to ⇧ as the disease progress.

Stooped posture: flexion of the head, stooping, tilting of upper trunk & tendency to hold the arm in flexed posture while waking is common. In advanced disease postural instability may lead to frequent falls & injuries.

Non motor features include

Loss of sense of smell (anosmia).

Sleep disorders: are common, may manifest as day time drowsiness, frequent napping, disrupted sleep & difficulty of turning over in bed.

Autonomic dysfunction: may manifest é orthostatic hypotension, constipation, urinary urgency & frequency & excessive sweating.

Neuropsychiatric system: depression in 50% of pts. Anxiety disorders.

Cognitive abnormalities: affect many pts & it may manifest é difficulty of doing complex tasks, long term planning, memorizing or retrieving new information.

Dementia is 6 X more common than their age matched controls.

Psychotic symptoms: affect 6-40% of pts, visual hallucination are common, depression & dementia are risk factors for developing psychotic symptoms.

Treatment

The goal of therapy is to maintain function & quality of life &to avoid drug induced complications. PD is progressive disease, therefore the Rx protocols vary depending on pt`s symptoms & extent of functional impairment.

Pharmacotherapy for motor symptoms

Initiated as soon as the pt's symptoms begin to interfere é the quality of life.

(a) Selegilline: is selective & irreversible monoaminoxide inhibitor, it slow the clinical progression of PD & delay the need for other medication. Used as initial Rx or added to alleviate tremor of Carbidopa/Levodopa associated wearing effect. 45 mg PO X 2.

(b) Dopamine agonists: have direct post synaptic effect on dopamine receptors. Dopamine agonist monotherpay is well tolerated & significantly ⇩ the risk of later treatment-related complications as motor fluctuation & dyskinesia associated é Levodopa/Carbidopa.

(3)Non Ergot alkaloids: o***Rupinirole:*** initial dose 0.25 mg PO TID to maximum target dose as monotherapy is 12-45 mg/day. o***Parmipexole:*** initial dose 0.125 mg PO TID maximum target dose as monotherapy is 1.5-4.5mg/day.

(4) Ergot alkaloids: o***Pergolide:*** initial dose 0.05mg PO TID to maximum target dose

1.5-6 mg/day o***Bromocriptine***: the initial dose 1.25mg PO BID or TID to maximum target dose as monotherapy 7.5-15mg/day. When dopamine agonists used as mono-therapy, higher doses are required to control symptom. However the dose should be titrated gradually. Most pts require the addition of Levodopa or another agent, within 1-3 yrs of initiating Bromocriptine. Older pts & those é akinetic rigidity have low risk of motor complications & dyskinesia & may be satisfactorily treated é Levodopa.

Advanced therapy

Levodopa/Carbidopa formulation (Sinemet®, Atamet®)

****Levodopa***: is converted to dopamine by presynaptic neuron & therefore ⇧ the amount of neurotransmitter available to the postsynaptic dopamine receptor.

****Carbidopa:*** blocks conversion of Levodopa to dopamine, thereby ⇩ the undesirable systemic effects of Levodopa such as nausea & orthostatic hypotension.

****Carbidopa/levodopa*** **IR** 25/100 mg initial dose: ½ tab PO TID, to maximum target dose of 1-2 tab PO TID.

****Carbidopa/levodopa*** **CR** 50/200 mg, 1 tab BID or TID, the dosage of these drugs should be escalated gradually.

Wearing-off effects: management becomes increasingly difficult as the disease pr-ogresses. Late treatment related complications include; dyskinesia***:*** refers to ch-orieform & dystonic movements that occur as a peak dose effect or at the beginni- ng or end of the dose. Motor fluctuation: (on & off) these are wide random swings in the pt's mobility experienced by many pts between doses of antiparkinson medication. >50% of pts treated é Levodopa for >5 yrs develop these complications.

Levodopa Augmentation

i) Catechol O- Methy Transferase (COMT) inhibitors: **Estacapone & Tolcapone:** offer augmentation of the effect of Levodopa by blocking enzymatic degradation of Levod-

opa & Dopamine. These drugs are used in conjunction é Carbidopa/Levodopa, they alleviate the wearing off symptoms.

ii) Anticholinergics **"Bezhexol"**: is given as adjuncts to dopamine mimetic therapy, useful in controlling resting tremor & dystonia.

iii) Amantadine: has anticholinergic & dopamine mimetic properties, helps to reduce drug induced dyskinesia, can be effective early in the course of the diseases.

Neuro-protective therapy

Reducing the progression of PD through neuro-protective or restorative therapy, is a major focus of research. Some of the neuro-protective therapy trails are:-

- ***NSAIDs.***
- ***Oestrogens replacement therapy*** in post-menopausal women.
- ***Selegilline therapy*** delays the need for Levodopa therapy by 9-12 months in newly diagnosed pts. Studies demonstrated that pts who remain on Selegilline for 7 yrs experienced slower motor decline.

Therapy of non-motor symptoms

Insomnia due to nocturnal akinesia: treated é night time supplemental dose of Carbidopa/Levodopa.

Depression: responds to antidepressants like Amitriptyline.

Psychotic pt*:* first remove Anticholinergics & Amantadine if the pt is taking. ⇩ The dose of dopaminomimetic if pt is not responding. If still the pt has psychotic symptoms & signs, start antipsychotics é minimal extrapyramidal side effects.

Dietary manipulation

limiting protein intake during the day may improve Levodopa's efficacy.

Physical Rx: Exercise program help to optimize mobility.

Surgical Rx: Pallidotomy & thelamothomy may be Rx option for refractory PD.

Tremor

Benign Essential Tremor: characterized by posture related 5-9 Hz oc-illation of hands & forearms, impairing performance of fine motor tasks. This type of tremor is familial, may be accompanied by titubation (head tremor/bobbing). Consumption of alcohol may temporarily suppress the tremor. Stress, caffeine or sleep deprivation may exac-erbate tremors. β- blockers are effective in controlling tremor.

An Action (kinetic) Tremor: is evident when the pt. moves his or her arms; there may be a relatively mild accompanying postural & intention component. Clonazepam treatment can be useful.

Myoclonus

Is brief, lightning-like contraction of a muscle or group of muscles. Occur normally as a person falls asleep (nocturnal myoclonus). Hiccup is a form of myoclonus affecting diaphragm muscles.

Action myoclonus: myoclonus that ⇧ é intended movements, occurs typically after brain injury. Palatal myoclonus: a continuous rhythmic contraction of posterior phar-yngeal muscles.

Aetiology: •Metabolic derangements (e.g. uraemia). •Degenerative diseases (e.g. Alzheimer). •Slow virus infections (Creuzfeldt-Jakob, subacute sclerosing panence-phalitis). •Severe closed head trauma. •Hypoxic ischemic brain injury.

Treatment: correct underlying metabolic abnormalities. Clonazepam 0.5-2 mg PO. TID or Valproate.

Tics

Is brief, rapid, simple or complex involuntary movements, ẃ are stereo typical & re-petitive, but not rhythmic.

Simple motor tics: (eg blinking) often begin in as nervous mannerisms in childhood

or later & disappear spontaneously.

Complex motor tics: often resemble fragments of normal behaviour as touching, smelling & jumping.

Simple phonic tics: include throat clearing, sniffing, grunting & complex phonictics include the repetition of words & coprolalia.

Tourettesy : complex type of tics disorder characterized by multiple motor & one or more phonic tics that may occur many times a day, nearly every day for **>**1 yr.

Treatment: pt & family education. Drugs as Clonidine or Haloperidol.

Chorea & Athetosis

Chorea: is brief, purposeless involuntary movements of the distal extremities & face, which may merge imperceptibly into purposeful or semipurposeful acts that mask the involuntary motion.

Athetosis: is writhing movements, often é alternating postures of the proximal limbs that blend continuously into a flowing stream of movement. Both often occur together (choreoathetosis).

Causes: •Huntington's disease •Thyrotoxicosis •SLE •Drugs (antipsychotic).

Chorea gravidarum

Choreiform movement occurring during pregnancy, often in pt é history of rheumatic fever. Usually begins during the 1st TM & resolves spontaneously by or after delivery. Rarely, a similar disorder occurs in women taking OCP. The treatment consists of sedation é Barbiturates, as other drugs may harm the foetus.

Hemiballismus

It is violent, continuous proximal limb flinging movements confined to one side of the body, usually affecting arm ›leg. It is caused by a lesion, usually an infarct, in the region of the contralateral subthalamic nucleus of Luys. Differential diagnosis includes

acute hemi chorea ẃ is usually due to tumour or infarct of the caudate nucleus & focal seizure. Although disabling, is usually self-limited, lasting 6-8 wks. Treatment is through antipsychotics drugs (often effective).

Huntington's disease

Also called Huntington's chorea. Is AD disorder characterized by choreiform movements & progressive intellectual deterioration, usually beginning in middle age. It develop insidiously, dementia or psychiatric disturbances may precede the disease or develop during the course. Motor manifestations as flicking movements of the extremities, a lilting gait, motor impersistence (inability to sustain a motor act, such as tongue protrusion), facial grimacing, ataxia & dystonia. Disorder is always progressive; pt ultimately lose physical & mental abilities to care for themselves. Rx is through the use of antipsychotics drugs ẃ may control behaviour problems (as Chlorpromazine 100-900 mg/day or Haloperidol 10-90 mg/day, PO).

Dystonia

Sustained abnormal posture & disruptions of ongoing movement, resulting from alterations in muscle tone.

Generalized Dystonia: rare, progressive,often hereditary, characterized by movements that result in sustained, often bizarre postures. Symptoms usually begin in childhood é inversion &plantar fixation of the foot while walking. In its severe form, pt may become twisted into grotesque fixed postures. Mental function usually preserved.

Focal Dystonia: affects a single body region. Rarely, dystonic movements spread to an adjacent region **(segmental Dystonia)** & even more rarely, the process generalizes. Rx often unsatisfactory. For generalized dystonia, high-dose anticholinergics &/or the dopamine-depleting drug Reserpine 0.1-0.6 mg/day PO are most often used.

Levodopa & Carbamazepine benefit a few pts. For focal or segmental dystonias or for

generalized dystonia that severely affects specific body regions, local injection of purified Botulinum toxin is the treatment of choice.

NEUROPATHY

A general term indicating peripheral nerve disorder of any cause

Classification

Based on symptoms or signs

Clinical pict	*Causes*	
	Acute	Chronic
Sensory		DM, Leprosy, Uraemia, Alcohol abuse, Vit def: B1 ,B6, B12. HIV, Hereditary, Paraneoplastic sy, Isplatin, Phenytoin.
Motor	GBS, Critical Illness, Polio	CIDP, Lead intoxication
Sensory / Motor		DM, Uraemia, Vasculitis, Hypothyroidism, Paraprotinemias, CIDP, Drugs, Toxins
Autonomic	GBS, Porphyria	DM, Amyloidosis, Familial dysautonomia

Based on distribution

Mononeuropathy

As a result of trauma, localized injury to single nerve. Violent muscular activity, forcible overextension of joint & repeated small traumas. Or from pressure or entrapment paralysis affecting superficial nerves at bony prominences or at narrow canals; also from tumours, bony hyperosteosis, casts, crutches, prolonged cramped postures. May result from Hge into a nerve or exposure to cold or radiation or Tumour invasion.

Mononeuritis Multiplex

As a result of collagen vascular disorders (polyarteritis nodosa, SLE, Sjörgen sy, Rh^{ed} arthritis). Sarcoidosis. Metabolic diseases (DM, amyloidosis), or infectious diseases (HIV, leprosy).

Polyneuropathy

As a result of acute febrile diseases: from toxin (e.g. diphtheria), autoimmune rea-

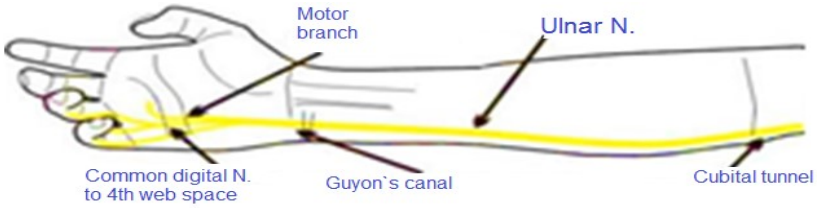
ction (GBS), immunization, toxic agents; Barbital, Phenytoin, heavy metals, Carbon monoxide, nutritional deficiency, metabolic disorders; DM, Vit B deficiency, Hypothyroidism, Sarcoidosis, Amyloidosis, Uraemia, Malignancy.

Signs & symptoms

Specific Mononeuropathies

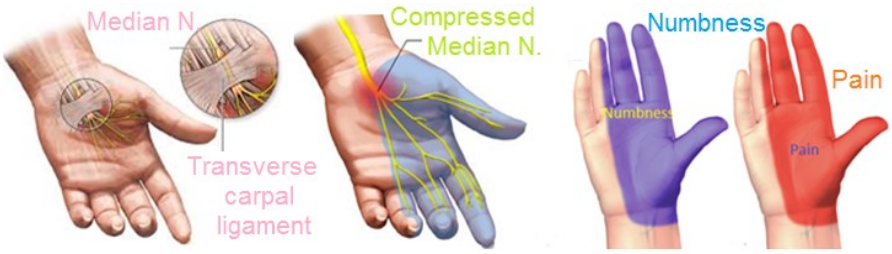
Characterized by pain, weakness & paraesthesia in distribution of affected nerve; multiple mono-neuropathy is asymmetric; nerves may be involved all at once.

Ulnar Nerve Palsy



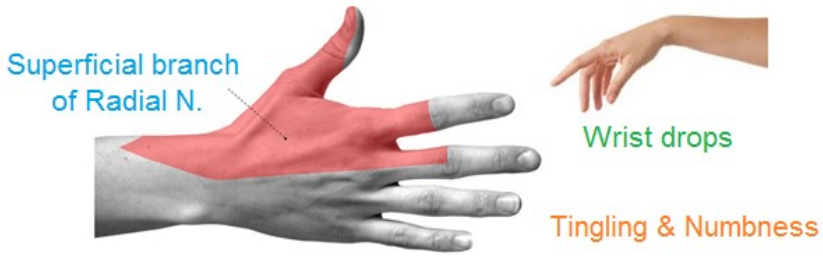
Often caused by trauma to nerve in the ulnar groove of elbow, or compression at cubital tunnel; characterized by paraesthesia & sensory deficit in the 5th & medial half of the 4th fingers is a common finding. Thumb adductor, 5th finger abductor & interossei muscles are weak & atrophied. Claw hand deformity.

Carpal Tunnel Syndrome



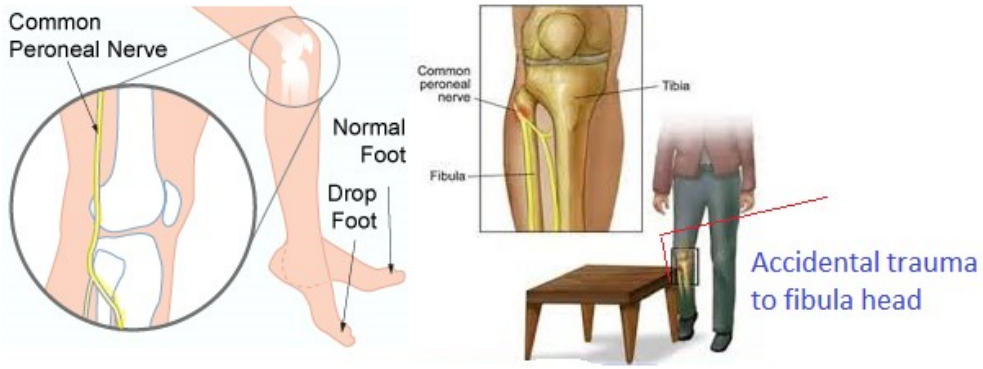
Compression of median nerve in volar aspect of wrist, it may be unilateral or bilateral. Paraesthesia in radial-palmar aspect of hand, pain over the wrist & palm. Pain may be more severe at night. Sensory deficit in palmar aspect of the first three fingers may follow; thumb abduction & opposition, may become weak & muscles atrophied. Conservative treatment should be tried first, surgical exploration in case of no success or worsening of symptoms occurs.

Radial Nerve Palsy



Is due to compression of nerve against humours; weakness of wrist & finger extensors (wrist drop). Sensory loss over dorsal aspect of 1st finger.

Peroneal Nerve Palsy



Usually caused by compression of the nerve against fibular neck, or as a result of accidental trauma. Result in weakness of foot dorsiflexion & eversion (foot drop). Sensory deficit over anterolateral aspect of lower leg & dorsum of foot or web space between 1st & 2nd metatarsals can occur.

Specific Polyneuropathies

Are relatively symmetric, often affecting sensory, motor & vasomotor fibres simultaneously. They may affect axon cylinder or myelin sheath in either form, may be acute as in GBS or chronic as in CRF.

Diabetic Neuropathy

Symptoms: burning sensation, numbness, constipation or nocturnal diarrhoea, impotence & foot ulcer.

Classification

a) Polyneuropathy; the commonest, characterized by distal symmetrical, manifests é tingling sensation, numbness & burning sensation. It is often progressive & may lead to total loss of sensation & absence of deep tendon reflexes.

b) Radiculopathy: neurogenic pain, is often self-limiting.

c) Amyotropy: atrophy of proximal muscles mainly hip girdle.

d) Autonomic neuropathy: may manifest é; -Postural hypotension -GIT; gustatory sweating, gastroparesis & nocturnal diarrhoea. –Genitourinary; neuropathic bladder, erectile dysfunction.

e) Mononeuropathy: paralysis of a specific nerve or nerves e.g. diplopia, squint due to 3^{rd} & 6^{th} cranial nerves palsies.

Sensory Polyneuropathy

Develops slowly over months or yrs. The sensory abnormalities are common, usually starting in the lower extremities, more severe distally than proximally. Peripheral tingling, numbness, burning pain, or deficiencies in joint proprioception & vibratory sensation are often prominent. Pain is often worse at night & may be aggravated by tou-c hing the affected area or by temperature changes. In severe cases, there are objective signs of sensory loss, typically é stocking & glove distribution. Charcot's joints may develop when sensory loss is profound. Tendon reflexes are diminished. Painless ulcers on the digits or sensory or proprioceptive deficits may lead to gait abnormalities.

Motor Neuropathy

Results in distal muscle weakness & atrophy.

Autonomic Neuropathy

Autonomic nervous system may be additionally or selectively involved, leading to; nocturnal diarrhoea, urinary &faecal incontinence. Impotence (erectile dysfunction).

Postural hypotension. Vasomotor symptoms vary. Skin may be paler & drier than normal, sometimes é dusky discoloration; sweating may be excessive. Trophic changes (smooth & shiny skin, pitted or ridged nails & osteoporosis) are common in severe, prolonged cases.

Nutritional Polyneuropathy

Commonly seen among alcoholics & malnourished pts. Wasting & symmetric weakness of the distal extremities is usually insidious but can progress rapidly, may accompanied by sensory loss, paraesthesia & pain. Aching, cramping, coldness, burning & numbness in the calves & feet may be worsened by touch. Multiple vitamins may be given when aetiology is obscure, but they have no proven benefit.

Diagnostic approach

CBC: megaloblasts in pernicious anaemia may suggest Vit B_{12} deficiency. Stippled RBCs indicate lead poisoning.

Liver & Renal functions tests: to assess liver & kidneys.

Glucose & Urine analysis: to assess DM & UTI.

Serum protein & electrophoresis (e.g. multiple myeloma).

Thyroid function tests: if suspicion of thyroid dysfunction.

Electromyography, Muscle biopsy: nerve conduction velocity. Sural nerve biopsy.

Treatment

Of the underlying/systemic disorder; recovery usually slow. Traumatic lesions é complete transection of nerve require surgery. Entrapment neuropathies may require corticosteroid injections or surgical decompression. Physical therapy & splints reduce the likely-hood or severity of contractures. If impaired sensation renders the pt prone to injury, protective measures should be taken.

Also called Landry's ascending paralysis. Is the most common acquired demyelinating neuropathy. Is an acute inflammatory demyelinating polyradiculoneuropathy. Is predominantly motor neuropathy characterized by muscular weakness & areflexia (loss of deep tendon reflexes). It has an acute onset & it is usually rapidly progressive in nature. There may be also mild distal sensory loss.

Aetiology & pathogenesis

The aetiology is unknown but it is believed to be due to autoimmune damage to the myelin sheath of peripheral nerves. In about 2/3 of cases, the disease begins 5 days -3 wks following an antecedent event such as; nonspecific viral syndrome, HIV infection, surgery, vaccination, campylobacter jejuni infection, SLE, lymphoma, infectious mononucleosis, hepatitis, mycoplasma pneumonia infection.

Signs & symptoms

Relatively symmetric weakness é paraesthesia usually begins in the legs & progresses to the arms. Weakness typically evolves over hrs to a few days & for 90% of pts, weakness is maximal at 3 wks after ẃ the pt reaches a plateau & further progression is unlikely. Weakness (motor) is always more prominent than sensory abnormalities & legs are usually more affected than the arms. Deep tendon reflexes are lost. Sphincters (both bladder & bowel) are usually sparred. 50 % or more of pts é severe disease have facial muscles weakness. Lower cranial nerves are also frequently involved, causing bulbar weakness, difficulty of swallowing, difficulty of handling secretions & maintaining the airways. Most pts need hospitalization & 30 % require ventilator care at some time during their illness due to possible respirat- ory failure. Autonomic dysfunction include: wide fluctuation in BP, postural ⇩ BP

& inappropriate ADH secretion, cardiac arrhythmia & pupillary changes occur in

severe cases. These complications need close monitoring as they may be fatal. Pain is another common feature of GBS. The usual type of pain is deep aching pain in the weakened muscles. Back pain involving the entire spine may occur. Respiratory paralysis/autonomic dysfunction may be life threatening. About 5% of pts die.

Diagnosis

Presumptive diagnosis is based on **history & physical examination** in addition to;

CSF analysis: ⇧ protein but few (<50 mononuclear cells) or no cells (albuminoc- ytologic dissociation).

Nerve conduction test: slow nerve conduction, evidence of conduction block, prolonged distal latencies, ẃ suggest demyelination.

Differential diagnosis: •Toxins (organic phosphate, botulism) •Acute poliomyelitis.

Treatment

Its medical emergency, requiring constant monitoring & support of vital functions.

General supportive measures

•The airway must be kept clear & vital capacity should be measured frequently, so that respiration can be assisted if necessary.

•Fluid intake: sufficient to maintain urine volume at least 1-1.5 L/day.

•Extremities: should protected from trauma & pressure of bed rest.

•Heat helps relieve pain, making early physical therapy possible.

•Immobilization, ẃ may cause ankylosis, should be avoided.

•Passive full-range joint movement should be started immediately.

•Active exercises begun when acute symptoms subside.

•Heparin 5000u SC BID to avoid thromboembolism in bed ridden pts.

Immunotherapy

Plasmapheresis, can shorten length of time that pt is dependent on respirator and

unable to ambulate. Criteria to initiate it include; the inability of the pt to walk or rapid deterioration.

Immunoglobulin Rx: it is also effective, ⇩ morbidity, hastens recovery. Plasmapheresis & immunoglobulin Rx may be given together.

Steroids are not effective in GBS: but in chronic relapsing polyneuropathy, corticosteroids improve weakness & may be needed for long time. Immunosuppresive drugs (Azathioprine) & plasmapheresis benefit some pts.

SPINAL CORD DISEASES

Spinal cord is part of the CNS contained in the spinal canal. Has 2 parts, white matter & gray matter, é central canal at the centre. The white matter contains ascending sensory & descending motor fibres. The gray matter contains nerve cell bodies. Spinal cord is organized into 31 somatotropic segments, i.e. 8 cervical, 12 thoracic, 5 Lumbar, 5 sacral & 1 coccygeal segments. Diseases of the spinal cord are frequently devastating, because it contains, in a cross-section, almost the entire motor output & sensory input of trunk & limbs.

Characters of diseases of spinal cord

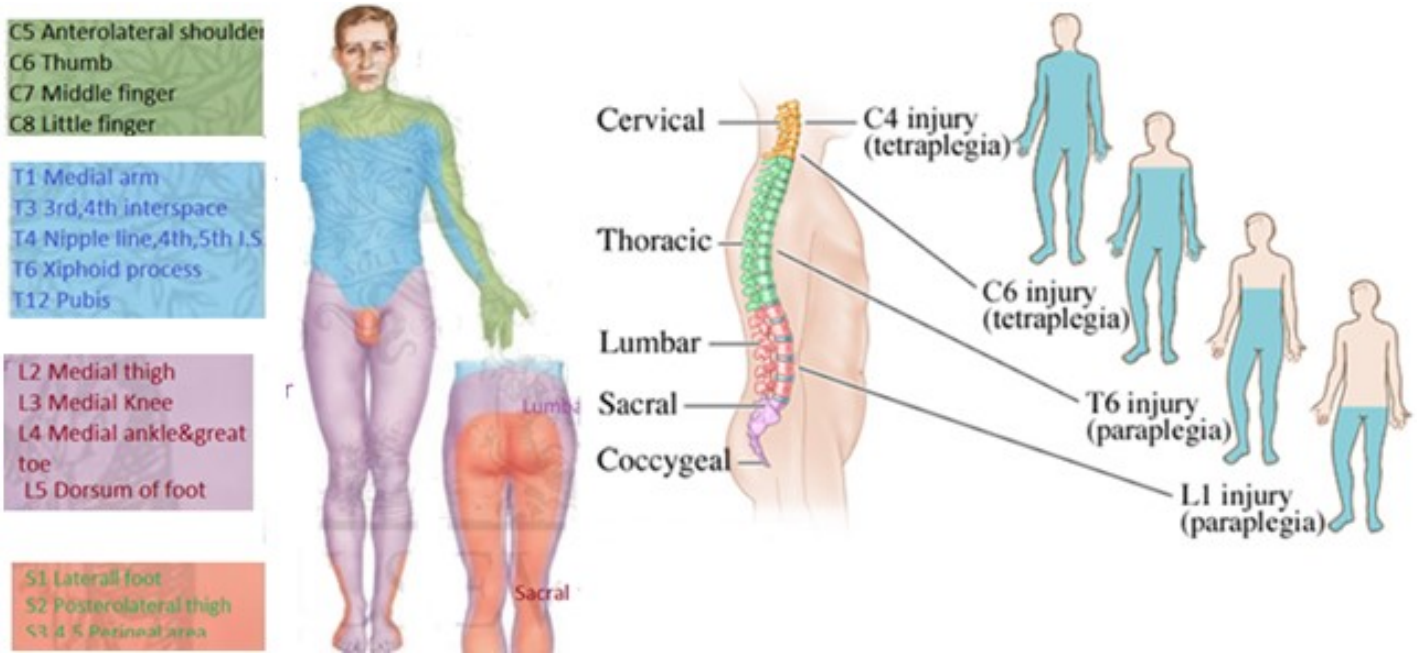
Presence of level below ẃ motor/sensory &/or autonomic function is disturbed.

1. Motor disturbance: causes weakness (paraplegia, quadriplegia), spasticity, hyperreflexia & extensor plantar response, ẃ is due to disruption of descending corticospinal fibres.

2. Impaired sensation: results from disordered function of ascending spinothalamic & dorsal column pathways.

3. Autonomic disturbance: leads to disturbed sweating, bladder, bowel & sexual dysfunction.

Key for Diagnosis



Causes

(1) Compressive: lesions may be epidural, intradural or intramedullary; TB spondylitis, Neoplasms, Epidural abscess, Epidural Hge. (e) Cervical spondylosis. (f) Herniated disc/disc prolapse. (g) Fractured or displaced vertebral body.

(2) Vascular: (a) AV-malformation. (b) Spinal artery thrombosis or emboli.

(3) Inflammatory: (a) Transverse myelitis. (b) Vasculitis. (c) MS.

(4) Infections: either Viral as; varicella zoster, HSV ”1 or 2”, CMV, HIV. or Bacterial as é mycobacterial or Parasitic as; Schistosomaisis, Toxoplasmosis.

(5) Developmental: syringomyelia, meningomyelocel.

(6) Metabolic: Vit. B_{12} deficiency.

Neoplastic spinal cord compression

(1) *Extramedullary:* tumour outside the spinal cord include:-

(a) *Epidural:* outside the dura, commonest cause of neoplastic compression of spinal cord in adults. Usually results from metastasis to adjacent vertebral bone or direct compression of the spinal cord. Commonest neoplasm include: breast, lung, prostate, kidneys, lymphoma & multiple myeloma. Most frequently involved site is

thoracic cord.

(b) *Intradural:* inside the dural layer. Are slowly growing benign tumours like meningioma, neuroblastoma & lipoma.

(2) *Intramedullary:* tumours within the spinal cord, are uncommon, include; ependymoma, hemangioblastoma, low grade astrocytoma.

Clinical feature

Initial symptom is backache, localized & worsens é movement, coughing or sneezing. Pain may radiate to the legs, trunk or following dermatomal distribution. Pain may be severe & awaken pt at night. As the compression progresses the pt develops progressive weakness, sensory abnormalities & autonomic disturbances, change in bladder function & constipation. Physical findings reveals; weakness, spasticity & hyperreflexia. Loss of or ⇩ sensations to pin prick in the lower limbs. Extensor plantar response (+ve Babiniski) & loss of abdominal reflexes & anal sphincter tone. Urine retention.

Investigations

- Check for primary tumour sites.
- Plain X-ray of spine.
- Myelography.
- Radionuclide bone scan.
- CT/MRI of spine.
- Biopsy usually unnecessary in pt. known pre-existing cancer.

Management

Depends on site & type of tumour.

Steroids: help to reduce the interstitial oedema. Should be started immediately within the first 12 hrs of occurrence of symptoms. Prednisolone 45 mg PO BID, or Dexamethasone 12 mg IV followed by 45 mg IV QID may be used.

Radiotherapy: effective even for classically radio resistant tumours. Prevents new weakness & may give recovery of function.

Surgery: decompression or vertebral body resection. Useful especially for intradural & intramedullary tumours. The Rx should started as soon as possible (within 12 hrs). Fixed motor deficits (paraplegia or quadriplegia), once established for >12 hrs, do not usually improve & beyond 48 hrs the prognosis for substantial motor recovery is poor.

TUBERCULOSIS OF SPINE

Pott's disease is one of commonest causes of myelopathy in developing countries. Often involves two or more adjacent vertebral bodies. Commonest site is lower thoracic & upper lumbar vertebrae.

Clinical features

Pt present é insidious onset of back pain, ẃ progressively get worse. Gibus deformity (kyphotic swelling over the back). Numbness & loss of sensation é a sensory level. Weakness of the lower limbs, often spastic in nature é exaggerated deep tendon reflexes & up going plantar (+ve Babiniski sign). Bladder/bowel dysfunction (urinary retention é overflow incontinence, constipation or faecal incontinence). In about 65% of cases evidences of extra spinal TB is present.

Diagnostic workup

•Plain X ray show characteristically destructive process of the vertebrae, disc spa-ce & deformity. •CT/ MRI may show the lesion more clearly.

Treatment

Medical Rx: short course anti TB drugs is mainstay. Steroids can be added if there is neurological deficit.

Surgical Rx: for spinal instability or deformity.

PROLAPSE OF INTERVERTEBRAL DISC

As result of trauma or sudden severe strain or degenerative changes. Commonest site for disc prolapsed is the lumbar region.

Clinical feature:

localized back pain aggravated by straining é/éout radiculopathy, segmental sensory loss, changes in deep tendon reflexes (asymmetrical). The straight leg raising sign is +ve: the pt will have back pain, when stretched leg is raised or flexed at the hip joint.

Diagnostic workup

- Myelography: may help to localize the site of prolapse.
- CT/ MRI: can easily demonstrate the prolapsed disk.

Therapy:

Medical Rx: often supportive, include; bed rest, adequate analgesics, physiotherapy & supporting belts/corsets.

Surgical Rx: definitive Rx for disk prolapse.

TRANSVERSE MYELITIS

Is an acute or subacute inflammatory disorder of spinal cord. Occurs associated é:-

- Antecedent infection (viral or mycoplasmal).
- Recent vaccination.
- MS.
- SLE.

Clinical feature

Initial symptom is localized back or neck pain or radicular pain followed by various co-mbinations of paraesthesia, sensory loss, motor weakness & sphincter disturbances, ẃ can evolve within hrs to several days.

Investigation: CSF: may be normal or show pleocytosis & ⇧ protein.

Treatment: Steroids can be used in moderate to severe cases.

METABOLIC & TOXIC MYELOPATHIES

Subacute combined degeneration of spinal cord

Neurologic disease mainly affecting the spinal cord, result from severe Vit B_{12} deficiency. Results in abnormalities on myelin basic protein leading to swelling of myelin sheath followed by demyelination &gliosis. The changes mainly affect posterior & lateral columns of spinal cord

Clinical feature: pt present é; paraesthesia in the hands & feet. Early loss of position & vibration senses. Progressive spastic & ataxic weakness. Some pts may develop optic atrophy & encephalopathy.

Treatment: Vit B_{12} 1000 µg IM/day for 5-10 days, followed by 1000 µg IM/wk for 1 month & then 1000 µg IM/month lifelong.

Neurolathrism

Neurolathrism is syndrome that affects the CNS of man due to consumption of peas of the lathyrus species (“Guaya”seeds) that contains neurotoxic amino acid. Excessive consumption of these seeds occurs during times of food shortage. It affects predominantly young men.

Clinical feature: onset can be acute/subacute usually ppt by manual labour, febrile illness or diarrhoea then the pt. will develop weakness, spasticity & rigidity progressively preventing them from walking. Usually no sensory abnormality was seen. Some of severely affected cases may develop incontinence & impotence.

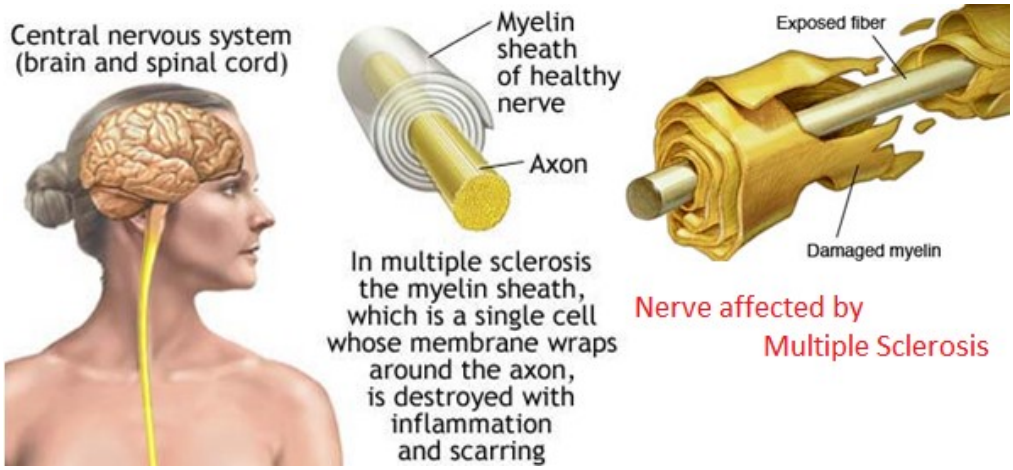
Investigation: no specific laboratory test required. Diagnosis is by exclusion of other causes & taking proper dietary history & understanding the geographic distribution of the diseases (common in certain parts of Africa)

Treatment: no cure once established.

Prevention: banning cultivation & consumption of the seed (Guaya). Breeding of non

toxic variant if possible. Use of certain preparation methods (cooking or soaking in excess water) makes the seed less toxic.

MULTIPLE SCLEROSIS



Aetiology

An immune-mediated disease of the CNS, predominantly affects young adults during their most productive years. Usually diagnosed between 20 & 50 yrs age. Occasionally affect young children & older adults. More common in women than men >2:1 (women are in general more likely to have an autoimmune diseases). Most common in those of Northern European ancestry. More common in Caucasians than Hispanics or African Americans; rare among Asians. More common in temperate areas of the world (5 times more likely). Attributed to infection (viral) or autoimmune disorder. The genetic & environmental factors also participate in its aetiology. Lower Vit D exposure? The Delayed reaction to viral infection contracted during childhood by a genetically susceptible person especially shingles, chicken pox, measles, or herpes can cause of MS. It was found also that the disease is least common in the lower socioeconomic class & rural residence. The risk of MS 1/750 of general population. 1/40 for those é 1st degree relative é MS & 1/4 for an identical twin. 20% of pts é MS have a blood relative é MS. The risk ⇩ is higher in any family in ẃ there are several family members é the disease.

Pathological changes

Immune cells are made throughout the body (tonsils, thymus, bone marrow, sple- en & lymphoid tissue of the gut), except in the brain & spin-al cord. MS is charactterized by the presence of areas of demyelination & T-cell predominant perivascular inflam-mation in the brain white matter. Some axons may be spared from these pathological processes. Disease begins most commonly é acute or subacute onset of neurologic abnormalities. Initial & subsequent symptoms may dramatically vary in their expres-sion & severity over the course of the disease, that usually lasts for many yrs.

Clinical picture

It is important to note that pt é MS have subjective complaints & objective signs that frequently are not attributable to one specific lesion in the CNS. It is usually possible to distinguish at least 2 or more separate foci of involvement based on the clinical as-sessment of the pt.

Initial symptoms: certain signs & symptoms are more common in the early stages of the disease. Pt may be complaining of double or blurred vision, numbness, wea- kness in one or two extremities, instability in walking, tremors & problems é bladder con-trol, heat intolerance. As is well known, sensory examination is the most difficult one to perform reliably & accurately in evaluation of pts é neurologic complaints. Howev-er, certain distributions of sensory problems can be suspicious for early MS. Among those are: ascending numbness starting in the feet; or bilateral hand numbness; hem-iparethesia; generalized heat intolerance. Objectively the most common sensory find-ings in the "numb" areas are dorsal column signs, such as reduction of vibration, pro-rioception & stereogensis, rather than problems é spinothalamic tract. Usually doub-le vision in MS pt results from a unilateral or bilateral par tial or complete internucle-ar ophthalmoplegia. The 6th cranial nerve (Abducent) paresis & palsy also have been

described as presenting symptoms,while the 3rd & 4th cranial nerve (oculomotor & trochlear) palsy are uncommon.

Optic Neuritis: is frequent presenting symptom of MS. characterized by blurred vision, a change in colour perception, visual field defect as central scotoma. Possible headaches & retroorbital pain ppt by eye movements. These symptoms may require neuroophthalmologic evaluation, MRI imaging & visual evoked potential studies to establish a degree of optic nerve function.

Motor weakness: often is accompanied by UMNL signs, such as mild spasticity, hyperreflexia & pathologic signs. The most common initial presentation is paraparesis. Weakness can also found in one extremity (monoparesis) or all the four extremities (quadriparesis).

Ongoing symptoms & signs: as the disease progresses, the original signs & symptoms may worsen & new ones may appear. The most common symptoms & signs include:-

- Motor system: weakness (variable severity mono, paraparesis, hemiparesis, quadriparesis).⇧spasticity resulting in spastic gait. Pathologic signs (Babinski's, Chaddock's, Hoffmann, Oppenheim's). Dysarthria.
- Cerebellar signs: incoordination (dysdiadochokinesia, problems é heel-to-shin test). Slowing of rapid repeating movements. Cerebellar ataxia (ataxic gait). Scanning speech. Loss of balance.
- Sensory systems: Lhermitte's sign sometimes called the barber chair phenomenon, is an electrical sensation that runs down the back & into the limbs. The sensation can feel like it goes up or down the spine. It is generally considered uncomfortable. Dysesthetic pain. Paraesthesia. Numbness. Dorsal column signs (i.e. severe ⇩ or loss of vibratory sense & proprioception, positive Romberg's test).
- Urinary: incontinence, incomplete emptying & ⇧ frequency of urine. All of these

problems may result in UTI.

- Optic disc: pallor, atrophy, blurred vision, diplopia, nystagmus, oscillopsia, intranuclear ophthalmoplegia, central scotomas.
- Cognitive & emotional abnormalities: emotional lability, depression.
- Fatigue & sexual dysfunction: uncommon symptom s.
- Signs may include; bowel incontinence, difficult swallowing, seizures, trigeminal neuralgia, dystonia, hearing loss & facial palsy.

All of the above mentioned symptoms can be ppt by heat, i.e. being in a hot, humid environment.

Diagnosis

MS most often characterized by episodes of neurological dysfunction followed by periods of stabilization or partial to complete remission of symptoms. These symptoms can appear over a few hrs or days, can be gradually worsening over a period of a few wks, or sometimes can present themselves acutely. Depending on a course & the subtype of the disease, these symptoms will either persist or slowly resolve over wks or months & may even culminate as complete remissions. A rela-psing-remitting pattern is the most common & is characteristic for this disease. Depends upon; neurological findings, clinical observation, results of MRI (the presence of areas of demyelination in the CNS), LP (CSF exam shows presence of oligoclonal bands &/or ⇧ IgG index) & sometimes tests of evoked potentials constitute the basis for diagnosis.

Course: listed below are the different paths that MS can take:-

Relapse-remitting: attack ẃ undergo complete or partial remission, then have the symptoms return.

Primary-progressive: progressive deterioration, there may be a temporary relief in symptoms & few pts have malignant MS é quick decline & pt severely disabled or

even lead to death.

Secondary-progressive: starts é progressive relapsing, end by 1ry progressive.

Progressive-relapsing: rare, progressive course ẃ made worse by acute attacks.

Differential diagnosis

Other demyelinating diseases of the nervous system, often of a viral or post-infectious origin, among them are encephalomyelitis, transverse myelitis, as well as other immune mediated conditions, ẃ affect CNS, as sarcoidosis, SLE, Vit B_{12} def.

Prognosis

5-20% of all pts will develop benign MS, show little progression after the first attack. 33% will have little to no disabilities allowing them to live independently while not in relapse. Only 33% of MS pts will have a severe disability.

Management

There is no curative Rx available for MS. However, a number of medications can used to treat the disease symptomatically.

Corticosteroids are medications of choice for treating exacerbations.

For Spasticity: Baclofen, Tizanidine, Diazepam.

Optic neuritis: Methlyprednisolone, oral steroids.

Fatigue: Antidepressant, Amantadine.

Pain: Codeine, Aspirin.

Sexual dysfunction: Viagra, Pravatine.

For Tremors: Isoniazid, Primidone, Propranolol.

Disease-modifying drugs

Interferon Beta 1a (Avonex & Rebif)

Is a protein that is a replica of human interferon. It suppress the immune system & helps to maintain the blood-brain barrier. You inject Avonex into the muscle once a

wk & Rebif is injected under the skin 3 times a wk. This drug is useful to people who have definite PPMS. One side effect of the drug is a flu like symptom.

Interferon β-1b (Betaseron)

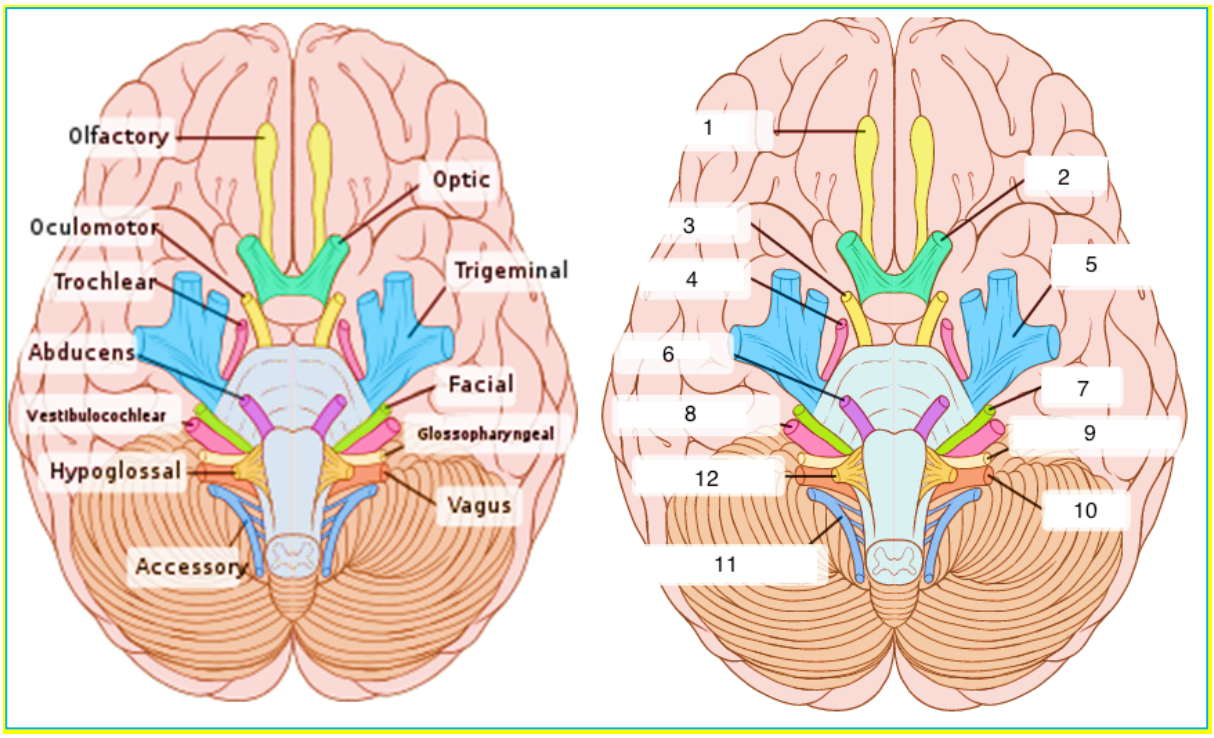
Is slightly different from our own interferon. This medication does the same thing as β-1a, but is injected just under the skin every 2 days, its side effects include irritation, bruising & redness at the site of injection & the flu like symptoms. This is also given to people who have definite PPMS.

Glatiramer Acetate (Copaxone)

Is a small fragment of a protein that resembles a protein in myelin. It ⇩ the reoccurrence of relapse. Injected just under the skin every day. There is no flu like symptoms but occasional redness may occur at site of injection.

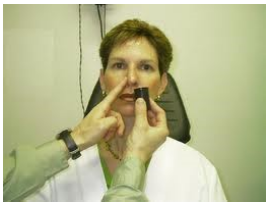
In summary all the above 3 drugs ⇩ relapses by 33%, have manageable side effect, are injected, stabilize the disease & tend to be costly. In the future, medications aimed at reducing specific autoimmune response & possibly, medications design-ed to assist in re-myelination will help improve the quality of life of MS pts.

EXAMINATION OF THE CRANIAL NERVES



#	Cranial Nerve	Popular Mnemonic	One of my Mnemonics
I	Olfactory	Oh	Only
II	Optic	Oh	Overgrown
III	Oculomotor	Oh	Orangutans
IV	Trochlear	To	Try
V	Trigeminal	Touch	To
VI	Abducens	And	Aggravate
VII	Facial	Feel	Fat
VIII	Vestibulcochlear	A	Vagrants
IX	Glossopharynx	Girls	Getting
X	Vagus	Vagina,	Vodka
XI	Accessory	Ah	And
XII	Hypoglossal	Heaven	Hamburgers

OLFACTORY NERVE (1ST)

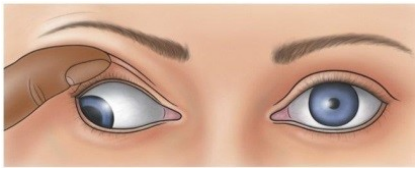


Affected in fracture base skull, ICHge. To diagnose, ask the pt. to take breath or blowing from each nostril separately, notice movement of nose wall, air coming outside, ask him to smell certain food stuffs coffee, tea, peppermint each nostril separately.

OPTIC NERVE (2nd)

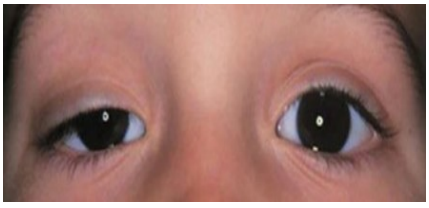
Special sensory nerve, is part of the CNS, responsible for vision, supply pupillary sphincter, affected by ICHge, brain tumor, glaucoma, DS. Damage result in blindness or loss of visual acuity as tested by card, Visual field defect (confrontation test). Loss of light reflex (direct, consensual), loss of accommodation, opticokinetic nystagmus in infants.

OCCULOMTOR NERVE (3rd)



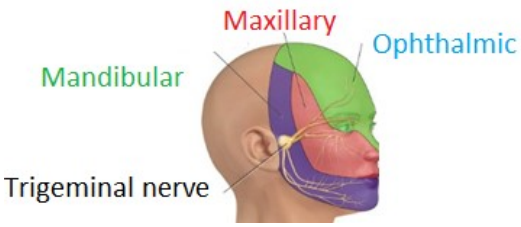
Is motor nerve, supply all extensor muscles of eye except superior oblique & lateral rectus, supply levator palpebral superiors muscle. Damage result in drooping eyelid, divergent squint, dilated pupil, double vision, difficult focusing & inability to move eye in certain direction.

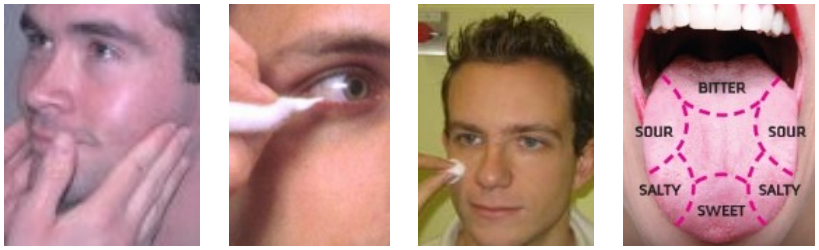
TROCHLEAR NERVE (4TH)



Motor, supply superior oblique muscle. Damage result in convergent squint, inabi-lity to move eye downward when it is internally rotated, in addition to double visi-on & blurring of vision.

TRIGEMINAL NERVE (5th)





Mixed nerve (motor & sensory). Motor to masseter, petyrgoid, temporalis muscles. Sensory to cornea, taste sensation to anterior 2/3 of tongue. Damage result in paralysis of masseter, petyrgoid muscles result in impaired mastication (clench your teeth & feeling masseter). Paralysis temporalis (inability to raise eye brow & feeling no contraction in temporalis muscle). Loss of corneal reflex. Loss of sensation on anterior 2/3 of the tongue.

ABDUCENT NERVE (6th)

Motor nerve, supply lateral rectus muscle. Damage result in convergent squint (as seen in the picture), inability to rotate eye laterally, at rest eye rotate medially. Diplopia & blurring of vision.

FACIAL NERVE (7th)

Mixed nerve, arise from pons, pass in conjunction é 8th cranial nerve in the internal auditory canal then through parotid gland. Motor to muscles of expression. Senso

ry to tongue, gives superficial touch sensation to anterior 2/3 of tongue (chorda tympani branch). Damage may be central affecting the entire half of face. Or Peripheral affecting the lower 1/4, inability to wrinkle brow, loss of normal forehead wrinkle, dropping of eye lid, inability to close eye & sleep é open eye, exposure ke-ratitis, drop of the angle of mouth, loss of nasolabial fold & inability to puff mouth.

AUDITORY (VESTIBULOCOCHLEAR) NERVE (8th)

Special sensory nerve, arise from pons, pass in conjunction é 7th Cranial nerve through internal auditory canal then through parotid gland. May affected by accident, fracture base skull, acoustic neuroma. Damage result in deafness, dizziness, loss of balance, nystagmus. Audiogram is diagnostic.

Rinne`s test: using tuning fork 256, normally air conduction is better & twice in duration than bone conduction, put tuning fork over mastoid process, when pt stop hearing vibration put it in front of ear.

Weber`s test: put fork over vault of skull, test hearing in both sides, in conductive deafness, bone conduction is better in diseased ear.

Type	RinneT.	Weber T.	Possible cause
Conductive	Bone>Air	Localizes to affected ear	Wax, cholesteatoma, otosclerosis, external/ middle ear tumour, rupture tympanic memb., otitis media.
Sensorineural	Air>Bone	Localizes to unaffected	Menieres disease, acoustic neuroma, ototoxic dru-gs, & presbycusis.

GLOSSOPHARYNGEAL NERVE (9TH)

Mixed nerve, motor to pharynx, sensory to posterior 1/3 of tongue. Damage result in difficult swallowing, absence gag reflex (touch posterior pharyngeal wall by ton-gue depressor). Ask pt to say ahh as long as he can (observe contraction & elevation of soft palate while uvula remain in middle position), also will lead to loss of general sensation of posterior 1/3 of the tongue(loss of bitter & sour taste).

VAGUS NERVE (10th)

Mixed nerve, originate in the medulla, motor to palate, uvula & sensory to all inte-rnal organs, the only cranial nerve that runs into thorax & abdomen. Damage cau-se hoarseness/loss of voice, impaired swallowing, GIT dysfunction & BP changes.

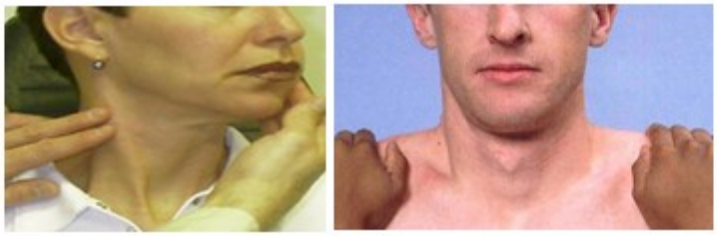
ACCESSORY NERVE (11th)

Motor to shoulder & sternocleidomastoid muscles. Damage result in impaired neck & shoulder movement, ask the pt to press é his head side over your hand & feel the sternomastoid muscle, also ask him to elevate his shoulders against the pressure of your hands (feel trapezius & shoulder muscles).

HYPOGLOSSAL NERVE (12th)

Motor to tongue. Damage result in deviation of tongue toward the injured side, ask pt to move his tongue in different directions.

9th



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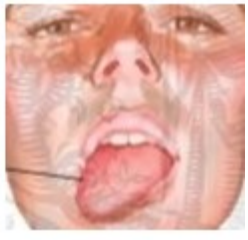

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Chapter IX.

CONNECTIVE TISSUE & JOINTS DISEASES

- Systemic Lupus Erythromatous
- Rheumatoid Arthritis.
- Systemic Sclerosis,
- Mixed connective tissue disorders.
- Gout.

Introduction: connective tissue & joints diseases are a group of medical disorders resulting from immunologic damage to the connective tissue of the body. They overlap é each other, may affect many organ systems & often respond to immu- nosuppressives. Their pathologies vary. The following are some of the connective tissue disorders:- SLE. Rh^{ed} arthritis. Systemic sclerosis (scleroderma). Polymyositis. Mixed connective tissue disorder. Primary Sjörgen's sy. & Behcet's disease.

SYSTEMIC LUPUS ERYTHREMATOSIS

SLE is a chronic immune disorder characterized by multisystem involve ment & clinical exacerbations & remission. Circulating immune complexes & autoantibodies cause tissue damage & organ dysfunction.

Epidemiology

Familial tendency & concordance rate among identical twins is 50%. Prevalence in the young women of child bearing age is 8-10 X that of men (F : M ratio is 10:1).

More common in black than white women & in pregnancy.

Aetiology

No single cause identified for SLE, it results from complex interaction of environmental, genetic factors & hormonal influences. The environmental factors include virus, drugs or toxins. It may be induced by drugs (Isoniazid, Hydralazine, Chlorpro- mazine etc.). There is genetic predisposition to SLE. Autoimmunity due to loss of tolerance to auto-antigens is central to the pathogenesis. The disease more common in women of child bearing age & oestrogen play a role in pathogenesis.

Signs & symptoms

Systemic symptoms: fatigue, WT loss & fever are prominent.

Skin: photosensitive malar butterfly rash (facial erythema over the cheeks & nose), chronic potential scarring discoid lesions, alopecia, livedoreticularis, Raynaud's ph-

enomena, purpura, oral ulcers, urticaria, conjunctivitis & bullae.

Musculoskeletal: joint/muscle pain, non-erosive polyarthritis, myositis, proximal myopathy& aseptic bone necrosis.

Renal: different types glomerulonephritis ẃ may manifest ē proteinuria, casts, oedema &later on to CRF.

CNS: focal or diffuse neurologic disorders in about 50% of cases:-Generalized manifestations; severe headache, reactive depression, psychosis, seizure& cognitive disturbance. Focal neurological signs: focal seizure, hemiparesis, paraparesis, cranial nerve lesions, ataxia, chorea may also be seen. Peripheral nerves: sensory or sensorimotor neuropathies.

Lung: pleurisy, lupus pneumonitis, fibrosing alveolitis.

CVS: hypertension from renal involvement, pericarditis, non-infective endocarditis, myocarditis, coronary vessel vasculitis.

Blood: anaemia, leukopenia, lymphopenia, thrombocytopenia, ⇧ ESR.

GIT: intestinal vasculitis, pancreatitis.

Other: fever, splenomegaly, lymphadenopathy, recurrent abortion.

Symptome of SLE may vary widly with the individuals

Diagnosis

•***Serology:*** ANA nearly 99% of pts are positive. Antibodies against double strand DNA. Low complement components (C3,C4).

•**Haematology:** anaemia, ⇧ ESR, ⇩ platelet count.

•***Urinalysis:*** proteinuria, haematuria.

•***Renal function test***: BUN & creatinine may be ⇧.

Treatment

If the SLE is believed to be due to drug-induced, stop the drug. Give sun-block creams or sunscreens.

NSAIDs used in full anti-inflammatory dose for fever, joint complaints & serositis. Hydroxychloroquine if joint/skin symptoms are not controlled by NSAIDs, e.g. 400 mg/day PO for 6 months, then 200 µg/day.

Corticosteroids: high-dose prednisolone in life-threatening conditions 1mg/kg/day for 6 wks, then taper. May be combined é immunosuppressives. Low-dose is of va-lue in chronic disease.

Cytotoxic drugs: Azathioprine, Cyclophosphamide sometimes are employed for severe refractory cases particularly renal diseases.

Prognosis

Early diagnosis & Rx ⇩ morbidity & mortality. The renal diseases & infectious complications are major causes of death.

RHEUMATOID ARTHRITIS

Chronic multisystemic inflammatory disease of unknown cause, characterized by persistent inflammatory synovitis, usually involving peripheral joints in symmetric-

al distribution. The potential of the synovial inflammation to cause cartilage damage & bone erosion & subsequent changes in joint integrity.

Epidemiology

The prevalence of RA is approximately 0.8% in the population.

Women more affected than men é F : M ratio of 3:1.

The prevalence ⇧ é age. Sex difference diminishes in the older age group.

Aetiology

The cause of RA remains unknown. It is suggested that RA may be a manifestation of a response to an infectious agent in a genetically susceptible host.

Genetic factors: the genetic susceptibility to altered immune response may play a role; concordance rate among monozygotic twins is 4 X & first degree relatives of pts é RA have a very high chance for RA. Presence of HLA-DR4 allogen is associated é high incidence of RA.

Infectious agent: may play a role in triggering an autoimmune reaction. Infectious agents such as Rubella, Mycoplasma, CMV may play a role in the pathogenesis.

Clinical Features

Insidious onset: in about 2/3 of pts, the RA begins insidiously é prodromal nonspecific symptoms as fatigue, weight loss, anorexia, generalized body weakness & vague musculoskeletal symptoms, for wks or months before the occurrence of sp-ecific joint symptoms.

Acute onset: in about 10% of pts, RA has an acute onset, é rapid development of polyarthritis, associated é constitutional symptoms, including fever, lymphadenop- athy & splenomegaly.

Joint manifestations: result from persistent inflammatory synovitis. Pain, swelling, tenderness of involved joints, aggravated by move. Generalized joint stiffness of

ten seen after period of inactivity. Morning stiffness ẃ lasts ›1 hr, ẃ is a feature of inflammatory arthritis is a common complaint. Bilateral, symmetrical small joint involvement is typical for RA. The commonly affected joints are the wrist joints, MPJ & PIPJ. While the DIPJ are often spared. synovitis of wrist joint is very common & may lead to limitation of movement, deformity & median nerve entrapment (carpal tunnel sy.). Elbow joint involvement may lead to flexion contracture. Keen joint commonly involved é synovial hypertrophy, chronic effusion & frequent ligamentous laxity. Pain & swelling behind the knee may be caused by extension of

inflamed synovium into popliteal space (Baker's cyst). Arthritis of the forefoot, ankles & subtalar joint scan produce severe pain é ambulation & as well as a number of deformities. Axial involvement is limited to cervical spine, atlantoaxial ligament involvement, in the cervical spine can lead to instability between C1 & C2 vertebr- ae & potential neurologic complaints.

Joint deformities: é persistent inflammation, a variety of characteristic joint chan- ges develop due to damage or weakening of ligaments, tendons & joint capsule. These deformities include:- Z-deformity: radial deviation at wrist é ulnar deviation of digits. Swan neck deformity: hyperextension of PIPJ, é compensatory flexion of DIPJ. Boutonnière deformity: flexion contracture of PIPJ & extension of DIPJ.

Extra-articular features: since it is a systemic disease, a variety of extra-articular manifestation may be seen. Although these occur frequently, not all of them have clinical significance. However, occasionally they may be the major evidence of disease activity & source of morbidity. More often, these manifestations occur in pt who have high titre of Rh^{ed} factor & pt who have more severe disease.

Rh^{ed} nodules: the commonest features of extra-articular diseases, found in 20-25% of cases. These firm subcutaneous masses typically are found in areas on periartic-

ular structures & on areas exposed to repetitive trauma (e.g. extensor surface of fingers, forearm, olecranon process of the elbow, proximal ulna, Achilles tendon & occiput). In some pts Rh^{ed} nodules may found on the viscera (lungs).

Rh^{ed} vasculitis: affect any organ, seen é severe RA & high titre of Rh^{ed} factor.

Peripheral nerves; distal sensory neuropathy.

Skin; cutaneous ulceration, dermal necrosis. Digital gangrene.

Visceral infarction. may involve lungs, bowel, liver, MI etc..

Eye involvement: Keratoconjuctivitis sicca is seen in 10-15% of RA pts. who have a secondary form of Sjogren sy. Scleritis or episcleritis occur less common.

Lungs: pleuritis & pleural effusion may be seen is some pts. The pleural fluid typic- ally has low glucose conc. The Rh^{ed} nodules may appear on the lung on X ray.

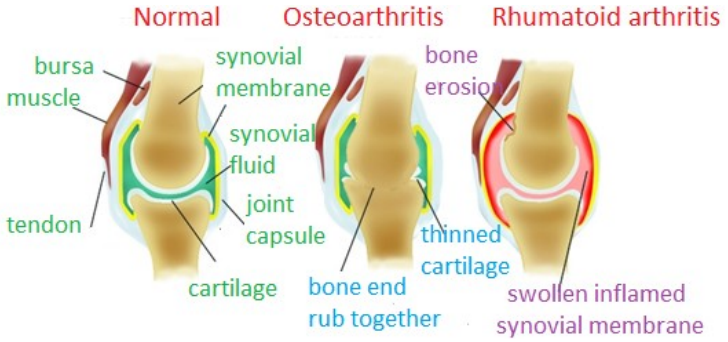
Heart: asymptomatic pericarditisis fund in 50% of pts on autopsy. It is often associated é pleural effusion. Myocarditis & Valvular dysfunction are rare findings.

Neurologic manifestations: peripheral nerves affected through entrapment (carpal tunnel sy.) or vasculitis related mononuritis multiplex. Atlantoaxial sublaxation may lead to compression of spinal cord.

Hematologic features: anaemia of chronic diseases. Thrombocytosis. Felty's sy is a CRA é splenomegaly & neutropenia, thrombocytopenia & anaemia.

Constitutional symptoms: like wt loss, fever & fatigue are common complaints & may be severe in pt é extra-articular manifestations.

Rheumatoid arthritis Vs Osteoarthritis



	Osteoarthritis	Rheumatoid Arthritis
Age	Usually begins after age 40	Usually begins age 25-50
Development	Develops slowly over years	Develop quickly within months
Inflammation	Mild	Swollen & Tender
Joints	Hips, knees, spine & fingers most common. Affect either/or both	Primarily fingers & small joints, affect both hands, both wrists
Stiffness	Tends to lossen after a short time of use	May be for hrs, morning stiff-ness

Diagnostic approach

(1)Proper history taking & physical examination: play a crucial role in making the di-agnosis of RA.

(2) Laboratory findings

a) CBC: normocytic normochromic anaemia, leucocytosis, thrombocytosis.

b) ESR ⇧ indicating chronic inflammation

c) Rh^{ed} factor: it is autoantibodies against the Fc component of IgG. Typically present in 60% of pts in the 1st year & 80% of pts é long standing diseases. Note that 30% of pt é RA may be -ve for Rh^{ed} factor.

(3) Radiographic findings

Early: characteristic changes include soft tissue swelling & loss of bone in periarti- cu-lar areas (periarticular osteopenia).

Late: sustained inflammation leads to loss of bones at joint margins (erosion) & joint space narrowing as a result of cartilage loss & joint deformity.

Revised American criteria for classification

4 of the following 7 criteria required to classify pt as having RA & the presence of 2 or more of those criteria, the clinical diagnosis of RA is not excluded.

(1) Morning stiffness: lasting>1 hr.

(2) Arthritis of ≥ 3 joint areas.

(3) Arthritis of hand joints: wrist, MCP &PIP.

(4) Symmetrical arthritis.

(5) Rh^{ed} nodules: SC nodules over bony prominences.

(6) Serum Rh^{ed} F.

(7) Radiologic changes: peri-articular bony erosion & other findings.

Management

Goals of therapy

Short term: controlling pain & ⇩inflammation éout causing undesired side effects.

Long term: preservation of joint function & the ability to maintain life-style.

Pharmacotherapy

(1) First line: NSAIDs used to control symptoms & signs of local inflammatory process. Rapidly effective in alleviating pain & symptoms, but there effect on long term disease progression is minimal. Aspirin, Ibuprofen, Diclofenac, Indomethacin may be used. Aspirin 900 mg PO TID, Ibuprofen 400mg PO BID or Diclofenac 50mg PO BID or TID. Side effects:-dyspepsia, renal dysfunction & bone marrow toxicity.

(2) Second line: low dose oral corticosteroids have potent anti-inflammatory effect, but they have equally predictable unwanted side effects. Systemic administration are given in severe progressive disease & extra-articular involvement. start 5-10 mg once daily in the morning. If pt improve, attempt should be made to taper the dose. Local injection of steroids may be used occasionally to severely affected joint.

(3) Third line: DMARDs (Disease Modifying Antirheumatic Drugs), this group of agents include; Methotrexate, Gold compounds, D-Penicillamine, Antimalarial & Sulfasalazine. These are drugs, ẃ have no analgesic effect & generally require wks to months

before anti-inflammatory effects are evident. Hence, NSAIDs should continue during the administration of DMARDs. They have the capacity to alter the

course of RA. Used in pt é RA, who are not responding to NSAIDs (é/éout steroid). These drugs may be used singly mostly, but they may be prescribed in combinations in pt é bad prognosis or refractory cases. The disease progression is delayed é these drugs & acute phase reactants such as ESR & CRP frequently decline. Methotrexate is the most frequently DMARD used, ẃ is relatively rapidly acting, given in intermittent low dose: 7.5-30 mg once weekly. Side effects: GI upset, oral ulcer, LFT abnormalities & insidious liver fibrosis. Administration of folic or folinic acid may diminish the frequency of some side effects.

(4) Fourth line: Anticytokine agents, effective in controlling signs & symptoms of RA in pt who failed to respond é DMARDs.

(5) Fifth line: immunosuppressive therapy; these include drugs such as Azathiopr- ine, Cyclosporine & Cyclophosphamide. They have the same therapeutic effect as DMARDs, but they are not more effective than DMARDs. Are prescribed to pt who fail to respond to DMARDs.

Non pharmacologic therapy

Pt Education: description of the illness & the chronicity of the diseases. Rest & exercise; pt should be advised to rest or splint acutely involved joints. Exercise to strengthen muscle surrounding involved joints, when the arthritis is resolved.

Physiotherapy & Occupational therapy: to reduce disability.

Assessment of response

Resolution of Symptoms: reduction/disappearance of joint pain, stiff ness & swell.

Functional Status: ability of pt to perform daily activities.

Laboratory: anaemia may be corrected & ESR declines.

Surgical therapy

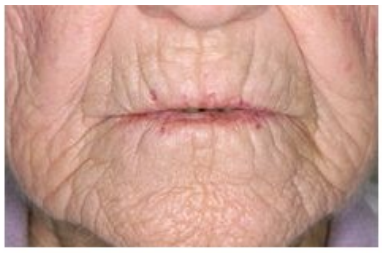
Early: synovectomy may ⇩ the inflammatory process in joints or tendon sheaths that remain inflamed despite drug therapy.

Late: arthroplasty or total joint replacement may be appropriate to relive pain or help restore function in structurally deformed joints.

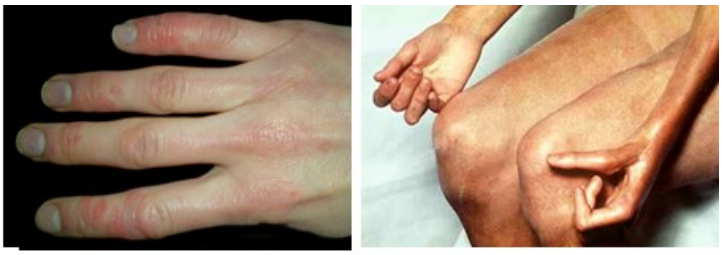
Poor prognostic factors include:

- Many persistently inflamed joints.
- Poor functional status.
- Low educational status of the pt.
- Rh^{ed} factor is +ve.
- HLA-DR4 is +ve.
- Radiologic evidence of erosion.
- Extra articular diseases
- Persistently elevated acute phase reactants (ESR &CRP).

SYSTEMIC SCLEROSIS



Morphia
(localised scleroderma)



In scleroderma, the abnormal build-up of fibrous tissue in the skin can cause the skin to tighten so severely that the fingers curl and lose their mobility

Systemic sclerosis (scleroderma) defined as a CT disease, characterized by widesp-read small vessel obliteration & fibrosis of the skin & multiple internal organs.

Diffuse scleroderma

Skin thickening present in the trunk in addition to face & extremities. Renal, gut in-volvement; associated é malignant hypertension, Raynauld's, myocardial disea-se. No effective treatment known.

Limited scleroderma

Skin thickening limited to sites distal to elbows & knee, face & neck also involved. Formerly CREST syndrome (calcinosis, Raynauld's, oesophageal motility disorder,

Sclerodactyly & Telangiectasia).

Sinus scleroderma: no skin changes but characteristics internal organ involvement.

Overlap scleroderma: presence of systemic sclerosis ē features of other CT diseases (SLE), Rh^{ed} arthritis, inflammatory myositis.

PRIMARY SJÖRGEN'S SYNDROME

Association of CTD (in 50% Rh^{ed} Arth.) é Keratoconjuctivitis sicca (dry eyes) or xerostomia (dry mouth) due to lymphocyte & plasma cell infiltration into secretory glands.

Signs & symptoms

Dry eyes, mouth & skin dyspareunia, dysphagia, otitis media, pneumonia, others; neuropathy, renal involvement, hepatosplenomegaly, drug reactions, lymphoma, ⇩ wellbeing, headache.

Diagnosis: History & physical exam, Schirmer's test to quantify tear production, biopsy of salivary glands.

Treatment

Artificial tears, occlusion of punctum ẃ drains tears.

Xerostomia may respond to frequent cool drinks/artificial saliva spray.

POLYMYOSITIS & DERMATOMYOSITIS

Polymyositis is an idiopathic inflammatory muscle diseases. characterized by insidious, symmetrical, prominent proximal muscle weakness resulting from muscle inflammation, ⇧ muscle enzymes & characteristic EMG finding.

Signs & symptoms

Skin: rash of dermatomyositis consists of erythematous patches ẃ sometimes are scaling or atrophic & distributed over face, neck, upper chest & extensor surfaces & light-exposed areas may be seen.

Lung: chronic interstitial lung diseases.

Joints: mild symmetrical inflammatory arthritis.

Muscles: most pts have gradual but steady progression of muscle weakness.

Pharyngeal muscle weakness: can lead to a problem in swallowing & aspiration & respiratory muscle dysfunction. Pt may have also dysphonia & facial oedema.

Other features: retinitis & myocardial involvement may occur.

Diagnosis

• Muscle enzyme (⇧CK) • Muscle biopsy • EMG characteristic.

Treatment

Prednisolone (start é 1 gm/kg/D PO). Immunosuppressive.

MIXED CONNECTIVE TISSUE DISEASE

MCTD combines features of SLE, systemic sclerosis & polymyositis. Renal or CNS involvement is rare. Antibodies against ribonucleic protein are present.

Treat é immunosuppressive including steroids.

RELAPSING POLYCHONDRITIS

Relapsing Polychondritis attacks pinna, nasal septum & larynx, the last causing stridor. Is associated é aortic valve disease, arthritis & vasculitis. Treat é steroids.

BEHCET'S DISEASE

A multiorgan disease associated é certain HLA-types & thrombosis. More common in men. Male to female ratio 2:1.

Signs & symptoms

•***Joints:*** arthritis. •***Eyes:*** pain, ⇩ vision, floaters, iritis, retinal vein occlusion.

•***Mouth, scrotum, labia***: painful ulcers ẃ heal by scarring. •***Gut:*** colitis.

•***CNS:*** meningoencephalitis, ⇧ ICP, brainstem signs, dementia, myelopathy, encepha lopathy, cerebral vein thrombosis.

Treatment: Colchicine, steroids (topical & oral), other immunosuppressive.

GOUT

A group of disorders of purine metabolism that are characterized by ⇧ serum uric acid, urate deposits in articular or extra articular tissues. Elevation of serum uric acid alone is not sufficient for diagnosis of gout; only 10% of pts é hyperuricemia develop gout. Some unknown factors predisposes some pts to urate deposition & articular inflammation, in the setting of hyperuricemia.

Etiology

All gout syndromes are characterized by either episodic or constant ⇧ of serum uric acid >7 mg/dl. Pts é ⇧ serum uric acid are mainly due to:-

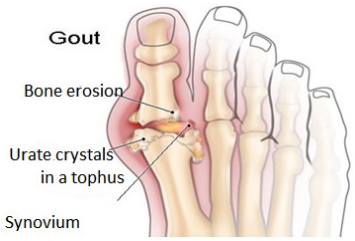
Overproduction: account for 10% of pts. These pts synthesize more than the normal amount of uric acid. The urinary excretion of urate is **>**1000 mg/day. The defect causing uric acid overproduction may be; •Primary; purine pathway enzyme defect. or •Secondary due to ⇧ cell turn over or cellular destruction associated é alcohol use or hematologic malignancies, or chronic haemolysis, or chemotherapy.

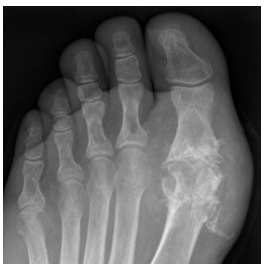
Under secretion of uric acid: account for 90% of pts. é ⇩ renal excretion of uric acid is the underlying reason for hyperuricemia (urinary excretion of uric acid is <700 mg/dl). Drugs as Diuretic, Aspirin & alcohol interfere é tubular handling of urate. Renal diseases as CRF, Lead nephropathy or inherited diseases as Lesch Nyhan sy. (IEM result from deficiency of enzyme Guanine hypoxanthine phosphoribosyl tran-sferase, causing accumulation of uric acid).

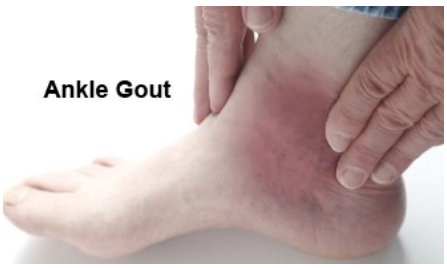
Conditions associated é Gout

- ***Obesity:*** serum uric acid level ⇧ é body weight.
- ***DM***: more common in gout pts.
- ***Hypertension:*** more common in gout pts.
- ***Hyperlipidaemia & Atherosclerosis***

Clinical stages of gout







Asymptomatic hyperuricemia

Characterized by ⇧ serum uric acid level in the absence of clinical evidences of deposition diseases (i.e. arthritis, tophi, nephropathy or uric acid stones). These pts have an ⇧ risk of having nephrolithiasis or acute obstructive uropathy.

Acute gouty arthritis

Is the primary manifestation of gout, is an extremely painful é acute onset arthritis. Most pts (80-90%) are middle aged or elderly men who have sustained asymptomatic hyperuricemia for 20-30 yrs before the 1st attack. Premenopausal women are not affected by gouty arthritis, perhaps due to the effect of oestrogen on uric acid clearance. However gout may be seen in postmenopausal elderly women who have mostly associated hypertension. Onset of acute gouty arthritis in teens or 20s is unusual & when it occurs it is often associated é 1ry or 2ry causes of uric acid overproduction. Several events may ppt acute gouty arthritis include: dietary excess, trauma, surgery, excessive alcohol ingestion, ACTH or glucocorticoid withdrawal, hypouricemic therapy & serious medical illnesses like MI & stroke. An acute onset of severe, painful & tender joint swelling, affecting the 1st MCPJ (called podagra). Other joints also may be affected including tarsal joints, ankle & knee. The fingers joints may be inflamed in elderly pts. Many attacks occur suddenly at night é rapid evolution of joints é erythema, swelling, tenderness & warmth. Intense joint inflammation can extend into the soft tissue & mimic cellulitis or phlebitis. Fever can occur in sever attacks. Polyarticular involvement can occur in some

cases & typically progression from monoarticular to polyarticular involvement occurs by extension to adjacent joints. Acute attacks usually resolve spontaneously in few days (3-10 days), although some can extend over several wks. The affected joint usually returns to normal between attacks & pt don`t have residual symptoms until the next episode. Intercritical gout: the third stage of gout is asymptomatic period after the initial attack. Recurrence of new attacks may occur during this stage. 7% of pts never experience a new attack of acute gouty arthritis after the 1st attack. However 62% experience recurrence within one yr. Typically the pt is asymptomatic between attacks, but attacks become more frequent & abate more gradually if urate deposition untreated.

Diseases progression

Attacks tend to become polyarticular & more sever overtime. Some pts develop chronic inflammatory arthritis éout asymptomatic intervals leading to a condition ẃ may resemble Rhed arthritis.

Chronic tophaceous gout

Develop in untreated pts & is the final stage of gout. The tophus is a collection of urate crystal masses surrounded by inflammatory cells & fibrosis. Typical locations for tophaceous deposits are:-

- The pinna of the ear.
- The surfaces of chronically involved joints.
- The extensor surface of the forearm.
- The olecranon process.
- The intrapatellar & Achilles tendons.

Renal complications

May arise at any stage of gout, nephrolithiasis is the only common clinical presentation of renal involvement. Proteinuria & impaired ability to concentrate urine related to urate deposition in the renal interstitial have been described in gout pts.

Investigations

•***Blood tests:*** as WBCs count, CRP, ESR, uric acid level are helpful in supporting diagnosis if elevated, but if normal can`t definitively R/O gout or pseudo gout.

•***24 hrs urine for Uric A:*** **<**600 mg is under excretion & **>** 600 mg is overproduction

•***Joint aspiration:*** (synovial fluid) for identification of the needle shaped yellow crystals under polarized light is diagnostic.

•***Serum uric acid:*** not diagnostic & may be normal during attack (N: 3.5-6.7mg/dL).

•***X ray of joint:*** destructive lesion in joint or punch-out lesions (tophi).

•***CT scan/MRI:*** for differential diagnosis of gout, pseudo gout, osteoarthritis & RA.

•***DECT:*** (Dual Energy Computerized Tomography) identify where uric acid has collected & replacing aspiration of fluid to confirm diagnosis.

Management:

Gouty diet & hydration: are very important in preventing gout attacks, drinking lots of water helps to dilute urinary uric acids, thus ⇩ the chance of attacks.

Avoidance of purine rich foods: as red meat, kidney, liver, mackerel, sardines, shellfish, oily fish, mushrooms & dried beans

⇧ Intake of high potassium foods: as cherry, orange, apple, bananas, apricot, figs, mangoes, leafy green vegetables, potato, milk & milk products ẃ enhance alkalinisation of urine preventing precipitation of uric acid & ⇧ its solubility in urine.

Drugs used in acute attack: NSAIDs are the first line, tapered gradually as symptoms allows, Indomethacin cap 25 mg 1X4 for 5-7 days, if contraindicated, the use of corticosteroid is effective, the intraarticular steroids is an alternative therapy when systemic therapy is contraindicated, colchicine has been the medication traditionally used for acute gout, but it has significant GIT toxicity & delayed onset of action. Colchicine should be given é caution in pt é hepatic, renal, or CV disease.

Intervals between flares (free stage): the focus in this stage is prophylactic.

Chronic gout (advanced gout & complications): Allopurinol (xanthine oxidase inhibitor) is the drug of choice, ⇩ uric acid production, Zyloric tab 100, 300 mg, 300-800 mg/day as single or divided doses, used in case of normal renal functions & ⇩ urate clearance by the kidneys. Uricosuric drugs, ⇧ renal excretion of uric acid through inhibition of renal proximal tubular reabsorption of uric acid, as Probenecid, 1-2 gm/day, pts taken uricosuric agents are at risk for urolithiasis. This risk can be ⇩ by ensuring high urinary output & sodium bicarbonate 1 gm TID. Colchicine 1500 mg tab 1 X 1

PSEUDO GOUT (CHONDROCALCINOSIS)

The deposition of CPPDC "Calcium Pyrophosphate Dihydrate Crystals" in the hyaline cartilage or fibrocartilage, is a metabolic disease where CPPDC are formed within the joint space, most often affect the knee, occur more in older pts leading to calcification of fibrocartilage (chondrocalcinosis) may associated é hyperparathyroidism, RA, or gout. The crystals are rhomboid shaped & positively birefringent, crystals will be blue when placed under polarized light. The X ray in pseudo- gout shows thin calcification in the articular cartilage or menisci é involvement of the patella-femoral joint. Management is similar to gout.

Food cause or trigger Gout


Foods good for Gout

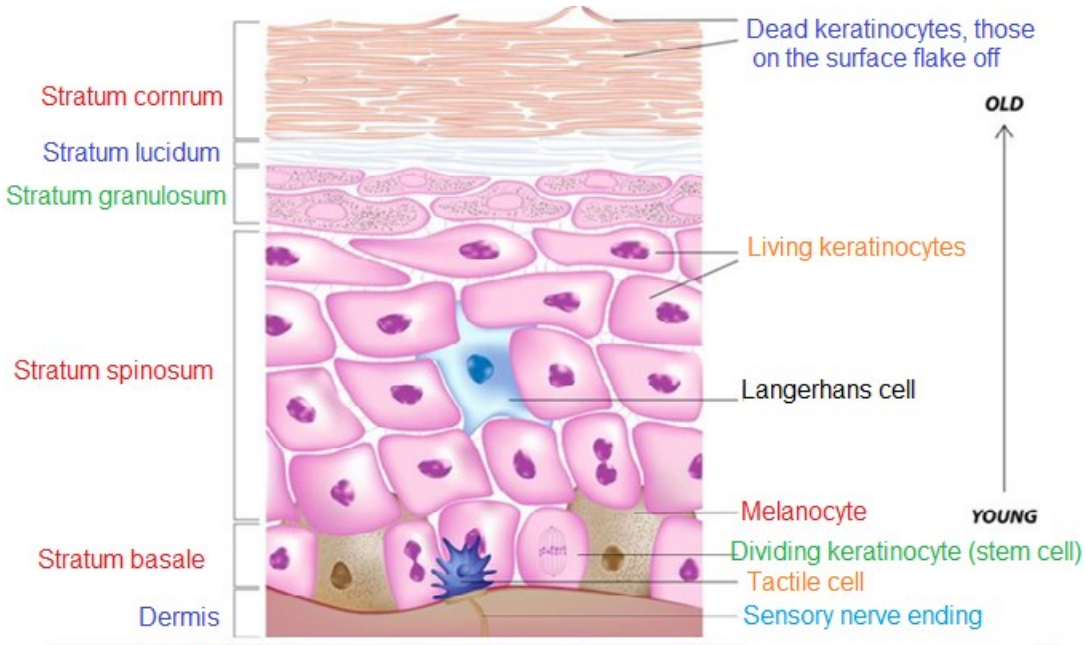
CHAPTER X

DERMATOLOGY

- ☆ Introduction
- ☆Definition & Terminology
- ☆ Fungal Infection
- ☆ Viral Infection
- ☆Cellulitis
- ☆Erysepelas
- ☆ Psoriasis
- ☆ Acne
- ☆Erythema
- ☆ Contact Dermatitis
- ☆Vitiligo
- ☆Pityriasis
- ☆ Alopecia
- ☆Ecthyma
- ☆Icthyosis
- ☆Epidermolysis
- ☆Cancer of skin
- ☆ Burns

INTRODUCTION

Structures & Functions of the skin



The skin is the largest organ in the body. It comprises about 15% of body weight. All skin is made up of these 3 layers (epidermis, dermis & subcutaneous tissue). Although there is a considerable regional variation in their relative thickness: the epidermis is thickest on the palms & soles, very thin on the eyelids. The dermis is thickest on the back. The amount of fat is generous on the abdomen & buttock compared ē the nose & sternum. It is composed of three layers: The epidermis, the outer most layer is directly contiguous ē the environment. Cells of the epidermis are; ***Keratinocyte*** ẃ is formed by an ordered arrangement of cells - produces keratin ẃ forms the outer most skin layer covered by thin lipids to give the skin protective capacity from water & heat loss, penetration of microbial agents & other trauma by physical mechanisms. Another type of cells is the ***Langerhans' cells*** -are cells ē dendrite processes specialized in antigen processing & presentation(building immunity to infection). They are found in the epidermis but they constantly move as a result, they transport antigens to the regional LNs & present them to naïve T lymphocytes in the regional LNs & consequently the naive T lymphocytes become recruited to the specific antigen & the

resultant immunologic response occurs "They take the offenders to the police station for investigation & appropria- te response". e.g. when a child receives BCG vaccination & develops a scar. In this way, the skin is very crucial part of the immune system because of the large surface area that it spans. Countless varieties of external antigens can be sensed by the immune system via the Langerhans' cells in the epidermis. Another cells in epidermis is the ***Melanocytes*** - ẃ are melanin (pigment) producing cell. The number of melanocytes in the epidermis is the same, regardless of the person's race or skin color; it is the number, shape & size of melanosomes (melanin containing granules) & the type of melanin that determine difference in skin colour. The dermis is the middle layer, composed of collagen, tough & resilient part of the skin lies on the SC tissue ẃ is principally composed of lobules of fat cells.

Physiological functions of skin

1. Display: enables us to assume our own identity & to recognize among our selves & ēout it, the emotional expressions wouldn't be possible.
2. Protection: from many environmentally unfavourable factors; such as, thermal, chemical, ultra violet radiation & different disease-causing microorganisms. It also protects from unnecessary entry & egress of fluids into & from the body.
3. Thermoregulation: because it bears receptors to detect temperature, it conveys sensory input to the CNS so that the thermoregulatory centre can respond appropriately. The skin is a peripheral thermoregulatory organ through sweating, vasodilation & shivering.
4. Immunologic: the skin is an end organ for many immunologically mediated disorders as well as a tool for immunologic research. Because it bears immunologic cells (lymphocytes, langerhans' cells & mast cells) it has an active role in immunologic field of action. The skin can be viewed as a peripheral arm of the immune system involved

in normal homeostasis & host defence.

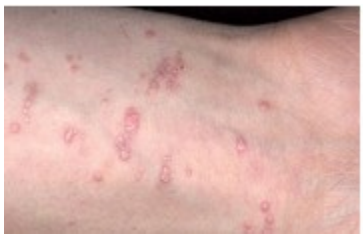
5. Synthetic function: the skin synthesizes Vit D, different hormones, melanin & other substances.

DEFINITIONS/TERMINOLOGY

Macule

Change in the colour of the skin. Flat, non-palpable, if you were to close your eyes & run your fingers over the surface of a purely macular lesion, you could not detect it (not raised or depressed compared to the skin surface). Lesions are <10 mm in diameter. A macule >10 mm is referred to as a patch. A patch is a large macule. Examples include freckles, flat moles, tattoos, & port-wine stains, rashes of rickettsial infections, rubella, measles (can also have papules & plaques) Macules are seen also as allergic drug eruptions.

Papules

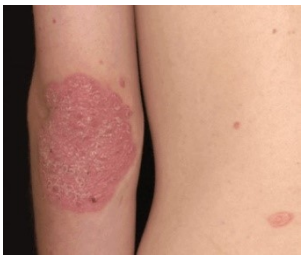


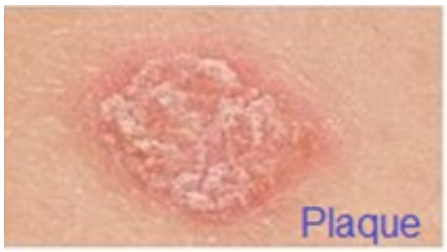
Are elevated lesions usually < 10 mm in diameter that can be felt or palpated. Examples include nevi, warts, lichen planus, insect bites, seborrheic & actinic keratoses, some lesions of acne & skin cancers. The term maculopapular is often loosely & improperly used to describe many red skin rashes; because this term is nonspecific & easily misused, it should be avoided.

Nodules

Are firm papules. Raised solid lesion > 10 mm, may be in the epidermis, dermis, or SCT. Examples include cysts, lipomas & fibromas.

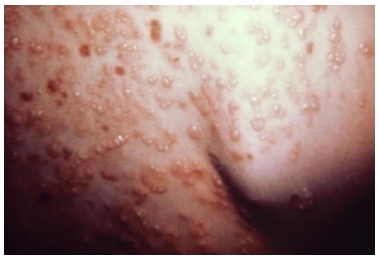
Plaques

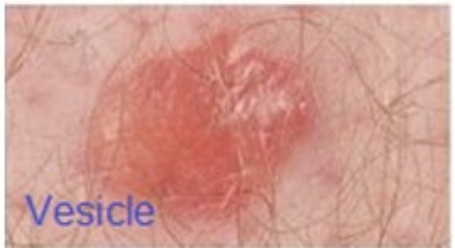




Are palpable lesions >10mm in diameter that are elevated or depressed compared to the skin surface. Plaques may be flat topped or rounded. Lesions of psoriasis & granuloma annulare commonly form plaques.

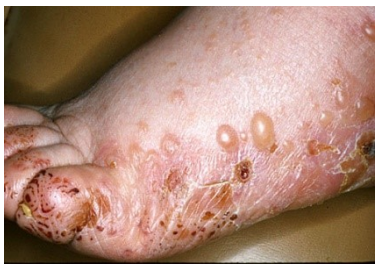
Vesicles





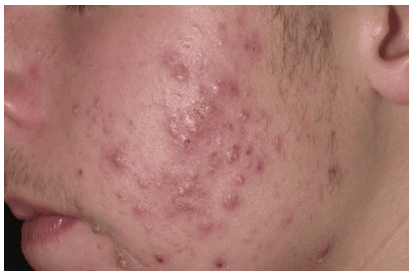
Are small, raised, clear, fluid-filled blisters < 10 mm in diameter. Vesicles are characteristic of herpes infections, acute allergic contact dermatitis, & some autoimmune blistering disorders (e.g., dermatitis herpetiformis).

Bullae



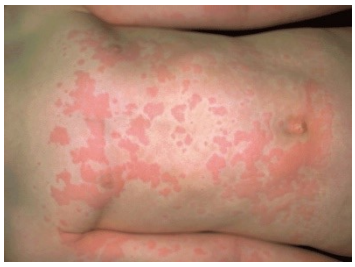
Are clear fluid-filled blisters > 10 mm in diameter. These may be caused by burns, bites, irritant or allergic contact dermatitis & drug reactions. Classic autoimmune bullous diseases include pemphigus vulgaris & bullous pemphigoid. Bullae also may occur in inherited disorders of skin fragility.

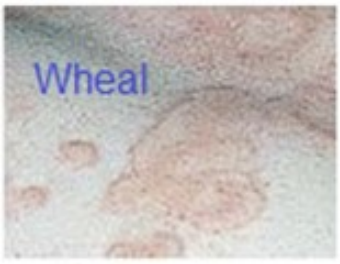
Pustule



Pustules are vesicles (<10 mm in diameter), that contain pus. Pustules are common in bacterial infections, folliculitis & may arise in some inflammatory disorders including pustular psoriasis (as sterile pustule).

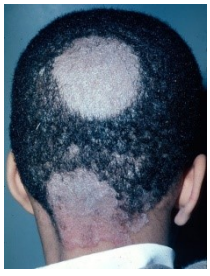
Urticaria





Wheals or hives area of oedema in the upper epidermis. Oedematous, transient papule or plaque caused by infiltration of dermis by fluid. Wheals are pruritic & red. Wheals are common manifestation of hypersensitivity to drugs, stings or bites, autoimmunity & less commonly, physical stimuli including temp, pressure & sunlight. The typical wheal lasts < 24 hr.

Scales



Excessive number of dead keratinocytes produced by abnormal keratinization, heaped-up accumulations of horny epithelium. Scaling is an ⇧ in the dead cells on the surface of the skin (stratum corneum). May be psoriatic-type (large white or silver flakes),pityriasis-type (branny powdery), or lichenoid (tightly adherent to skin surface)

Lichenification is caused by chronic rubbing ẃ results in palpably thickened skin ē ⇧ of skin markings & lichenoid scale. It occurs in chronic eczema e.g. atopic dermatitis, seborrheic dermatitis & fungal infections.

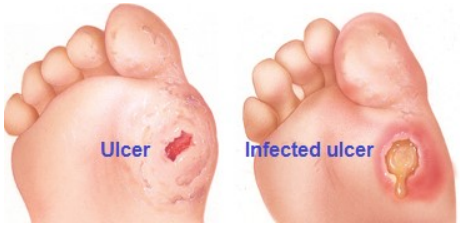
Crusts

Scabs occurs when plasma exudes through an eroded epidermis. It is rough on surafa-ce & yellow or brown in colour. Bloody crust appears red, purple or black. Crusting can occur in inflammatory or infectious skin diseases (e.g. impetigo).

Erosions

Are open areas of skin that result from loss of part or all of the epidermis. it is a sh-allow moist or crusted lesion. Erosions can be traumatic or can occur ē various infl-ammatory or infectious skin diseases. An excoriation is a linear erosion caused by scratching, rubbing, or picking.

Ulcer



Result from loss of the epidermis & at least part of the dermis. It may be covered ē a dark-colured crust called an eschar. Causes include venous stasis dermatitis, physical trauma ē or ēout vascular compromise (eg, caused by decubitus ulcers or peripheral arterial disease), infections & vasculitis.

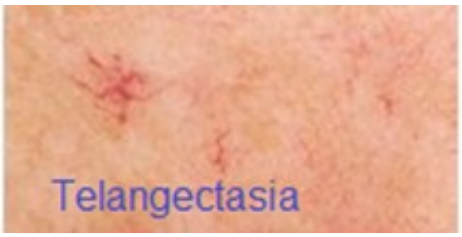
Petechiae

Bleeding into the skin. Are non-blanchable punctate foci of Hge. Causes include platelet abnormalities (e.g. thrombocytopenia, platelet dysfunction), vasculitis & infections (e.g. meningococcemia, Rocky Mountain spotted fever, other rickttsioses).

Purpura

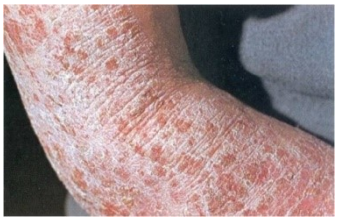
Is a larger area of Hge that may be palpable. Palpable purpura is considered the hallmark of leukocytoclastic vasculitis. Purpura may indicate a coagulopathy disorder. Large areas of purpura may be called ecchymoses or, colloquially, bruises.

Telangiectases



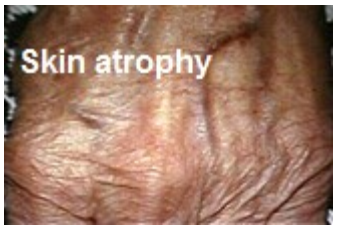
Are foci of small, permanently dilated blood vessels that may occur in areas of sun damage, rosacea, systemic sclerosis, hepatic disease (spider naevi), or inherited diseases (e.g. ataxia-telangiectasia, hereditary haemorrhagic telangiectasia) or after long-term therapy ē topical fluorinated corticosteroids (is the name given to prominent cutaneous blood vessels).

Lichenification



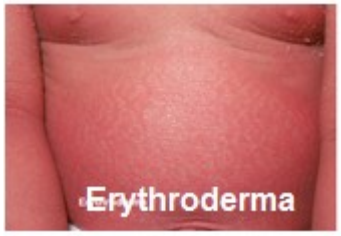
Is thickening of the skin ē accentuation of normal skin markings; it results from repeated scratching or rubbing.

Atrophy



Is thinning of the skin, ẃ may appear dry & wrinkled, resembling cigarette paper. Atrophy may be caused by chronic sun exposure, aging, & some inflammatory & neoplastic skin diseases, including cutaneous T-cell lymphoma & SLE. Atrophy also may result from long-term use of potent topical corticosteroids.

Erythroderma

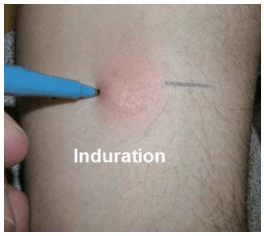


Is a term used to indicate red skin over the entire body.

Scars

Are areas of fibrosis that replace normal skin after injury. Some scars become hypertrophic or thickened & raised. Keloids are hypertrophic scars that extend beyond the original wound margin.

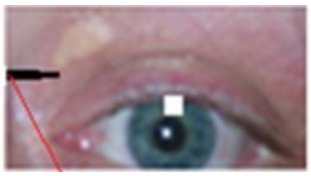
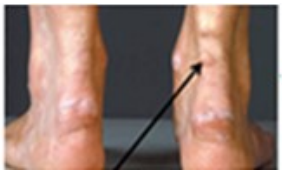
Induration



Deep thickening of the skin, can result from oedema, inflammation, or infiltration.

Indurated skin has a hard, resistant feeling. Induration is characteristic of panniculitis, some skin infections, tuberculin test & cutaneous metastatic cancers.

Xanthomas

Xanthelasma   Tendinous xanthomas

Yellowish, waxy lesions, may be idiopathic or in pts who have lipid disorders.

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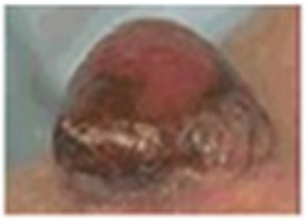
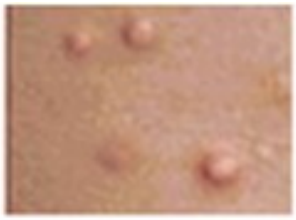
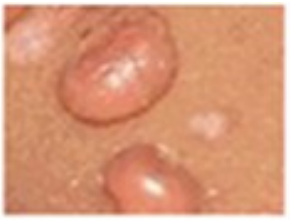
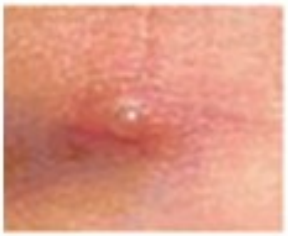
Macule

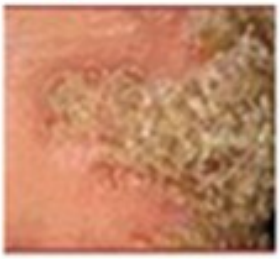

Nodule

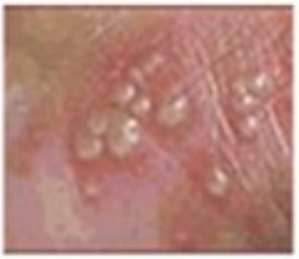

Papule


Bulla

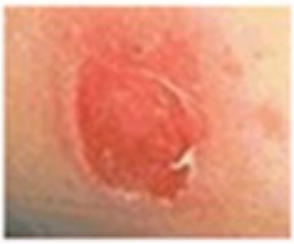

Vesicle


Scale

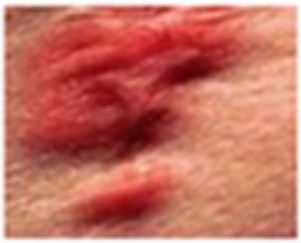

Crust


Pustule

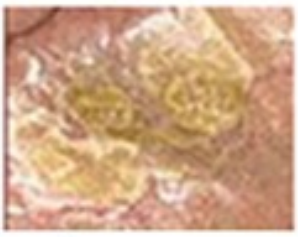

Excoriation

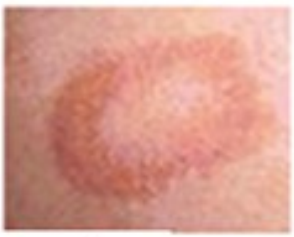

Erosion


Lichenification


Scar


Fissure


Plaque


Patch

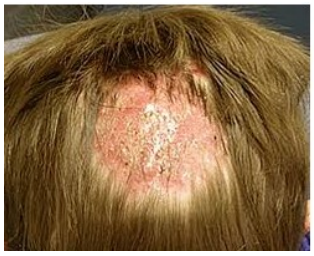
FUNGAL INFECTION

Superficial fungal infections of the skin are one of the most common dermatologic conditions seen in clinical practice. Therefore, recognition is important for primary care physicians. However, making the correct diagnosis can be difficult, because these infections can have an atypical presentation or be confused ē similar-appearing conditions. Superficial fungal infections can be divided into 3 categories:-

•Dermatophytic infections. •Pityriasis versicolor. & •Candidiasis.

Dermatophytes specifically Trichophyton, Epidermophyton & Microsporum species, are responsible for most superficial fungal infections. The term "Tinea" refers exclusively to dermatophyte infections as explained below.

TINEA CAPITIS



Tinea Capitis is a dermatophytic infection of the head & scalp, usually found in infants, children & young adolescents. Most infections occur in preschool-aged children. Around puberty. Commonest presentation is scaly patches on the scalp ē variable degree of hair loss & generalized scaling that resembles Seborrheic dermatitis may occur on the scalp. Cervical lymphadenopathy can occur when there is secondary bacterial infection. Keroin is a form of Tinea Capitis ē accentuated inflammatory response. It is boggy, nodular tender mass ẃ may form pus. An unusual scaling reaction known as favus may give the scalp a waxy or doughy appearance ē thick crusted areas. Differential diagnosis of Tinea Capitis includes seborrheic dermatitis, dandruff, scalp psoriasis, atopic dermatitis, scalp impetigo & alopecia areata. The finding of large areas of alopecia that have early pustule formation favors a diagnosis of Tinea

capitis over alopecia areata.

Investigation: KOH examination of hair pulled not cut to look at the root. Looking for the fungal elements from skin scraping, nail or hair.

Treatment

Topical do not penetrate deeply enough. Griseofulvin in a dose of 10-20 mg/kg for 6-8 wks is the first-line of treatment. Griseofulvin should be taken after fatty meal. Ketoconazole 2-4 mg/kg for 10 days. Concurrent use of Selenium sulphide 2.5% reduces spore formation & shedding. There is high risk of recurrence. Topical treatment can be added to ⇩ the transmission & accelerate resolution. Whitefield ointment is preferred in the absence of 2ry bacterial infection. Other family members should also be examined and treated.

TINEA CORPORIS

Tinea corporis is dermatophytosis of the glabrous skin of the trunk & extremities. Lesions are round, scaly patches that have a well-defined, enlarging border & a relatively clear central portion. The active edge often contains follicular papules. Itching is variable & not diagnostic. Tinea corporis can assume a giant size when steroids are applied for cosmetic reasons or as a result of miss diagnosis.

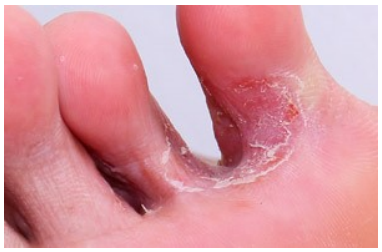
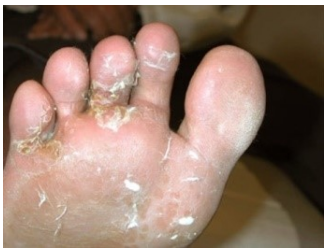
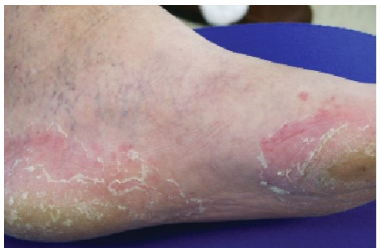
Differential Diagnosis: •Lichen planus •Atopic eczema •Psoriasis.

Investigation: KOH from active edge of lesion. Culture for fungus only in doubtful cases if the KOH is negative.

Treatment

Small & single lesion can be treated ē topical agents. Clotrimazole 1%, ketoconazole 2%, Miconazole 1%. BID for 2 wks. Systemic: ketoconazole 2-4 mg/kg of BW, for 10 days. Itraconazole & fluconazole are choices if available. Griseofulvin is also effective for the treatment of Tinea corporis.

TINEA PEDIS

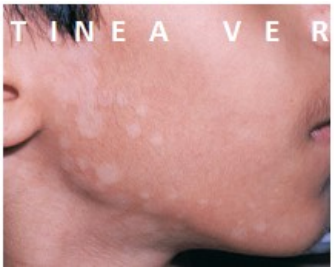




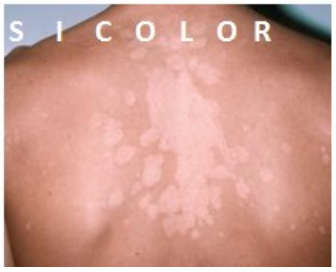
Tinea pedis is fungal infection of the feet & is usually related to sweating & warmth & use of occlusive footwear. Men between 20- 40 yrs of age are most frequently affected. The infection often presents as white, macerated areas in the 3rd or 4th toe webs. It may also present ē a classic pattern on the dorsal surface of the foot or as chronic dry, scaly hyperkeratosis of the soles & heels. Itching is also common ē vesicular or hullous lesion. It is transmitted by direct contact or sharing of shoes, towels or bath.

Treatment

- Topical antifungal creams or ointments applied regularly for 4-6 wks.
- Systemic treatments provide better skin penetration than most topical preparations, Itraconazole, terbinafine & Griseofulvin are good choices for oral Rx.
- Itraconazole & Terbinafine are more effective than Griseofulvin. Once-weekly dosing ē Fluconazole is another option, especially in noncompliant pts.
- Personal hygiene (foot hygiene) is highly advised.

TINEA VERSICOLOR





Is a common superficial infection caused by the organism Pityrosporum orbiculare ẃ is a saprophytic yeast that is part of the normal skin flora. Lesions can be hypop-

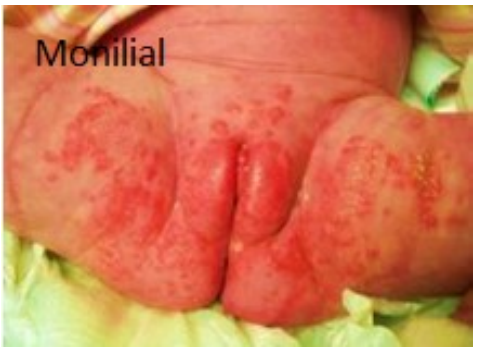
igmented, light brown or salmon coloured macules. A fine scale is often apparent, especially after scraping. Individual lesions are typically small, but frequently coalesce. Lesions are limited to the outermost layers of the skin. Most commonly found on the upper trunk, extremities & less often on the face & intertriginous areas. While most pts are asymptomatic, some complain of pruritus.

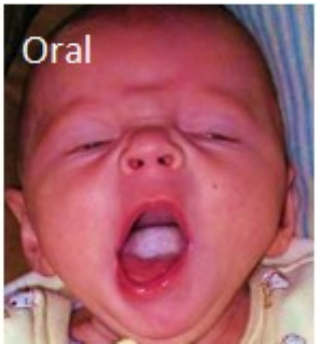
Diagnosis: direct microscopic examination of scale ē 10% potassium hydroxide.

Differential diagnosis: ■Seborrhoea ■Eczema ■Pityriasis Rosea ■2ry Syphilis.

Treatment: Topical antifungals. Oral antifungals can be used for more extensive disease: Ketocanozole 400 mg x 1 dose. Fluconazole & Itraconazole also effective.

CANDIDIASIS





Candidal Dipar Dermatitis: appears as confluent bright red & plaques, scattered pustules, overlying scales & satellite lesions on the periphery. Involving the skin folds. Flourishes in warm moist environment. Babies who have recently taken antibiotics are more likely to develop a yeast infection.

Oral Monaliasis: creamy white sores over the tongue & in mucosal buccal cavity.

Differential diagnosis

- Prolonged contact é urine or faeces.
- Irritant/Contact dermatitis.

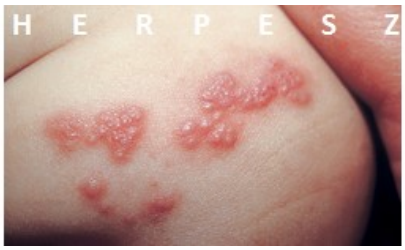
Treatment

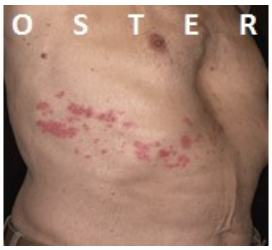
❄ Local antifungal ointment or oral drops, or Gel for oral monaliasis.

❄ Diaper area to dry between changes. Using topical barrier oint. as zinc oxide.

VIRAL INFECTION

HERPES ZOSTER

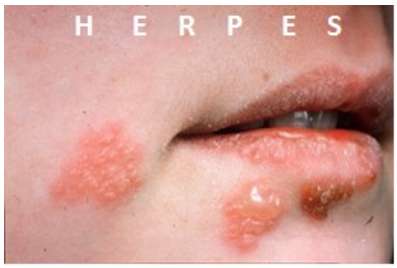


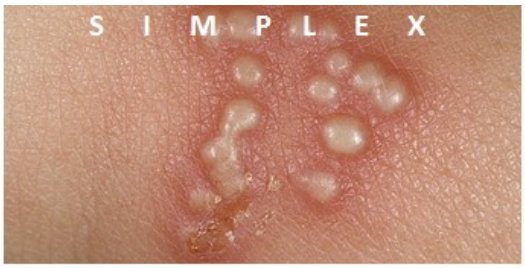


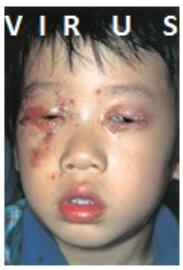
Reactivation of endogenous latent VZV infection within the sensory ganglia results in herpes zoster or "shingles", a syndrome characterized by a painful, unilateral vesicular eruption in a restricted dermatomal distribution. How the virus emerges from latency is not clearly understood. Pts frequently experience a prodrome of fever, pain, malaise & headache ẃ precedes the vesicular dermatomal eruption by several days. The rash initially appears along the dermatome as grouped vesicles or bullae ẃ evolve into pustular or occasionally haemorrhagic lesions within 3-4 days. The thoracic & lumbar dermatomes are the most commonly involved sites of HZ. The complications of HZ include ocular, neurologic, bacterial superinfection of the skin & post herpetic neuralgia.

Treatment: •Antivirals: Acyclovir/Famciclovir/Valacyclovir. •Antivirals ē Corticosteroids. •Analgesics: Opioids/Acetaminophen.

HERPES SIMPLEX







❄<u>HSV- 1 Primary infection:</u> oropharyngeal sores (children), IP is 2-12 days. Presented ē gingivostomatitis, pharyngitis, or multiple small vesicles in clusters or singly ẃ resolves in 10-14 days. Symptoms may include; fever, vesicular & ulcerative lesions, oede-

ma, lymphadenopathy, malaise, recurrence in some people throughout adult life. May presented ē Keratoconjunctivitis & self-transmission (autoinoculation) to eye, causes lesions, scarring can cause visual impairment, may lead to autoimmune response against eyes.

❄Genital HSV-2 Primary Infection: HSV-2: genitalia (adults), IP is 2-7 days. Vesicular lesions anywhere in genital tract, may associated ē fever, malaise, tender bilateral inguinal adenopathy, lesions may ulcerate & become very painful, lesions may involves urethra leading to urinary retention. May persist for wks. Liability for recurrence.

Complications: IUI as a result of inoculation of virus to the baby during labour, it carry very high mortality to the baby ẃ can presented ē aseptic meningitis, or visceral herpes. If mother is suspected to have genital herpes SC is highly indicated.

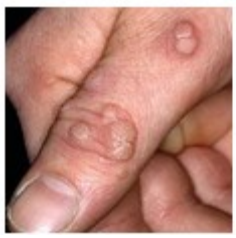
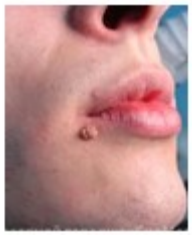
Diagnosis: •Cytopathology: multinucleated giant cells from skin scrapings •Virus isolation •Immunofluorescence •PCR; used for systemic or encephalitic disease •Serology; IgG appears in 4-7 days, cannot discriminate HSV-1 from HSV-2.

Management: i) Supportive: education, psychological support, analgesics, keep ar-ea clean & dry. ii) Antiviral (Acyclovir/Famciclovir/Valacyclovir), topical, oral, or IV.

VIRAL WARTS

Warts are tumours or growths of the skin caused by infection ē Human Papilloma Virus. More than 70 HPV subtypes are known. Warts can have several different forms based upon location & morphology (flat, mosaic or filiform). Lesions may occur singly or in groups, or as coalescing lesions forming plaques. Scrape off any hyperkeratotic debris & reveal thrombosed capillaries (seeds). Warts are particularly common in childhood & are spread by direct contact or autoinocculation. This means if a wart is scratched, the viral particles may be spread to another area of skin. It may take as long as 12 months for the wart to first appear (IP following exposure is 2-6 months).

In children, even ēout treatment, 50% of warts disappear within 6 months while 90% are gone in 2 yrs. They are more persistent in adults but they clear up eventually. Cutaneous warts also more common among certain occupations as handlers of meat, poultry & fish. Predisposing conditions include atopic dermatitis & any condition in ẃ there is ⇩ cell-mediated immunity.

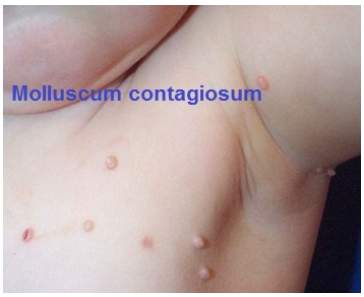



Diagnosis: is based upon clinical appearance.

Differential Diagnosis: •Lichen Planus. •Seborrheic Keratosis. •Acrochordon or skin tag. •Clavus or corn.

Management: many people don't bother to treat them because treatment can be more uncomfortable &troublesome than the warts. They are hardly ever a serious problem. However, warts may be painful & they often look ugly & cause embarrassment. Treatment include; Salicylic acid, Liquid nitrogen, Cantharidin. Cyrotherapy, curettage, laser therapy. Immunotherapy, intra-lesional injections.

MOLLUSCUM CONTAGIOSUM

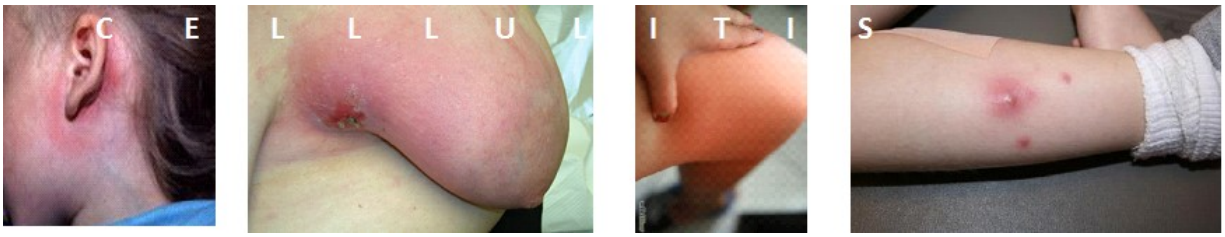


Poxvirus, sharply circumscribed single or multiple skin-colored, dome-shaped papules ē waxy surface.Usually umbilicated centre although can have protruding white centre. Areas: trunk, axillae, face, & genitals. Contagious, spread by scratching so often in linear pattern. Curd like core often expressed (typical Molluscum bodies under microsc-

ope). Occurs in HIV pt é low CD4 count ē ẃ atypical presentations are common, commonly seen in children & tends to be generalized, giant molluscum contagiosum & 2ry infection in association ē HIV infection.

Treatment: Cryosurgery, Curettage or Electrosurgery. Cantaridine or 5-Fluorourcil.

CELLULITIS



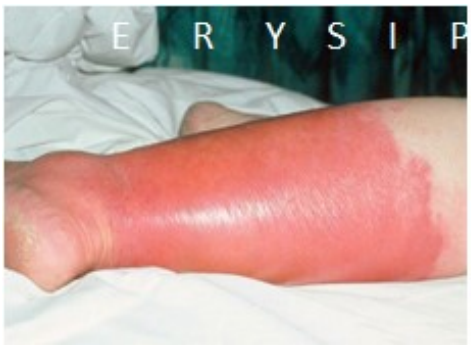
Is an infection of the skin ē some extension into the subcutaneous tissues. An extremity is the most common location but any area of the body can be involved.

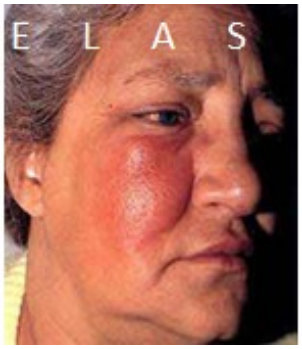
Five factors were identified as independent risk factors:- Lymphedema, Site of entry (leg ulcer, toe web intertriginous & traumatic), Venous insufficiency, Leg oedema, & Being overweight. Cellulitis is a recognizable clinical syndrome ē both local & systemic features. Systemic symptoms include: Fever & chills, Myalgias, ⇧ WBC count. The local findings include: Macular erythema that is largely confluent, Generalized swelling of the involved area, Warmth to the touch of the involved skin, Tenderness in the affected area, Tender regional lymphadenopathy is common, Lymphangitis may be present & Abscess formation also may be present. Cellulitis in the majority of pts is caused by β- haemolytic streptococci groups A, B, C, G & Staphylococcus aureus. Other less common pathogens include H. influenza, P. Aeruginosa, Aermonas hydrophilia, Pasturella multocida.

Diagnosis: is clinical.

Treatment: Anti-strep/Anti-staph; Cefazolin, Nafcillin, Vancomycin, Fluoroquinolones (3rd & 4th gen), or Macrolides (Azithromy) , for a duration of 10-14 days.

ERYSIPELAS



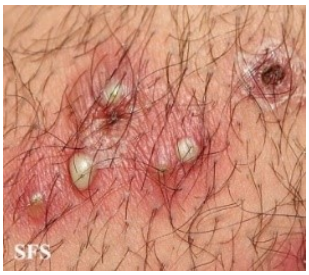


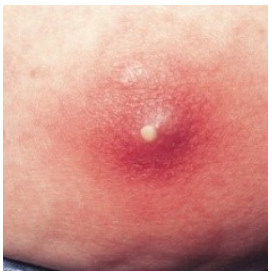
Erysipelas is a characteristic form of cellulitis that affects the superficial epidermis, producing marked swelling. Caused by bacterial organisms; β-haemolytic streptococci group A, Group C & G less commonly, Staph. Aureus, Streptococcus pneumoniae, enterococci, gram negative bacilli. The erysipelas skin lesion has a raised border ẃ is sharply demarcated from normal skin. This is its most unique feature & allows it to be distinguished from other types of cellulitis. The demarcation is sometimes seen at bony prominences. The affected skin is painful, oedematous, intensely erythematous, & indurated (peau d' Orange appearance). The face historically was the most common area of involvement.

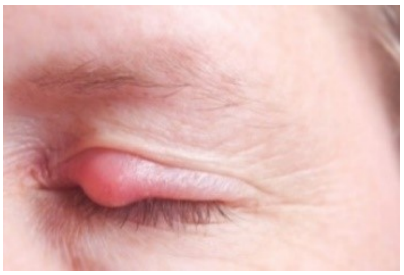
Diagnosis: is clinically. It can mimic other skin conditions as: herpes zoster (5th cranial nerve), contact dermatitis, or urticaria.

Treatment: Penicillin is the preferred treatment, Erythromycin, Clindamycin, or Fluoroquinolones. Erysipelas does have the propensity of recur.

ABSCESS







Localized collection of pus at the infection site (characteristically a staphylococcal

infection). Most common sites on hairy parts of the body exposed to irritation, pressure, friction, or moisture.

Types

Furuncle (*boil*): abscess in a hair follicle & adjacent subcutaneous tissue.

Carbuncle: several furuncles in adjoining hair follicles ē multiple drainage sinuses.

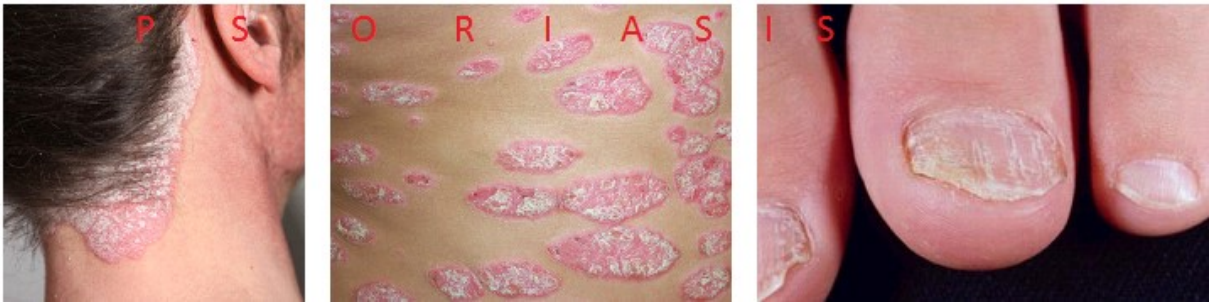
Signs & symptoms: affected portion of skin possibly extremely tender, painful & swollen. Abscess possibly enlarged, softened & open, discharging pus & necrotic material. Erythema & oedema possibly persisting at the site for days or wks. Possibly may accompanied by mild fever.

Treatment

- Cleaning infected area thoroughly ē soap & water.
- Applying hot, wet compresses to the area to promote vasodilation & drainage.
- Administering topical antibiotics.
- Incision & drainage possibly necessary after the lesion has matured.

" Once there is pus , it must be evacuated".

PSORIASIS



Is a common chronic skin disorder, typically characterized by Circumscribed red patches covered by thick, dry, silvery, adherent scales. Epidermal cells produced 6-9 times faster than normal. Commonly a family history is seen. May begin at any age, condition possibly severe if onset is in childhood

Types: ⅄ Plaque psoriasis: symmetrically distributed plaques involving the scalp,

extensor sor elbows, knees, & back. ⅄Guttate psoriasis: abrupt appearance of multiple small psoriatic lesions ⅄Pustular psoriasis: most severe form of psoriasis. Characterized by erythema, scaling & sheets of superficial pustules ē erosions ⅄Inverse psoriasis: refers to a presentation involving the intertriginous areas. ⅄Nail psoriasis: the typical nail abnormality in psoriasis is pitting ē colour changes & crumbling of the nail. Most pts ē psoriasis tend to have the disease for life. There is variability in the severity of the disease overtime ē complete remission in 25% of cases.

Signs & Symptoms

Excessive development of the basal layer of the skin. Affected areas that typically appear dry, cracked & encrusted. Build-up of skin composed of living &dead tissue. Pruritus (common). Common sites on scalp, knees, elbows, umbilicus & genitalia.

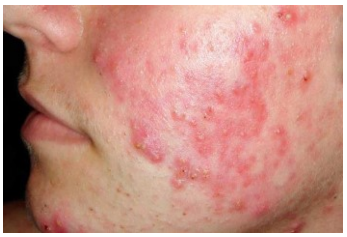
Diagnosis

Made by physical examination & in some cases by skin biopsy.

Management

Depends on type, disease extent & effect on pt. Palliative only; no cure. Topical application of medications, such as coal tar, Vit D, steroids & wet dressings. Calcipotriol (Daivonex) affects the growth & differentiation of keratinocytes via its action at the level of Vit D receptors in the epidermis. Tazarotene, is a topical retinoid, systemic retinoids. Methotrexate, Cyclosporine. Ultraviolet (UV) light therapy to retard cell production. Exposure amount depends on condition, pigmentation, & susceptibility to burning. UVB light or natural sunlight to the point of minimal erythema. UVA light from an artificial source, such as special mercury lamps. Excrimer laser, a more powerful form of UVB light therapy, directed to eliminate stubborn plaques & control scaling & inflammation. Immunmodulator therapy (Em-brel, Remicade).

ACNE VULGARIS



Common inflammatory skin disease of the sebaceous glands and their hair follicles Characterized by appearance of comedos (blackheads or whiteheads), papules (solid elevation less than 1 cm) & pustules (small raised areas of the skin filled ē pus),as shown in the illustration. Usually on the face, chest, upper back & shoulders. Most commonly caused by hormone changes during puberty, but can appear at any age. Underlying cause of genetic predisposition. Possible contributing factors, including stress & external irritants, such as soaps & cosmetics.

Classification

Type 1: Mainly comedones ē an occasional small inflamed papule or pustule; no scarring present.

Type 2: Comedones & more numerous papules & pustules; mild scaring.

Type 3: Numerous comedones, papules & pustules, spreading to the back, chest & shoulders, ē an occasional cyst or nodule; moderate scarring.

Type 4: Numerous large cysts on the face, neck & upper trunk; severe scarring.

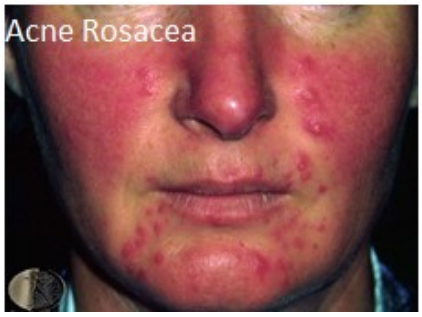
Signs & symptoms

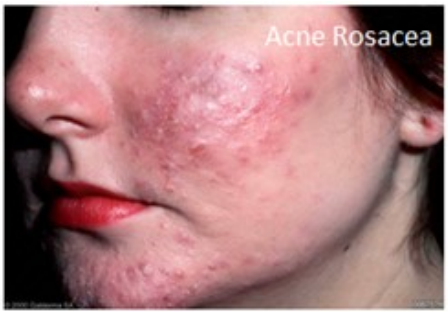
Acne plug that commonly appears first as an open comedo (black head) or a closed comedo (whitehead). Colour of comedo is caused by the melanin produced by hair follicle, not by dirt. Eventual enlargement & rupture or spreading of contents to dermis. Resulting in inflammation & acne pustules or papules. Development of scars if chronic irritation, continues over a period of time.

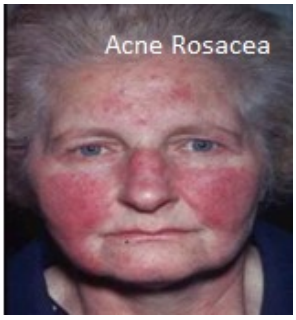
Management: Goals of reducing bacterial count, decreasing sebaceous gland activ-

ity & preventing inflammation of the follicle. Antibacterial sol. applied to the skin, orally administered antibiotics, or both. Topical agents ẃ may be used alone or in combination (ē clean hands). Skin kept as clean & dry as possible.

ACNE ROSACEA







Rosacea is an acneiform disorder of middle-aged & older adults. It is a chronic dis- order ē periods of exacerbation & remission. Characterized by vascular dilation of the central face, including the nose, cheek, eyelids &forehead. The cause of vascular dilatation in rosacea is unknown. ⇧ susceptibility to recurrent flushing reactions that may be provoked by a variety of stimuli including hot or spicy foods, drinking alcohol, temperature extremes & emotional reactions. The earliest stage is characterized by facial erythema & telangiectasia. Pts ē rosacea may develop severe sebaceous gland growth that is accompanied by papules, pustules, cysts &nodules.

Diagnosis

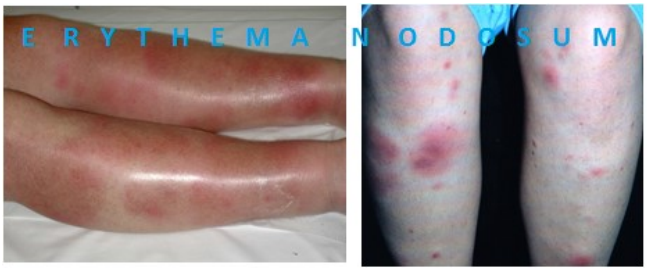
Based upon 1 or more of the following):-

- Flushing (transient erythema).
- Non-transient erythema.
- Papules & pustules.
- Telangiectasia.

Management

Topical antibiotics or benzoyl peroxide are the initial treatments of choice. Tretinoin cream is used in pts ē papular or pustular lesions that are unresponsive to other treatments. The chronicity of rosacea requires that medical therapy to be continued long-term, not just for flare-ups of the condition.

ERYTHEMA NODOSUM



Characterized by the presence of painful, erythematous, non-ulcerative nodules, often symmetric distribution, located bilaterally below the knees (mainly on the anterior tibial surface). Lesions evolve from bright red to brown-yellow, resembling old ecchymosis. Old & new lesions often coexist. Ps may also present ē fever, fatigue & arthralgia. The morphology of the lesion, a deep nodule, identifies EN as an inflammatory disease of the fat (called a panniculitis). Can occur at any age, but most cases appear between 2^{nd} & 4^{th} decades. It is 15-20 X more common in women than men. EN is not a disease, but a reaction pattern to a variety of factors.

Causes: ● Infections; streptococcal infections, TB, Histoplasmosis or Coccidiomycosis. Streptococcal disease is the most common cause of EN in children.

● Medications as oral Contraceptive pills, Sulphonamides, Aspirin & Phenobarb.

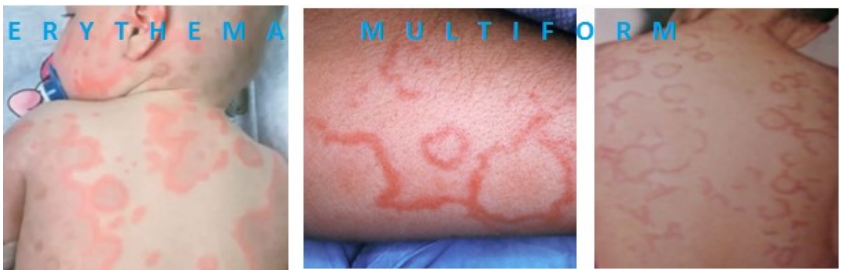
● Systemic diseases as sarcoidosis, inflammatory bowel disease are commonly associated disorders in adults ē EN.

● Neoplasms as lymphoma, leukaemia & renal cell carcinoma. ● Idiopathic > 50%.

Diagnosis: should always be followed by a search for the underlying etiology.

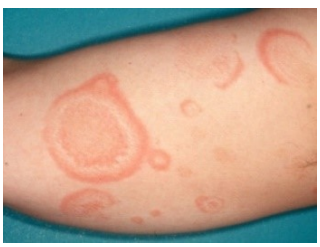
Management: it is usually self-limited or resolves ē Rx of the underlying disorder. The lesions heal ēout atrophy or scarring. Eruption generally lasts from 3 to 6 wks & recurrences are frequent. Treatment is typically symptomatic, supportive measures & pain control are recommended. The use of systemic steroids should be weighed against the possibility of masking an underlying neoplastic, inflammatory, or infectious condition. Oral potassium iodide therapy is another treatment option.

ERYTHEMA MULTIFORM



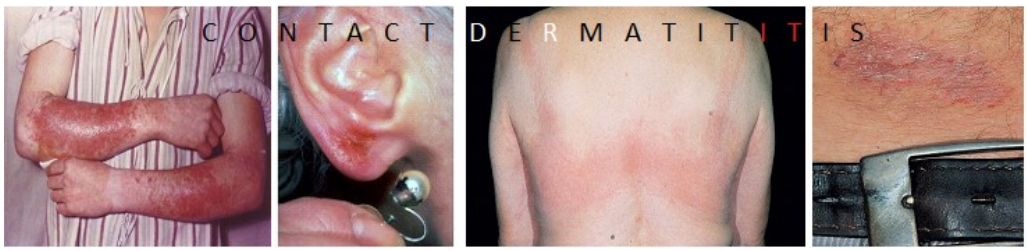
EM is a hypersensitivity reaction, commonly seen in the trunk, lower limbs, usually triggered by infections, most commonly herpes simplex virus. It presents ē a skin eruption characterised by a typical target lesion. There may be mucous membrane involvement. It is acute & self-limiting, usually resolving ēout complications. It is divided into major & minor forms & is now regarded as distinct from Stevens Johnsonn Sy. & toxic Epidermal Necrolysis. EM most commonly affects young adults (20–40 yrs of age), however all age groups can be affected. There is a male predominance but no racial bias. There is a genetic tendency to EM. The triggers for EM include; Infections associated ē 90% of cases & the commonest is herpes simplex infection, usually herpes labialis (cold sore on the lip) & less often genital herpes. Mycoplasma pneumonia (bacterial lung infection) is the next most common trigger. Others triggers including: Para poxvirus, varicella zoster, adenovirus, hepatitis viruses, HIV, CMV, Viral vaccines. Also reported in association ē Tinea, rheumatic fever, malignancies. Medications are probably an uncommon cause (<10%) of EM. Many drugs have been reported to trigger EM, including; barbiturates, penicillins, NSAIDs, sulphonamides, Phenothiazines & anticonvulsants.

ERYTHEMA MARGINATUM



Occurs commonly in trunk, lower limbs, It is associated ē rheumatic fever, malignancy, herpes simplex, mycoplasma pneumonia, or may be drug induced as ē Sulpha & Phenobarbitone, it clear from centre & spread peripherally. Appears as rings, lasting for months. Face, soles of feet & palms of the hands are usually unaffected. It is painless, itchy, hence often goes unreported & ignored.

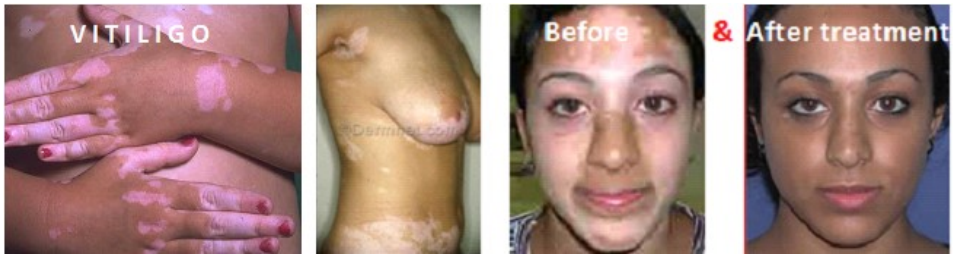
ALLERGIC CONTACT DERMATITIS



Contact dermatitis refers to any dermatitis arising from direct skin exposure to a substance. It can be allergic or irritant-induced. An allergen induces an immune response, while an irritant directly damages the skin. The most common sensitizer are the plant oleoresin urushiol found in poison ivy, poison oak & poison sumac. Other common sensitizers are; Nickel (jewellery). Formaldehyde (clothing, nail polish), Fragrances (perfume, cosmetics). Preservatives (topical medications, cosmetics). Rubber. Chemicals in shoes (both leather & synthetic).

Treatment: avoidance of exposure to the offending substance, use of corticosteroids topical or oral in the acute phase of the reaction may be helpful, cooling of the skin by using calamine lotion or aluminium acetate.

VITILIGO



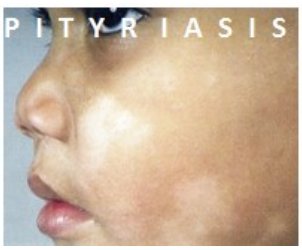
Autoimmune disease, tends to occur in families, the pigment cells in single or mul-

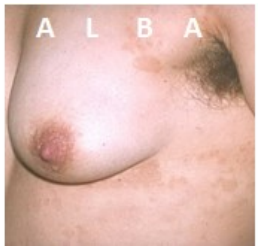
tiple areas of the body is destroyed. Vitiligo is acquired skin depigmentation that affects all races but is far more disfiguring in blacks. The precise cause of Vitiligo is unknown. Genetic factors appear to play a role. 20-30 % of pts may have positive family history. The pathogenesis is thought to involve an autoimmune process directed against melanocytes. Its peaks in the 2nd & 3rd decade of life. The depigmentation has predilection for acral areas & around body orifices (mouth, eyes, nose, anus). The course usually is slowly progressive.

Diagnosis: based upon the clinical presence of depigmented patches of skin.

Management: repigmentation therapies include:- Topical steroid, exposure to UV rays for 15 min after 2 hrs from taking oxysoralen capsules. Ultrameladinine 10 lotion (local). Surgery-minigrafting techniques. Depigmentation Rx ē Hydroquinone.

PITYRIASIS ALBA

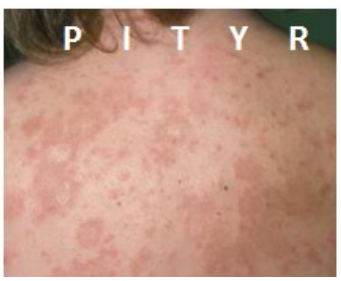


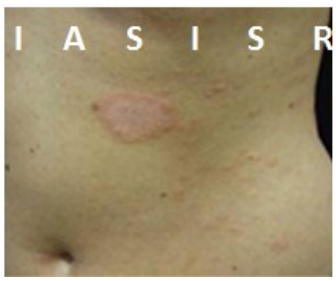


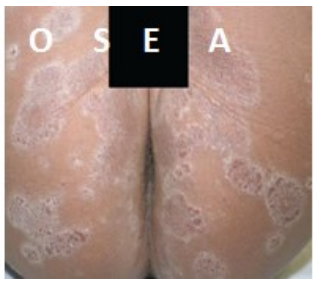
Seen in 80% of children 1-5 yrs age, as hypo pigmented lesions on light exposure areas of the body,? exposure to sun after putting perfume, may associated ē parasite infestation, or Vit A deficiency.

Management: Ultracare cream, Triderm cream, Zinc oxide ointment.

PITYRIASIS ROSEA







Pityriasis rosea is an acute, self-limited, exanthematous skin disease characterized

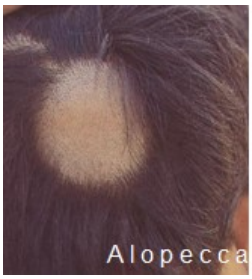
by the appearance of slightly inflammatory, oval, papulosquamous lesions on the trunk & proximal areas of the extremities. The eruption commonly begins ē a "herald" or "mother" patch, a single round or oval, rather sharply delimited pink or salmon-colored lesion on the chest, neck, or back. 2-5 cm in diameter. A few days later lesions similar in appearance to the herald patch, appear in crops on the trunk & proximal areas of the extremities. The eruption spreads centrifugally or from the top down in just a few days. The long axes of these oval lesions tend to be oriented along the lines of cleavage of the skin, like a Christmas tree pattern. Then the lesions fade ēout any residual scarring.

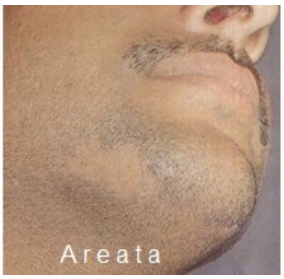
Diagnosis: ⅄The presence of a herald patch by history or on examination. ⅄The characteristic morphology & distribution of the lesions. ⅄The absence of symptoms other than pruritus make an easy diagnosis in most instances.

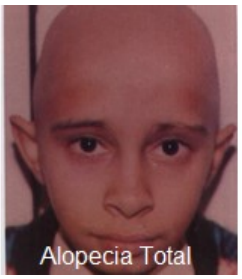
Differential diagnosis: •Psoriasis •Secondary Syphilis •Tinea Corporis •Lyme disease & •Drug eruptions.

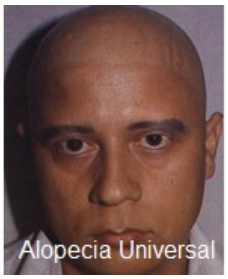
Treatment: usually reassurance, topical steroids, antipruritic lotions, phototherapy, Erythromycin in severe cases. The rash usually persists for 2-3 months.

ALOPECIA









Types

•Alopecia Areata: localized loss of hair. •Alopecia totalis: total loss of scalp hair.

•Alopecia universalis: loss of entire body hair including scalp hair.

Alopecia areata: rapid & complete loss of hair in one or most often several round

or oval patches, usually on the scalp, bearded area, eyebrows, eye lashes & less commonly on other hairy areas of the body. Approximately 1.7% of the population will experience an episode of alopecia areata during their life time.

Etiology

Exact cause is still unknown. It is autoimmune disease- mediated by the cellular arm (T-cell, macrophages), or modified by genetic factors (HLA-R4, DR 11,DQ7), or trigge-red by environmental factors e.g. trauma, neurogenic, or infection.

Associated disease: higher incidence of alopecia areata in pts ē:-

- Atopic dermatitis.
- Autoimmune disease (SLE, Thyroiditis, Vitiligo, Myasthenia gravis).
- Lichen planus.
- Down sy.

Differential Diagnosis

Tinea capitis. Trichotilomania. Secondary syphilis. Congenital triangular alopecia. Alo-pecia neoplastica. Early SLE.

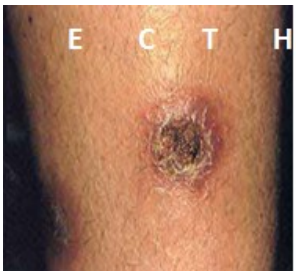
Treatment

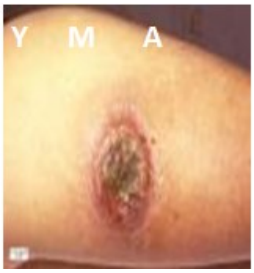
Spontaneous recovery is extremely common for patchy alopecia areata. For localized patchy alopecia areata- steroid- both local (intralesional & topical) & systemic (in short course). High potent topical steroid used as first line therapy. Intralesional ster-oid given at 4-6 weeks interval. Systemic steroid (Short course, < 8 wks) alone or ē topical steroid. If lack of response after several months therapy- Topical 1% Anthralin cream applied for 15-20 min & then shampooed off the treated side. 5% topical Minoxidil as a single agent or as an adjuvant ē topical Anthralin. PUVA.

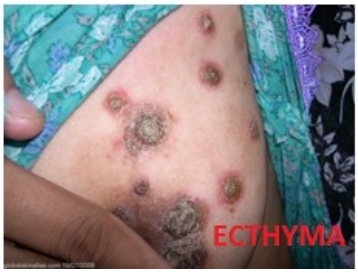
Prognosis: poor prognostic marker include:-

- Early onset (Prepubertal). - Extensive involvement. - Prolong duration (> 5 yrs).

ECTHYMA



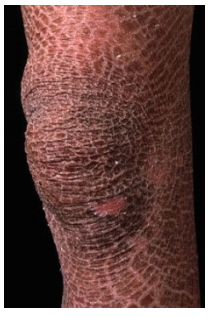
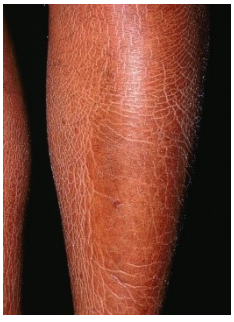
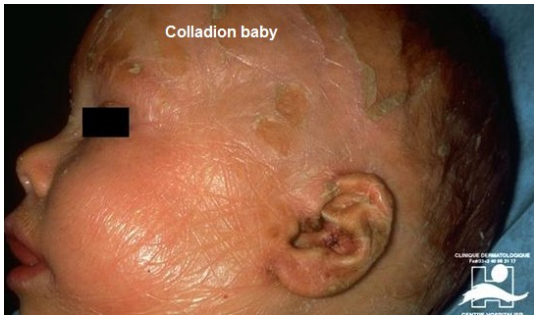




Ecthyma is an ulcerative pyoderma of the skin caused by group A β -haemolytic streptococci. Because Ecthyma extends into the dermis, it is often referred to as a deeper form of impetigo. Pre-existing tissue damage (excoriations, insect bites, dermatitis) & immunocompromised states (diabetes, neutropenia) predispose pts to the development of Ecthyma. Ecthyma begins as a vesicle or pustule overlying an inflamed area of skin that deepens into a dermal ulceration ē overlying crust. A shallow, punched-out ulceration is apparent when adherent crust is removed. The deep dermal ulcer has a raised & indurated surrounding margin. Ecthyma can remain fixed in size or can progressively enlarge to 0.5-3 cm in diameter. Ecthyma heals slowly & commonly produces a scar. Regional lymphadenopathy is common.

Treatment: •Topical mupirocin ointment. •Gentle surgical debridement. •Oral/IV antibiotics (Penicillin, Clindamycin, Macrolides, or Cefazolin).

ICTHYOSIS

Icthyosis Vulgaris is the most common genetic skin disorder. The gene is inherited as AD, the abnormality is found on chromosome Iq21 & is related to an abnormality in levels of the protein filaggrin. The abnormality in the gene causes skin to regenerate

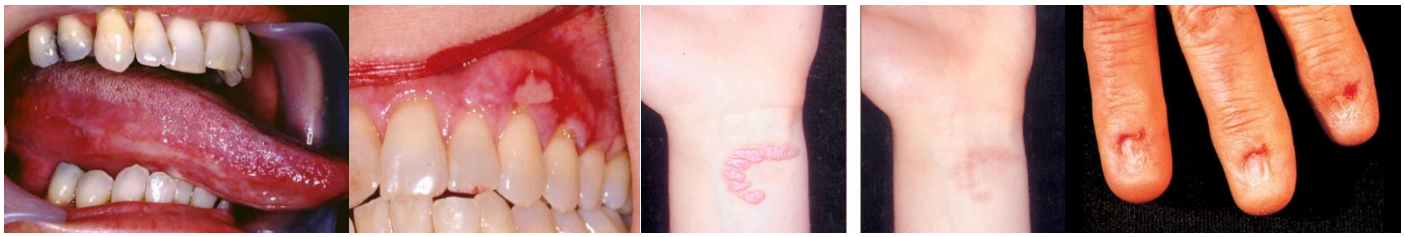
(go through mitosis) faster than it sheds. So many people affected by it (1 out of every 250), it's hard to find out when & where the disorder originated. Icthyosis that is not due to a genetic mutation is called acquired Icthyosis & is extremely rare.

Clinical picture: •Dry Skin. •Scaly Skin. •Discoloration of Skin. •Flaky Scalp. •Painful deep cracks in palms & soles. • Collodion baby is rarely predicted during pregnancy.

Diagnosis: although many cases of Ichthyosis go unreported, it can be diagnosed through:- •Skin examinations. •Skin biopsy/ •Researching family history (has anyone in the family had Ichthyosis before?)

Treatment: there is no known cure, but the following can aid in easing the pain of ichthyosis vulgaris: •Retinoids (from Vit. A). • Constant moisture to affected area

LICHEN PLANUS



A benign, chronic disease affecting skin & oral mucosa. Unknown cause. ?Immunological. ? Familial tendency. Lesions have characteristic Wickham striae. Most com monly on buccal mucosa, lesions may be on the tongue, lips, floor of mouth & gingiva. Present in about 1% of the population, most common in middle age, slightly more common in women. Mostly subside within few weeks- months, but may turn chronic & turn premalignant.

Types

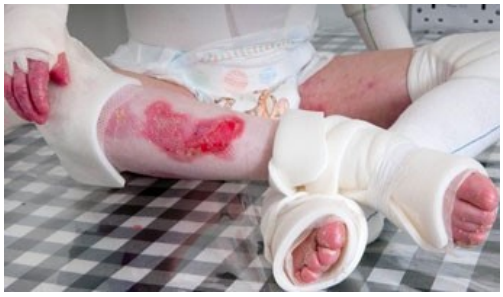
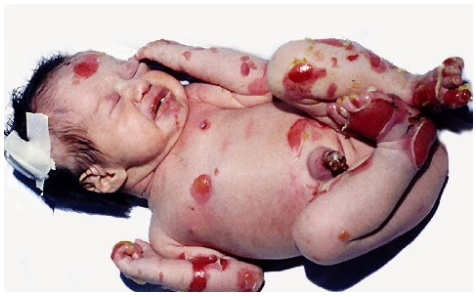
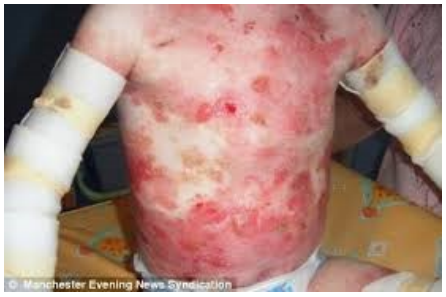
- Reticular lichen planus is the most common form.
- Erosive & bullous lichen planus.
- Epithelium separates from connective tissue.
- Desquamative gingivitis can be caused by lichen planus.

•Skin lesions are 2 to 4 mm papules most commonly in lumber region, flexor surfaces of the wrist, anterior ankle.

Diagnosis: based on clinical appearance & possibly biopsy. These lesions may be premalignant (SCC).

Treatment: •Steroids (topical & systemic). •PUVA . •Cyclospoin. •Azothioprin.

EPIDERMOLYSIS BULLOSA

EB is rare genetic condition encompasses many clinically distinctive disorders ē three features in common:-

1) Genetic transmission.

2) Blister formation.

3) Mechanical fragility of the skin.

The skin & sometimes the m.m. (such as the lining of the mouth), blister in response to mild friction or trauma. A genetic defect prevents the layers of the skin from adhering properly. Blisters form as the layers of the skin split apart in response to friction or trauma. This condition is not contagious. An estimated 1/ 50,000 is born ē some form of EB. The disorder occurs in every racial & ethnic group throughout the world & affects both sexes equally. There are 3 main forms of inherited EB. These different subtypes are defined by the depth of blister within the skin layer:-

•EB Simplex: where blistering occurs in the upper layer of the skin (the epidermis). This is the most common type of EB, accounting for 70% of cases, and tends to be milder than the other types. Blistering may be localized to the hands &/or feet, or

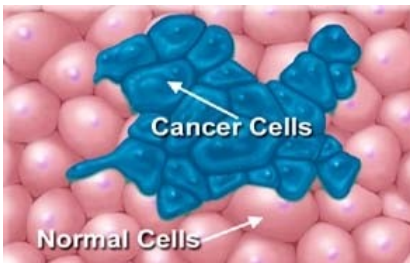
may be generalized & affect the entire body. While blistering can be continuous, the skin heals ēout significant scarring.

- Junctional EB: where blistering occurs at the junction between the epidermis & the dermis, in a layer of skin known as the basement membrane zone. JEB accounts for around 5% of cases and is usually considered the most severe type of EB is fatal in infancy or early childhood. These children develop blisters ẃ heal ē scars. They may have significant mobility problems & may have airway involvement, as well.
- Dystrophic EB: where blistering occurs below the basement membrane zone in the upper part of the dermis. DEB accounts for around 25% of cases. Blistering is extensive, both internally & externally, heal ē scarring, very obvious damage to the skin. Fingers may fuse & contract, causing mitten deformities of the hand. Feet may be similarly affected.

Management

There's currently no cure for EB, so treatment aims to relieve symptoms & prevent complications developing, such as infection. Require lengthy & painful daily skin care regimes including extensive bandaging & wrapping under aseptic conditions.

CANCER OF SKIN

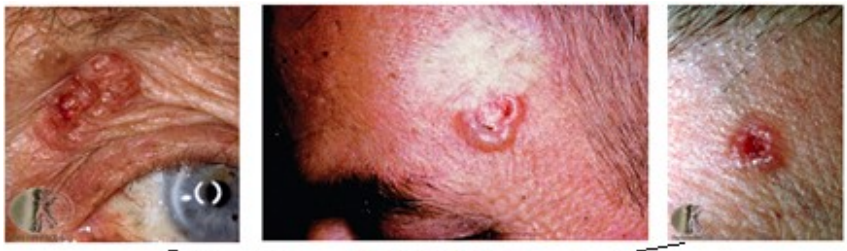


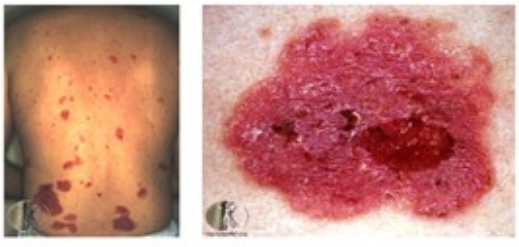
Cancer occurs when cells in a body part begin to grow out of control & crowd out normal cells. Cancer of skin is the most common type of cancer & represents 50% of all new cancers detected each yr. It is the most common of all cancers. According to the latest statistics available from the National Cancer Institute, more than 1 million cases are diagnosed in the US each year. Most skin cancers are: slow-growing, easy

to recognize & relatively easy to treat when detected early. Cancer skin has one of the highest cure rates, ē rather simple & economic treatments.

Types

Basal Cell Carcinoma





Most common type of skin cancer, arises in basal cell layer of the epidermis, found on sun exposed parts of body like the head & neck. Occurs most commonly in blonde, fair -skinned individuals who have had a lot of sun exposure or repeated episodes of sunburn. Flesh coloured (early stage shown in the figure) or brown. Can be fast or slow growing & destructive over months or yrs, but rarely spread, it is rarely metasta-sizes but is invasive. Gorlin's syndrome- inherited tendency to BCCs.

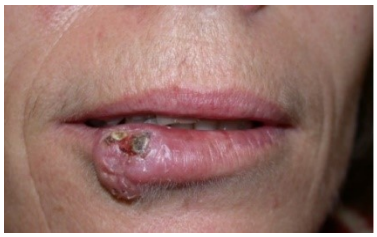
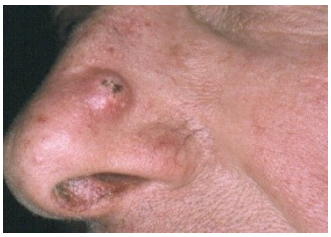
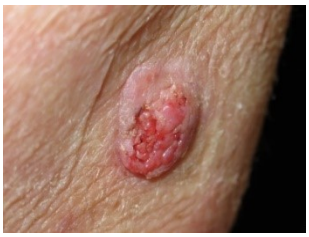
BCC include the following types; Nodular (most common type) or Superficial (com-mon) or Morphoeic (waxy, scar-like), or Pigmented (can resemble melanoma), or mixed BCC/SCC. The first 2 types are seen commonly in general practice.

Signs & symptoms: tumour mainly seen on sun-exposed areas of the body, especially the face. Can also occur on parts of the body rarely exposed to sunlight. Small, shiny, skin-coloured swelling, Telangiectasia cross the edge. Pearly white or waxy bump ẃ may bleed or develop a crust, or form a depression in the centre. May have central ulcer or scab so edges appear rolled ẃ often bleed spontaneously, then heal over. Rodent ulcer is an open sore. BCC may presented as multiple superficial ulcers, the upper trunk or shoulders are the commonest site but can appear anywhere, ulcers appears pink/red scaly patch ē raised edge on close examination.

Management: Goal of complete eradication of the lesions. Type of treatment determined by size, shape, location & invasiveness. Curettage & Electrodesiccation. Cryotherapy & Laser therapy. Chemotherapeutic drugs. Surgical excision (used in 90% of cases). Irradiation or Chemosurgery.

Remember-BCCs don't kill but can be locally destructive.

Squamous cell carcinoma

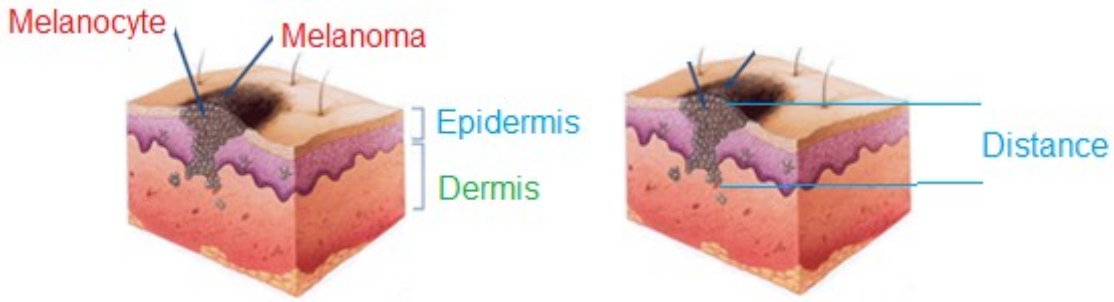
Common type of skin cancer. It develops in the epidermis from squamous cells ẃ produce keratin. Usually presented as a slowly growing scaly or crusted lump. Can present as a non-healing sore or ulcer "punched out" in appearance. Sometimes growth is rapid over a matter of weeks. Metastatic SCC occur in 5% of cases, most commonly from primary lesion on ear or lip & is commoner in transplant pts, or pt ē CLL, Also metastatic SCC is associated ē increasing age & associated ē alcoholism.

It is more likely if multiple skin cancers present

Causes: •UV radiation-damages DNA in skin. •May develop in an actinic keratosis or patch of Bowen's disease. •Genetic predisposition. •Smoking-especially SCC lip. •Thermal burns. •Chronic leg ulcers. •Immunosuppression-Azathioprine/Ciclosporin. •Organ transplantation pt is highly susceptible. •HPV infection implicated in genital SCCs. • Pre-existing skin conditions e.g. lichen sclerosus & lichen planus can predispose to development of genital & oral SCCs.

Treatment: if you suspect a possible SCC, refer for histological diagnosis confirmed in Dermatology department. Joint dermatologist/plastic surgeon assessment ideal. Surgery, possibly ē skin graft. Radiotherapy may be needed.

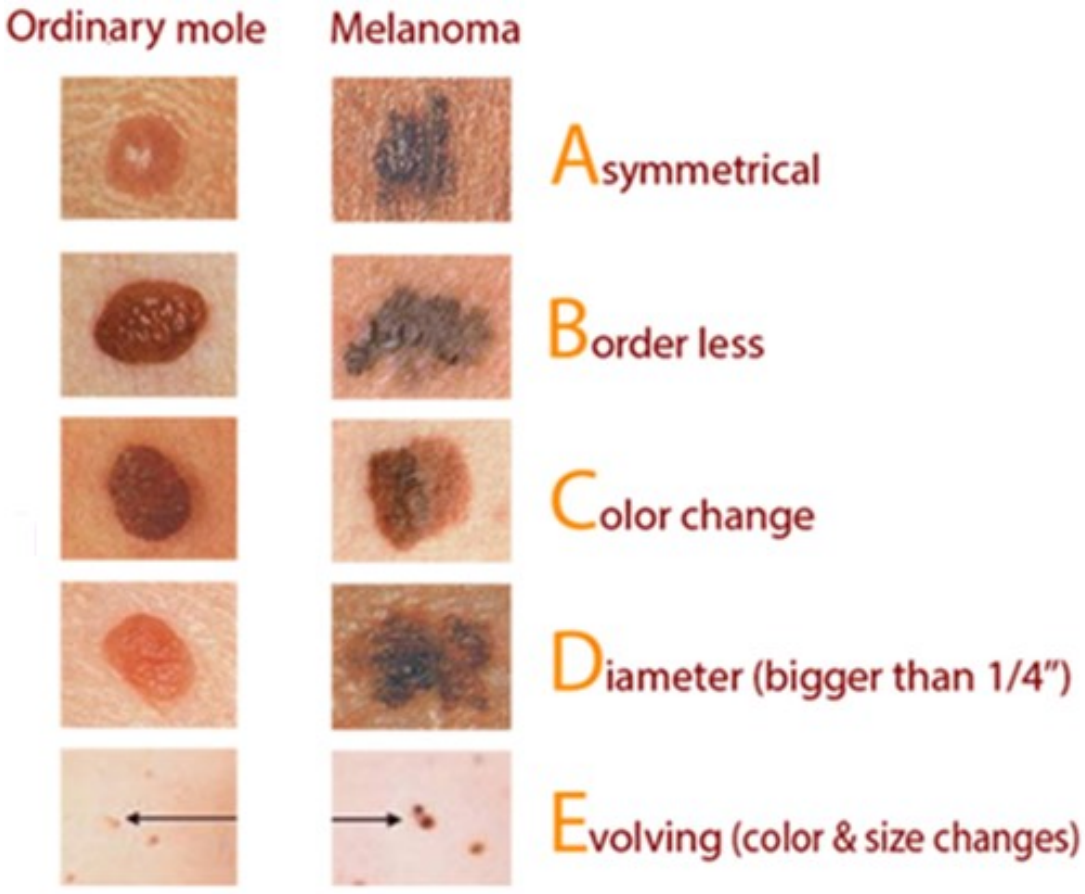
Melanomas



Can occur anywhere on the body, it is less common, but more serious. Almost always curable when detected early. More likely to spread to other parts of the body. Melanocytes are found in the basal layers of the epithelium, Cancerous growth of melanocytes results in malignant melanoma (while non-cancerous growth of melanocytes results in moles or freckles).

Diagnosis

- Clinical – ABCDE of melanoma.
- Skin biopsy.



Risk factors

- Sun exposure, particularly during childhood.
- Fair skin ẃ burns easily. Blistering sunburn, especially when young.
- Previous melanoma.
- Positive family history of melanoma.
- Large numbers of moles/dysplastic moles.

Common sites

*In men commonest site is the back. In women commonest site is the leg. Can occur on mucous membrane*s, e.g lips or genitals. Can occur under the nail. Can occur in eye, brain or mouth

Management

- Refer suspected case for surgical excision by Dermatologist ē 2-3 mm margin.
- Wider excision if histology confirms melanoma.
- Thicker melanomas > 1 mm-wider excision +/- sentinel node biopsy.
- Widespread melanoma-surgery/chemotherapy.

Prognosis

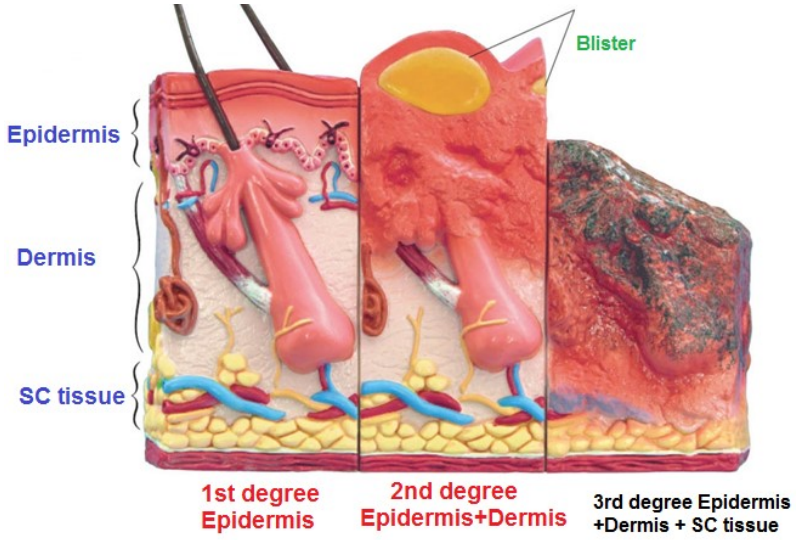
Breslow's depth was used as a prognostic factor in melanoma of the skin. It is a description of how deeply tumour cells have invaded, it measures in millimetres (1 mm equals 0.04 inch) the distance between the upper layer of the epidermis & the deepest point of tumour penetration. The thinner the melanoma, the better the chance of survival.

Breslow thickness < 1mm, almost 100 % 5 year survival

Breslow thickness > 4 mm, only 50 % 5 year survival

Remember,melanoma is a major cause of death from malignancy in young people.

BURNS



Causes

Friction burns: • Rubbing of the skin • Outer layer • Anti-inflammatory creams.

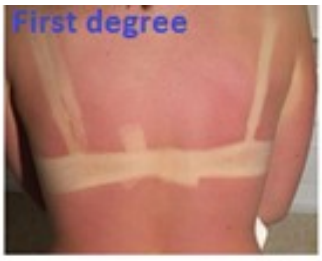
Thermal burns: • Flames • Hot liquids • Hot objects • Gases.

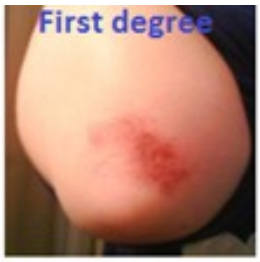
Electrical burns: accidental electrical contact, depend on: strength of electrical current & duration of contact

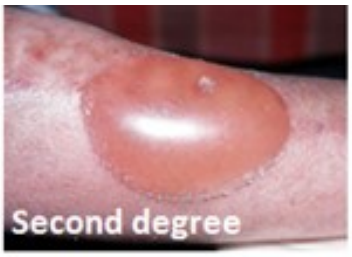
Radiation burns: •UV light. •X-rays. •Sunlamps. •Radiation therapy.

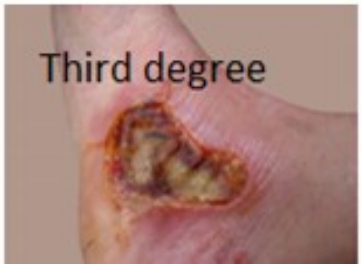
Chemical burns: •Strong acids. •Strong bases. •Detergents. •Solvents.

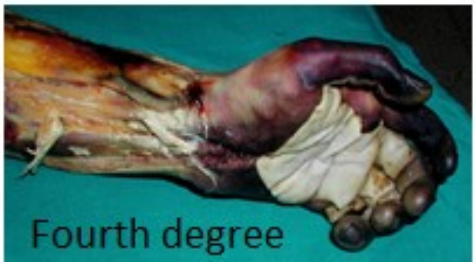
Types











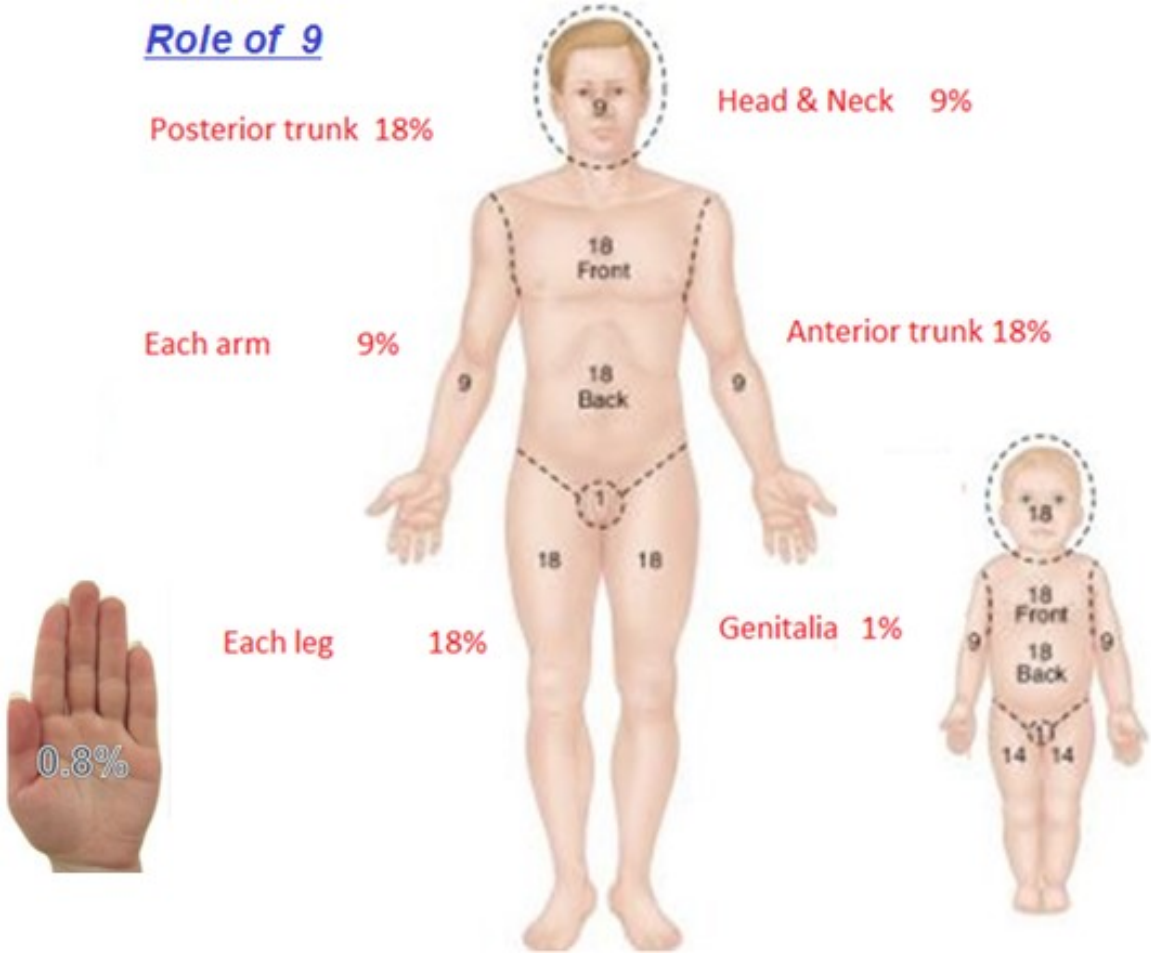
First-degree burns: affect epidermis (superficial). Characterized by; redness, pain, dry skin, no blisters, no scars. Example -mild sunburn, friction burn.

Second degree burns: affect epidermis & part of the dermis (partial thickness). Characterized by blisters, deep redness, wet & shiny, very painful to touch, no scars. Example: contact ē hot objects or flame.

Third degree burns: affect epidermis & entire dermis (full thickness). Characterized by; dry, leathery skin, swelling, black, white, brown or yellow skin, lack of pain. Examples include; electrical or chemical sources or flames.

Fourth degree burns: affect epidermis, dermis & underlying tissue (SC tissue, muscles & bones). Characterized by; black skin, no sensation. Example: flames.

Size of burned area



For practical purpose, the size of pt`s hand is equal to 1% (0.8%).

Management

▲Resuscitation volume needed for pts ē burns covering > 20% of the body's surface. During the first 24 hrs, the pt need:

4 mL × body weight (kg) X %of body surface burned.

Half is given during first 8 hrs.

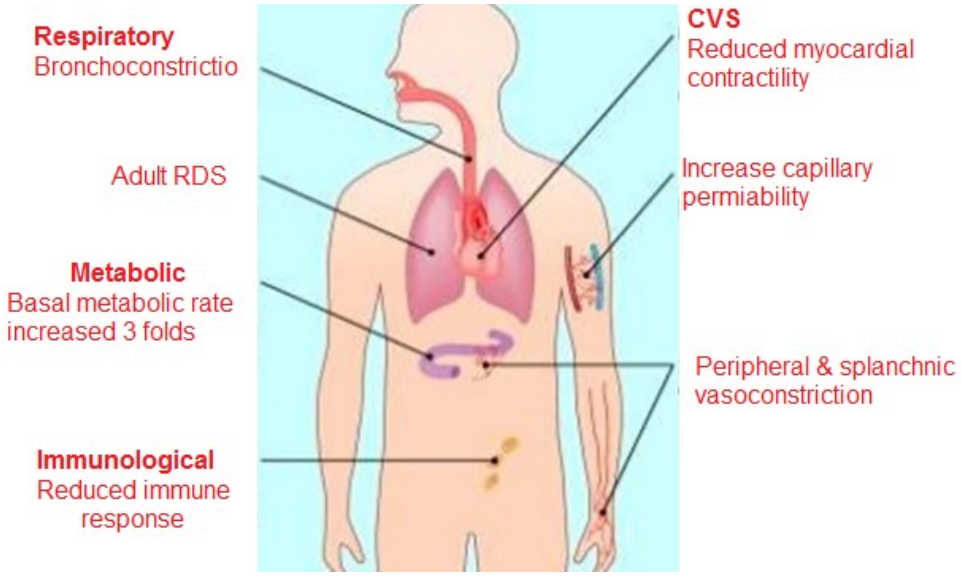
Half given over the subsequent 16hr

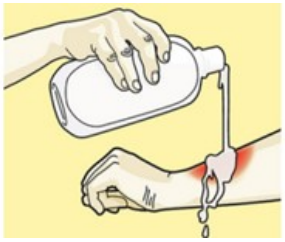
For practical purpose the size of your hand is equal to 1%.

Using either ringer lactate or glucose saline.

- Tetanus toxoid: 0.5 ml IM.
- Tetanus Immunoglobulins.
- For burn >10% associated ē hypovolemic shock & release of myocardial depressant factors, give Dopamine if perfusion is poor + Plasma 20 ml/Kg every 12hrs + Urine catheter (10-12 FG for children & 14-18 FG for ad-ults) for accurate calculation of fluid requirement.
- Flamazine oint to the site of burn.
- Keloid formation after healing may may require plastic surgery.
- Conractubex gel locally ē massage few times daily or med gel coat for mild cases of keloid may be helpful.

Systemic Response





Chapter XI

OPHTHALMOLOGY

Introduction

Diseases of the Eye Lid

Diseases of the Lacrimal Apparatus

Diseases of Conjunctiva

Orbital Cellulitis

Red Eye

Keratitis & Corneal Ulcer

Iridocyclitis

Glaucoma

Scleritis

Blindness

Cataract

Trachoma

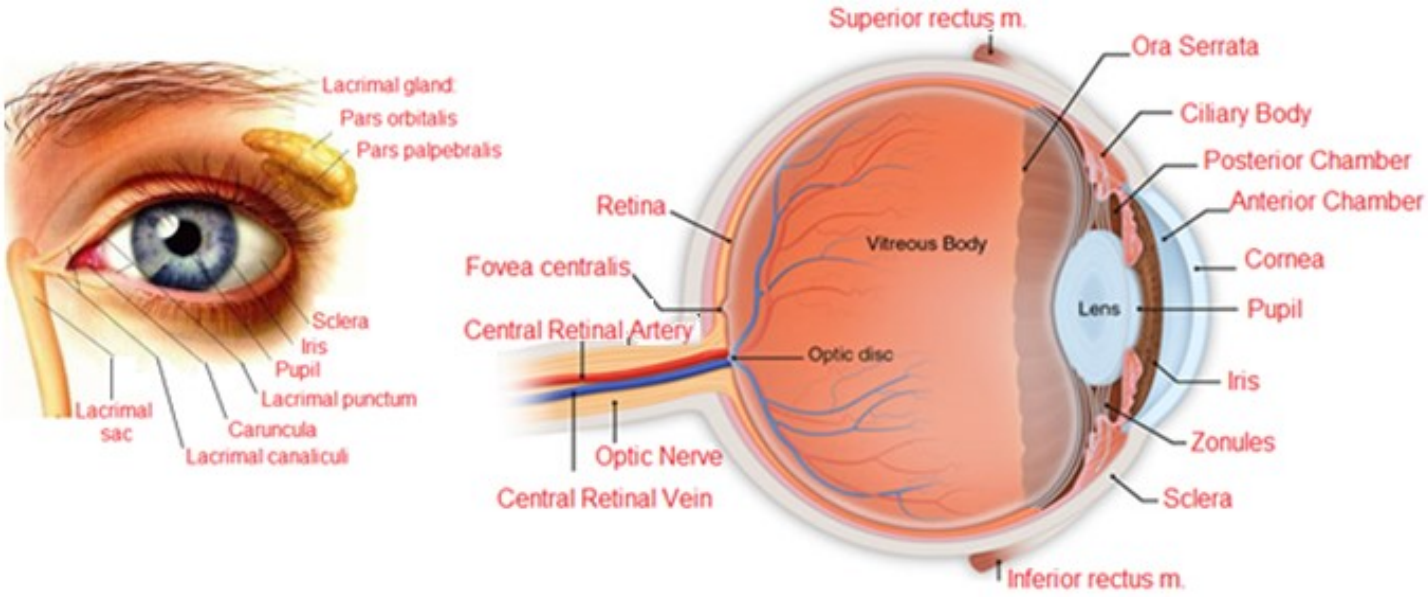
Vitamin A Deficiency Disorder

Refractive Errors

Colour Blindness

Systemic Diseases & the Eye

Introduction



The eye ball, or globe, sits in a protective bony structure known as the orbit. The orbit is about 4 cm in height, width & depth. It is shaped roughly like a 4 sided pyramid surrounded on three sides by the sinuses: the ethmoid (medially), the frontal (superiorly, & the maxillary (inferiorly). The optic nerve & the ophthalmic artery enter the orbit at its apex through the optic foramen.

Eyelids protect the anterior portion of the eye, composed of thin elastic skin that covers striated & smooth muscles & the tarsal plates.

Tears are vitally important to the health of the anterior segment of the eye. They are formed by the main lacrimal gland & the accessory lacrimal glands.

Conjunctiva, a mucous membrane, provides a barrier to the external environment & nourishes the eye.

Sclera, commonly known as the “white of the eye”, is a dense fibrous structure that composes the posterior five sixths of the eye.

Cornea, a transparent avascular domelike structure, forms the most anterior portion of the eyeball & is the main reflecting surface of the eye.

Anterior chamber, lies behind the cornea, filled ē a continually replenished supply of clear aqueous humour, ẃ nourishes the cornea.

Uvea, consists of the iris, ciliary body & choroid. The iris, or coloured part of the eye, is a highly vascularized, pigmented collection of fibres surrounding the pupil.

Pupil, is a space that dilate & constricts in response to light.

Lens, directly behind the pupil & iris lies the crystalline lens, a colourless & almost completely transparent biconvex structure held in position by zonular fibres. It is avascular & has no nerve or pain fibres. The lens is suspended behind the iris by the zonules & is connected to the ciliary body.

Ciliary body, controls accommodation through zonular fibres & the ciliary muscles.

Posterior chamber, is a small space between the vitreous & the iris. Aqueous fluid is manufactured in the posterior chamber by the ciliary body.

Choroid, is layered between the retina & the sclera. Is highly vascularized tissue, supplying blood to the adjacent outer portion of the retina.

Ocular fundus, is the largest chamber of the eye & contains the vitreous humour, a clear gelatinous substance, mostly water, encapsulated by a hyaloid membrane, the vitreous humour.

Visual pathway

Good vision is not dependent solely on a healthy functioning eyeball but also on an intact visual pathway. This pathway is made up of the retina, optic nerve, optic chiasma, optic tracts, lateral geniculate bodies, optic radiation & the visual cortex of the occipital lobe. The pathway is an extension of the central nervous system. The optic nerve is the 2^{nd} cranial nerve. Its function is to transmit visual impulses from the retina to the higher centres in the brain.

Blood supply

Arterial blood supply: the eye is supplied by anastomosing vessels from internal & external carotid arteries. The retina supplied by the central retinal artery, a branch of

ophthalmic artery & enters the eye ē optic nerve & divides on the optic disc into its branches. The uvea is supplied by the ciliary circulation, from ophthalmic artery. The eye lids gets its blood supply from facial & ophthalmic arteries.

Venous blood supply: almost the entire blood from the Anterior & posterior uvea drains through four vortex veins via superior & inferior orbital veins to cavernous sinus. The eye lid drains through facial vein into cavernous sinus.

Lymphatic drainage: there is no lymphatic vessels inside the globe. The lymphatic drainage of the medial eye lid is to sub mandibular LNs & that of lateral one is to the superficial pre-auricular LNs & then to deeper cervical LNs.

Nerve supply

A- Motor

- Oculomotor (CN III) Innervate- medial rectus, superior rectus, inferior rectus, & inferior oblique.
- Trochlear (CN IV) nerve- innervates superior oblique.
- Abducent (CN VI) -innervates lateral rectus.
- Facial (CN VII) -innervates orbicularis oculi M.

B- Sensory

- Ophthalmic branch of trigeminal nerve is the sensory nerve of the globe & adnexa & has three branches -frontal, lacrimal & nasociliary.
- Optic nerve (CNII) - responsible for vision.

C- Autonomic

(I) Sympathetic nerve- supplies Muller's muscles & dilator pupillae.

(II) Parasympathetic comes via occulomotor & innervates the ciliary muscle & sphincter pupillae.

Extra ocular muscles; Are six & their action is so complex. Control eye movement.

Form cone behind the eyeball. Include the following;

Extra ocular muscles & their action (monocular action)	
Superior rectus	for upward movement of the eye
Inferior oblique	inward and upward movement of the eye
Medial rectus	inward movement of the eye
Lateral rectus	outward movement of the eye
Inferior rectus	downward movement of the eye
Superior oblique	inward & down ward movement of the of the eye

Definition/Terminology

Visual acuity: this term refers to the ability to see fine detail.

Visual field: this is the area your vision covers, normally about 180 degrees.

Stereoscopic vision: the ability to see with both eyes allows judgments to be made about distance

Colour vision: the ability to distinguish different colours.

Contrast sensitivity: black on a white background provides good contrast. Some people need better contrast than others to assist ē vision.

Light sensitivity: the pupil expands & contracts to allow light into the eye, this can be painful for some people.

Visual perception: the ability of the brain to make sense of visual information.

Testing the vision

A. Visual Acuity (V/A): test the visual acuity in each eye separately. Measured ē a snellen chart, showing letters, 'E' chart or pictures for pt who cannot read. Pt should sit at 6 meters. Start ē the right eye by closing the left eye ē the palm of hand. Use commonly 'E' chart & ask the pt to show the direction of the 'E' (right, left, up or down) & then record the last line that the pt sees. Repeat for the left eye. The human finger is about the same size as the top letter on the chart, so counting fingers at 6 meters is

about equal to 6/60 vision & abbreviated as CF. If vision is below 1/60, use the pt to detect motion of hand in front of the eye; 'hand motion' (HM). If the pt can't see HM, the final test is to shine a light into his eye. If he can perceive light –LP- If he can't perceive light –NLP. Projection of the light from four quadrants of the eyes should be examined to test the peripheral retina & optic ne-rve function. Test for red &/or green colour discrimination, macular function test.

Interpretation of V/A. The WHO classification of Visual impairment & Blindness.

- 6/6 - 6/18 : normal.
- < 6/18 - 6/60 : visual impairment.
- < 6/60 - 3/60 : severe Visual impairment.
- < 3/60 - NPL : blindness

Blindness is defined as visual acuity of < 3/60 in the better eye ē the best possible correction

B. Visual Field

Is that portion of one's surroundings that is visible at one time during central vision. Not a routine test in all pts. Important to do in any pt ē suspected glaucoma, diseases of the optic nerves & certain retinal diseases.

Confrontation test: is simple & no need of special equipment. Will detect serious visual field defects. Works by comparing the pt's visual field ē the examiner's.

Steps: sit facing the pt at one meter distance. If the pt's left eye is being tested, he should cover his right eye & you should cover your left eye. Pt looks straight into your eye & you look straight into his to make sure he is fixing your eye. Then hold your fin-

gers at an angle equidistant between you & the pt & ask him to say visible or not as your fingers move. If you can see them & the pt cannot, then he has a defect. Move in different quadrant - Do the same ē the other eye.

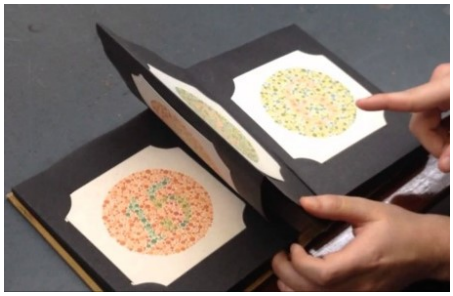
Perimetery

Difficult to test in children, old or non-comprehending people. In all visual field test, each eye is tested separately. The pt must fix his gaze on a target or spot in front of him. The examiner then sees at what angle objects come into the pt`s range of vision.

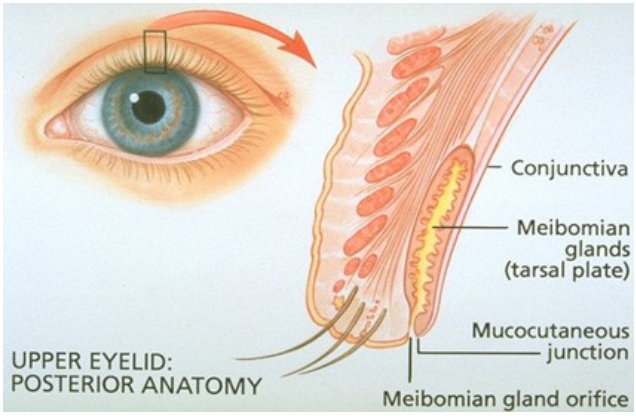
Tonometer test

For measuring the eye pressure- R/O Glaucoma.

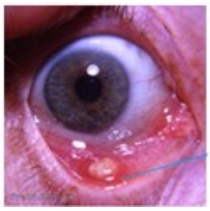
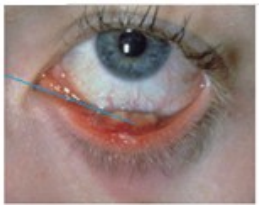
C. Colour Vision: done by using a chart called 'Ishihara chart'. Simple macular test is to ask the pt for red & green colour perception.



DISEASES OF THE EYE LIDS



INTERNAL HORDEOLUM

A small abscess collection in the Meibomian glands. Caused by staphylococcus.

Symptoms: Pain, redness, swelling within eye lid.

Signs: Tender, inflamed mass within the eye lid.

Treatment: Hot compress . Topical antibiotics. If the above treatment fails, referral for incision & curettage under local anaesthesia

EXTERNAL HORDEOLUM/STYE

Acute staph infection of a lash follicle & its associated gland of zeis or moll.

Symptom: Pain, redness, lid margin swelling of short duration.

Signs: Tender inflamed mass in the lid margin ẃ points anteriorly through the skin. More than one lesion may be present &occasionally minute abscesses may involve the entire lid margin. In severe cases a mild pr septal cellulitis may be present.

Treatment

•Warm compression.

•Topical antibiotic -Chloramphenicol eye oint.

•Systemic antibiotic -Cloxacillin 50 mg/kg divided in four doses for 7 days if secondary eye lid cellulitis develops.

•Epilation of the eyelash associated ē the infected follicle may enhance drainage..

•If the above management fails & if there is an abscess, referral for surgical drainage.

CHALAZION

A chronic lipogranulomatous inflammatory lesion caused by blockage of meibomian gland orifices & stagnation of sebaceous secretion - Pt ē acne roscea or seborrheic dermatitis are at ⇧ risk of Chalazion ẃ may be multiple or recurrent.

Symptom: Painless nodule within the eye lid.

Sign: Non tender, firm, roundish mass within the eye lid.

Treatment: Hot compression & referral for surgical incision& curettage.

MOLLUSCUM CONTAGIOSUM

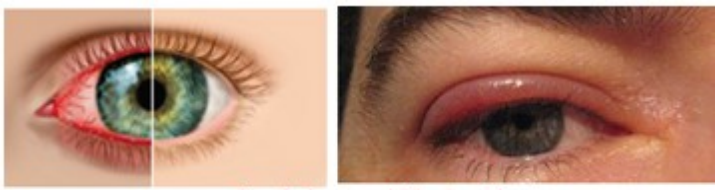
Uncommon skin infection caused by a poxvirus. It is common in children & immunocompromized pt. In immunocompromised pt, it is multiple, large size, bilateral, recurrent & resistant to treatment.

Symptoms: painless, raised, skin lesion.

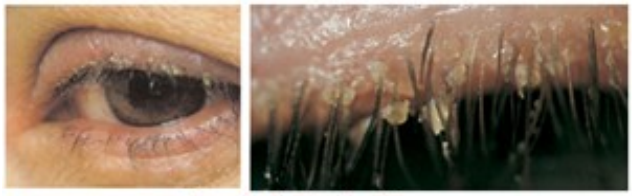
Signs: single or multiple, pale, waxy, umblicated nodules. If the nodule is located on the lid margin it may give rise to ipsilateral chronic follicular conjunctivitis & occasionally a superficial keratitis.

Treatment: expression. Shaving & excision. Destruction of the lesion by cauterization, Cyrotherapy.

BLEPHARITIS



Staphylococcal Blepharitis

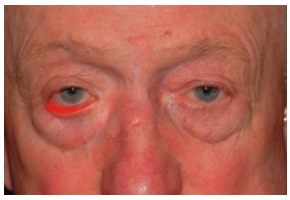
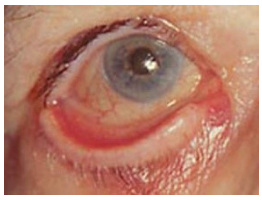


Seborrheic Blepharitis

A general term for inflammation of the eyelid. Can be associated ē conjunctivitis. There are two main types of Blepharitis. 1. Staphylococcal Blepharitis: caused by Staph. aureus, is ulcerative in type ē redness of lid margins ē scales & easily pluck able lashes. 2. Seborrheic Blepharitis: is associated ē seborrhea of the scalp, bro-ws & ears. Is nonulcerative. The scales are greasy ē less marked redness of the lid margin. A pt may present ē a mixed type of Blepharitis. Both types of pts could present ē:- Symptoms: Irritation. Burning. Itching of the lid margins. Signs: Scales on lid margin. Eye lid margin ulceration & redness. Treatment: Lid hygiene. Topical antibiotics (Erythromycin or Chloramphenicol eye drops QID) -for infectious. Systemic antibiotics-Doxycycline 50-100mg/day for 4 wks for infectious. Topical steroid (Terracortril eye suspension once twice a day) for seborrheic blepharitis.

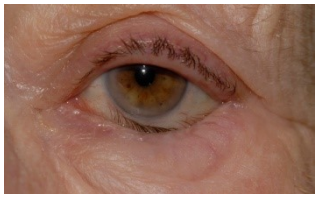
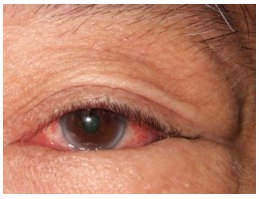
ABNORMALITY IN THE FUNCTION & POSITION OF THE EYELIDS

ECTROPION

Means eversion of eyelid. Treatment - Referral for surgical correction.

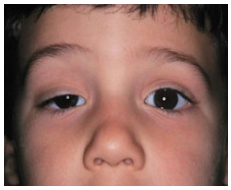
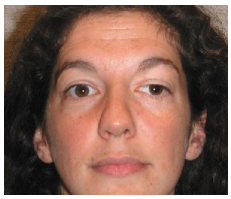
ENTROPION

Means the eyelids turn in wards then the eyelashes rub & damage the globe.

Treatment - Referral for surgical correction.

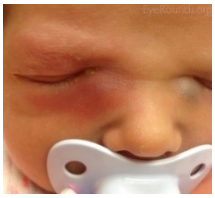
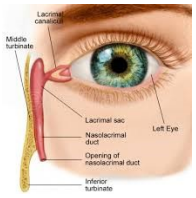
PTOSIS

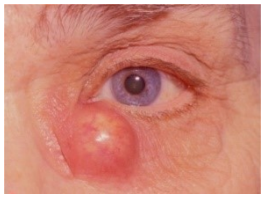



Means drooping of the upper eye lid due to Levator muscle weakness. It can cause amblyopia if it is unilateral. Treatment - Referral for surgical correction

DISEASES OF THE LACRIMAL APPARATUS

DACROCYSTITIS



Inflammation of the lacrimal sac that occurs primarily because of Nasolacrimal duct obstruction. Chronic tear stasis & retention leads to 2ry bacterial infection.

Etiology: Staphylococcus, Pneumococcus, Streptococcus .etc.

Acute Dacrocystitis

Symptoms: painful, swollen mass below the medial side of the eye, conjunctival injection, & tearing. Signs: tender mass on the medial side of the eye, pressure on the sac will often fail to result in regurgitation of mucopurulent material.

Treatment: hot compression. Systemic antibiotic. Incision & abscess drainage may be required. Complication: preseptal cellulitis. Orbital cellulitis.

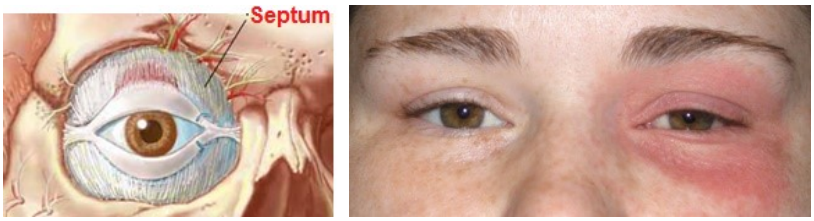
Chronic Dacrocystitis

Symptoms: tearing, swelling over the medial aspect of the eye, mucoid or purulent discharge ē pressure on the lacrimal sac area. Signs: non tender mass on medial aspect of the eye. Treatment: referral for surgery (dacryocystorhinostomy).

ORBITAL INFECTION

Etiology: H. influenza, S. aureus, S. pneumonia etc. Predisposing factor: -trauma, stye, dacrocystitis, sinusitis, etc. The orbital septum: orbital septum + Tarsus = " middle lamella" of the eyelid. Originate at the arcus marginalise (periosteum). The septum fuses superiorly ē the levator aponeurosis, inferiorly ē inferior border of tarsus, laterally is inserted anterior to the lateral canthal tendon, & medially to the posterior lacrimal crest (i.e. lacrimal sac is outside the orbit).

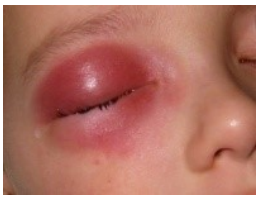
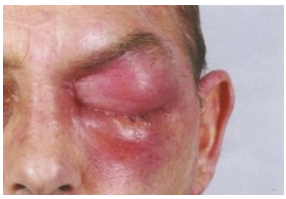
Preseptal cellulitis



It is infection of the tissues anterior to the orbital septum. Symptoms: no visual reduction, mild periorbital pain, localized eyelid redness & swelling. Sign: V/A is normal, tender & hot eyelid, ocular motility is normal. Treatment - Ciprofloxacillin 500 mg PO

bid for 7 days. If no improvement within 48 hrs, It needs early referral.

Orbital cellulitis

An infection of orbital tissue posterior to the orbital septum.

Symptom: pain, Proptosis, fever, limited ocular movement, visual reduction.

Sign: V/A is reduced, tender eye, reduced to absent ocular motility.

Treatment: it is an ophthalmic emergency that needs admission; IV antibiotics. So early referral to ophthalmic centre is highly recommended.

Complication: if it is left untreated, it is vision & life threatening. -Loss of vision -Meningitis -Brain abscess -Cavernous sinus thrombosis.

THE RED EYE

The differential diagnoses of red eye are protean ranging from trivial conditions like sleeplessness & fatigue to life threatening conditions as cavernous sinus thrombosis & carotid cavernous fistula.

PAINLESS RED EYE

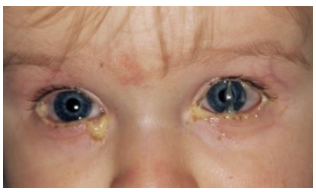
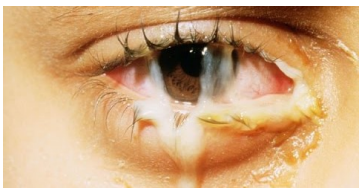
Causes are mostly self-limiting. If they are neglected & mismanaged they will complicate to the extent of sight threatening condition. Appropriate evaluation & management is recommended. Those pts who will not have improvement in < 48 hrs need referral to a better centre for better management.

CONJUNCTIVITIS

Is a general term for any inflammation of the conjunctiva.

Epidemiology: the prevalence of each is different in paediatric & adult population. The vast majority of paediatric cases are bacteria, while in adult's bacterial & viral causes are equally common.

BACTERIAL CONJUNCTIVITIS

Commonly caused by Staphylococcus Aureus, Streptococcus Pneumonia, Hemophilus Influenza & Moraxella Catarrhalis. S. Aureus is common in adults. Highly contagious from secretions or ē contaminated objects & surfaces.

Symptoms: pts typically complain of redness & discharge in one eye; although it can also be bilateral. The affected eye often is “stuck shut” in the morning. Purulent discharge continues throughout the day. The discharge is thick; it may be yellow, white or green. No real pain as the conjunctiva has few sensory nerve supplies but complain of irritation, itching & discomfort. Vision is almost normal.

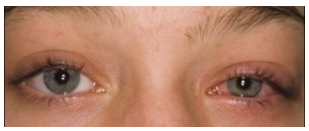
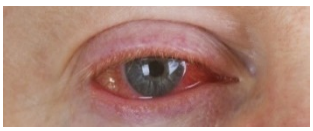
Sign: on examination, pts will typically have purulent discharge at the lid margins & in the corners of the eye. More purulent discharge appears within minutes of wiping the lids. Red eye – due to dilatation of superficial blood vessels as apart of inflammation. Oedema of the conjunctiva (chemosis) & eyelids swelling. Cornea is mostly clear; but if it is involved, there will be different degree of corneal opacity it is common special in untreated and delayed pts.

Diagnosis: mostly clinical-Gram stains.

Course: it lasts for 1 - 2 wks & then it usually resolves spontaneously.

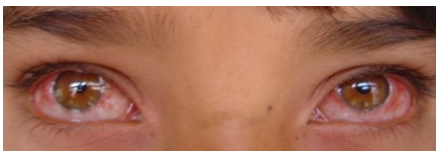
Treatment: Chloramphenicol eye drop or ointment QID - Ciprofloxacillin eye drop QID - If the above drugs are not available, one can use tetracycline eye ointment BID - Evaluate the pt after 48 hrs & if no improvement, refer to ophthalmic centre for better evaluation N.B. Don’t use steroid or steroid containing antibiotic as they will reduce local immunity & encourage micro-organism to multiply.

VIRAL CONJUNCTIVITIS

It is highly contagious, spread by direct contact ē the pt & his or her secretions or ē contaminated objects & surface. Pt usually presents ē watering, photophobia, irritation & mostly associated ē URTI. Treatment: self-limiting, prophylactic topical antibiotics, Chloramphenicol TID. Never use steroid or steroid containing antibiotics.

ALLERGIC CONJUNCTIVITIS



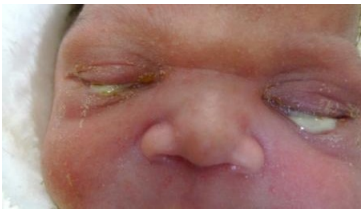
Caused by air borne allergy contacting the eye. With specific IgE, causes local mast cell degranulation & release of chemical mediators including histamines, eosinophil chemo tactic factors & platelets activating factors.

Symptoms: red eye, severe persistent itching of both eyes, mucoid eye discharge, no visual reduction.

Signs: V/A is normal, papillary reaction to hypertrophy on tarsal conjunctiva.

Treatment: Cold compress, vasoconstrictor-antihistamine like Cromolyn Sodium, topical steroid -Terracortril eye suspension.

NEONATAL CONJUNCTIVITIS
(Ophthalmia Neonatorum)



Conjunctivitis in a new-born (in the first 28 days of life).

Etiology: gonococcus &Chlamydia are the commonest cause of ẃ Gonococcal is most serious.

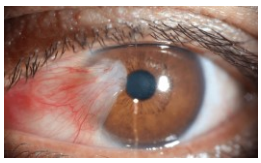
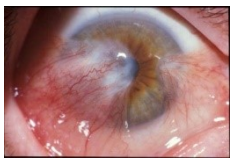
Symptoms: profuse thin to thick purulent eye discharge.

Sign: purulent eye discharge, eye lids are swollen. If cornea is involved, ulcer, scarring, lately cornea will shrink.

Treatment: it is sight threatening condition that needs systemic antibiotic & close follow up in better ophthalmic centre - start ē tetracycline eye oint. 3-4 times a day - Urgent referral to ophthalmic centre may be needed.

Prevention: the eye lids should be cleaned ē saline swabs as soon as the head was born & before the infant‘s eyes opened. - then apply TTC eye oint. It should be applied routinely whenever there is risk that mother had infection during pregnancy.

PTERYGIUM

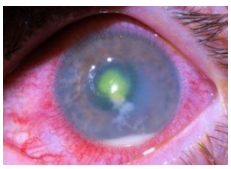
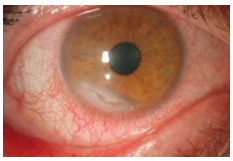
Fleshy growth of the conjunctiva that encroaches the cornea & cover cornea (Pterygium means wing). It usually starts nasally, but occasionally temporally in the 3 o'clock or 9 o'clock. More common in dry, hot & dusty environment. Pt com-plains slight cosmetic blemish, irritation of the eye. If it grows into the pupil, it will cause blurring of vision to blindness.

Treatment: protection from sun ē eye glass. If irritated, topical steroid, Terracotril eye suspension BID. Extensive crossing the limbus, will needs surgical excision.

PAINFUL RED EYE

Painful red eye may be sight threatening conditions. The diagnosis of such diseases need experienced ophthalmic worker, appropriate instruments & especial diagnostic tests & procedures. Their visual outcome highly depends on the time interval between onset of the disease & initiation of treatment & subsequent close follow up. So early referral to best centre may salvage their vision.

KERATITIS AND CORNEAL ULCER

The cornea is exposed to the atmosphere & so often suffers from injury, inflammation or infection. Common terms used in corneal disease. - Keratitis -is the general word for any type of corneal inflammation. Corneal ulcer-is loss of some of corneal epithelium & inflammation in surrounding cornea. -Corneal scar is white & opaque cornea, ẃ is the final result of any serious inflammation.

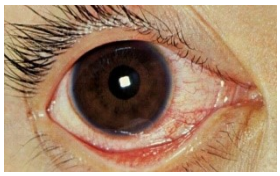
Etiology: Virus, bacteria, fungi.

Symptoms: Pain -sharp & severe. Blurred vision -because the ulcer makes the corneal surface irregular & less transparent. Photophobia. Red eye.

Signs: red eye -circumcorneal injection. Cornea -greyish to whitish infiltrate, hazy ē loss of clarity & opacity of different degree.

Treatment: start ē Gentamycin or Ciprofloxacillin eye drop frequently. For proper diagnosis, it needs slit lamp examination & culture. So early referral to ophthalmic centre is recommended.

IRIDOCYCLITIS



Inflammation of the iris & ciliary body.

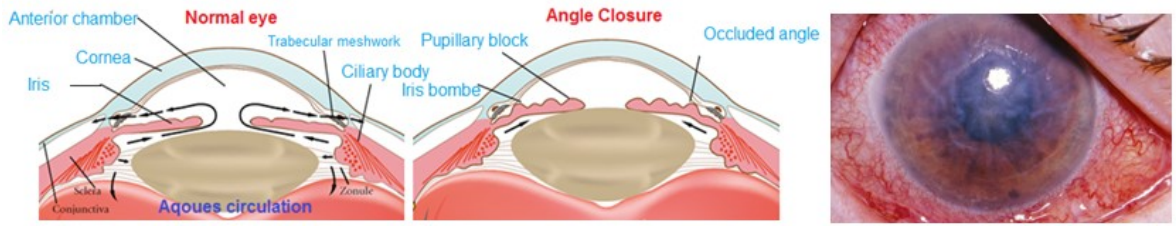
Etiology: associated ē systemic diseases - Infection -Mostly idiopathic.

Duration: acute duration less than 6 wks . Chronic duration above 6 wks.

Symptoms: Painful red eye. - Photophobia - Reduction of vision Sign - V/A may be reduced - Cornea is relatively clear -Circumcorneal injection -Meiosis (small pupil), may be irregular -Anterior chamber may be hazy or loss of clarity.

Treatment: Start ē topical steroids e.g.-Dexamethasone eye drop QID –Atropine drop 1% BID to prevent adhesion & ⇩ pain. Refer as soon as possible to ophthalmic centre.

ACUTE ANGLE CLOSURE GLAUCOMA



Glaucoma is commonly defined as a condition in ẃ the intra ocular pressure is suficiently high to cause optic nerve damage followed by visual field changes. Closed angle glaucoma is an ⇧ of IOP as a result of obstruction of aqueous outflow.

Symptoms: Painful red eye. Sudden reduction of vision. Rapid progressive visual impairment. Ocular pain. Nausea, vomiting & ipsilateral headache. Rain–bow (haloes) vision around light.

Signs: ⇩ of V/A . Firm to hard eyeball on digital palpation. Circumcorneal injection. Cornea is hazy or loss of its clarity. Anterior chamber will be shallow. Pupil is mid dilated, sluggish & fixed. Difficult to evaluate the fundus due to cornea oedema.

Treatment: Timolol eye drop 0.25% every 30 minutes + Acetazolamide (Diamox) 500 mg PO stat & then 250 mg PO QID. & urgent referral to ophthalmic centre.

OPEN ANGLE GLAUCOMA

It is characterized by - Adult onset of age above 40 yrs - Repeated IOP > 21 mmHg - Bilateral but severe in one eye.

Symptoms: usually asymptomatic. In advanced cases, constriction of visual fields.

Signs: V/A is reduced in advanced case. IOP is raised. Visual field constriction. Optic disc cupping.

Treatment: urgent referral for medical & surgical treatment.

CONGENITAL GLAUCOMA

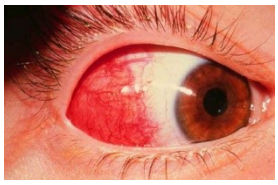
Cause: mal development of trabeculum including iridocorneal junction.

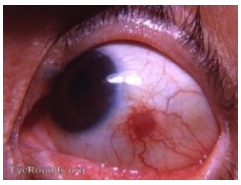
Symptoms : Triad of - Epiphora - Photophobia - Blepharospasm.

Signs: Triad of -Megalocornea (buphthalmos) -Haab's striae (descemenet membrane break) - IOP > 20 mmHg.

Treatment: early referral for surgical management.

EPISCLERITIS



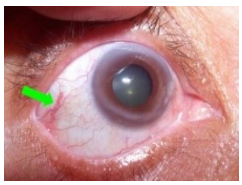


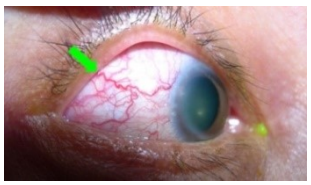
Inflammation of the episclera below the conjunctiva. Ocular redness ēout irritation or pain & the redness typically persists for 24- 72 hrs then resolves spontaneously.

Treatment

Not sight threatening. Self-limiting process. Topical vasoconstricting agent may reduce redness.

SCLERITIS





Inflammation of the sclera.

Symptoms

Painful disorder, typically a constant severe boring pain that worsens at night or in the early morning hours & radiates to the face & periorbital region. Pain is severe

enough to limit activity & often to prevent sleep. Watering, redness, & photophobia. Highly associated ē systemic disease like rheumariod arthritis, SLE, etc.

Signs: Sclera oedema. Tenderness.

Treatment: early referral for better management.

Summary of differential diagnosis of the red eye

Symptoms	Conjunctivitis	Cornea lesions	Acute iritis	Angle closure Glaucoma	Episcleritis/ Scleritis
Pain	Discomfort	Pain,Photophobia	Pain, photophobia	Severe pain	Aching pain. Locally tender
Discharge	Mucopurule-Nt	Watery	Watery	Slightly watery	Slightly Watery
Vision	Never impaired	May be Impaired	Impaired	Severely Impaired	Normal
Hyperaemia	Generalized	Ciliary/localized near-est to lesion	Ciliary	Ciliary	Near Affected area
Cornea	Normal	Alteration of surface re-flection &/ or opacity	Normal	Steamy- loss of Lustre	Normal
Pupil	Normal	May be irregular or Meiotic	Small &/or Irregular	Dilated & Non-Reactive	Normal
IOP/tension	Normal	Normal	May ⇧	⇧	Normal

BLINDNESS

Blindness is defined as visual acuity of less than 3/60 in the better eye with the best possible correction.

Epidemiology: every 5 seconds one person in our world goes blind & a child goes blind every minute. An estimated 45 million people world wide are blind. Every year, an additional 1-2 million persons go blind. Around 80% of blindness is treatable & preventable. A majority of the blind live in the poorest section of the devel oping world. Without proper interventions the number ⇧ to 75 million by 2020.

Causes: of world wide blindness:- 1.Cataract -19.34 million. 2.Trachoma- 6 million. 3.Glaucoma -2 million. 4.Measles/Vitamin A deficiency. 5.Others.

Vision 2020: WHO & International Agency for the Prevention of Blindness have

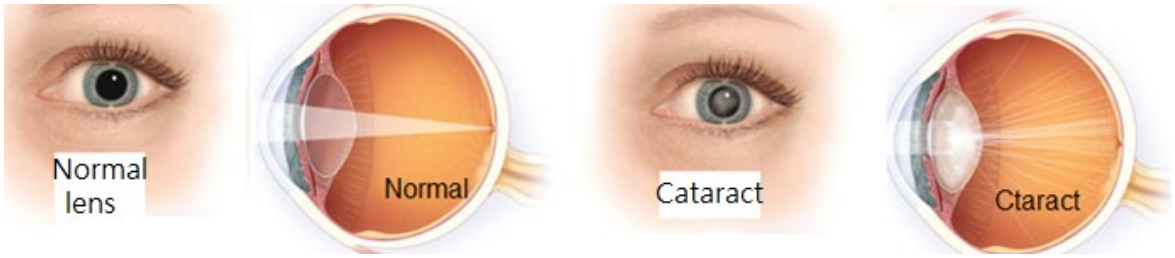
launched the plan called “vision 2020 the right to sight”. 20/20 represents normal visual acuity recorded by the Snellen’s method &measured in feet equivalent to 6/6 in meters. The hope is that by the year 2020 most of the avoidable blindness in the world should be eliminated, so that everyone in the world except those ē untreatable & unavoidable disease should have a visual acuity of 20/20 by the year 2020. The three main components (priorities) of Vision 2020 are:-

1-human resources development.

2- Infrastructure & appropriate technology.

3- Disease control (cataract, trachoma, Onchocerciasis, childhood blindness…).

CATARACT



It is lens opacity that causes visual impairment or blindness. The word cataract is derived from Latin “catarracta" ẃ means "water fall".

Epidemiology

Around 19.34 million people are bilaterally blind (< 3/60 in the better eye) from age related cataract. This represents 43% of all blindness. The number of blind people in the world & the proportion due to cataract is increasing due to:-•Population growth •Increasing longevity. The result of these 2 factors means that the population aged over 60 yrs will double during the next 20 yrs from approximately 400 million now, to around 800 million in 2020. This ⇧ in the elderly population will result in a greater number of the people ē visual loss & blindness from cataract that will need eye services. A figure of 1000 new blind people from cataract per million populations/year is used for planning purpose in developing countries.

Risk factors: •Aging. •Trauma. •Ultraviole exposure. •DM.

Classification

Anatomically: •Cortical cataract. •Nuclear cataract. •Post subcapsular cataract.

Etiologically: ▪Age related/senile. ▪Congenital. ▪Traumatic. ▪Metabolic cataract.

Clinically: •Immature cataract is when there is area of clear lens part in between opacities; vision better than 3/60, still allows view of posterior pole(+ve red reflex) •Mature cataract is when the whole cortical lens is opaque obscuring the part of the lens & vision worsen than 3/60.

Progress of the disease: some pt develops mature cataract only in a few months after a sign of opacity in the lens, others ē early opacity may persist in the lens for many yrs ēout obvious progress at all. However if opacity has formed it doesn't normally disappear spontaneously.

Symptoms: progressive painless vision reduction. Dazzling/glare/in nuclear cataract, in bright light the pupil constricts & vision deteriorates; become well in dim light.

Signs: Reduced V/A - Whitish opacity seen through the pupil.

Complication of unoperated cataract

•Dislocation or sub-laxation of lens. •Glaucoma. •Uveitis.

Treatment: Surgery-cataract extraction ē intra- ocular lens implantation.

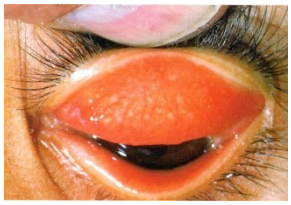
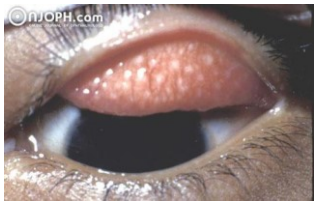
CONGENITAL CATARACT

Etiology: cong. infection (TORCH). Trauma or anoxia at birth. Genetic disorders.

Clinical features: whitish Pupillary reflex - increased eye movement (nystagmus).

Treatment: early referral for surgical management.

TRACHOMA

Trachoma is a chronic infectious Keratoconjuctivitis caused by Chlamydia trachomatis .It is a Greek word meaning 'rough' ẃ describes the appearance of the conjunctiva.

Epidemiology

Very common disease, particularly in developing countries. Affects about 600 million people. About 150 million people suffer from active trachoma. Operable trichiasis & entropion in 11 million people, 6 million of whom have gone blind due to the disease. Trachoma is the 2nd largest cause of blindness in the world, after cataract & leading cause of preventable blindness.

How does the disease develop?

Trachoma tends to be found in dry rural areas, where lack of water & bad living conditions may facilitate the spread of the disease. In communities where trachoma is common, infection starts in early child-hood. The first signs can be found in children of less than one year old. Trachmatos inflammation becomes increasingly intense in children up to the age of 6-8 years. Scars on the inside of the eye lids, caused by trachoma, can be found in children from the age of 4 years. Scarring is increasingly common in older children, but the serious complication of in turned eye lashes & corneal scarring do not usually appear before adult age. Thus, blindness due to trachoma is most common in adults.

Trachoma in the community

The severity of trachoma can vary from one community to another because of differences in the eases of spread of infection. Repeated infections ē C. trachomatis, or other causes of conjunctivitis, increase the intensity of inflammation, ẃ leads to more

scarring & blindness. Children are the main reservoir of Trachomatous infection, as they are commonly & heavily infected. Compared to men, women tend to have more severe trachoma, including inturned eyelashes &blindness, probably reinfected by children for whom they care.

Risk factors: Poverty - Poor hygiene at individual, family or community level. Lack of water supply.Age & sex; common in children & women. Environmental factors the 4 Ds (Dust, Dry, Dirty, Discharge).

Transmission of trachoma

Flies: eye to fly to eye - Fomite eye to clothing to eye - Finger: eye to finger to eye.

Common symptoms: varies from a mild condition ē hardly any symptoms at all, to a severe & blinding disease; -slightly mucopurulent discharge. –Tearing. -Foreign body sensation. -In severe cases, eyelid oedema, pain, red eye & photophobia.

Signs: follicles (whitish spots beneath the conjunctiva). Oedematous & thickened tarsal conjunctiva. -Upper tarsal conjunctival scaring. Pannus- vascular growth into the cornea. Herbert's pit-irregular upper limbus. Trichiasis (misdirected eyelash ē or ēout entropion). Corneal opacity.

Simplified WHO Grading of Trachoma

1- Active trachoma ē follicles/TF/. Must be at least five follicles in the upper tarsal plate & the blood vessels of the conjunctiva are visible.

2- Active trachoma intense/TI/. Oedematous & thickened tarsal conjunctiva ob scuring > 50% of blood vessels.

3- Trachomatous scarring/TS/. White scar in the upper tarsal plate.

4- Trachomatous Trichiasis/TT/. Evidence of one or more eye lash rubbing or touching the eye ball. History of eye lashes Epilation.

5- Corneal opacity/CO/. Central & sufficiently dense to obscure the part of pupil.

Management

•Local antibiotics, including:- Tetracycline 1% eye ointment, either twice per day for 6 wks or twice a day for 5 consecutive days per months, or a once daily for 10 consecutive days, each month for at least 6 consecutive months per year.

•Identify & treat families where there are one or more members ē TF or TI; treat the whole family ē one of the topical antibiotic regimens for mass treatment.

•Systemic antibiotics

A. Doxycycline 100mg PO/day for 21 days, don't give for children < 7 yrs, pregnant & lactating mother. Or Tetracycline 250 mg PO QID for 21 days, don't give children < 7 yrs, pregnant & lactating mother.

B. Erythromycin 250 mg QID for 3 wks

C. Azithromycin 20 mg/kg PO single dose- don't give to pregnant lady & those < 6 months of age. Maximum dose one gm &may require repeat dose after 6 months.

•Face washing- regular face washing to keep the eyes & face clear of discharge.

•Environmental change -provide adequate water supply, improve community sanitation (building & using VIP latrines & proper waste disposal); exclude cows & goat from the home. For community treatment of trachoma, mass distribution of tetracycline ointment is carried out especially during epidemics of conjunctivitis at intervals for five consecutive days per month for six months.

VITAMIN A DEFICIENCY DISORDER

VADD is change in the eye & other systems from vit A deficiency.

Dietary sources of retinol: Animal foods -contain the active vit retinol - Liver is the best source ẃ stores retinol - Milk products are also very rich in retinol. Plant foods - are particularly important because they are the staple diet for poor people Contain carotene pigment ẃ is converted into retinol - The best source is red palm oil, others;

carrots, mangoes, papaya. -Poor sources include; rice, cassava, yams & white maize ẃ are staple diet of the poor.

Function of Vit A: maintenance of healthy epithelium & formation of visual purple.

Clinical signs & symptoms:

Night Blindness -poor dark adaptation &poor night vision (nyctalopia). Is the earliest symptom of vit. A deficiency.

Conjunctival Xerosis: dryness of the conjunctiva causes to lose its normal shiny lustre & look like wax or paint instead. It is reversible ē treatment.

Bitot's Spot ē Conjunctival Xerosis: Bitot's spot is a foamy plaque on the temporal aspect of bulbar conjunctiva .

Corneal Xerosis: corneal surface looks rough, dull &irregular.

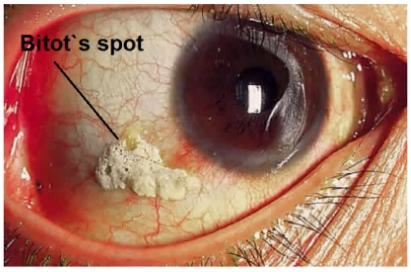
Corneal ulceration ē Xerosis: the ulcers are bilateral & central.

keratomalecia: liquefaction of part of cornea.

Xerophthalmia scar: bilateral, central or lower part of cornea. It is the last & severe sign ē melting of the cornea.

Xerophthalmia fundus: a pale yellow spot appear near the course of retinal vessels & also in the retinal periphery.

Bitot`s spot



Treatment Indications

All children ē any active corneal ulceration. All children ē signs of Xerophthalmia. All children ē measles since they are prone to develop Xerophthalmia. All severely ill or malnourished children from areas where Xerophthalmia occurs, even if there is no clinical evidence of Xerophthalmia

Recommended dose of vitamin A for age< one year or weight < 8 Kg.

	Mg	IU
Day 1	55	100,000
Day 2	55	100,000
Day 7	55	100,000

Recommended dose of vitamin A for age > one year or weight > 8 Kg

	Mg	IU
Day 1	110	200,000
Day 2	110	200,000
Day 7	110	200,000

Preventive treatment in the community

- Children under one year old; 55 mg or 100,000 IU, repeat every 4-6 months.
- Children over one year old; 110 mg or 200,000 IU, repeat every 4-6 months.
- Children at birth 27.5 mg or 50,000 IU.
- Mothers just after giving birth 165 mg or 300,000 IU.
- Pregnant and lactating mother 5.5 mg or 10,000 IU daily for 2 wks.

Prevention of blindness from Xerophthalmia

-Distribution of massive dose capsule.

-Fortification of food; identify pertinent food & process ē Vit. A.

-Horticulture & agriculture to grow & eat the right sort of food.

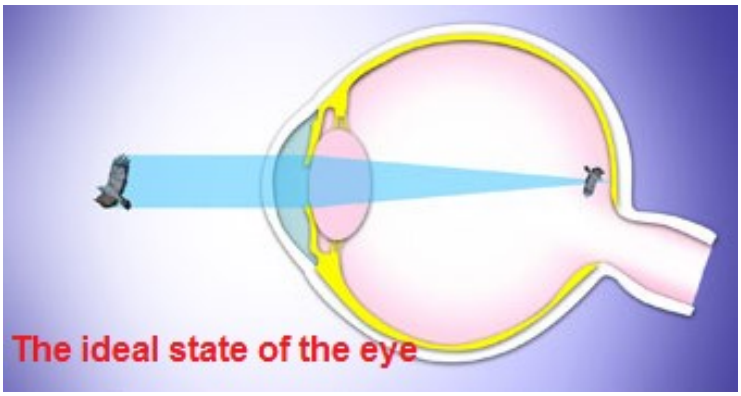
-Nutrition & health education.

-Immunization especially measles.

REFRACTIVE ERROR

INTRODUCTION

Emmetropia



The normal refractive state of the eye. The eye acts as a convex lens & parallel rays of light are focused on the retina. Light rays coming from 6 meter or more is considered to be parallel. For this reason during distance vision testing the pt is seated 6 meters from the test chart. Most of the refraction in the eye is done by the cornea (2/3) the rest being by the lens (1/3).

Accommodation

Rays of light from an object close to the eye is divergent & will be focused behind the retina. The eye adjusts the image by:-

-Contraction of ciliary muscles thereby loosens the suspensory ligaments so that the lens will be more spherical & strong.

-Decreasing the size of the pupil.

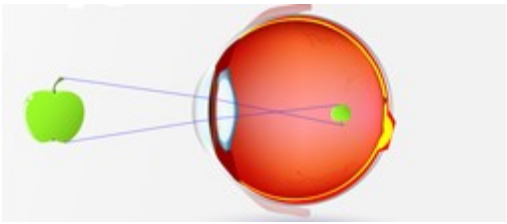
-Contraction of the medial recti.

All these muscles are innervated by Occulomotor nerve

Refractive Errors

In states of refractive error rays of light cannot be focused on the retina & the image appears blurred. The main types of refractive errors are:-

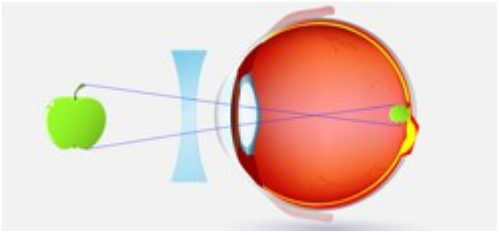
MYOPIA



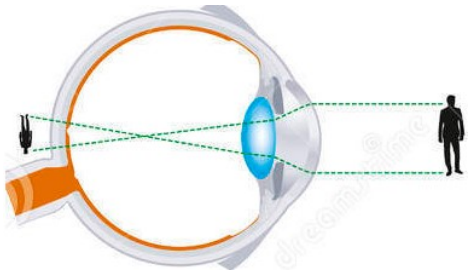
Short sightedness. In myopic eye the refractive power is so high that parallel rays of light focused in front of the retina.

Symptom: poor distant vision.

Treatment: spectacle- concave or negative lens.



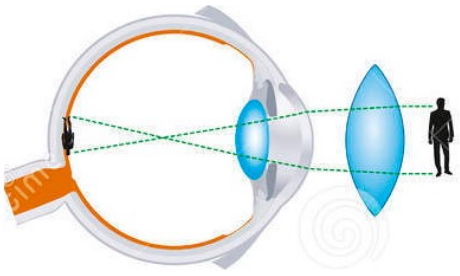
HYPERMETROPIA



Long-sightedness. In hypermetropia rays of light are focused behind the retina because the power of the optical system is too low for the length of the eye.

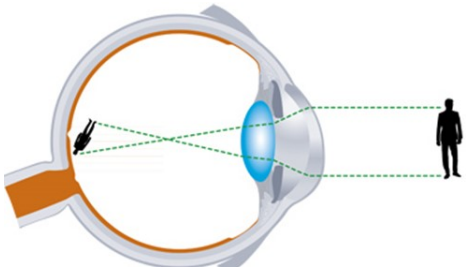
Symptoms: complain about near vision tasks. In advanced state they will have poor distant vision.

Treatment: Convex lens or positive lens.



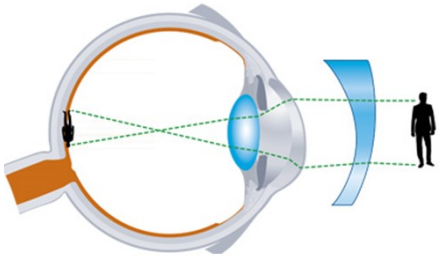
ASTIGMATISM

In astigmatism the rays of light coming to the eye are focused differently in different meridians or has two focal points.



Symptom: distortion of image -Poor vision at any distance.

Treatment: Spectacle ē cylindrical lens.



PRESBYOPIA

This is the result of the natural aging process of the lens where it becomes harder & less elastic. Accommodation will be ineffective and the person fails to do near work like reading. There is no difficulty of distant vision. Treatment-convex lens.

STRABISMUS

Symptom: deviation of the eye. Could have Diplopia. Poor vision.

Signs: V/A may be normal or reduced. Deviated eye.

Types of strabismus: Medial deviation (Esotropia), Lateral deviation (Exotropia), Upward (Hyperopia) & Down ward (Hypotropic).

Treatment: early detection & referral for for spectacle &/or surgery.

AMBLYOPIA

Amblyopia affects
one in every 40 children

Lazy eye. A reduction of vision of one or both eyes despite normal ocular finding.

Causes: certain types of refractive error. Strabismus . Cataract, Ptosis.

Treatment: Early referral to better centre.

COLOUR BLINDNESS

X - Chromosome Gene, OFN1LW, Location Xq28

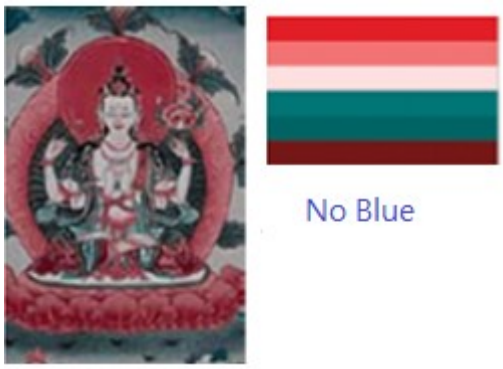
Described by, English Chemist, John Dalton in 1798

Incidence 5% in males & 0.5% in females •Inability or ⇩ ability to see colour, or perceive colour differences under normal lighting conditions •People usually have 3 types of cone cells in the eye, each type senses either red, green or blue light (the 3 basic colours) & most of cone cells are found in macula, ẃ is the central part of retina.

Normal

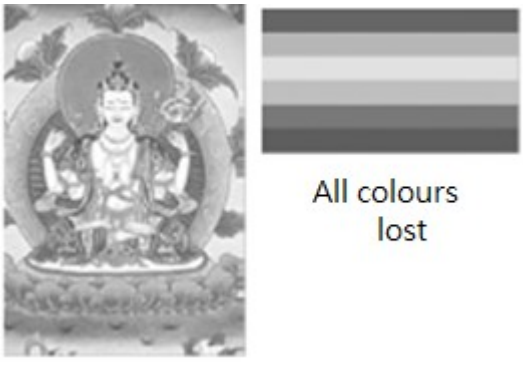
Green colour blindness (Deuteranopia) the commonest 95%

BLUE COLOR BLINDNESS (TRITANOPIA)



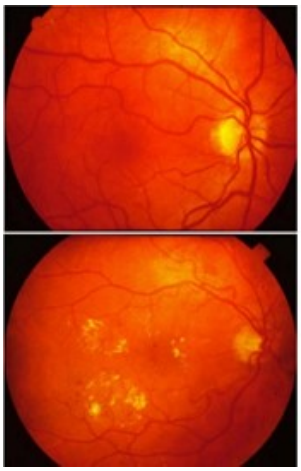
Red colour blindness (Protanopia)

Total colour blindness (Monochromacy): only as if it were on a black &white television as 2-3 cone pigments are missing .



SYSTEMIC DISEASES & THE EYE

DIABETES MELLITUS



Normal

Background diabetic retinopathy. There are areas of hard exudates and some evidence of macula involvement.

DM is a metabolic disorder ē hyperglycemia due to peripheral tissue resistance to insulin action or failure of insulin secretion or both that leads to micro vascular & cardiovascular complications. Ophthalmic manifestation of DM:-

1- Diabetic retinopathy

It is a disorder of the retinal vasculature that eventually develops to some degree in nearly all pts ē longstanding DM.

Pathogenesis: the cause of diabetic microvascular disease is unknown. It has been suggested that exposure to hyperglycemia over an extended period of time results in ultimate vascular damage ẃ is a microangiopathy of retinal vessels that result in micro vascular occlusion & leakage. Microvascular occlusion will cause hypoxia of the retina & stimulate new blood vessel formation. These vessels are fragile & bleed easily.

Epidemiology: it is the leading cause of legal blindness in developed world. The situation is increasing in our country.

Risk factors: •Duration of DM. •Age of onset. •Blood glucose control. •Comorbid illness like; •Pregnancy, •hypertension, •Renal diseases •Smoking etc.

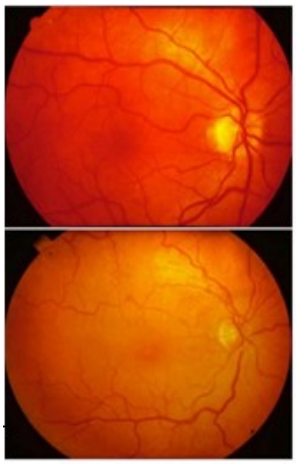
Clinical symptoms & signs: normal or reduced vision. Retinal findings include exudates, Hge, new vessel formation.

Management: strict blood glucose control. Avoid risk factors. Refer to ophthalmic centre for evaluation. Follow up

2-Diabetic cataract.

3- Others- refractive error, cranial nerve palsy, Neovascular Glaucoma.

HYPERTENSION



Normal

Hypertensive retinopathy.
The retinal arteries have become narrow & tortuous. In more advanced cases Hge & 'star burst' exudates occur together with papilloedema.

An acute or chronic elevation of systemic blood pressure leading to characteristic ophthamoscopic alteration over the fundus & other systemic complications.

Hypertensive retinopathy

Retinal vascular change ē arterial thickening, leakage & Hge over the fundus.

Symptoms: normal or reduced vision, nausea. headache, vomiting.

Signs: normal or reduced V/A, elevated blood pressure, vascular thickening, exudates, Hge, papilledema etc on the retina.

Management: control of BP. Refer to ophthalmic centre for better evaluation.

HIV/AIDS & THE EYE

HIV/AIDS is a disease caused by the human immune deficiency virus/HIV/. Pts will have recurrent opportunistic infections or of unusual tumours in association ē a dys-functional cellular system. HIV has been demonstrated in tears, conjunctival epithelial cells, corneal cells, aqueous, retinal vascular endothelium & retina.

Ophthalmic manifestation is classified as:-

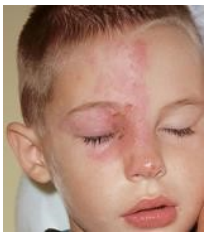
1. Microvasculopathy.

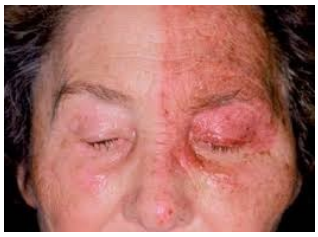
2. Tumour e.g. Kaposi's sarcoma, Squamous cell carcinoma.

3. Neuro-ophthalmopathy e.g. cranial nerve palsy, optic atrophy.

4. Opportunistic infection e.g. herpes zoster ophthalmicus, herpes simplex infection, toxoplasmosis etc. Over 70% of AIDS cases have some form of ophthalmic manifestation. Some of the commonest diseases will be discussed.

1. Ophthalmic herpes zoster





Is caused by varicella zoster - eye is affected through ophthalmic branch of trigeminal nerve, it is unilateral, common in immunocompromised pt., 90% are sero positive for HIV infection & most are young. **Symptoms**; prodromal symptoms of URTI. The rash appears 2-3 days after the pain, the rash is not different in sero positive & sero negatives but recurrent in sero positives. **Signs:** in chronological order;

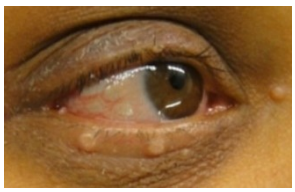
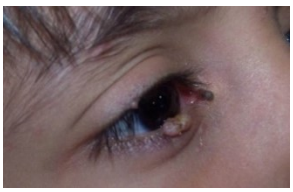
1. Maculopapular rash in the forehead.

2. Development of vesicles, pustules & crusting ulceration.

3.In severe cases- periorbital oedema due to 2ry bacterial cellulitis. It can also cau-se Keratitis, Uveitis, Keratouveitis, cataract, vitritis etc.

Treatment: analgesics-Aspirin 600 mg Q 4hr. -Paracetamol 1 gm Q 4hr. Gentian violet- 0.5% to clean the wound. Topical antibiotics. Systemic antiviral should be given within 72 hrs after rash because the drug needs active viral replication, Acy -clovir 800 mg 5X/day/for 7days. Refer to ophthalmic centre for further evaluation.

2. Molluscum Contagiosum

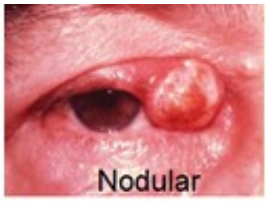
In immunocompromised pt, it is multiple, large size, bilateral, recurrent & resistant to treatment.

Symptoms: painless, raised, skin lesion.

Sign: single or multiple, pale, waxy, umblicated nodules. If the nodule is located on the lid margin it may give rise to ipsilateral chronic follicular conjunctivitis & occasionally a superficial keratitis.

Treatment: expression. Shaving & excision ¾ destruction of the lesion by cauterization, Cyrotherapy

3. Squamous Cell Carcinoma

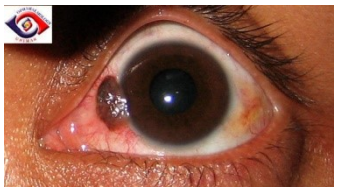
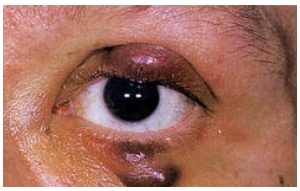



Conj. Squ. Cell Carcinoma

Malignant neoplasm of keratinizing cells of the epidermis, high chance to metastasize.

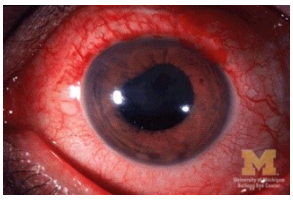
Symptoms & signs: painless plaque or nodule ē variable degree of scale, crust & ulceration. ***Treatment:*** referral for surgical excision & biopsy.

4. Kaposi's Sarcoma

A malignant vascular tumour that develops on the skin, m.m., LNs & visceral organs. It appears like flat or raised non tender, purple red -dark reddish lesion over the eye lid or conjunctiva. Referral for surgical excision & biopsy.-

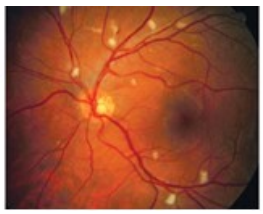
5. Uveitis



Causes: - herpes simplex - Herpes zoster – Toxoplasmosis.

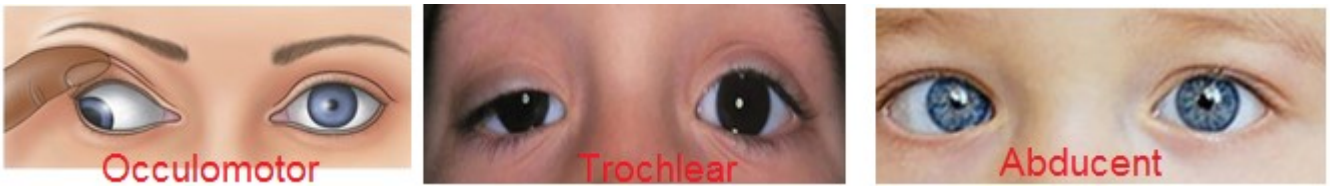
6. HIV retinopathy

Several cotton wool spots, typical of HIV retinopathy



It is a non-infectious micro vascular disorder characterized by cotton wool spots, microaneurysms, retinal haemorrhages, & area of capillary non-perfusion. These micro vascular changes are the most common retinal manifestations of HIV disease & are clinically apparent in about 70% of persons ē advanced HIV disease.

7. Cranial nerve palsy



If the third, fourth, or sixth nerves are affected, there will be diplopia. If optic nerve is affected, there will be loss of vision.

Causes: CMV or other infections.

Diagnosis: serology (ELISA) for HIV. Clinical diagnosis.

Treatment: of opportunistic infection accordingly -Antiretroviral drugs -Health education about the syndrome

8. Other Systemic Diseases

- Collagen/vascular diseases: Rh^{ed} arthritis, SLE.
- Infectious: TB, Syphilis Leprosy.

Chapter XII

SURGERY

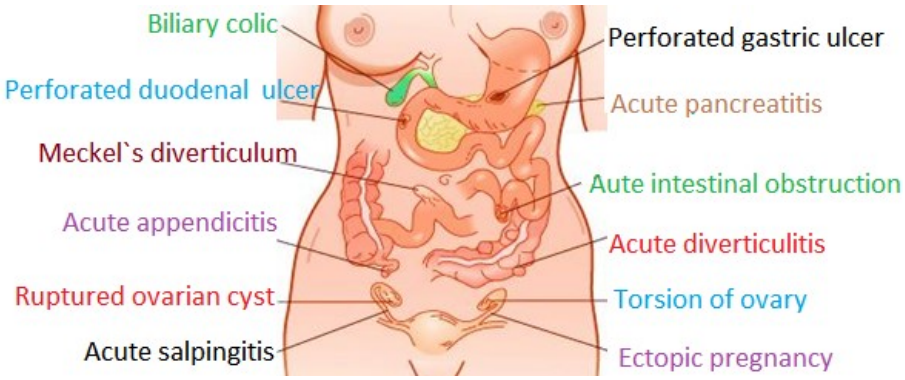
- Acute Abdomen
- Appendicitis
- Cholecystitis
- Pancreatitis
- Peritonitis
- Hernia
- Intestinal Obstruction
- Benign Prostatic Hyperplasia
- Anal Fissure
- Piles
- Abdominal Pain In Elderly
- Mesenteric Ischemia
- Abdominal Aortic Aneurysm
- Gastric tumors
- Colorectal Cancer
- Bleeding Per Rectum

ACUTE ABDOMEN

Pts é an acute abdomen comprise the largest group of people presenting as a general surgical emergency. Acute abdomen is condition of abrupt onset associated é severe abdominal pain (resulting from inflammation, obstruction, infarction, perforation, or rupture of intra-abdominal organs). It requires urgent evaluation & diagnosis because it may indicate urgent surgical Rx.

Sudden onset of abdominal pain indicates peritoneal irritation.

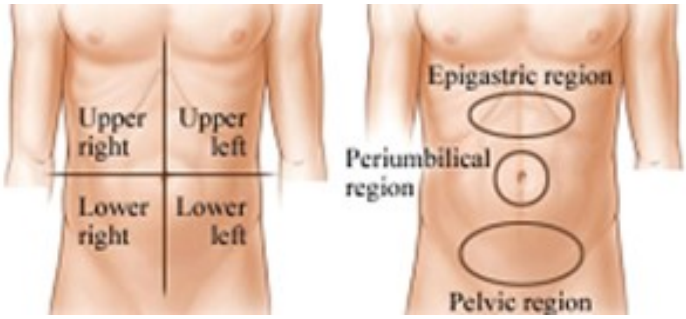
Causes: It's Huge!: use history & physical examination to narrow it down.



Most common causes

•Non-specific abdominal pain 34%	•Pancreatitis 3%
•Appendicitis 28%	•Renal colic 3%
•Biliary tract disease 10%	•Perforated ulcer 3%
•Intestinal obstruction 4%	•Cancer%
•Gynaecological disease%	•Others 6%

Investigations



Upper right quadrant pain: •Upright chest XR. •Upright & supine abdominal XR. •CBC. •Urine. •S. Amylase • S. Creatinine. •BUN. & •S. Electrolytes.

Lower right quadrant pain: •Urine. •Pregnancy test. •U/S •CBC.

Upper left quadrant & epigastric pain: •Upright CXR. •Upright & supine abdominal XR. •CBC. •S. Amylase & Lipase.

Lower left quadrant pain: •Pregnancy test. •Urine. •U/S. •CBC. •Upright & supine abdominal XR. •CT scan abdomen if diverticular disease suspected.

Periumbilical pain: •CBC. •Serum amylase &lipase. •XR Abdomen up right & supine. •stool analysis.

Common gynaecologic causes

•Ruptured ovarian cyst. •Ovarian torsion. •Ectopic pregnancy.

•Acute salpingitis. •Pyosalpinx. •Endometritis. •Uterine rupture.

Extra-abdominal causes

•MI. •Pericarditis. •Left lower lobe pneumonia.

•Pneumothorax. •Pulmonary infarction.

•Hematologic; sickle cell disease, acute leukaemia.

•Drugs. •Metabolic. •Herpes Zoster.

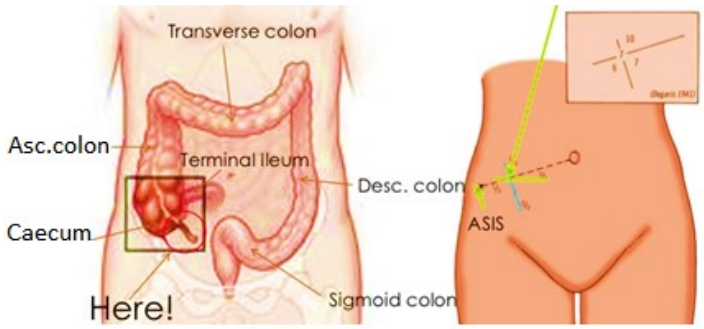
•Tabes dorsalis. •Nerve root compression.

•Endocrinal causes as diabetic ketoacidosis, addisonian crisis.

Immediate Management

1. Start large bore IV é either saline or lactated ringer's solution.
2. IV pain medication.
3. Nasogastric tube if vomiting or concerned about obstruction.
4. Foley catheter to follow hydration status (fluid chart).
5. Antibiotic if suspicious of inflammation or perforation.
6. Definitive therapy or procedure will vary é diagnosis.
7. Close observation, urgent investigations & surgical consultation.

ACUTE APPENDICITIS



Approximately 7% of the population will have appendicitis in their life-time é the peak incidence between the ages of 10 & 30 yrs. It is the commonest surgical condition in children need operation.

Symptoms

•Central abdominal pain moving to right iliac fossa. •Nausea, vomiting, anorexia. •Low grade fever.

Physical examination

Findings depend on duration of illness prior to examination. Early, the pts may not have localized tenderness, é progression there is tenderness to deep palpation over the McBurney's point.

McBurney's point: just below the middle of a line connecting the umbilicus & ASIS.

Rovsing's sign: pain in right lower quadrant é palpation to left lower quadrant.

Rectal examination: pain can be most pronounced if the pt has pelvic appendix.

Rebound tenderness, Voluntary Guarding, Muscular Rigidity.

Psoas sign: place pt in left lateral decubitus & extend right leg at the hip. If there is pain é this movement, then the sign is +ve.

•***Obturator sign:*** passively flex the right hip & knee & internally rotate the hip. If there is increased pain then the sign is positive.

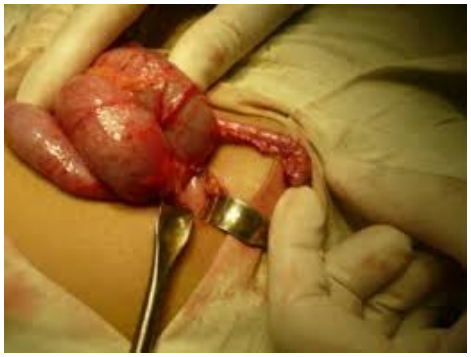
•***Fever:*** at the onset of pain fever is usually not found & is late finding, temp. 39^{o}C is uncommon in the 1st 24 hrs but not uncommon after rupture.

Diagnosis

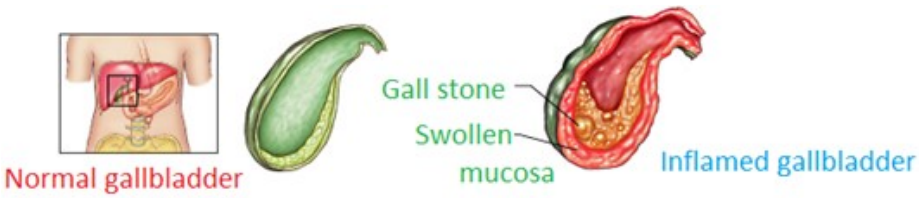
- Should be suspected in anyone é epigastric, periumblical, right flank, or right sided abdominal pain who has not had an appendectomy.
- Women of child bearing age need a pelvic exam & pregnancy test.
- ***CBC:*** the WBC is of limited value, sensitivity of ⇧ WBC is 70-90%, but specificity is very low.
- ***CRP***: independent surgical indication marker for appendicitis.
- ***ESR:*** have been studied é mixed results.
- ***Urine analysis:*** abnormalities found in 19-40%, include; pyuria, hematuria, bacteriuria, presence of >20 WBCs/field should ⇧consideration of UTI.
- ***X-ray abdomen:*** abnormal in 24-95%, the abnormal findings include; fecalith, appendicular gas & free air.
- ***U/S:*** reported sensitivity 94.7% & specificity 88.9%, limitations of U/S is retrocec-al appendix may not be visualized & perforation may be missed.
- ***CT:*** is of greater sensitivity & accuracy.

Treatment

- Appendectomy is the standard of care.
- Pts should be NPO, given IV fluid & preoperative antibiotics.
- Antibiotics are most effective when given preoperatively & they ⇩ postoperative infection & abscess formation.



ACUTE CHOLECYSTITIS



Inflammation of gall-bladder, 90% of cases are associated é calculi. Common in fertile, fatty, above forty, females.

Symptoms & signs

Pain: characteristic for its great acute pain in right hypochondrium & epigastric area ẃ radiate to the right supraclavicular area & right shoulder.

Dyspepsia: frequent symptoms ẃ disturb a pt, are nausea, frequent vomiting, at first by gastric maintenance & later é bile. Afterwards feelings of swelling of stoma- ch, de- lay of emptying & gases.

Murphy's sign: delay of breathing during palpation of gallbladder on inhalation.

•Kehr's sign: is strengthening of pain at pressure on the area of gallbladder, especially é deep inhale.

Diagnosis

+ve Morphy`s sign: insinuate your fingers below the right costal margin, ask pt to take deep breath, he will feel severe pain & stop breathing at certain point. It is +ve é cholecystitis or liver disease.

U/S abdomen: dilatation of biliary system, presence of stones or fluid.

CBC: leucocytosis.

LFTs: ⇧ serum bilirubin & alkaline phosphatase.

Serum Amylase, Lipase.

Urine analysis: bilirubin.

Plain XR abdomen: radiopaque gall stones may be seen.

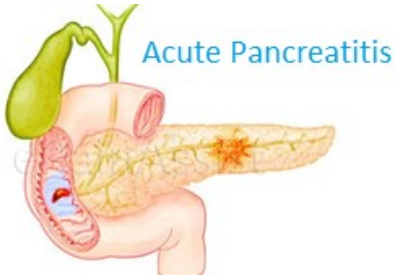
Management

Cholecystectomy: is a major surgery, removal of gallbladder through 4-7 inches incision, drainage tube & stay in hospital for few days.

Laparoscopic cholecystectomy: the first choice of Rx for gall stones & inflammation of the gallbladder, requires several small incisions in the abdomen to allow the insertion of the laparoscope.

Non-surgical Rx: include pain medicines, low-fat diet & antibiotics.

ACUTE PANCREATITIS



Causes

•Biliary tract disease especially stones •Alcoholism •Drugs: Furosemide, Valproic Acid, Azathioprine, Sulfasalazine •Infection (mumps) •Hypertriglyceridemia •Structural abnormalities of pancreatic duct (stricture, cancer) •Abnormalities of common bile duct & ampullary region •Surgery of stomach or biliary tract •Vascular disease •Trauma •Hyperparathyroidism & Hypercalcaemia are aetiological causes.

Clinical picture

•Fever.

•Severe abdominal pain radiating to the back; sudden in biliary pancreatitis, developing over wks in alcoholism. Pain is steady, boring, persistent, relieved by leaning forward & accentuated by coughing or movement or deep breathing. •Abdominal tenderness é muscular rigidity. •Hypoactive bowel sounds. •Nausea & vomiting •Tachycardia & tachypnea. •Jaundice may present. •Lung examination may reveal limited diaphragmatic excursions & evidence of atelectasis.

Complications

•Early death may be due to cardiovascular instability or respiratory failure or later death due to pancreatic or pseudo cyst infection.

•Pancreatic infection of devitalized retroperitoneal tissue é sepsis.

•Pancreatic pseudo cyst may be secondary infected, bleed or rupture.

Diagnosis

•⇧ Serum Amylase & Lipase. •WBC: ⇧ 12,000 -20,000/mm^3

•Hyperglycaemia. •⇩ Serum calcium. •⇧ Serum bilirubin.

•X-rays abdomen (supine & upright). •Chest X ray. •U/S abdomen. •CT abdomen.

Differential diagnosis

The following diseases can mimic acute pancreatitis:- •Perforated gastric or duodenal ulcer. Mesenteric infarction. •Strangulating intestinal obstruction. •Ectopic pregnancy.•Dissecting aneurysm. •Biliary colic. •Appendicitis.•Diverticulitis. •Inferior wall MI. •Haematoma of abdominal muscles or spleen.

Prognosis

Ranson's 11 prognostic signs.

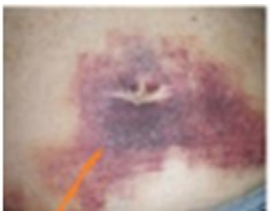
5 Signs at admission	6 Signs within 48 hrs from admission
• Age>55 years	• Hct drop by >10%
•BG >200 µg/dl	• BUN rise >45 mg/dl
•Serum LDH >350 u/L	• Serum Ca <8 mg/dl
• AST >250 u/L	• PO_2< 60 mmHg
• WBC count >16,000/µL	• Base deficit >4 meq/l
	• Estimated fluid sequestration >6 L.

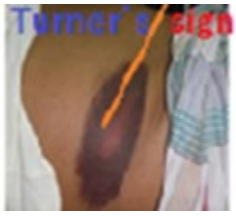
The mortality according to Ranson`s 11 prognostic signs ⇧ é the number of +ve signs: if < 3 signs are +ve, the mortality rate is < 5%. If 3-4 signs are +ve, the mortality is 15-20% If 7-8 signs are +ve, the mortality is 100%.

Acute pancreatitis associated é necrosis & Hge has mortality rate 10-50%, the diagnosis is suggested by:-

- Progressive ⇩ in Hct.
- Presence of haemorrhagic fluid within ascites.
- Reduction of serum Ca level.
- Presence of Grey Turner &/or Cullen sign (indicating extravasation of haemorrhagic exudates to the flanks or umbilical region respectively.

Cullen`s sign





Turner`s sign

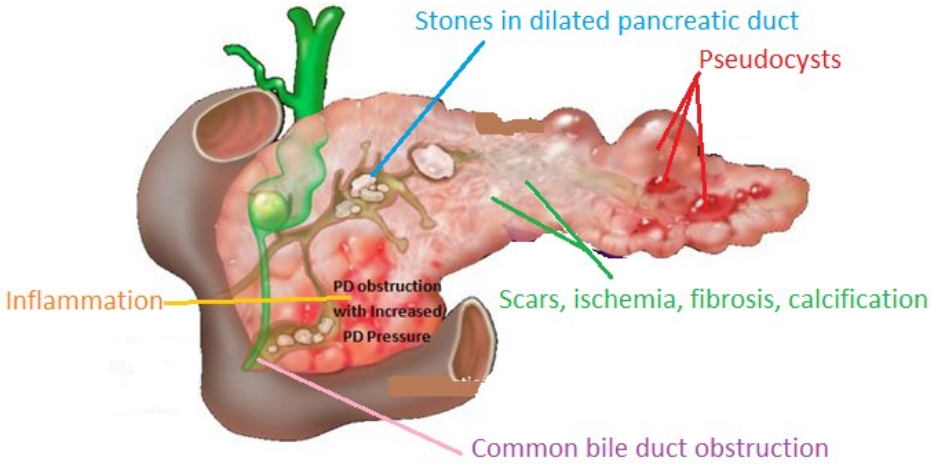
Management

Mild oedematous pancreatitis: •Keep pt NO until manifestations of acute inflammation subside •Give sufficient IV fluids •Insert NGT.

Severe acute pancreatitis: •Refer to hospitals for admission to ICU. •Vital signs & urine output are monitored at least/1 hr. •Accurate metabolic flow sheet, to be checked every 8 hrs. •ABG is determined as necessary. •Hct, BG, electrolytes (Ca, Mg), CBC, platelet, coagulation parameters, total protein é albumin, BUN, creatinine, amylase & lipase studies performed daily. •Keep pt on NPO é NG tube. •IV fluids may be given up to 6-8 L/day. •Give H2 receptor blockers IV •Give O_2 as needed •Severe pain should be treated é Pethidine 50-1500 mg IM/4-6 hrs & as needed in pt é normal RFTs (morphine causes the sphincter of oddi to contract & should be avoided). •Treat hyperglycaemia >250mg/dl. •If symptoms of calcium depletion appear give calcium gluconate 10-20 ml IV in 1 litre of replacement fluid.

Surgery: indicated for: •Trauma. •Uncontrolled biliary sepsis. •Inability to distinguish acute pancreatitis from other causes. •To drain a pseudo cyst that is expanding rapidly, secondary infected, or associated é bleeding or impending rupture.

CHRONIC PANCREATITIS



Causes

- Alcoholism: 70-80% of cases are associated é alcoholism.
- Idiopathic.
- Hereditary.
- Microlithiasis.
- Hyperparathyroidism.
- Main pancreatic duct obstruction (stenosis, stones, or cancer).

Signs & symptoms

Persistent or recurrent epigastric or Left upper abdominal pain, nausea, vomiting, anorexia, constipation, flatulence & wt loss are common. In advanced disease, pts may develop steatorrhoea, recurrent acute attacks of pain ẃ become more constant later & insulin secretion is ⇩ é impaired glucose tolerance.

Diagnosis

Laboratory tests are frequently normal, but inflammation markers may be minimally elevated.

- X ray abdomen: may visualise pancreatic calcification (30% of cases).
- U/S or CT abdomen: for calcifications, dilated ducts & atrophy.
- Tests of pancreatic function: to assess endocrine & exocrine function, including

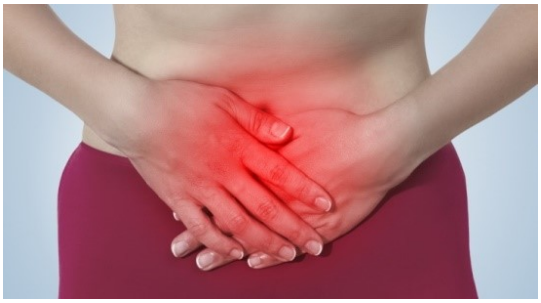
glucose tolerance.

- Stool tests: faecal chymotrypsin.

Management

- IV fluids & fasting prove beneficial.
- Oral pancreatic enzymes é each meal (30.000 u of lipase).
- If steatorrhoea is severe & refractory, medium chain triglycerides ẃ are absorbed éout pancreatic enzymes, can be provided as an alternative source of fat.
- Supplementation é fat-soluble Vitamin A, D, K sometimes required.
- Relapse may require Rx similar to that of acute pancreatitis.
- A Pancreatic pseudo cyst, ẃ causes chronic pain, needs referral to centres é surgical facilities & expertise.
- DM rarely occurs in chronic pancreatitis. For most pts, BG level of 200-250 mg is acceptable & does not require treatment. It is better to maintain the pt in a slightly hyperglycaemic range than run a risk hypoglycaemia caused by over-zealous administration of insulin.
- Pts é chronic pancreatitis are at ⇧ risk for pancreatic cancer. Worsening of symptoms, especially é development of a pancreatic duct stricture should prompt an examination for malignancy.

PERITONITIS



The peritoneum is a thin, double layer of serous membrane in the abdominal cavity. The area of the peritoneum is around 2 square meters. The peritoneum tissue is a typical connective tissue; covered by polygonal mesothelium; has very good plastic peculiarities & has a very good blood supply. The parietal peritoneum is inervated by the sensitive somatic nerves. The pain as a result of the parietal peritoneum irritation is localized (somatic pain), while the pelvic peritoneum has no so-matic innervations. The visceral peritoneum has vegetative (parasympathic & sympathic) innervations & the pain of visceral peritoneum irritation is not localized.

Peritonitis is an inflammation of the peritoneum, the serous membrane that lines part of the abdominal cavity. It may be localized or generalized &may result from infection & from a non infectious process.

Infective peritonitis the causative organism are;

- Pyogenic bacteria.
- E-coli.
- Aerobic & anaerobic strept.
- Staph.

Non infected peritonitis result from leakage of sterile body fluids into the peritoneum , such as blood, gastric juice (e.g. peptic ulcer, gastric carcinoma), bile (e.g. liver),urine (pelvic trauma), pancreatic juice (pancreatitis). Note: while these body fluids are ster-ile at first, they frequently become infected once they leak out of their organ, leading to infectious peritonitis within 24-48 hr. Also sterile abdominal surgery under normal circumstances, causes localized or minimal generalized peritonitis through foreign bo-dy reaction or fibrotic adhesion.

Pathophysiology

- In normal conditions, the peritoneum appears greyish & glistening. It becomes dull 2-4 hr after the onset of peritonitis, initially ē serous or slightly turbid fluid.
- Peritonitis is caused by leakage of contents from abdominal organs into abdominal cavity, as a result of inflammation, infection, ischemia, or tumour perforation.
- Bacterial proliferation occurs.
- Oedema of the tissues results & exudation of fluid develops in a short time.
- Fluids in peritoneal cavity becomes turbid ē increasing amounts of protein, WBCs, cellular debris & blood. The immediate response of the GIT is hypermobility, followed by paralytic ileus ē an accumulation of air & fluid in the bowel.
- Later on the exudate becomes creamy & suppurative. It may spread to the whole peritoneum. Secondary peritonitis is the more common type of peritonitis, happens when the infection comes into the peritoneum from the GIT or biliary tract.

Risk factors

Liver disease. Fluid in the abdomen. Weakened immune system. Pelvic inflammatory disease. Appendicitis. Stomach ulcer. Twisted intestine. Pancreatitis. Inflammatory bowel disease. Injury caused by operation. Peritoneal dialysis. Trauma.

Clinical picture

Signs & symptoms depend on the location & the extent of inflammation.

- Abdominal pain & tenderness. At first, a diffuse type. Pain tends to become constant, localized & more intense near the site of the inflammation.
- Diffuse abdominal rigidity, swelling & abd. tenderness & pain ranging from dull aches to severe, sharp pain is often present, especially in generalized peritonitis.
- Fever & chills, loss of appetite, thirst, nausea & vomiting.
- Reduced urine output.
- Not being able to pass gas or stool.

- Sinus tachycardia.
- Development of paralytic ileus ẃ causes nausea, vomiting & abdomen distension.
- Auscultation reveals absent of bowel sounds.
- In neglected cases the pt will present by sunken eyes.

Diagnosis

Based on the clinical manifestations

- CBC: leucocytosis.
- Hypokalaemia,hypernatremia &acidosis may present but are not specific findings
- Abdominal XR may reveal dilated, oedematous intestines.
- CT scan may be useful in differentiating causes of abdominal pain.
- In pt ē ascites, a diagnosis is made via paracentesis.
- Culture of peritoneal fluid can determine the microorganism & its sensitivity.

Management

✓Pt is placed on the side ē knees flexed; this position ⇩ tension on the abdominal organs & maximize comfort.

✓IV rehydration &correction of electrolyte disturbances.

✓Fluid chart & CVP assessment ẃ assists in calculating fluid replacement.

✓Nasogastric tube to deflate the stomach & bowels .

✓Foley catheter is inserted to check the urine output & the adequacy of IVF.

✓Antibiotics IV, but may also infused directly into peritoneum a combination of Ampicillin, Aminoglycoside & Metronidazole can cover all aerobic & anaerobic.

✓Analgesics are given for pain relive.

✓Monitor pt mental, cardiac, pulmonary status, GIT. (temp, pulse, intestinal sounds, softening of the abdomen), also monitoring for signs & symptoms of shock.

✓Laparotomy is needed to perform a full exploration & lavage of the peritoneum.

HERNIA

Etiology

All hernias occur at the site of weakness of the abdominal wall ẃ are acted on by repeated ⇧ in abdominal pressure as a result of:-

- Chronic cough or Straining or Vomiting or Pregnancy.
- Bladder neck or urethral obstruction.
- Severe muscular effort.
- Ascetic fluid.

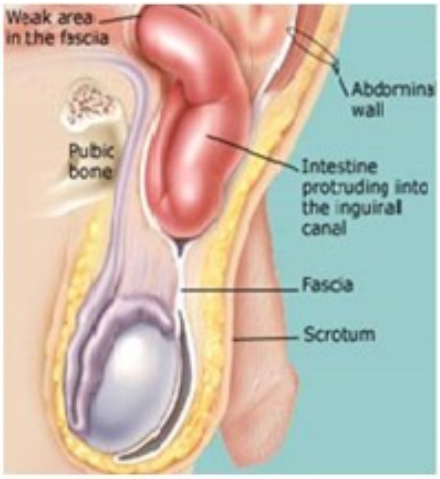
Common abdominal hernia

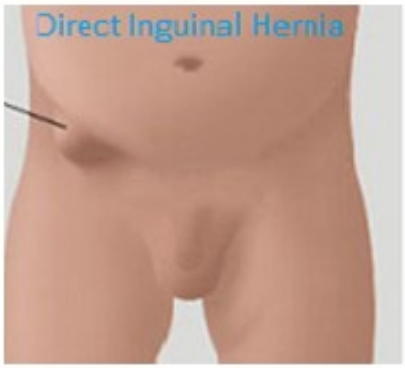
Inguinal hernia

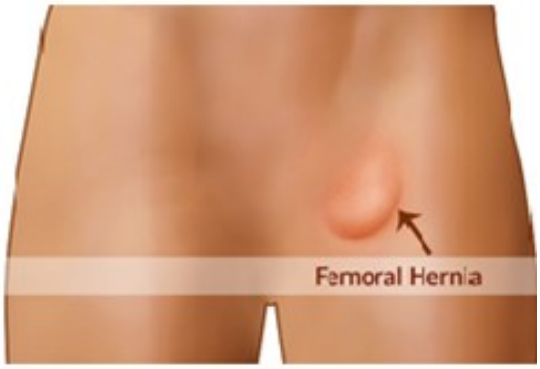
Makes up 75% of all abdominal hernias & occurring up to 25 times more often in men than women.

Indirect inguinal hernia

Is the most common form of hernia & it's usually congenital due to patent processus viginalis, it protrude through the inguinal ring & is ultimately the result of the failure of embryonic closure, it follow the pathway that testicles made during pre-birth development & sometimes the hernia sac protrude into the scrotum.







Direct inguinal hernia

Occur slightly to the inside of the site of indirect hernia, in a place where the abdo-

minal wall is naturally slightly thinner, it rarely will protrude into the scrotum, almost always occur in the middle age elderly because there abdominal wall weakness as they age.

Femoral Hernia

The major feature of the femoral canal is the femoral sheath. This sheath is a condensation of the deep fascia (fascia lata) of the thigh & contains, from lateral to medial, the femoral artery, femoral vein & femoral canal. The femoral canal is a space medial to the vein that allows for venous expansion & contains a LN (node of Cloquet). Other features of the femoral triangle include the femoral nerve, ẃ lies lateral to the sheath. Femoral hernia occur through the femoral canal in the femoral triangle, medial to femoral vessels & under inguinal ligament (appears between the thigh & groin region), is more common in females.

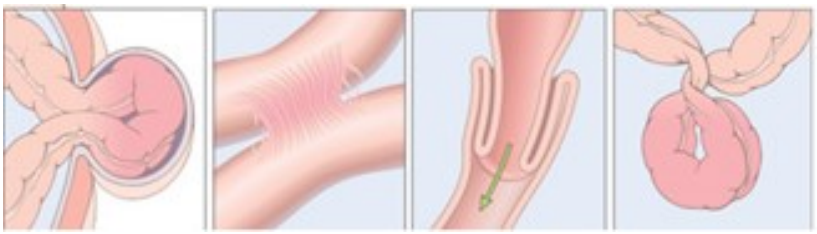
Femoral hernia versus inguinal hernia

INGUINAL HERNIA	FEMORAL HERNIA
1-More common in males	1-More common in females
2-Pass through the inguinal canal	2-Pass through the femoral canal
3-Neck of the sac is above & medial the pubic tubercle	3-Neck of the sac is below & lateral the pubic tubercle
4-Less common to be strangulated	4-More common to be strangulated
5- Can be treated éout surgery	5- Must be treated surgically
6-The 2 diagnostic signs of hernia +	6-The diagnostic signs of hernia
7-The sac mainly contain bowel	7-The sac mainly contain omentum

Diagnostic Procedures

•Physical exam reveals the herniated area. •Medical history of sharp abdominal pain when lifting or straining also may help confirm the diagnosis. •X-ray or CT is ordered if bowel obstruction is suspected.

INTESTINAL OBSTRUCTION



Herniation *Adhesions* *Intussusception* *Volvulus*

Any condition interferes é normal propulsion & passage of intestinal contents. Can involve the small bowel, colon or both as in generalized ileus.

Classification

- According to cause of obstruction: mechanical or functional (Ileus).
- According to duration of obstruction: acute or chronic.
- According to extent of obstruction: partial or complete.
- According to type of obstruction: simple or closed loop or strangulation.

Aetiology

Neonate: •Meconium ileus •Hirschprung's disease •Malrotation •Intestinal atresia

Age from 2-24 months: •Intussusception (>2 yrs old) •Hirschsprung disease.

Children: Hernia.

Adults: Mechanical bowel obstruction: Small bowel obstruction: •Adhesion 60%. •Hernia 20%. •Neoplasm or Volvulus 10%. •Others: Gall stone. Foreign body. Intussuception. Large bowel obstruction: •Cancer 60%. •Diverticular disease 15%. •Volvulus 15%. •Others: Hernia. Fecal impaction. Inflammatory. Functional bowel obstruction: •Vascular occlusion ileus. •Spastic ileus (intestine remain contracted & no propulsive) as a result of: uremia, porphyria, heavy metal poison. •Adynamic or inhibition ileus: post operatively, mostly after abdominal surgery, or metabolic causes as diabetic ketoacidosis, hyponatremia, hypokalemia, hypomagnesaemia, or as a result of drugs as morphine, antacid, anticonvulsant. Also may result from intraabdominal inflammation, sepsis, occult wound infection, pneumonia or renal stone or as a result

of retroperitoneal hematoma or fracture spine or ribs.

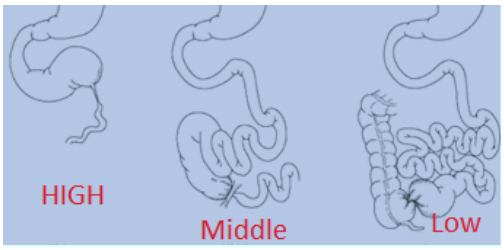
Diagnosis

4 Cardinal symptoms; **Pain.** **Vomiting.** **Distension.** **Constipation.**

With proximal obstruction, earlier symptoms é prominent vomiting & less distension. While vomiting uncommon in colon obstruction till late stage. The location & characteristic of pain differentiate between mechanical & functional obstruction (ileus), severe cramp & localized in mid of abdomen (mechanical) while diffuse & mild in (ileus).

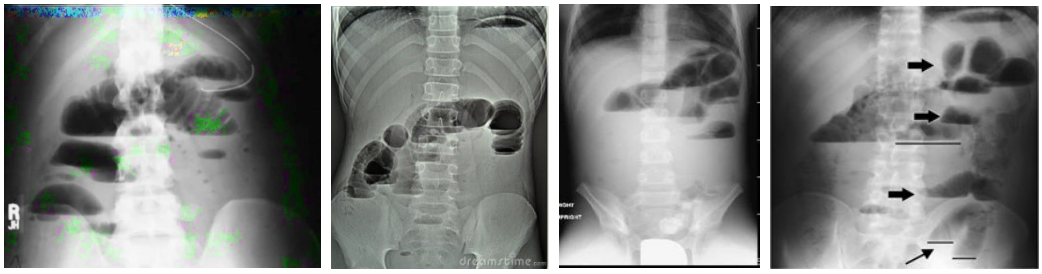
Examination

- Vital signs (RR, temp & BP).
- Hydration status.
- Abdominal & rectal examinations.



High	Middle	Low
Frequent vomiting. No distention. Intermittent pain but not classic crescendo type.	Moderate vomiting. Moderate distention. Intermittent pain (crescendo, colicky) with free intervals.	Vomiting late, feculent. Marked distention. Variable pain; may not be classic crescendo type.

Investigations:



Air fluid level & dilated loops at different levels of intestinal obstruction

CBC: ⇧ PCV (dehydration), ⇧ WBC.

Kidney function tests: ⇧ BUN & creatinine.

X-ray abdominal (supine & upright): small bowel considered dilated when diameter

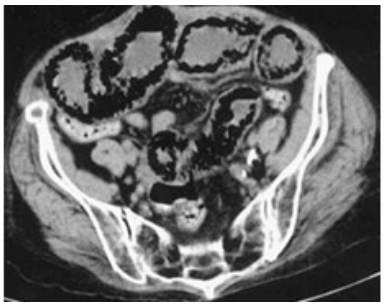
>3 cm while proximal colon 9 cm & the sigmoid 5 cm. The dilated small bowel tend to be in the central portion of abdomen recognized by presence plicae circularis. Dilated colon tend to be in the periphery of abdomen & recognized by haustral marking. X ray can be diagnostic in 50-80% of pts. The cause of bowel obstruction can often determined. Presence of pneumobilia suggest gall stone ileus. The sigmoid & cecal volvulus produce pathognomonic images. Presence of pneumoperitoneum indicates perforated viscous.

CXR: detect extra-abdominal condition & bowel obstruction e.g. pneumonia.

Contrast studies: indications are controversial. Identify site & often the cause of obstruction. Differentiate between colonic & distal small bowel obstruction. Differentiate between ileus-partial & complete obstruction.

Computed tomography: recently become valuable in bowel obstruction especially when plain films failed in diagnosis or suspect strangulation. Sensitivity 93% & spe- cificity 100%. Accuracy 94% in diagnosis of bowel obstruction.

CT: Pneumatosis Intestinalis;
dilated Loops of small bowel,
air in wall of small bowel,
no air in colon



Management

Initial management is 'drip & suck'.

Supportive Rx: •NPO. •NG tube to decompress the stomach.

•Send blood for electrolyte & urea.

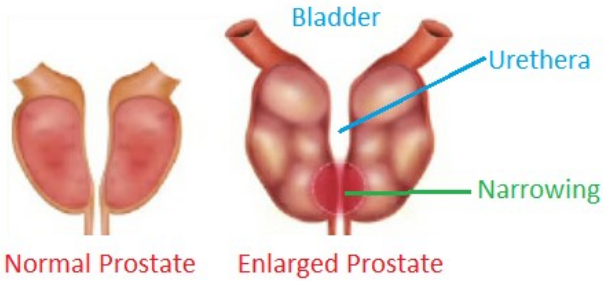
•IVF(rehydration), replace electrolyte losses. •Fluid chart, urine output monitoring

•Cross match blood & transfusion if required. •IV antibiotics if indicated.

Symptomatic Rx: analgesics after confirming diagnosis.

Specific Rx: surgical interference.

BENIGN PROSTATIC HYPERPLASIA



Male sex gland, pear-shaped, weight 7-16gm- size of walnut. Helps control of urine flow, produces fluid component of semen, produces prostate specific antigen.

Hyperplasia

It is an ⇧ in the size of an organ or tissue due to ⇧ in the number of constituent parenchymal cells. May be physiological or pathological (hypertrophy is an ⇧ in the size of an organ or tissue due to enlargement of individual cells). Benign prostatic hyperplasia is non-malignant enlargement of the prostate gland caused by cellular hyperplasia of both glandular & stromal elements. It is the most common benign tumor in men & is not a precancerous condition.

Etiology

Hormone theory: as age advances the male hormone (androgen) ⇩ while the quantity of the oestrogenic hormone is not ⇩ equally. According to this theory the prostate enlarges because of predominance of oestrogenic hormone. The prostatic enlargement can be regarded as involuntary hyperplasia due to disturbance of the ratio & quantity of the circulating androgens & oestrogens & induction of prostatic growth factors.

Neoplastic theory: postulates that enlargement is a benign neoplasm “fibromyoadenoma” (as prostate is composed of fibrous, muscular & glandular tissues).

Incidence

- 50% of all men have an enlarged prostate by age 60.
- 80% of all men have an enlarged prostate by age 80.

•Only 10% of them present é symptoms.

Symptoms

Voiding symptoms: •⇩ in the urinary stream. •Straining. •Dribbling at the end of urination. •Intermittency. •Hesitancy. •Pain or burning during urination. •Feeling of incomplete bladder emptying.

Irritative symptoms: •Urinary frequency. •Urgency. •Dysuria. •Bladder pain. •Nocturia. •Incontinence. •Symptoms associated é infection.

Diagnosis

•History & Examination.

•Digital rectal examination.

•Validated symptom questionnaire.

•Urinalysis.

•Urine culture.

•BUN, Creatinine.

•PSA.

•Transrectal U/S biopsy.

•Uroflometry.

•Post void residual.

Prostate Specific Antigen

Generally, PSA is **<** 4 ng/ml & this is considered normal. When prostate cancer develops, the level usually is **>** 4, but a level **<**4 does not mean that cancer isn`t present- as about 15% of men é a PSA **<**4 will have prostate cancer on biopsy. Men é a PSA level in the borderline range 4-10, have about a 1 in 4 chance of having prostate cancer. If the PSA is **>** 10, the chance of having prostate cancer is over 50%.

Age specific PSA

Normal level according to age is as follow:-

- 40-49 Yrs old <2.5 ng/ml.
- 50-59 Yrs old <3.5 ng/ml.
- 60-69 Yrs old <4.5 ng/ml.
- 70-79 Yrs old <6.5 ng/ ml

Complications

•Urinary retention. •UTI. •Sepsis secondary to UTI. •Residual urine. •Calculi. •Renalfailure. •Hematuria. •Hernias. •Hemorrhoids.

Treatment

∝ blockers: •Improve bladder & prostate smooth muscle tone also relaxes smooth muscles & ⇩ urethral resistance. •More effective than 5 α reductase inhibitors. •Tamsulosin & Alfuzosin require no dose titration. •Doxazocin (Cardura) 1mg/day, maximum 8 mg/day.

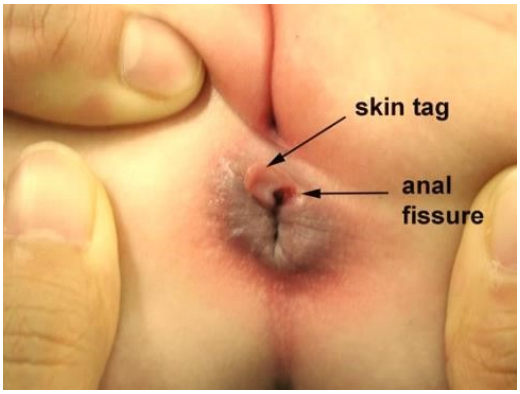
5 α reductase inhibitors: •Reduce prostate volume, involution of epithelial component. •Reduces risk of prostate cancer, but ⇧ risk of high grade disease.

•Finestride (Proscar 5 mg tab/day).

Combined therapy: large prostate **>**40 gm or PSA **>**4 or moderate to severe symptoms combined therapy is used. Much less effective for men é smaller prostate.

Surgical therapies: •Transurethral resection of prostate still the gold standard therapy. •Laser therapy significantly reduced blood loss, catheter may be required post operatively. •Open prostatectomy rarely required.

ANAL FISSURE



Anal & perianal disorders makeup about 20% of all outpatient surgical referrals. Extremely distressing & embarrassing pt, often put up é symptoms for long time, before seeking medical advice. Fissure is a tear in the anal canal extending from just below the dentate line to the anal verg. Most commonly in young & middle age adults.

Aetiology

•The initiating factor is trauma, typically overstretching of the anoderm by a large hard stool.

•The proposed explanation for the posterior midline predominance is a lack of tissue support & maximal stretching at this site.

•Failure to heal is 2ry to poor perfusion of the anoderm in the posterior midline.

Clinical picture

•Anal bleeding, bright red blood is common, pain & discomfort.The cardinal symptom is pain during & for minutes to hours following defecation

•Perianal itching & irritation. Pt feel something coming down.

•Perianal discharge.

Management

•Warm bath & diet sufficiently high in fibre to achieve soft bulky stools allows approximately 50% of acute anal fissures to heal within 3 wks.

•Stool softeners & fibre supplements are reasonable additions.

•Recurrence is common, in the range of 30-70%, but can be reduced to 15-20% by maintaining a high fibre diet.

•Topical application of nitroglycerine, a nitric oxide donor, causes a transient lowering of resting anal pressure &an ⇧ in anodermal blood flow.

•Topical Ca Ch Bl (2% Diltiazem, 0.3% Nifedipine).

•Botulinum toxin: in chronic cases has been inject into the external & internal sphincters & é short term follow up, healing rates of 80% have been achieved.

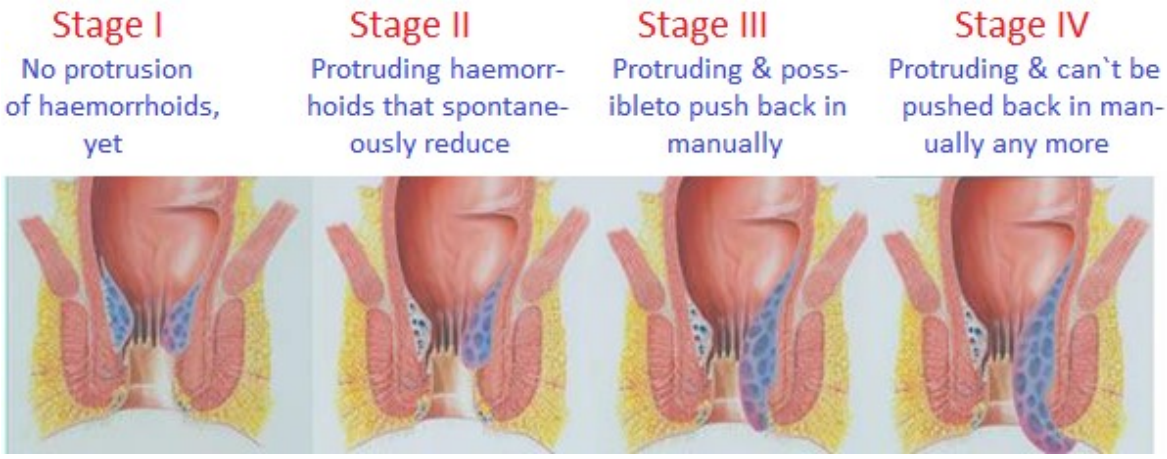
•Internal sphincterotomy: achieve healing in about 95% within several wks.

PILES / HAEMORRHOIDS

Dilated or enlarged veins in the lower portion of the rectum or anus. Peak ages: 45 - 65 yrs. ½ of adults experience haemorrhoids by age 50. Common among pregnant women-temporary.

Causes: •Constipation. •Diarrhea. •Sitting or standing for long periods of time. •Obesity. •Heavy lifting. •Pregnancy.

Types



Symptoms

•Rectal bleeding. •Bright red blood in stool. •Pain during defecation. •Anal itching. •Rectal prolapse. •Thrombosis.

Signs & Tests

•Rectal examination: visual & digital. •Stool, Sigmoidoscopy, Anao & Proctoscopy.

Treatment

Mild cases are controlled by; •Preventing constipation. •Drinking fluids. •High-fiber diet. •Stool softeners. •Local application of cream or suppository containing cortisone. •Keeping anal area clean. •Soak in warm water. Use sitz bath é warm water. •Apply ice packs or compresses X 10 min. •If prolapse, gentle push back into anal canal. •Use moist towelettes or wet toilet paper instead of dry paper.

Painful or persistent hemorrhoids

•Tying off a haemorrhoids (Baron Band ligation). •Sclerotherapy. •Infrared light photocoagulation/electrocoagulation. •Laser light. •Cryosurgery (Freezing).

Surgery; haemorrhoidectomy, removal of enlarged veins around the anus.

ABDOMINAL PAIN IN ELDERLY

Mortality rate for abdominal pain in the elderly is 11-14%. •Perception of pain is altered. •Altered reporting of pain: stoicism, fear, communication problems.

Causes

Don't miss these

•Appendicitis- do not exclude it because of prolonged symptoms.

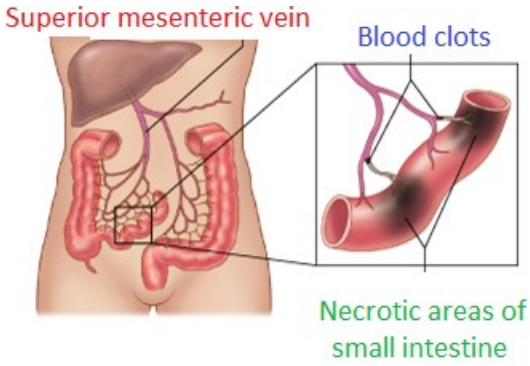
•Acute cholecystitis - most common surgical emergency in elderly.

•Perforated peptic ulcer-only 50% report a sudden onset of pain. Missed diagnosis was leading cause of death.

•Mesenteric ischemia - we make the diagnosis only 25% of the time. Early diagnosis improves chances of survival.

•⇧ frequency of Abdominal aortic aneurysms in elderly & may look like renal colic.

MESENTERIC ISCHEMIA



Consider this diagnosis in all elderly pts é the following risk factors:-

•AF. •Recent MI. •Atherosclerosis. •CHF. •Digoxin therapy. •Hypercoagulability. •Prior deep venous thrombosis. •Liver disease.

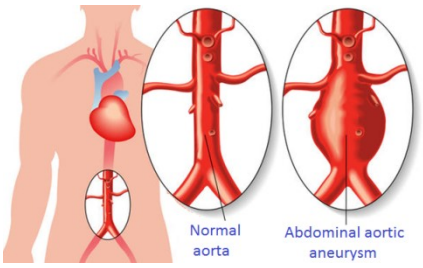
Clinical picture

•Severe pain, often refractory to analgesics. •Relatively normal abdominal examination. •Embolic source: sudden onset (more gradual if thrombosis). •Nausea, vomiting & anorexia are common. •50% of cases will have diarrhea. •Eventually stools will be guiaic +ve. •Metabolic acidosis & extreme leukocytosis when advanced disease is present (bowel necrosis).

Diagnosis

Requires mesenteric angiography or CT angiography.

ABDOMINAL AORTIC ANEURYSM



Risk factors ⇧ é age, women> 70 years & men > 55 years.

Symptoms & Signs

•Abdominal pain, sudden onset of significant pain. In 70-80% it is abdominal (not back pain!), back pain in 50%. Atypical locations of pain include: hips, inguinal area,external genitalia. •Syncope can occur & Hypotension may be present. •May be

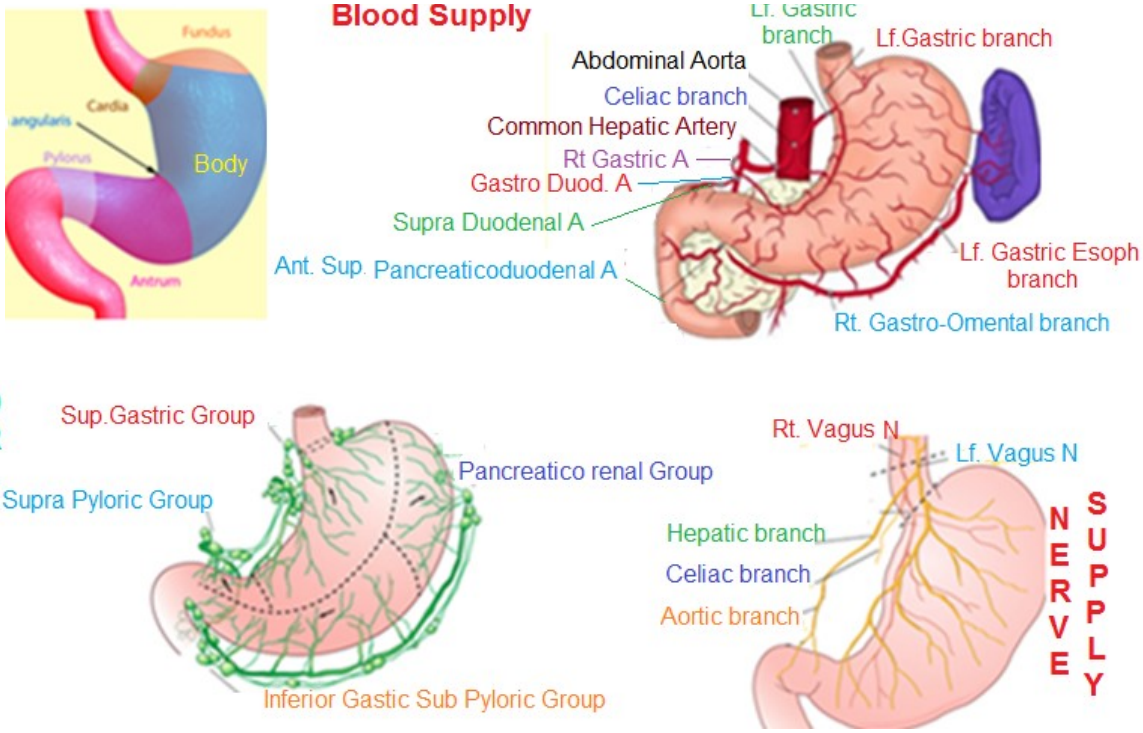
present é hematuria. •Palpation of a tender, enlarged aorta on examination is an important finding. •Suspect it in any older pt é abdominal pain especially é renal colic-flank - or back pain.

Diagnosis

U/S: can reveal the presence of abd. aortic aneurysm but not helpful for rupture.

CT- Scan: abdomen/pelvis éout contrast for stable pts. High suspicion in an unstable pt requires surgical consult & emergent surgery.

GASTRIC TUMORS



Stomach is J-shaped. Has 2 surfaces (anterior & posterior), 2 curvatures (greater & lesser), 2 orifices (cardia & pylorus). It has fundus, body & pyloric antrum.

Blood supply

Most of blood supply to stomach is from the celiac artery. The 4 main arteries are; left & right gastric along the lesser curvature. Left & right gastroepiploic along the greater curvature. Blood supply to the proximal stomach also comes from the inferior phrenic & short gastric arteries. Venous drainage parallels the arterial supply; left & right gastric veins drain into the portal vein. The right gastroepiploic drains into the superior

mesenteric vein & Left gastroepiploic drains into the splenic vein.

Lymphatic drainage

Is into 4 zones: Superior gastric, Suprapyloric, Pancreaticorenal & Inferior gastric/sub-pyloric. All the 4 drain into the celiac group of nodes & into the thoracic duct.Gastric cancers drain into any of these groups regardless of location of tumour.

Innervation

Parasympathetic via the vagus (Lf anterior & Rt posterior) & Sympathetic via the Celiac plexus.

Layers: 5 layers; ■Mucosa (Epithelium, lamina propria). ■Sub mucosa. ■Smooth muscle layer. ■Subserosa & ■Serosa.

Etiology

85% of gastric tumours are adenocarcinomas & 15% lymphomas & gastrointestinal stromal tumours. Gastric cancer is the 2nd most common fatal cancer in the world. There is tremendous geographic variation, ē highest death rates ⇧ ē age, peaking in the 7th decade & affect males twice as often as females.

Risk Factors

Diet: low fat or protein consumption, salted meat or fish, high nitrate consumption & High complex carbohydrate consumption.

Environment: poor food preparation (smoked/salted), lack of refrigeration, poor drinking water (well-water) & smoking.

Social: low social class (except in Japan).

Medical: prior gastric surgery, H. pylori infection, Gastric atrophy & Gastritis, Adenomatous polyps & Male gender.

Helicobacter pylori: presence of IgG to H. pylori in a given population correlates ē local incidence & mortality from gastric cancer, different strains elicit different antibody

responses. The cag A strain causes more mucosal inflammation & thus a higher risk of gastric cancer than cag A-negative strains.

Adenomatous polyps: there is 20% risk of developing cancer, especially in lesions >2cm. Multiple lesions ⇧ the risk of developing cancer. Presence of polyps ⇧ the chance of developing cancer in the remainder of mucosa. Endoscopic surveillance is required after removal of polyps.

Types

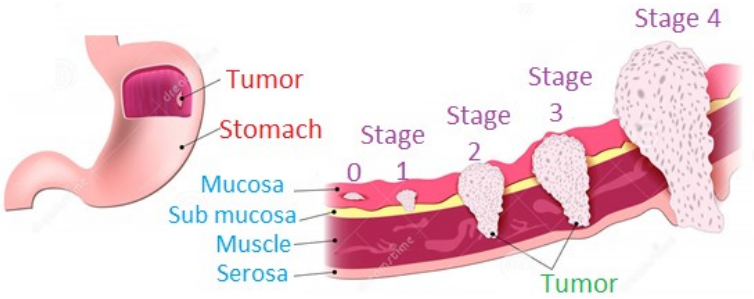
The gastric cancer may arise in the antrum (50%), the gastric body (30%), the fundus or oesophagogastric junction (20%).

a. **Adenocarcinoma.** b. **Leiomyosarcoma.** c. **Lymphomas.** d. **Carcinoid Tumours.**

The macroscopic forms are classified by (Bormann classification) into:-

- Polypoid or Proliferative.
- Ulcerating.
- Ulcerating/Infiltrating.
- Diffuse Infiltrating (Linnitus - Plastica).

Stages



Clinical Presentation

Symptom	Percent
Weight loss	62
Abdominal pain	52
Nausea	34
Dysphagia	26
Melena	20
Early satiety	18
Ulcer-type pain	17

Symptoms are often absent in early stages & when present are often ignored, missed, or mistaken for another disease process. ▪Vague discomfort &/or indigestion ▪Epigastric pain that is constant, non-radiating, & unrelieved by food ingestion. ▪Proximal tumours may present ē dysphagia. ▪Antral tumours may present ē outlet obstruction. ▪Diffuse mural disease may present ē early satiety due to ⇩ distensibility. ▪Up to 15% of pts develop hematemesis & 40% are anaemic at presentation. ▪Unfortunately most pts present in later stages of disease, ē evidence of metastatic or locally advanced tumour. ▪Palpable abdominal mass, ovarian mass, supraclavicular or periumbilical L.Ns. ▪Obstruction from tumour invasion into transverse colon. ▪Hepatomegaly, jaundice, ascites & cachexia.

Investigation

- Upper gastro intestinal endoscopy ē multiple biopsy & brush cytology. Endoscopy is the diagnostic method of choice ē multiple biopsies (seven or more) the diagnostic accuracy approaches 98%. Cytologic brushings can also be obtained. Size, morphology & location of tumour can be documented,as well as any other mucosal abnormalities.
- Radiology: CT Scan of the chest & abdomen. U/S upper abdomen. Barium meal. The double contrast barium swallow has 90% accuracy & is cost effective. No ability to distinguish between malignant & benign ulcers.
- Diagnostic laparoscopy.
- Serologic markers: CEA, CA-125, CA 19-9, CA 72-4 may be elevated but have low sensitivity/specificity, & none are diagnostic.

Treatment

Surgical resection is the only curative option. Distal tumours ẃ involve the lower ½ (subtotal or partial gasterectomy). Proximal tumours ẃ involve the fundus, cardia or body (total gasterectomy). The issue of extent of resection appears to have been sett-

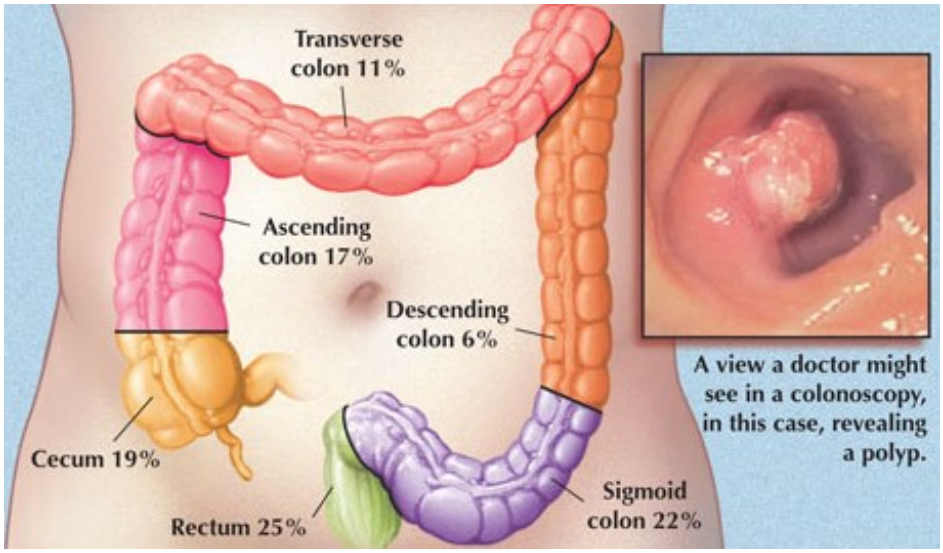
led. As long as adequate tumour margins are achieved, subtotal gastrectomy has the same survival as total, ē decreased morbidity.

Chemotherapy/Radiotherapy for gastric cancer, more recently pre & post-chemo-radiation therapy has been scrutinized to see if there is any benefit to survival.

Outcome

5-yr survival for a curative resection is 30-50% for stage II disease, 10-25 % for stage III disease. A recent study offers evidence of a survival benefit associated ē postoperative chemo radiotherapy.

COLON / COLORECTAL CANCER



Epidemiology

Carcinoma of large intestine is the most common tumour of the elementary tract & is the 3rd common cancer in old age group. In western countries its incidence is approaching 40 per 100.000. 90% of cases occur after age 50. Is the 2nd leading cause of cancer death. Men & women are affected equally. Women are more likely to have right sided colonic adenomas. 25% of CRC arise from rectum, 22% from sigmoid colon, 19% from cecum, 17% from ascending colon, 11% from transverse colon & 6% from descending colon. Distributed evenly among various racial groups. African Americans & Hispanics have lower survival rate.

Risk factors

- Established non-dietary causes of colorectal cancer (CRC) include; genetic predisposition, family history of colorectal adenomas or colorectal cancer in 1st degree relative, juvenile polyposis. Chronic ulcerative colitis & Crohn's diseases, schistosomiasis, personal history of, ureterosigmoidostomy, breast, ovarian & uterine cancers, all ⇧ the risk of CRC.
- Obesity, adult height, alcohol consumption, frequent eating & consumption of diets high in red meat, processed meat, diet high in sugar, eggs, total & saturated fat & use of cigarettes & other tobacco products, all possibly ⇧ risk of CRC.
- The evidence that diets high in vegetables & regular physical activity ⇩ the risk of CRC, is convincing.
- Diets high in starch, non-starch polysaccharides (fibre) & carotenoids all of ẃ possibly ⇩ risk of CRC.
- Aspirin & NSAIDs ⇩ risk of CRC.

Clinical picture

Symptoms vary depending on the site of carcinoma. In tumours of the left colon bleeding is common & obstruction is early. Tumours of the right colon present é anaemia, cachexia & alteration of bowel habit but obstruction is late because of the relatively fluid nature of the bowel contents. As a consequence left sided tumours tend to be diagnosed earlier. Carcinoma of the lower rectum will almost always cause early bleeding é mucous discharge; later there is tenesmus & a feeling of incomplete emptying of the bowel. The findings on physical examination range from no obvious abnormality to the signs of advanced malignancy é cachexia & signs of extra colonic spread. A mass may be palpable, rectal tumours may be palpated on digital examination. Fresh blood in the stool should always suggest the possibility of a tumour of the

rectum or pelvic colon. Occult blood is found in the stool if an ulcerating lesion is present higher in the colon. 15-20% of pts have distant metastatic disease at the time of presentation. The % of CRC manifestations include; abdominal pain 44%, change in bowel habit 43%, hematochezia or melena 40%, weakness 20%, anaemia ēout other GIT symptoms 11%, wt. loss 6%. Some pts have more than one abnormality.

Diagnosis

- Digital rectal examination.
- Barium enema ē/ēout air contrast: used primarily to locate deformities of intestinal topography polyposis colon is import- ant predisposing fact.
- Sigmoidoscopy, rigid type or flexible fibre optic type: used to visualize local rectal tumours or for routine screening.
- Colonoscopy: direct visual examination of the colon & rectum detects early polypoid tumours preoperatively & recurrences post-resection; Multiple biopsies may be performed at time of study to ⇧ sensitivity.
- CT scan: used to stage disease & identify metastases, is valuable to search for hepatic metastasis prior to surgery so that appropriate Rx can be planned.
- Transrectal U/S: excellent choice for preoperative staging of rectal carcinomas.
- Magnetic resonance imaging: very useful for diagnosing metastatic disease.
- Laparotomy: useful in detecting metastases to abdominal regions (especially omentum or liver) that often remain undetected by current imaging techniques.
- Tumour markers: CEA, CA 19 9, CA 50, & CA 19 5, have a low diagnostic ability to de

tect primary CRC, overlap ē benign disease, low sensitivity for early stage disease. An expert panel on tumour markers convened by the American Society of Clinical Oncology recommended that serum CEA levels not be used as a screening test for CRC. Tumour markers have prognostic utility.

Stages of CRC

TNM staging system

(T) Primary tumour

- TX - Primary tumour cannot be assessed.
- T0 - No evidence of primary tumour.
- Tis- Carcinoma in situ: intraepithelial or invasion of lamina propria.
- T1 -Tumour invades submucosa.
- T2-Tumour invades muscularis propria.
- T3 -Tumor invades through the muscularis propria into the sub serosa or into non-peritonealized pericolic or perirectal tissues.
- T4 -Tumour directly invades other organs &/or perforates visceral peritoneum.

(N) Regional lymph nodes

- NX - regional L.Ns. cannot be assessed.
- N0 - no regional LNs metastasis.
- N1- metastasis in 1 to 3 regional L.Ns.
- N2 - metastasis in 4 or more regional L.Ns.

(M) Distant metastasis

- MX - distant metastasis cannot be assessed.
- M0 - no distant metastasis.
- M1 - distant metastasis.

Management

Surgical excision: mainstay of curative Rx. Specific procedure depends on the anatomic location of the cancer, but typically involves hemi colectomy. Surgical resection of affected bowel è clear margins, along è the adjacent mesentery & at least 12 regional nodes. For rectal tumours, total mesorectal excision è a distal surgical margin of at least 2 cm is recommended. For tumours that are located within 6 cm of the anal verge, or involve the anal sphincter, wide surgical resection è abdominoperineal resection & permanent colostomy is recommended. Local excision, for palliative Rx or simple polyp removal.

Radiation therapy: postoperative radiation, ē or ēout chemotherapy, significantly reduces local recurrence rates. Common regimen incorporates infusional 5-Fluoro- uracil as a radio sensitizer to boost the efficacy of pelvic radiation. Administered as 45 to 55 Gy over 5 wks. Repeated as needed.

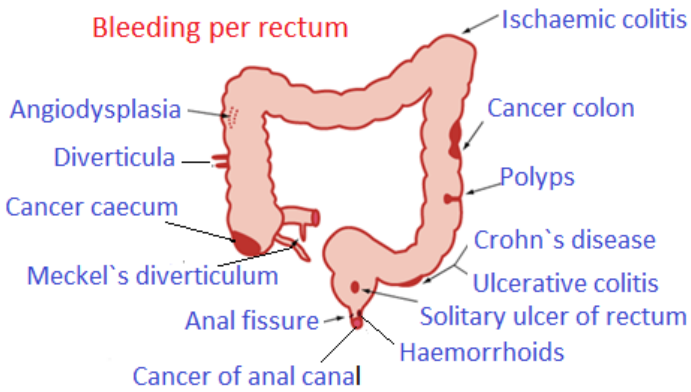
Systemic chemotherapy: 5-Fluorouracil has been the mainstay of systemic chemotherapy for CRC. Capecitabine was approved in 2001 as 1st line therapy for metastatic CRC. Irinotecan (Camptosar), Oxaliplatin (Eloxatin), Bevacizumab, Cetuximab.

Electrocoagulation: mostly palliative treatment for rectal carcinomas. Curative for small subset of pts.

Prognosis: **5 years survival rates for Colon Cancer:**

- Stage I (T1-2N0) -93%
- Stage IIA (T3N0) - 85%
- Stage IIB (T4N0) - 72%
- Stage IIIA (T1-2N1) - 83%
- Stage IIIB (T3-4N1) - 64%
- Stage IIIC (N2) - 44%.
- Stage IV - 8%.

RECTAL BLEEDING



Causes:

- Ischaemic colitis.
- Piles.
- Cancer colon - Cancer anal canal.
- Bleeding disorders.
- Ulcerative colitis -Diverticulosis - Rectal polyp.
- Bilharziasis.
- Crohn`s disease.
- Anal fissure.
- Dysentery-Amoebiasis-Giardiasis-Campylobacter-Enteropath. E Coli.

Investigations:

- CBC.
- Stool analysis.
- Coagulopathy studies.
- P-R examination.
- Lower endoscopy.
- In old age: R/O cancer colon (tumour markers, biopsy), in case of anaemia, anorexia, loss of wt., diarrhoea or constipation bouts.

CHAPTER XIII

GYNAECOLOGY

- Infertility
- Endometriosis
- Vaginal Discharge
- Uterine Bleeding
- Genital Prolapse
- Breast Cancer
- Ovarian tumours
- Uterine Tumours

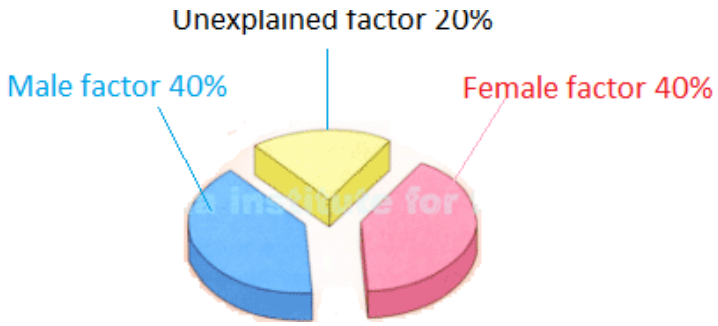
INFERTILITY

Failure to conceive within 2 yrs of regular unprotected intercourse. Either primary or secondary. 84% of couples will conceive within 1 year & 92% within 2 years.

Primary infertility: the inability to conceive after 1 yr of unprotected intercourse for a woman younger than 35 yrs, or after 6 months of unprotected intercourse for a woman 35 or older.

Secondaryinfertility: inability of woman to conceive who previously was able to do so

Etiology



Male factors

The causes of infertility are commonly referred to as factors. For example, when a pt has a partner ē abnormal sperm production or function, the problem is male factor infertility. Male factor infertility derives from three types of causes:- pretesticular, or testicular, or post-testicular.

- Pre-testicular causes include; problems ē the hypothalamus, pituitary, or gonadal axis ; an example is Kallmann sy. (gonadotropin-releasing hormone neuron def.).
- Testicular causes include genetic problems (e.g. Klinefelter sy) & nongenetic problems (e.g. chemotherapy, infection & varicocele).
- Post-testicular causes are obstructive to sperm (e.g. hypospadias, cryptorchidism, absence of the vas deferens, infections, surgery & trauma)

Female factors

Like male infertility, female infertility is classified into various factors on the basis of the anatomic location of the problem. The location can be anywhere in the female

reproductive tract ẃ includes the cervix, the uterus, the fallopian tubes, the ovaries & the peritoneum. Thus, women may have cervical factor, uterine factor, tubal factor, ovarian factor, or peritoneal factor infertility.

Cervical factor

Women ē cervical factor infertility typically have a diagnosis of cervical stenosis ẃ prevents the sperm from entering the uterus & reaching the egg. Cervical stenosis can be a consequence of surgery (e.g. a loop electrosurgical excision procedure, cervical infection ē resultant scarring, hypoestrogenism, or radiation-induced changes; in rare cases, it can be congenital). Cervical factor infertility can also involve having dysfunctional or inadequate cervical mucus. Fertile cervical mucus (often descriptively referred to as egg-white cervical mucus) is necessary for transport of the sperm upward from the vagina into uterus & is produced in response to the mid-cycle oestrogen surge.

Uterine factor

Infertility may result from a wide array of conditions. Congenital causes (e.g.müllerian anomalies) can range from minor conditions to very severe ones. For example, in Mayer-Rokitansky-Küster-Hauser sy, pts have normal ovaries but no upper vagina or uterus. Another congenital cause of uterine factor infertility is exposure to diethylstilboestrol in utero. Later in life, these so-called DES daughters are fou-nd to have T-shaped uteri that result in infertility, recurrent miscarriage & preterm deliveries. Acquired causes of uterine factor infertility include endometritis, Asherman syndrome (scarring of the uterine lining), fibroids, & polyps, as well as iatrogenic causes such as hysterectomy.

Tubal factor

Infertility derives from blockage or absence of one or both fallopian tubes. If both fallopian tubes are blocked, the embryo cannot travel into the uterus for implantation. Causes of tubal infertility include prior infection, previous tubal surgery, other tubal

injury, or (rarely) fallopian tube torsion & necrosis. One common cause is a dilated & fluid-filled fallopian tube on one or both sides, a condition known as hydrosalpinx. Even if one tube is normal, a hydrosalpinx on the opposite side will leak inflammatory fluid into endometrium, thereby decreasing pregnancy rates. Treatment of hydrosal-pinx consists of removal of proximal occlusion of the aff-ected fallopian tube

Ovarian factor

Infertility accounts for 40% of cases of female infertility. Ovarian reserve ⇩ ē age & the decline becomes steeper starting at approximately the age of 30 yrs. One of the most common causes of infertility is ovulatory dysfunction, including polycystic ovar-ian sy. Pts ē PCOS may have various other conditions as well, such as obesity & meta-bolic sy & should be carefully followed long after their infertility has been diagnosed & treated. Finally, medical disorders (e.g. malnutrition, excessive exercise, eating dis-orders, hypothyroidism & Hyperprolactinemia) can also contribute to anovulation by causing alterations in hypothalamic-pituitary-ovarian axis.

Peritoneal factor

Infertility is caused by diseases in the pelvis & peritoneum, such as PID, pelvic adhe-sions & endometriosis. Endometriosis is a condition in ẃ endometrial tissue is found outside of the uterus. Endometriosis-associated infertility has been hypothesized to be due to:-

- Distorted adnexal anatomy.
- Dysfunctional oocyte development.
- Reduced endometrial receptivity.

Endometriosis is characterized by dysmenorrhea, dyspareunia & dyschezia, among other symptoms. Pts ē suspected endometriosis should be referred to providers who can perform surgery for both diagnosis & treatment.

Diagnosis

The basic workup of a pt ē infertility begins ē a thorough history ẃ should include pregnancy, medical & surgical history, infection & sexual history, menstrual & paternal history. A thorough physical examination is essential.

Pelvic ultrasonography

May be performed to evaluate antral follicle count, ovarian cysts, fibroids, polyps & hydrosalpinx. Most pts need assessment of tubal patency by means of hysterosalpingography. Some pts need saline infusion Sonography to characterize intracavitary abnormalities. Initial laboratory work should include determination of levels of FSH, estradiol & possibly antimüllerian hormone for ovarian reserve(this is optional).

Urine based ovulation test detecting LH

Pts who have ovulatory dysfunction should also be assessed for abnormal TSH & prolactin levels ẃ are easily correctable causes of irregular ovulation. In pts whose ovulation status is unclear, it may be helpful to obtain a mid-luteal progesterone value (typically on cycle day 21) to determine whether a pt is ovulatory or not. Pts who demonstrate signs or symptoms of hyperandrogenism (e.g. hirsutism or virilization) should be referred to a specialist for assessment of androgen levels & targeted assessment of a possible neoplasm.

Semen Analysis

Semen analysis is imperative & one of the most important tests in a standard infertility workup. This test is useful in identifying abnormalities in sperm form & function that may be amenable to treatment aimed at improving a couple's fertility. Terms used to describe abnormal sperm include Azoospermia (absence of sperm), Oligospermia (⇩ sperm concentration, <15 million/ml), Asthenospermia (<40% ē normal motility) & Teratospermia (<4% ē normal morphology). Pts can also have a combination of abnormalities, such as oligoastheno-terato-spermia. The values of normal semen are:-

Volume >2.0 ml, pH 7.0-8.0, Total sperm count >20 million per mL, Motility 50% or greater, Normal forms 50% or greater, Fructose +ve, Liquefaction 1-20 minutes.

Treatment of the Infertile Couple

Depends on the specific diagnosis. the possible aetiologies include; Defect in spermatogenesis, Hypogonadism, Varicoceles, Endocrinopathies, Obstruction, Infection, Klinefelter sy, or Idiopathic. If the diagnosis is male factor infertility ē mild oligospermia or Asthenospermia, pts may benefit from:-

Sperm washing, & intrauterine insemination. Clomiphene citrate is occasionally used for induction of spermatogenesis, it carries 20% success. Severe male factor infertility often necessitates the use of invitro fertilization ē intracytoplasmic sperm injection. Women ē uterine factor infertility due to fibroids or polyps may require surgery.

Women ē ovarian factor infertility (anovulation) generally require ovulation induction ē medications such as Clomid, Letrozole, or Pergonal.

Clomid (Clomiphene) 50 mg tab daily for 5 days, starting from the 5th day of the menstrual cycle-if no ovulation- give 100 mg daily for 5 days in the next cycle. If no pregnancy in 6 months refer for advanced therapies. Clomid carry 7% risk of twins & 0.3% for triplets. It act through induction of ovulation, it has a competitive inhibiting action on oestrogen, it combines & blocks oestrogen receptors at the hypothalamus & pituitary causing a negative feedback causing an ⇧ in the FSH, result in follicle maturation, in turn ⇧ in LH peak ẃ stimulates the ovulation & the formation of corpus luteum. If no response ē Clomid then FSH e.g:-

Pergonal (FSH 75 IU+ LH 75 IU) administered IM. This is usually given under the guidanance of someone who specializes in infertility. This therapy is expensive & pts need to be followed closely. Adverse effects; in women ē excessive ovarian stimulation the use of LH activity ⇧ the risk of ovarian hyper stimulation sy, multiple gestation, fetal wastage, marked ovarian enlargement or cyst formation, rupture of ovarian cysts and

intraperitoneal Hge., usually after pelvic examination. Shock & thromboembolic disorders. Women ē tubal or peritoneal or anatomic abnormalities factor infertility generally require surgical correction e.g. Tuboplasty, Septoplasty, Lysis of adhesions, Myomectomy. Surgery may be performed through; laparoscopically or hysteroscopically. If the fallopian tubes are beyond repair one must consider in vitro fertilization.

Assisted Reproductive Technology

Explosion of ART has occurred in the last decade. Is a collective term for various technologies in ẃ eggs & sperm are handled outside the body. It includes IVF & variations such as Gamete Intrafallopian Transfer (GIFT) & Zygote Intra-Fallopian Transfer (ZIFT). Briefly, a single IVF cycle consists of the following steps: ovarian stimulation, follicular aspiration, oocyte classification, sperm preparation, oocyte insemination & fertilization, embryo culture & embryo transfer. The cycle general- ly takes about 2 wks. Success rates are largely dependent on pt age, starting at 35-50% in women < 35 yrs & gradually ⇩ to 5-10% in women older than 40 yrs.

Emotional Impact

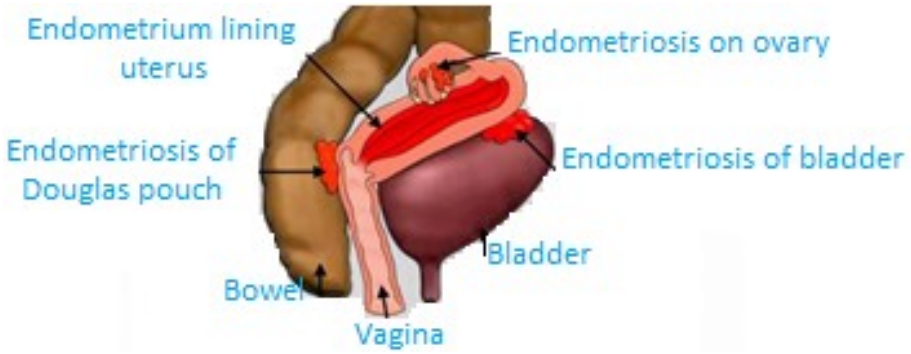
Infertility places a great emotional burden on the infertile couple. The quest for having a child becomes the driving force of the couple's relationship. It is important to address the emotional needs of these pts.

Conclusion

Infertility should be evaluated after one year of unprotected intercourse. History & physical examination usually will help to identify the etiology. If pts fail the initial therapies then the proper referral should be made to a reproductive specialist.

The evaluation & management of an infertile couple requires an understanding of the processes of conception & embryogenesis, as well as sensitivity to the emotional stress that can result from the inability to conceive.

ENDOMETRIOSIS



Introduction: Endometriosis is a disease in ẃ endometrial glands & stroma implant & grow in areas outside the uterus. Most commonly implants are found in the pelvis. Lesions may occur at distant sites: pleural cavity, liver, kidney, bladder, etc…

Features of Endometriosis: prevalence 2-50% of women; 21-47% of infertility cases. Found in 1/3rd or more women ē chronic pelvic pain.

Who Is at Risk For Endometriosis?

Risk factors for endometriosis are varied. It is most common in women:

- Who are in their 30s and 40s.
- Who have not given birth.
- Who have periods that last > 7 days.
- Who started menstruating before age 12.
- Who have short menstrual cycles (< 28 days).
- Who have a family history (mother or sister) of the condition.

Theories of Pathogenesis

*Retrograde menstruation (Sampson's Theory): endometrial fragments transported through fallopian tubes at time of menstruation & implant at intra-abdominal sites

*Müllerian (Coelomic) metapalasia theory (Meyer's Theory): metaplastic transformation of pelvic peritoneum

*Lymphatic spread (Halban's Theory).

The reason that endometriosis develops is not well understood. Hereditary factors seem to play a role & some areas of endometrial cells outside of the uterus may be present at birth. It is also possible that endometrial cells may travel to abnormal areas during menstrual bleeding, during surgeries, or through the bloodstream. Immunological factors may be involved, as a defect in the immune system could cause failure to eliminate the misplaced endometrial cells.

Symptoms: the most common symptom of endometriosis is pain (cyclic & non-cyclic) that occurs prior to, during, or after menstruation. The pain can occur during sexual intercourse, '75% of cases present ē dyspareunia', or during urination 'dysuria', or during bowel movements. 90% present ē severe dysmenorrhea, secondary dysmenorrhea, or premenstrual & postmenstrual spotting (in about 20%). , 70% of cases present ē chronic pelvic pain in the low back or pelvis, , About 30%- 40% of women ē endometriosis have some trouble conceiving, infertility can be the first sign of endometriosis in many women, the reason for this is not well understood, & scarring of the reproductive tract may play a role. Hormonal factors also may be involved. Some women have severe disabling pain. Other women have mild symptoms or no symptoms. *The classic Triad - dysmenorrhea, dyspareunia, dyschezia (*constipation associated ē a defective reflex for defecation).

Physical Examination: no pathognomonic finding, or may be associated ē tender, fixed adnexal mass, uterosacral nodularity, or uterus may fixed & retroverted on recto-vaginal exam!

Differential Diagnosis: severe menstrual pain can be caused by other conditions, including fibroid tumors. Fibroid tumors are noncancerous growths of the muscle tissue of the uterus. They can cause heavier than normal menstrual bleeding & cramping. Both endometriosis & fibroids can cause pain at other times of the month as well. The

differential diagnosis include also; Chronic pelvic inflammatory disease, recurrent acute salpingitis, hemorrhagic corpus luteum, benign or malignant ovarian neoplasm & ectopic pregnancy.

Diagnosis: pelvic Imaging: even though imaging studies cannot confirm the diagnosis of endometriosis, ultrasound, CT, or MRI scans are sometimes used to help in diagnosis as these scans can detect larger areas of endometriosis or cysts related to endometriosis. Laparoscopy, direct visualization (via laparotomy or laparoscopy), is the only way to definitively diagnose endometriosis, histologic & gross findings consistent ē endometrial tissue can be identified. In this procedure, the surgeon examines the inside of the abdomen & pelvis ē a viewing instrument inserted through a small incision (laparoscopy), small biopsies can be taken for examination by a pathologist to confirm the diagnosis. Other tests Ca125 - not specific nor sensitive. Sine qua non-sharp, firm, exquisitely tender “barb” (barbed wire) in uterosacral ligaments.

Management

Treatment goals;

To alleviate pains.

To delay recurrence as long as possible.

To help pts get pregnant.

Medical treatment: pts ē endometriosis who wish to get pregnant. Taking oral contraceptives to reduce the amount of menstrual flow can often reduce the pain associated ē endometriosis symptoms while producing shorter & lighter menstrual cycles. Sometimes the pills are taken continuously, without breaks for a menstrual period.

Other hormonal therapies mimic the hormonal state of menopause, eliminating menstrual periods & reducing the pain of endometriosis. GnRH agonists interrupt the production of female hormones ‘*GnRH Agonists’.*

*Excision: at the time of laparoscopy, the surgeon can remove endometriosis growths or scars. Most women will have pain relief after this is done, but recurrence of endometriosis symptoms occurs in about 45% of women a year later. Recurrence is more likely with time. Hormone treatments after surgery may reduce the chance that endometriosis symptoms will return.

*Open Surgery: fertility-preserving surgery: young pts ē severe endometriosis who wishes to have children.

Ovary-preserving surgery + medication: young pts ē severe endometriosis who does not wish to have children.

*Radical surgery: older pts ē severe endometriosis who do not wish to have children.

*Very severe cases of endometriosis may require open abdominal surgery to remove endometrial growths, or even a hysterectomy (removal of the uterus). Parts or all of the ovaries may also be removed in these cases. Even ē removal of the uterus & ovaries, endometriosis returns in about 15% of women.

VAGINAL DISCHARGE

The vagina is lined by non-keratinized stratified squamous epithelium influenced by oestrogen & progesterone. In children the pH of the vagina is 6-8 & the predominant flora is G +ve cocci & bacilli. At puberty, the vagina estrogenized & glycogen content ⇧ Lactobacilli (Duoderline Bacilli), convert glycogen to lactic acid, the pH of the vagina is 3.5-4.5, the vaginal discharge may be blood stained white cream, yellow, or greenish. It is wrongly called leucorrhoea ẃ is an excessive amount of normal discharge, never cause pruritus or bad odour & is white in colour.

Causes

*Physiological: ⇧ in pregnancy & mid cycle. Consists of cervical mucus endometrial & oviduct fluid +exudates from Bartholin's &Skene's glands, exudate from vaginal epith.

*Infection: Trichomonas, Candida, or Bacterial vaginitis, Neisseria gonorrhoea, Chlamydia, Trachomatis, syphilis, DM, AIDS (⇩ immunity).

*Antibiotics, Hormones, lack of hormones, Douches, Vaginal medication, Steroids.

*Foreign body: IUCD, neglected pessary, vaginal diaphragm.

*Pregnancy.

*Malignancy.

*Atrophic vaginitis.

*Urinary & feculent discharge.

Diagnosis

History: age, type of discharge, amount, onset (relation to antibiotics medication, or to menstruation), use of toilet preparation, colour of discharge, smell, pruritus.

General Examination: anaemia, cachexia.

Vulva inspection: speculum & bimanual examination, amount, consistency, odour

Investigation

- Swab for culture & sensitivity.
- Gram stain of discharge & Biopsy from suspicious area.
- Serological test.
- Test for gonorrhoea.
- Cervical smear.

Treatment

Directed to the cause:-

- Foreign body –remove.
- Leucorrhoea: reassurance, hygiene, minimize pelvic congestion by exercise.
- Specific according to a specific agent: e.g. in fungal infection; oral Fluconazole 150 mg as single dose, intravaginal Clotrimazole, for 1, 3, 7, or 14 days.

UTERINE BLEEDING

The onset of menses start by the age of 16 yrs é the 2ry sex characters. If the sexual development does not appear by the age of 14 yrs start your evaluation. The cycle length is 24-35 days & the menstrual days is 2-7 days. The menstrual flow is about 20-80 cc/menses. The phases of reproductive cycle include; follicular, ovulation, luteal & menses phases. Changes in menstrual period (flow, duration, frequency, or bleeding between cycles) defined as AUB & include:-

*Menorrhagia ẃ is prolonged duration of menses or ⇧amount of bleeding/day.

*Hypo menorrhea ẃ is shorter menses or less flow/day. The prevalence of abnormal uterine bleeding is 20 million office visits/yr & 25% of visits to gynaecologists in USA (in Egypt the situation ?).

Causes

❄Pregnancy; the age is not an issue!, never forget pregnancy, prove it !, assump-tions can lead to death.

❄FIGO classification system is used for causes of AUB in non-gravid women in the reproductive age, include;

PALM (structural):

P- Polyp. A- Adenomyosis. L- Leiomyoma (sub mucosal or other myoma).

M- Malignancy & hyperplasia.

COEIN: (non-structural):

C - Coagulopathy. O- Ovulatory dysfunction. E- Endometrial. I – Iatrogenic.

N-Not yet classified.

❄Iatrogenic: IUD related, post-instrumentation, post medical abortion.

❄Infection: endometritis, cervicitis, ascending/PID, haematogenously (TB).

❄Coagulation disorders: R/O VWD in any girl who requires transfusion for excessive

bleeding when first starting periods. The coagulation disorders may be inherited (haemophilia), Acquired (ITP, leukaemia), or drug induced (Heparin, Aspirin).

❄Bleeding from other sites: GIT (neoplasia or haemorrhoids). Genitourinary (urethral caruncle or diverticulum, renal lithiasis or haemorrhagic cystitis). Gynecologic-al from labia, cervix or vagina (trauma, infection, or neoplasia).

Diagnosis: is by exclusion.

- History: age of the pt, menstrual history, pattern & amount of menstrual loss.
- Examination of abdomen & pelvis.
- Ultrasonography.
- Hysteroscopy. Endometrial biopsy (to R/O hyperplasia & carcinoma).
- Hormonal assays: progesterone, LH, FSH & TFTs.
- Blood tests: CBC, CT, BT, PT, APTT.

Management

Medical Rx:

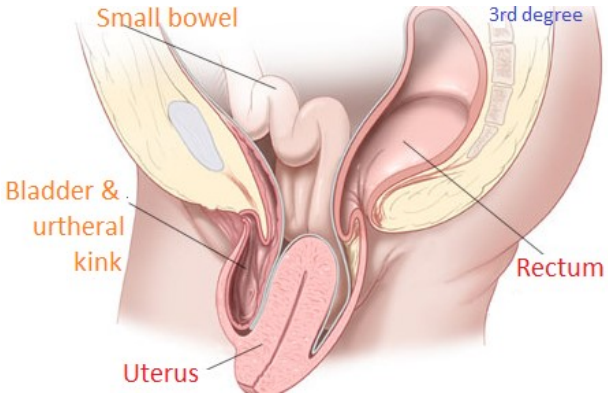
- Non-hormonal therapy: NSAIDs; Mefenamic acid (ovulatory DUB). For VWD use DDAV for type 1. Antifibrinolytic e.g. Tranexamic acid (to inhibit the ⇧ plasminogen activators & plasmin). Daflon tab Dicynone, 2 amp daily (⇧ capillary resistance). Konakion, 2 amp daily, (Vit K essential for formation of F 2,7,9, 10). Cyclokaprin, 2 amp. daily, (inhibit activation plasminogen).
- Combined oral contraceptive pills: low-dose oestrogen-progestogen is used (regulate the cycle & ⇩ the amount of blood loss). Progestogen dominant pills is used in progesterone deficiency & Oestrogen dominant pills are used in oestrogen deficiency.
- Progestogen: used in an ovulatory cycles to ⇩ blood loss. Norethisterone (Primulot N) 5 mg tid & Medroxy-Progesterone acetate 10 mg tid.
- Levonorgestrel-releasing IUCD: induces endometrial atrophy & ⇩ blood loss.

- Androgens & Gonadotrophine releasing hormone: used when the above medical therapy has failed or surgery is contraindicated. Androgens: Danazol & Gestrinone ⇨ amenorrhoea by -ve feedback & direct action on endometrium. Gonadotrophin releasing hormone ⇨ hypo gonadal state.

Surgical managementEndometrial ablation (resection): carried out under direct hysteroscopic vision using fluid for distension & irrigation. The techniques include:-

- Laser ablation, Endometrial loop resection using electro diathermy.
- Rollerball electro diathermy ablation.
- Thermal balloon ablation & Hysterectomy.

GENITAL PROLAPSE



The primary cause of prolapse is weakness of the supporting structures of uterus & vagina, usually as result of trauma during child birth.

Predisposing Factors

Weakness of the pelvic cellular tissue: the cervical ligaments ẃ act as the main support for the uterus may become weakened by the following:-

- Obstetric trauma. • Congenital weakness. • Postmenopausal atrophy.
- May result following an injury of the pelvic floor (surgical or accidental).

Types

Vaginal prolapse: can occur éout uterine prolapse but the uterus can`t descent éout carrying the vagina é it. The varieties include:-

- Anterior vaginal wall prolapse: either prolapse of the upper part of the anterior vaginal wall é the base of the bladder is called cystocele, or prolapse of the lower part of the anterior vaginal wall é the urethra is called urethrocele, or complete anterior vaginal wall prolapse-called cystourethrocele.
- Posterior vaginal wall prolapse: called rectocele if the anterior wall of the rectum is prolapsed é the middle third of the posterior vaginal wall or called entrocele (hernia of the pouch of Douglas) if the upper third of the posterior vaginal wall descends lined by peritoneum of the Douglas pouch & containing loops of intestine.
- Vault prolapse: descent of the vaginal vault, where the top of the vagina desc- ends, or inversion of the vagina after hysterectomy. The vault prolapse is more likely to occur after subtotal than after total hysterectomy.
- Uterine prolapse: the uterus gradually descends in the axis of the vagina taking the vaginal wall é it. It may present clinically at any level.

Classification

1st degree: cervix descent below its normal level on straining but does not protru- de from the vulva (external os of the cervix is at the level of ischial spines).

2nd degree: the cervix protrudes from the vulva on straining.

3rd degree: the whole uterus prolapsed outside the vulva & the vaginal wall becomes most completely inverted over it. Enterocele is usually present.

Clinical Picture

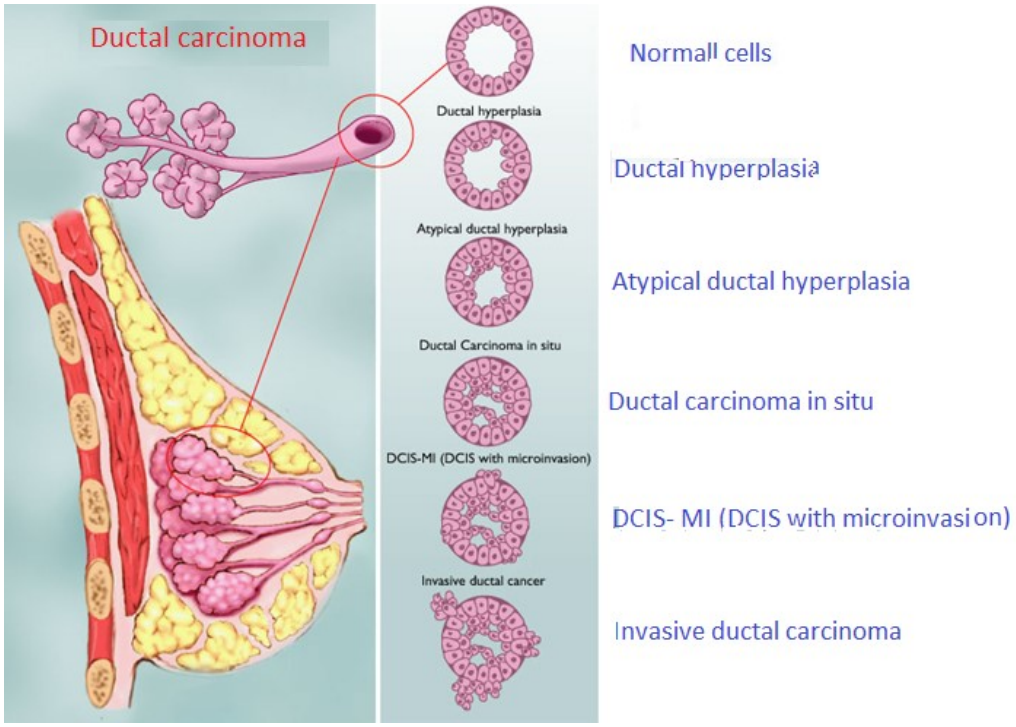
Before actual prolapse, the pt feels a sensation of weakness in the perineum, part icularly towards the end of the day. Later she notices a mass ẃ appears on straining & disappears when she lies down. Urinary symptoms are common & trouble some even é slight prolapse including:-

- Urgency & frequency by day.
- Stress incontinence.

- Inability to micturate unless the anterior vaginal wall is pushed upwards by the pt's fingers. Difficult micturition, defecation, she have to put her finger inside to help her in micturition or defecation according to the site of prolapse, urine pass when pt cough, sneeze, or carry heavy object. Cervicitis.
- Vaginal discharge & recurrent vaginal infection.
- Repeated UTI, frequency & scalding day & night when cystitis develops.
- Rectal symptoms are not so marked, pt always feels heaviness in the rectum & constant desire to defecate. Piles develop from straining.
- Back- ache, congestive dysmenorrhea & menorrhagia (common).

Management: prophylactic. Surgical: correction, fixation, excision in 3rd degree.

BREAST CANCER



Epidemiology

Breast cancer primarily affects women but about 1% of all cases effect men. It is the 2nd leading cause of death in women next to lung cancer. One out of nine women will develop breast cancer in their lifetime. The breasts are made of fat, glands & connec

tive (fibrous) tissue. The breast has several lobes ẃ are divided into lobules &end in the milk glands. Tiny ducts run from the many tiny glands, connect together & end in the nipple. These ducts are where 78% of breast cancers occur. This is known as infiltrating ductal cancer. Cancer developing in the lobules is termed infiltrating lobular cancer. About 10-15% of breast cancers are of this type. Another type of breast cancer is inflammatory breast cancer (often misdiagnosed & dangerous).

Risk factors

• Age. •Race. • Individual or family history of breast cancer. •History of ovarian cancer. •A genetic predisposition (mutations to the BRCA1 or BRCA2 genes cause 2% of all breast cancers). •Oestrogen exposure. •Atypical hyperplasia of breast. •Lobular carcinoma in situ. • Lifestyle factors (obesity, lack of exercise, alcohol use). • Radiation.

Hereditary breast cancer

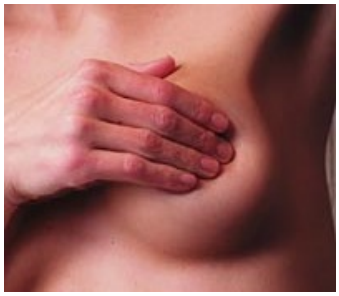
15% of breast cancers are inherited. Approximately 80% of hereditary breast cancer is caused by mutations in the BRCA1 or BRCA2 genes. Women who inherit a BRCA mutation have 75% chance of developing breast cancer in their lifetime. Women ē especially strong family history may consider preventive surgery to remove breast tissue &/or chemoprevention. Several other genetic syndromes can ⇧ breast cancer risk.

Early detection

Means a better chance of successful treatment. Mammography is the best tool doctors have to screen for breast cancer. Many organizations recommend that women obtain a mammogram each yr, starting at the age of 40. Regular clinical breast examinations & breast self-examinations are also recommended. Early detection include:-

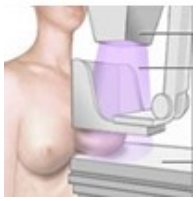
- •Self/Doctor examinations.
- •Mammography.
- •Biopsy. •Ultrasound & MRI.

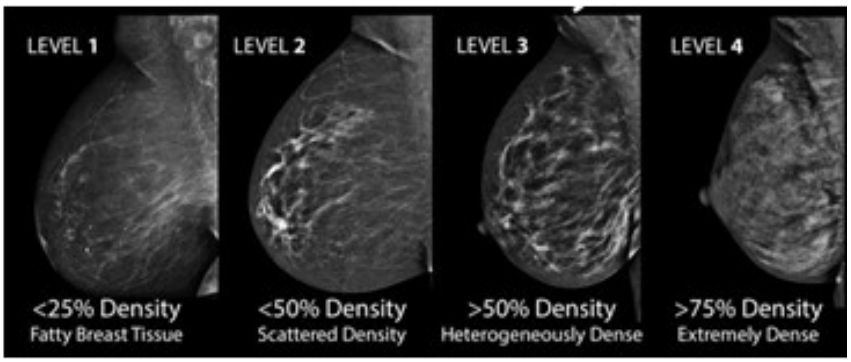
Breast self/doctor examination



Includes visual inspection & careful feeling of the breasts, the armpits & the areas around the collarbone. Looking for lumps or abnormalities around the breast. Most lumps are NOT cancerous. Best time for examination is immediately after the monthly period. Not 100% accurate.

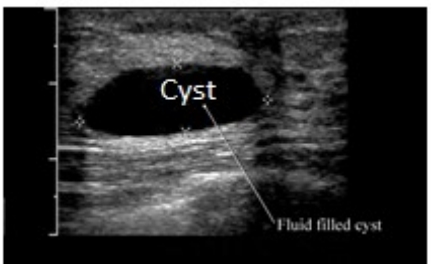
Mammography: X-ray of the breast taken from several angles by compressing the breast horizontally, diagonally & sometimes vertically. Not 100% accurate.

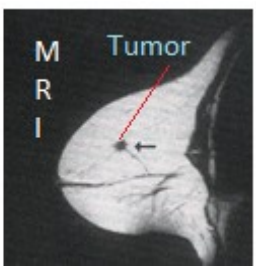




Ultrasound: usually done in addition to the mammogram. Shows whether a mass is filled ē fluid or solid. Cancers are solid. Not 100% accurate.

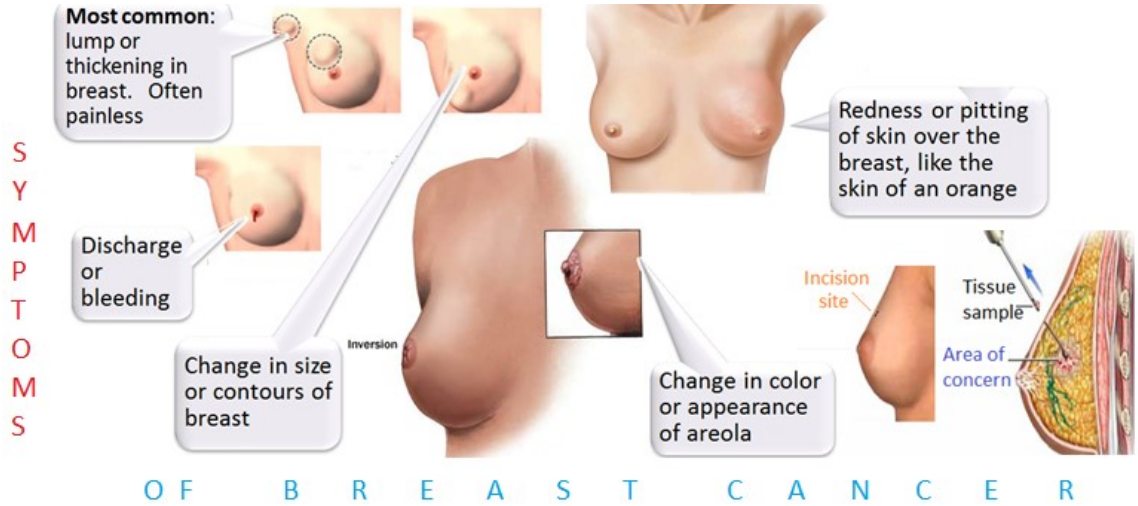
MRI: differentiates diseased tissue from normal healthy tissue. Is 100% accurate.





Biopsy: take a very small piece of tissue from the breast for examination & testing. Examined by a pathologist. 100% accurate.

Symptoms



- Early breast cancer has little or no symptoms. It is not painful.
- Breast discharge, especially if only from one breast or bloody.
- Sunken nipple, though a common variant of normal nipples a new development should cause concern.
- Redness, changes in texture & puckering. Usually caused by skin disease but sometimes can be associated ē breast cancer.
- Skin irritation or changes, such as puckers, dimples, scaliness, or new creases.
- Lumps on or around breast. Most lumps are not cancerous.
- Other lumps around the under arm or collarbone ẃ don't go away.
- Loss of smell ?
- No visible or obvious symptoms (asymptomatic).

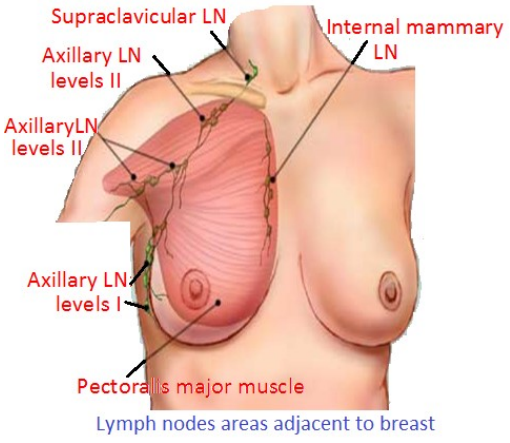
Inflammatory breast cancer

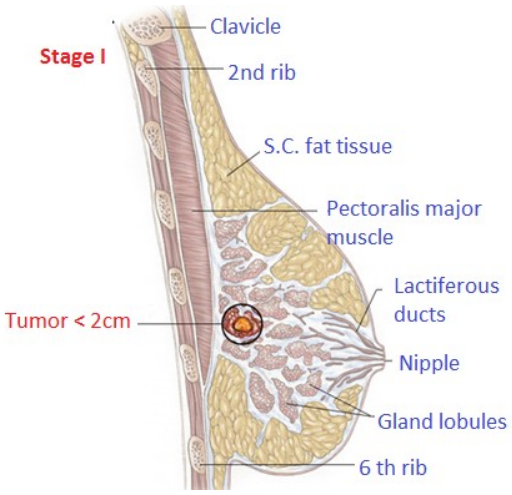
Rare, serious, aggressive form of breast cancer, the breast looks red, feels warm, associated ē thickening of skin, ridges, welts & hives may be observed, the skin may look wrinkled. Sometimes misdiagnosed as infection.

Metastasis

- The most common place for metastasize is into the LNs under the arm or above the collarbone on the same side of the cancer. Then comes; •Brain •Bones •Liver.

Stages



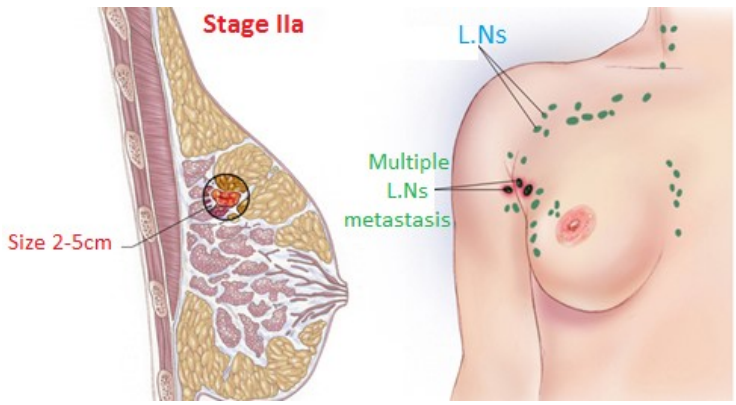


Staging is a way of describing a cancer, such as the depth of the tumour & where it has spread. Is the most important tool to determine a pt's prognosis. Described by the TNM system: the size of the tumour, spread to the nearby L Ns & whether the cancer has metastasized (to organs as the liver or lungs). The type of treatment depends on the stage of the cancer. Stages include:-

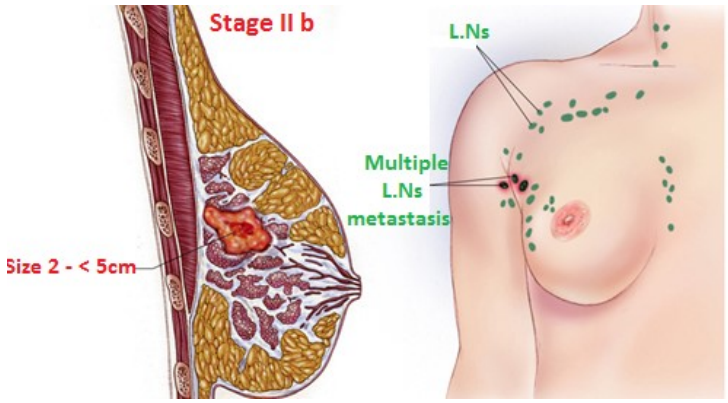
Stage 0: cancer in situ (non-invasive) meaning the cancer has not spread past the ducts or lobules of the breast. Ductal carcinoma in situ is the most common .

Stage I: the tumour is small & has not spread to the L Ns.

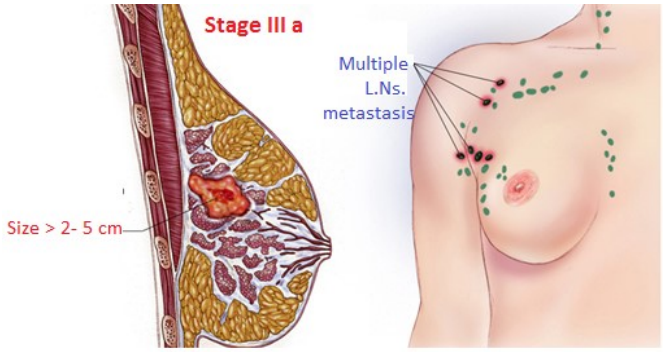
Stage IIa: describes a smaller tumour that has spread to the axillary L.Ns (under the arm), or a medium-sized tumour that has not spread to the axillary L.Ns. May also describe cancer in the axillary L.Ns ē no evidence of a tumour in the breast.



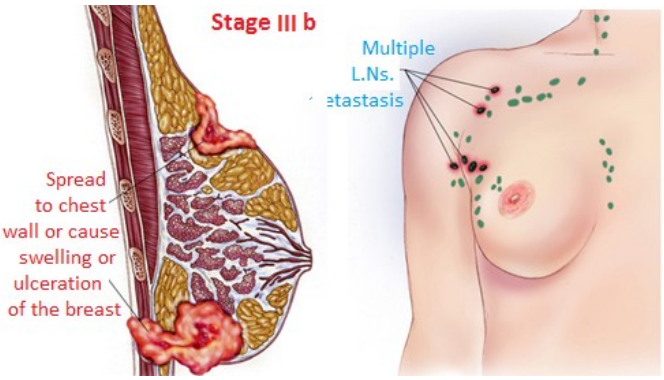
Stage IIb: describes a medium-sized tumour that has spread to the axillary LNs. Also describe a larger tumour that has not spread to the axillary L.Ns.



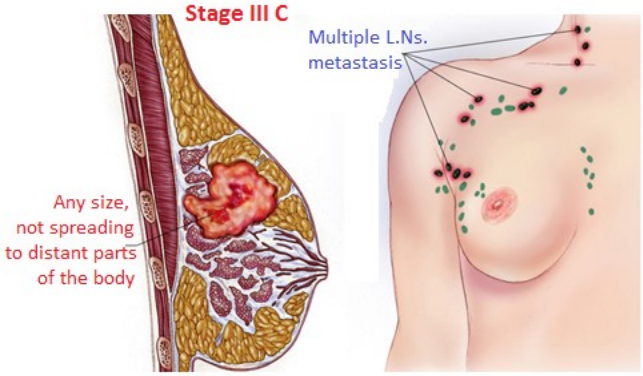
Stage IIIa: describes any size tumour that has spread to ⇨ the L.Ns.



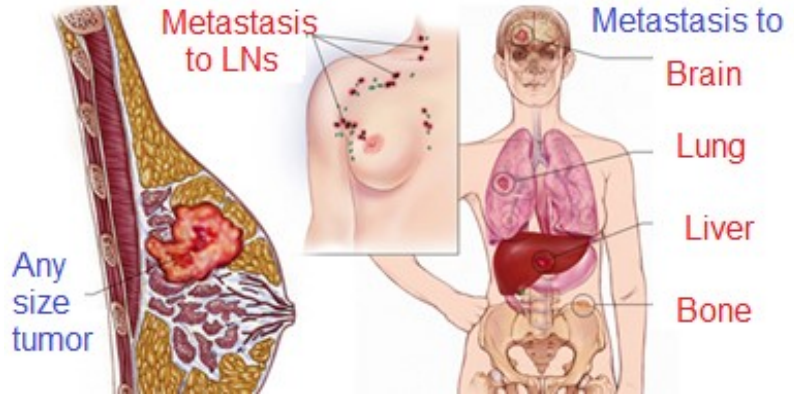
Stage IIIb: describes cancer spread to the chest wall, or caused swelling or ulcerat-ion of the breast, or is diagnosed as inflammatory breast cancer.



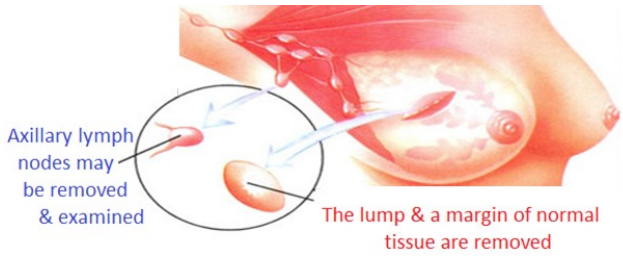
Stage IIIc: spread to distant L.Ns. but has not spread to distant parts of the body.



Stage IV: cancer of any size & spread to distant sites in the body, usually the bones , lungs or liver, or chest wall.



Management



Surgery

Removal of the tumour ē or ēout radiation therapy is initial Rx. For invasive cancer, L.Ns are removed & evaluated. More invasive surgery (mastectomy) is not always better. Breast reconstruction is an option after mastectomy.

Adjuvant Therapy

Rx given in addition to surgery to reduce the risk of recurrence. May include radiation, chemotherapy, biologic therapy & hormone therapy.

Radiation Therapy

The use of high-energy X-rays or other particles to destroy cancer cells. Usually used to treat breast cancer after surgery. Different methods of delivery. External-beam: outside the body or Internal using implants inside the body. Side effects may include fatigue, swelling & skin changes.

Chemotherapy

May be given before surgery to shrink a large tumour (neoadjuvant chemotherapy) or after surgery to reduce the risk of recurrence (adjuvant chemotherapy). Combination of medications is often used.

Hormone Therapy

To manage tumours that test +ve for either oestrogen or progesterone receptors. May be used alone or together ē chemotherapy. Tamoxifen (Nolvadex) is a common hormone therapy & is effective in many premenopausal & postmenopausal women. Aromatase inhibitors are also used alone or following Tamoxifen use as treatment for postmenopausal women, including Anastrozole (Arimidex), Letrozole (Femara) & Exemestane (Aromasin).

New Therapies: Targeted Therapy

Designed to target cancer cells while minimizing damage to healthy cells. Used to stop the action of abnormal proteins that cause cells to grow & divide out of control. Trastuzumab (Herceptin) for women ē a HER-2/neu +ve breast cancer either ē or after adjuvant chemotherapy. Bevacizumab (Avastin) blocks angiogenesis (the formation of new blood vessels) & is under evaluation in clinical trials.

Follow up care

Important to detect possible recurrence at the earliest stage, include; •Monthly breast self-exam. •Physical examinations. •Mammography. •Pelvic examinations.

OVARIAN TUMOURS

Normal ovaries

Normal size 5 X 3 X 3 cm. Variation in dimensions can result from:-

-Endogenous hormonal production (varies ē age & menstrual cycle).

-Exogenous substances e.g. ovulation inducing medications.

Ovarian masses

- Functional: Follicular cyst, Corpus Luteum cyst.
- Inflammatory: Tuboovarian abscess.
- Neoplastic: Benign, Borderline, Malignant.

Differential diagnosis of adnexal mass

Organ	Cystic	Solid
Ovary	Functional cyst Neoplastic cyst Benign, Malignant Endometriosis	Neoplasm Benign Malignant
Fallopian tube	Tubo ovarian abscess Hydrosalpinx Para ovarian cyst	Tubo ovarian Ectopic pregnancy Neoplasm

Epidemiology

Cancer of the ovary represents about 30% of all cancers of the female genital orga ns. A women has 5-10% risk of undergoing surgery for a suspected ovarian neoplasm. 13-21% of these will be found to have an ovarian malignancy. For all types of ovarian cancer, the 5-yr relative survival is 45%. Women diagnosed when they are younger than 65 do better than older women. If ovarian cancer is found & treated before the cancer has spread outside the ovary the 5-yr relative survival rate is 92%. However, only 15% of all ovarian cancers are found at this early stage.

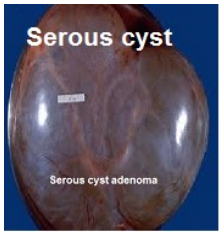
Risk factors

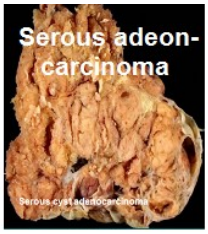
•Null parity.•Family history. •Child hood gonadal dysgenesis. •Cloiphene. •Hereditary non polyposis colon cancer. •BRCA1 & BRCA2 mutation. CA125 present in 80% of serous & endometrioid tumour. •Cytogenetics-gain of 12 & 8. Loss of chromosome X, 22, 18, 17, 14, 13, 12, 8. Benign/borderline tumours exhibit trisomy 12.

Types

Epithelial tumours

Serous

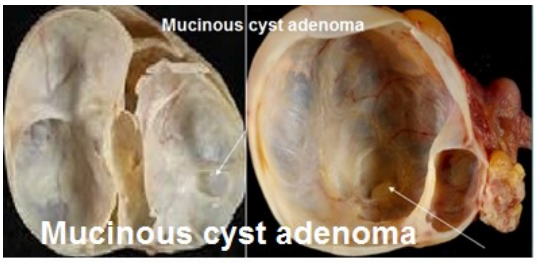




contain clear fluid, often bilateral, around age of menopause, malignant type is the

commonest ovarian cancer.

Mucinous



Large, multilocular filled ē mucin, if ruptured pseudomyxoma peritonei.

Brenner tumours

Usually benign, occur in reproductive life, they can be malignant, may be associated ē endometrial hyperplasia, may coexist ē mucinous cystadenoma.

Endometrial: few cases arise in endometriosis. 30% coexist ē primary endometrial cancer, the second most common type of epithelial ovarian cancer, occur primarily in women who are between 50-70 years of age.

Malignant Germ cell tumours

Rare represent 3% of ovarian cancers. Teratoma (peak incidence in 2nd decade). Malignant teratoma. Immature teratoma. Non gestational Choriocarcinoma; secrete HCG, may be component of solid teratoma. Yolk sac (endodermal sinus), highly malignant, affect young age, partly solid, secrete α fetoprotein

Clear cell carcinoma

Are part of the surface epithelial tumour, accounting for 6% of these cancers, polypoid masses that protrude into the cyst, on microscopic examination, composed of cells ē clear cytoplasm(that contains glycogen), Hob nail cells, the pattern may be glandular, papillary or solid.

Sex cord tumours

Androgen secreting tumours, Sertoli-leydig, Gynandroblastoma, cause virilization. Fibroma, solid tumour, may be associated è meigs syndrome, tend to have long pedicle. Granulosa-theca cell tumours; moderate to large size, Solid, as enlarge may have cystic spaces, Yellow ting on cut surface, Thecoma is benign, but granulosa cell is malignant, Occur at any age, 50% postmenopausal, secret oestrogen.

Classification

FIGO Staging

Stage 1	Growth limited to one or both ovaries
Stage 2	Growth limited to one or both ovaries ē pelvic extension
Stage 3	Growth limited to one or both ovaries ē peritoneal implants / +ve LNs
Stage 4	Growth limited to one or both ovaries ē distant metastasis

Diagnosis

Ovarian cancer has always been thought of as a symptomless disease,but research has shown this to be untrue. There are symptoms, unfortunately they may be so subtle that they are attributed to other benign condition. However 81% of the respondents realize in observation that symptoms existed before diagnosis, ē these symptoms being confused ē irritable bowel syndrome, endometriosis, gall bladder issues or other ailments. On examination; the benign tumour usually mobile, unle- ss large or complicated. Dermoid cyst may be felt anterior to the bladder. The malignant tumour usually bilateral, may associated è ascites, hard deposit in the pelvis, leg oedema, signs of bowel obstruction or ureteric obstruction.

Early detection

If a women shows ovarian cancer symptoms, you may monitor her ē one of the following tests or a combination:- ⅄Blood test. ⅄Trans vaginal U/S . ⅄Pelvic exam.

Screening tests: include;

- Trans-vaginal U/S.
- CA-125 blood test.

Complications

- Torsion.
- Severe abdominal pain/vomiting.
- Rupture, Haemorrhage, Impaction & Infection.

Management

The treatment of ovarian cancers based on the stage of the disease ẃ is a reflection of the extent or spread of the cancer to other parts of the body. Also depends on histologic cell type (biopsy), the pt's age & overall condition. There are basically 3 forms of treatment of ovarian cancer:-

1-Surgical.

2-Chemotherapy: first-line chemotherapy for ovarian cancer typically consists of 2 drugs given together. The combination =paclitaxel + platinum drug-either carboplatin or Cisplatin. Select women may benefit from administration of chemotherapy directly into the abdomen - called intraperitoneal Rx - in addition to conventional intravenous administration. Side effects: nausea, vomiting, diarrhoea, hair loss, loss of appetite, mouth sore & anaemia.

3-Radiotherapy: now, has a very small role since platinum based protocols & Paclitaxelhave improved the median survival. However it can be used as a palliative treatment for metastatic bone or brain lesions or of localized recurrence to alleviate the pain. Side effects include; bladder infection, diarrhoea, irritation, darkening of skin, nausea, frequent urination, abdominal pain.

UTERINE CANCER

Uterine cancer is one of the most common malignancies of female genital tract. The incidence is increasing worldwide in recent years. Overall, 2%-3% of women develop uterine cancer during their lifetime. A malignant epithelial disease that occurs in endometrial gland of uterus. Also called endometrial cancer.

Risk Factors

1. Medical conditions: Diabetes mellitus, hypertension. Overweight-obesity (excess oestrogen as a res-ult of peripheral conversion of adrenally derived androstenedione by aromatization in fat). Late menopause.

2. Gynaecologic diseases: Long-term endogenous oestrogen exposure. Polycystic ovary. Functioning ovarian tumours. An ovulating dysfunctional bleeding. Infertility, Null parity.

3. Prolonged use of oestrogen: Prolonged menopausal oestrogen replacement therapy ēout progestogen. Prolonged use of antiestrogen, Tamoxifen for breast cancer

4. Genetic factors & other factors: Endometrial & ovarian cancer are the simultaneously occurring ē other genital malignancy, reported incidence (1.4~3.8%). Family history of tumour is higher (12-28%).

Types

1. Endometrioid Adenocarcinoma: account for about 80~90%. Well differentiated & prognosis is better.

2. Mucinous carcinoma: rare (about 5%). Most of them are a well differentiated. Behaviour is similar to that of common endometrial carcinoma.

3. Serous adenocarcinoma: architecture is identical ē complex papillary. More aggressively ē deep myometrial & lymphatic invasion. Simulating the behaviour of ovarian carcinoma.

4. Clear cell carcinoma: rare subtype. High grade & aggressive. Prognosis is similar to or worse than of papillary serous carcinoma. Survival rate is lower 33%~64%.

5. Other rare subtypes: squamous adenocarcinoma, undifferentiated carcinoma & mixed adenocarcinoma.

Symptoms

- Asymptomatic (<5%).
- Abnormal vaginal bleeding (pre/or postmenopausal, minimal or non-persistent).
- Abnormal vaginal discharge (25% infection of uterine co-ntents).
- Pelvic pressure/discomfort (uterine enlargement or extrauterine pread).

Signs

- No evidence in early stage on physical examination.
- Slight enlargement of uterine size & soft Uterus.
- Fixed, immobile, adnexal mass in advanced stage.

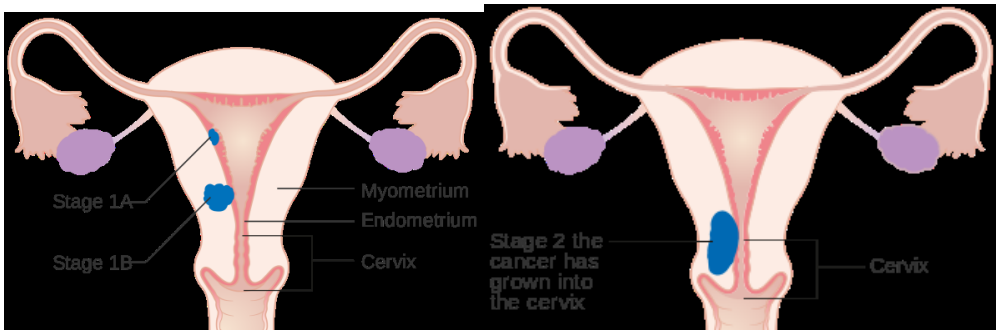
Special Examination

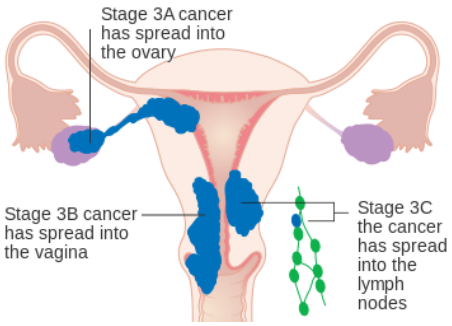
Dilation & Fractional curettage (D & C): most effective, definitive procedure & co-mmonly used. Established correct diagnosis, clinical stage. differentiated from cer-vical cancer or cervical involvement.

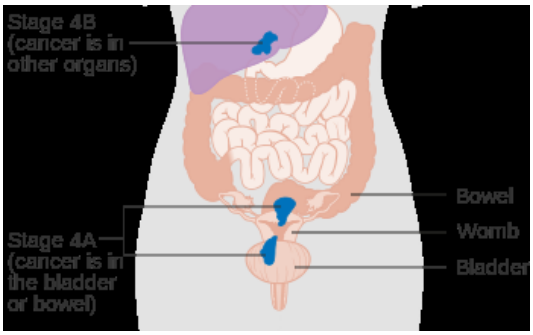
Ultrasonography: Identifying the size of lesion, invasion of endometrium or cervix.

Hysteroscopy: for direct observation, taking sample correctly, identifying polyps & sub mucous myoma. Pap test: unreliable diagnostic test, 30 - 50% abnormal pap test results. Others: MRI, CT, CXR, IVP, cystoscopy, & sigmoidoscopy.

Stages







Treatment

Stage I: abdominal hysterectomy+bilateral salpingoophorectomy + selective lymphadenectomy clear cell or papillary carcinoma-omentectomy + appendectomy.

Stage II: radical hysterectomy + pelvic & paraortic lymphadenectomy.

Stage III,IV: cytoreductive surgery.

Indications for radiation alone

○Elderly or obesity. ○Multiple chronic or acute medical illness (hypertension, cardiac disease, DM, pulmonary or renal disease). ○Advanced stage.

Hormone therapy

Most endometrial cancers are oestrogen dependent. Hormonal therapy is indicated for; advanced stage or early stage & desire for fertility. The used drug is MPA.

Chemotherapy

Used in case of; advanced stage or recurrent carcinoma, as postoperative adjunctive treatment for high risk factor. Drugs used include; DDP (Cisplatin), CTX (Cyclophosphamide), ADM (Doxorubicin), 5-Fu, Taxal MMC, VP16.

5-Year Survival Rate: Stage Ib: 94% . Stage Ic: 87% . Stage II: 84%. Stage III: 40%

Follow-up

75-95% disease will recur within 2-3 yrs after operation. Follow up include:-

•Main complaints. •Pelvic examination. •Vaginal discharge smear . •CXR. •Serum CA125. •Blood routine test. •Blood biochemistry examination. •CT/MRI.

Chapter XIV

PSYCHOLOGY

- Anxiety Disorders
- Somatoform Disorders
- Dissociate Disorders
- Mood Disorder
- Personality Disorders
- Substance Abuse
- Sexual & Gender Identity Disorder
- Eating Disorder
- Treatment Of Psychological Disorders

Introduction

The term psychology comes from the Greek roots psyche meaning soul or mind & logos meaning word or study. Psychology is the science of human behaviour & mental processes. The behaviour is anything we do- overt actions & reactions. The mental processes are our internal experiences- thoughts, feelings, memories……

This chapter will focus in certain topics. Anxiety. Obsessive-Compulsive Disorders. Stress related disorders. Mood Disorders. Personality Disorders. Substance Abuse.

ANXIETY DISORDERS

It is a feeling of dread, apprehension or fear. There are significant comorbid psychiatric conditions associated ē anxiety disorders! Manifested by physiological arousal like increased heartbeat, perspiration, muscle tension & rapid breathing. Anxiety affects cognition making problem solving difficult. We all experience moderate level of anxiety. Writing term papers, test taking (test anxiety) &several other day-to-day problems may give rise to mild forms of anxiety. Most people have difficulty in coping ē anxiety producing situations. These situations become major source of anxiety, taking more time & energy. Anxiety becomes severe or so persistent when it interferes ē every day function in family life, social activities, work or school. When this happens, it is characterized as anxiety disorder. Anxiety can have different forms.

GENERALIZED ANXIETY DISORDER

Affect 4-7% of general population. Median onset = 30 yrs but large range. The Female : Male ratio is 2:1

It is a widespread anxiety that is impossible to manage by avoiding specific situations. The person expresses a great many worries but cannot specifically tell the causes. Freud named such anxiety free-floating anxiety. Physiological & behavioural manifestations are aching muscles, being easily tired, difficulty to relax, indigestion, diarrhoea, frequent need to urinate, often complain of cold, clumsy hands and a racing heart. Such people expect the worst to happen. They fear that they will faint or lose control of themselves or worry that members of their family will develop some disease or be crashed by a car. As a result, they find it difficult to concentrate or fall asleep. In the morning they feel tired rather than relaxed.

PANIC DISORDER

50-60% have lifetime major depression. One third have current depression. About20 - 25% have history of substance dependence. The already existing state of tension as seen in generalized anxiety disorder reaches an acute & overwhelming level. Heart begins to pound faster & breathing becomes difficult. This condition may last from 15 min to an hour. When panic attacks are related to a specific stimulus, it is classified as phobias.

PHOBIC DISORDER

When anxiety is centred on a particular object or situation ēout any good reason, it is called phobia. Phobias sometimes develop after an initial association of fear ē some stimulus, for example, dog, elevator, high place or a situation that carries no danger at all. Common phobia types & stimuli in the environment include:-

Phobia types	Feared objects or situation
❑ Acrophobia	High place
❑ Claustrophobia	Enclosed places
❑ Ergasiophobia	Work
❑ Gramophobia	Marriage
❑ Haphephobia	Being touched
❑ Hematophobia	Blood
❑ Monophobia	Being alone
❑ Ocholophobia	Crowds
❑ Xenophobia	Strangers
❑ Ophidiophobia	Fear of snakes

OBSESSIVE-COMPULSIVE DISORDER



OCD seen 2% of general population. Mean onset 19.5 years, 25% start by age 14! Males have earlier onset than females. Female: Male 1:1. >70% have lifetime history of an anxiety disorder. >60% have lifetime history of mood disorder. Up to 30% have a lifetime Tic disorder. 12% of persons ē schizophrenia.

Obsession is an involuntary, irrational thought that occurs repeatedly. Sometimes it is mild. Example: a person locking & unlocking a door before leaving home. At other times it can be severe.

Compulsion is an action that a person uncontrollably performs again & again although she or he has no conscious desire to do so. The act is often senseless such as looking under the bed several times before going to sleep or locking & unlocking the door several times before going out. Or repeated hand washing for fear of contamination.

SOMATOFORM DISORDERS

It is a persistence of symptoms that have physical form, but in ẃ there is no actual physiological malfunction. The typical somatoform disorders are:-

Hypochondriasis

It is the pre-occupation ē bodily symptoms as possible signs of serious illness. The hypochondriac is perfectly healthy, but lives ē the conviction that cancer, heart disease, DM, or some other particular disorder is about to develop. If a hypochondriac has a headache, he believes it is due to some serious kidney disorders. The stomach ache will be taken as evidence of stomach ulcers or cancer. The behavioural manifestations are: •Reading every popular magazine concerning health •Adopt difficult health routines like hours of sleep & rest. •Stop eating certain foods & drinks. •Consume vast quantities of vitamins & medicine. •Frequently visits doctors.

Conversion disorders

When certain part of the body is not functioning well (blindness, deafness, paralysis or loss of sensation) ē no organic problems, it is called conversion disorder. The individual expresses some psychological problem, ẃ does not necessarily exist. There are no hard & enough evidences to verify the causes of such disorders.

DISSOCIATIVE DISORDERS

It is the dissociation or splitting of a certain kind of behaviour that are normally integrated. Example- cases indicate that people who are wandering in the streets ēout the notion of who they are or where they came from have dissociation disorders. Among the dissociate disorders are:

Amnesia

Is partial or total loss of memory concerning past experiences, such as an automobile accident or a battle. In the most severe forms, individual cannot recall his name, unable to recognize his parents & do not know his address.

Psychological amnesia

Is different from organic amnesia in that: it appears suddenly, often following serious stress, also disappears suddenly.

Organic amnesic syndrome

Is physiological, caused by some form of damage to brain tissues. Brain damage may result due to the disturbed proportion of acid to alkali in the blood. The insufficiency of oxygen may damage the brain tissue as well.

Fugue

It is related to amnesia. Fugue is the Latin word for flight. It is a sudden & unexpected leaving from home & taking a new identity elsewhere. The individual may be absent for days or months or yrs & may take up a totally new life at the new place. During the fugue the individual does not remember the earlier life. Later recalling what had happened earlier might come back home.

Multiple personality

Rare disorder; < 100 cases have been reported in literature. When the usual integrity of one's personality becomes so partitioned that 2 or more relatively independent sub personalities emerge, we name it multiple personality.

MOOD DISORDER

Experiences of being happy or upset in life are normal. In some people, however, changes of feelings are so long lasting that they affect everyday life. When disturbances in emotional feelings are so strong enough, we call them mood disorders. Mood disorders tend to run in families; thus, genetic factors play a role in their occurrences. The most common forms of mood disorders are:

MAJOR DEPRESSION

It is the most frequent problem diagnosed in out pt clinics. Interviews conducted in many parts of the world show that incidence of depression has increased significantly in the previous yrs. People who suffer from major depression may feel useless, worthless & lonely & may despair over the future. Depression also seems to involve disturbances in brain activity & biochemistry. Psychological factors such as learned helplessness, tendencies to attribute negative outcomes to internal causes & neglect active perceptions of one self & others are also involved. Suicide is a major cause of death among young people. Individuals are more likely to attempt suicide when they have recovered to some extent from depression than when they are in the depths of despair. The hallmark is that such feeling may continue for months & yrs. Women are found to experience major depression twice as men.

MANIA

It refers to an extended state of intense euphoric. People experiencing mania feel intense happiness, power & energy. People ē manic disorder may be involved in an activity much greater than their capacity believing that they will succeed at anything they attempt. Sometimes mania & depression can come alternatively. The swings between high & low moods may alternate over a period of few days or years. This is called bipolar depression.

SCHIZOPHRENIA

Evgen Bleuler (1911) coined the term schizophrenia. It is a general term for a number of psychotic disorders characterized by thought disturbance that may be accompanied by delusions, hallucinations, attention deficits & bizarre motor activity. Schizophrenia is splitting in the function of the mind, emotion on one hand & thinking on the other. Schizophrenia has complex origins, involving genetic factors, certain aspects of family structure, & biochemical factors. Schizophrenia may also be related to damage in several regions of the brain. Many homeless persons appear to be individuals suffering from serious psychological disorders such as schizophrenia or mood disorders. Schizophrenias are different & their causes & prognoses are also different. The distinct types are paranoid, disorganized, & catatonic. However the following features are taken as common properties.

a) Deterioration from previous levels of social, cognitive & vocational functioning.

b) Onsets before midlife (roughly 45-50 yrs of age).

c) Duration of at least six months & mostly noticeable.

d) A pattern of psychotic features including thought disturbances, delusions, usually auditory hallucinations, disturbed sense of self and a loss of reality testing.

Schizophrenia is manifested in different forms. These are:

Disorder of thought: a split among various ideas or between ideas & emotions; Incoherence or dissociation in the thought process. Concepts, ideas, symbols are sometimes put together simply because they seem similar. The tendency to jump from one track of thought to another.

Disorder of perception: distorted view of reality; the schizoid consistently reports distortions of sensory perception, auditory, somatic & tactile hallucinations. Auditory- takes the form of insulting. Tactile- feel burning sensations. Somatic- sensation of something crawling under the abdomen.

Disorder of affect: frequently show inappropriate emotional responses or none at all. Might laugh when told of the death of a favourite relative. Might get angry when given a present; Face remains immobile, voice becomes monotone. The external situation or stimulus fails to trigger an appropriate response

Disorder of motor behaviour: perform repetitive & inappropriate behaviour or acts. The schizoid might spend hours rubbing his forehead, slapping leg, or might sit all day, sometimes no physical activity (catatonic stupor).

PERSONALITY DISORDERS

It is an umbrella term for a number of psychological disorders. It is a class of behavioural disorders manifested as pathological developments in one's overall personality. When personality traits become so inflexible & maladaptive that they impair a person's functioning, we label it as personality disorder. Including:

Paranoid personality disorder: it involves mistrust of others. The paranoid suspects that virtually everyone around him is trying to deceive or take advantage of him in some way.

Schizoid personality disorder: it is a personality disorder in ẃ individuals become almost totally detached from the social world. They show little interest in friend-

ships, love affairs, or any other kind of intimate contact with other persons. They are indifferent to praise and criticism and often show emotional coldness and detachment. They perceive the people around them as obstacles to the goals they wish to reach.

Anti-social personality disorder: it is a personality disorder involving a lack of conscience & sense of responsibility, impulsive behaviour, irritability, & aggressiveness. Its essential feature is the violation of the rights of others. Typical patterns of behaviour are truancy from school, inability to hold a job, lying, stealing, aggressive sexual behaviour, drug & alcohol abuse, & a high rate of criminality. Its main feature is absence of emotion in social relationships. They show no concern over the most callous murder & no sadness at the death of a parent or friend. Even if they face prison terms, social sanctions, expulsion from school or face loss of jobs, they tend to repeat the same behaviour that resulted punishment upon them.

SUBSTANCE ABUSE

Psychoactive substances are those ẃ when introduced into the body, affect the mental wellbeing of the user. Abuse occurs when persistent use entails social, occupational, psychological or physical problems. Psychoactive substances include depressants, stimulants & hallucinogens, such as alcohol, tobacco, cannabis & khat. They are used for various ends. According to Nikowane & Jansen (1999); Street children use them to help them cope ē the frustration, boredom, & hardships of street life. For the unemployed such substances provide as a pass time & as an outlet for feelings of frustration. Other underlying reasons for using substances are poverty, ignorance & lack of organized recreational facilities or prog- rams. Psychological, environmental & biological factors all play a role. If consump-

tion of substances like tobacco, alcohol etc remains within reasonable bounds, the

practice is not psychological disorders. But if the individual is dependent on one of the above indicated substances & devoted to get & use it & then it fits the definition of abnormality.

Health consequences of substance abuse

1. Individuals using psychoactive substances are at risk for suicide, poisoning & acquisition of serious blood borne diseases, such as HIV , hepatitis B, C, especially when there is sharing of infection equipment. Example-Researchers found that sexual abuse has been linked to other behavioural problems, including excessive use of alcohol & other drugs, unprotected sex ē multiple partners, & prostitution.

2. Other consequences are death due to overdose, accidents & damage to the brain, liver lungs & heart.

3. Mental disorders are common & are often associated ē physical trauma, suicide, & other violent acts. Malnutrition is common among the children of smokers & drinkers, as income is used to buy cigarettes or alcohol.

Social damages of alcoholism

Family disruption; Decreased job productivity due to inefficiency. Accidents. Absence or low morale. Death. Injury. Property damage from alcohol related automobile accidents. Increased medical care for alcoholics.

SEXUAL & GENDER IDENTITY DISORDERS

Sexual disorders- It involves disturbances in sexual desire, sexual arousal, or the ability to attain orgasm. Some of these are:

a. Sexual desire disorders: involves a lack of interest in sex or active aversion to sexual activities. Persons suffering from these disorders report that they rarely have the sexual fantasies most persons generate, that they avoid all, or almost all-sexual activity, & that these reactions cause them considerable distress.

b. Sexual arousal disorders: involve the inability to attain or maintain an erection (males) or the absence of vaginal swelling & lubrication(females). Orgasm disorders involve the delay or absence of orgasm in both sexes & may also include premature ejaculation.

c. Paraphilias: sexual disorders involving choices of inappropriate sexual objects, such as young children, or the inability to experience arousal except in the presence of specific objects or fantasies. Paraphilias include:-

1.Fetishism: sexual gratification that is dependent upon an inanimate object or some part of the body other than the genitals.

2.Transvestitism: sexual gratification through dressing of the opposite sex.

3.Transsexuals: gender identification ē the opposite sex

4.Exhibitionism: sexual gratification through exhibiting the genitals to involuntary observer.

5.Voyeurism: sexual gratification through secretes observation of another person's sexual activities or genitals.

6.Pedophilia: sexual gratification obtained through sexual contacts ē children.

7.Incest: sexual relations among members of the immediate family.

8.Rape: sexual relations achieved by threatening or using force on another person.

9.Sadism: sexual gratification obtained through inflicting pain on another person.

10.Masochism: sexual gratification through having pain inflicted on oneself.

Gender identity disorder

Persons suffering from gender identity disorder feel that they were born ē the wrong sexual identity & seek to change this identity through medical treatment or other means. Advances in surgical techniques have now made it possible for such persons to undergo sex-change operations, in ẃ their sexual organs are actually altered to

approximate those of the other sex. Before their operations these individuals receive extended counseling, learning the mannerism of the other gender, how to wear its clothes & so on. Existing evidences indicate that these people are satisfied ē the results & happier than they were before. However, follow-up studies suggest that some persons who undergo such operations experience regrets & unhappiness, sometimes to the extent that they commit suicides.

EATING DISORDERS

These are serious disturbances in eating habits or patterns that pose a threat to individuals' physical health & well-being. Eating disorders include anorexia nervosa & bulimia nervosa. **Anorexia nervosa** is a disorder in ẃ individuals, intensely fearful of being or becoming fat, starve themselves, failing to maintain a normal body weight. In contrast, **Bulimia nervosa** involves episodes of binge eating followed by various forms of compensatory behaviour designed to avoid weight gain, such as self-induced vomiting or over use of laxatives. Eating disorders are much more common among females than among males. Both disorders seem to arise in part from dissatisfaction ē personal appearance & efforts to match the thin-is-in model promoted strongly in the mass media.

TREATMENT OF PSYCHOLOGICAL DISORDERS

Psychotherapy

Is a way of solving non-organic or psychological problems by utilizing different psychological approaches. Is the treatment of problems of an emotional nature by psychological means. The objective of psychotherapy is to bring: Ego strength. Self-integration. Self-direction. Therapy is directed towards modifying maladaptive behaviour & fostering adaptive behaviour. The primary goal of therapy is to help the client achieve more effective coping behaviour. The process is a professional relationship

between the therapist & the pt. Psychotherapy include; 1-Classical psychoanalysis, ẃ is based on the idea suggested by Freud, ẃ says that the basic sources of abnormal behaviour are unresolved past conflicts & anxieties. So it is used to explore & understand the unconscious, use a technique called free-association, to get rid of the anxiety-producing situations should bring unwanted impulses out of the unconscious part of the mind into the conscious part. The psychoanalyst recognizes all forms of information & makes connections between what the client says & the repressed feelings. Dream analysis is another technique. Freud assumed that during sleep hrs the use of defence mechanisms is low. This allows the repressed wants & desires to surface. The psychoanalyst moves beyond the surface description of the client's dream, & examines its underlying meaning.

2-Ego analysis: the goal of this therapy is to bring Ego strength so that individuals take active part in trying to control their environment. The therapist assists the pt in recognizing his/her conscious aims &capabilities, and controls the Id.

3-Play therapy: it is the application of psychoanalytic therapy on children who cannot speak out their problems. In play therapy, the therapist observes the child in a playroom. The therapist never criticizes the child, or stops the child from displaying any varieties of plays. From series of observations, the therapist tries to determine the root causes of the child's problems.

Comment on the psychoanalytic therapy

Psychoanalysis is time consuming & expensive. A pt meets ē his/her therapist an hour a day, four to six days in a week, for several days.

Behavioural therapy

It is concerned ē behavioural changes. From behaviourist point of view all positive & negative behaviours are primarily learned. The behavioural therapy is not concerned

ē case history. It is based on classical conditioning.

1. Systematic desensitization: It is the most successful treatment based on classical conditioning. Phobias, anxiety disorder, impotence & fear of sexual contact are often treated successfully using this technique. Pts are taught to relax & then are shown pictures of their feared object or problem, to desensitize them, or reduce their unfavourable response patterns. The threatening stimuli are systematically paired ē less threatening stimuli & proceed to more threatening representation of the real object.

2. Aversion therapy: it is mainly used for addictions or unwanted behaviours. In this technique a negative feeling is attached to stimuli, ẃ are supposed to bring undesirable behaviours. Example: for a person ē drinking problem, an alcoholic drink is paired ē a drug that causes severe nausea & vomiting. After few pairings the alcohol becomes associated ē vomiting.

Medication

Antidepressants are an option (most often for more severe cases) that can help ease the symptoms of depression & return a person to a better level of functioning. Medication is often crucial for cases of bipolar (typically a mood stabilizer). Antidepressants are not habit forming. The antidepressant first introduced 40 yrs ago. Also used for treatment of other disorders including: Anxiety disorders, dysthymia, chronic pain & behavioral problems.

Evolution of drug therapy: antidepressants discovered accidentally while investigating antipsychotic efficacy of modifications of Phenothiazines. Imipramine- first antidepressant discovered. Around the same time, monoamine oxidase inhibitors were identified. The 2nd generation antidepressants identified to address problemsē 1st generation antidepressants. . Late 1980's- SSRI's were developed. Now working on other antidepressant treatments.

Tricyclic Antidepressants

Effectively relieve depression ē anxiolytic & analgesic action. Is the 1st choice for treatment of depression. Imipramine & Amitriptyline.

Clinical Limitations of TCA's: slow onset of action. Wide variety of effects on CNS (adverse side effects): can directly impair attention, motor speed, dexterity & me mory. Cardiotoxic & potentially fatal in overdoses.

Pharmacokinetics of TCAs: well absorbed upon oral administration. Relatively long half-lives. Metabolized in the liver. Converted into intermediates that are later detoxified. Readily cross the placenta. In CNS: blocks presynaptic 5-HT, DA & NE receptors. Blocking of A Ch receptors leads to dry mouth, confusion, blurry vision &mental confusion. Blocking of histamine receptors leads to drowsiness & sedation. Other effects include; cardiac depression, increased electrical irritability.

Second Generation (Atypical) Antidepressants

Developed in the late 1970's & 1980's

Maprotiline-one of the first clinically available antidepressants, has a long half-life & blocks NE reuptake. ***Amoxapine-*** primarily a NE reuptake inhibitor. ***Trazodone -*** not a potent blocker of NE or 5-HT,its active metabolite blocks a subclass of 5-HT receptors. .***Bupropion-***selectively inhibits DA reuptake, used for ADHD, side effects include: anxiety, restlessness, tremors & insomnia. ***Clomipramine-***structurally a TCA but exerts inhibitory effects on 5-HT reuptake. ***Desmethyclomipramine -***active metabolite; classified as a mixed 5-HT & NE reuptake inhibitor. Used to treat OCD, depression, panic disorder & phobic disorders. ***Venlafaxine*** – also a mixed 5-HT & NE reuptake inhibitor, also inhibits the reuptake of DA. Produ- ces improvements in psychomotor and cognitive function

Serotonin - Specific Reuptake Inhibitors

SSRI's available for the past 15 yrs. Allows for more serotonin to be available to stimulate postsynaptic receptors. Available to treat depression, anxiety disorders, ADHD, obesity, alcohol abuse, childhood anxiety, etc.

Fluoxetine (Prozac) – 1st SSRI available, long half life, slow onset of action, can cause sexual dysfunction, anxiety, insomnia & agitation.

Sertraline (Zoloft) – 2nd SSRI approved, low risk of toxicity, few interactions, more selective & potent than Prozac.

Paroxetine (Paxil) – 3rd SSRI available, more selective than Prozac, highly effective in reducing anxiety & posttraumatic stress disorder (PTSD) as well as OCD, panic disorder, social phobia, premenstrual dysphoric disorder & chronic headache. ***Fluvoxamine (Luvox)*** – structural derivative of Prozac, became available for OCD, also treats PTSD, dysphoria, panic disorder & social phobia.

Citalopram (Celexa) – well absorbed orally, few drug interactions, treats major depression, social phobia, panic disorder.

Serotonin syndrome: at high doses or combined ē other drugs, an exaggerated response can occur, this is due to increased amounts of serotonin. Alters cognitive function , autonomic function and neuromuscular function. Potentially fatal.

Serotonin withdrawal syndrome: ē discontinuation of any SSRI onset of withdrawal symptoms occur within few days & can persist 3-4 wks. Symptoms include; disequilibrium, GIT problems, flu-like symptoms, sensory & sleep disturbances.

Dual Action Antidepressants

Nefazodone – a unique antidepressant, resembles a TCA as an inhibitor of 5-HT & NE reuptake, no therapeutic superiority over TCA's & SSRI's.

Mirtazapine – increases noradrenergic & serotonergic neurotransmission by blocking

the central α autoreceptors & heteroreceptors, a potent antagonist, rapidly absorbed orally.

Monoamine Oxidase Inhibitors

MAOI's are long acting, irreversible inhibitors of monoamine oxidase. Have been used since the 1950's but have a controversial past. Has potential for serious side effects & potentially fatal interactions ē other drugs & food. MAO is one of 2 enzymes that break down neurotransmitters 5-HT & NE. Two types; MAO-A: inhibition causes anti-depressant activity. MAO-B: inhibition causes side effects.

Irreversible MAOI's

Nonselective: block both A & B types. Form permanent chemical bond ē part of the MAO enzyme (enzyme function returns only as new enzyme is biosynthesiszed). Have rapid rate of elimination, excess drug is rapidly metabolized. Inhibition occurs slowly.

Phenelzine (Nardil), Tranylcypomine (Parnate), Isocarboxazid (Marplan).

Reversible MAOI's

Highly selective in inhibiting MAO-A. Much safer than irreversible MAOI's.

Side effects are minimal.

Brofaromine, Pirlindole, Toloxatone & Moclobemide.

New Drug Treatments

COMTI –second of two enzymes that catalyze the inactivation of DA & NE by decr easing neurotransmitter levels.

Tolcapone – specific inhibitor of COMT used in treatment of Parkinson's.

SNRI -soon to be available for clinical use.

Reboxetine - block NE reuptake ēout also blocking DA or 5-HT reuptake.

Serotonin 5-HT$_1$ Agonists – appear to be responsible for acute antidepressant effects.

DHEA – a major glucorticoid hormone secreted by the adrenal glands, function uncle-

ar. Precursor to estrogen & testosterone. Increases feelings of physical & psychological well-being.

SAM, SAMe- plays key intermediary role in many metabolic reactions that involve the transfer of the methyl groups between molecules. Not generally recommended for treatment of depression.

Generalized anxiety disorder management: Buspirone, Benzodiazepines, Antidepressants (SSRIs, Venlafaxine, Imipramine). Cognitive-behavioural therapy.

Panic disorders management: education, reassurance, elimination of caffeine, alcohol , drugs, OTC stimulants.

Cognitive-behavioral therapy: SSRIs, Venlafaxine, Tricyclics, MAOIs, Benzodiazepines, Valproate, Gabapentin

Obsessive-Compulsive Disorder: 40-60% treatment response. Serotonergic antidepressants. Behaviour therapy. Adjunctive antipsychotics, psychosurgery.

MULTIPLE CHOICE QUESTIONS

1- The following are recognized causes of eosinophilia (true or false).

A) Malaria.

B) Visceral leishmaniasis.

C) Churg-Strauss syndrome.

D. Drug hypersensitivity.

E. Visceral larva migrans (Toxocariasis).

2- Consumption of raw fish or shellfish is associated ē infection caused by:

A) Clonorchis Sinensis.

B) Ancylostoma duodenale.

C) Schistosoma Japonicum.

D) Vibrio parahaemolyticus.

E) Paragonimus Westermani.

3- Concerning anti-tuberculous chemotherapy (true or false)

A) Pyrazinamide causes hyperuricemia.

B) Isoniazid causes a lupus-like syndrome.

C) Twice weekly regimens should be continued for at least 12 months.

D) Pyridoxine is only needed by slow acetylators.

E) Rifampicin can only be given orally.

4- Following splenectomy for trauma (true or false)

A) Thrombocytopaenia is typical.

B) Pneumococcal vaccine should be given.

C) Malaria is more severe.

D) Prophylactic penicillin should be taken for 6 wks.

E). Heinz bodies are characteristically seen on the blood film.

5. Steroids are of benefit in the treatment of (true or false);

A) visceral leishmaniasis.

B) Eschericia coli septicaemia.

C) Cerebral malaria.

D) Severe typhoid fever.

E) Herpes zoster recrudescence (shingles).

6- Subcutaneous nodules are a typical finding in (true or false);

A) Neurofibromatosis.

B) Hydatid disease.

C) Cysticercosis.

D) Onchocerciasis.

E) Trichinosis.

7- Concerning tuberculin skin testing (true or false);

A) Pts ē tuberculous pericarditis are usually tuberculin positive.

B) Previous BCG vaccination usually results in a strongly positive reaction.

C) Pulmonary sarcoidosis gives a positive tuberculin test in about 30% of cases.

D) If the sputum microscopy & culture are negative for mycobacteria, pulmonary tuberculosis can only be diagnosed if the tuberculin test is positive.

E) The test is usually negative in miliary tuberculosis.

8- Hookworm (true or false);

A) Is usually spread by the faeco-oral route.

B) Is usually diagnosed by microscopy of adhesive tape taken from the perianal area.

C) May block the pancreatic duct causing pancreatitis.

D) Eggs can be readily distinguished microscopically from those of Strongyloides sp.

E) Commonly causes diarrhea in non-immunes.

9- The following are associated ē ⇧ risk of vertical transmission of HIV (true or false);

A) Breast feeding.

B) High titres of p24 antigen in maternal serum perinatally.

C) Low maternal CD4 counts during pregnancy.

D) Prolonged labour.

E) HIV-1 compared to HIV-2.

10- A fever of 2 wks' duration associated ē neutropenia is characteristically due to (true or false);

A) Disseminated tuberculosis.

B) Brucellosis.

C) Malaria.

D) Influenza B.

E) Amoebic liver abscess.

11- The following drugs are contraindicated or should be used ē caution in epileptics (true or false);

A) Doxycycline.

B) Chloroquine.

C) Ciprofloxacin.

D) Mefloquine.

E) Metronidazole.

12- Hepatocellular carcinoma (true or false);

A) Is more common in men than women.

B) Is radiosensitive.

C) Is associated ē intake of aflatoxin.

D) Usually presents ē weight loss, right hypochondrial pain & hepatomegaly.

E) Progress of the disease can be monitored by serial measurement of the tumor marker inhibin.

13. Blindness is a recognized complication of (true or false);

A) Leprosy.

B) Onchocerciasis.

C) Vitamin A deficiency.

D) Cysticercosis.

E) Toxoplasmosis.

14- Legionnaires disease (true or false);

A) Can be acquired by drinking infected water.

B) Smokers are more susceptible.

C) Most cases are sporadic.

D) Hyponatraemia is typical.

E) May cause rigors.

15- A positive VDRL (venereal disease research laboratory) test ē negative TPHA & FTA (Treponema pallidum haemagluttinin & fluorescent treponemal antibody) tests is consistent with: (true or false)

A) Early infection primary syphilis.

B) Treated syphilis.

C) Glandular fever.

D) Late syphilis.

E) Previous yaws infection.

16- Genital ulcers (true or false);

A) May be due to herpes simplex virus.

B) Are associated ē an ⇧ incidence of HIV.

C) If painful & associated ē lymphadenopathy, are likely to be due to chancroid.

D) Are found in gonorrhea.

E) If well-defined & beefy red, are likely to be due to granuloma inguinale.

17- A 20-year-old man was referred for investigation of lifelong haemolytic anaemia. Jaundice accompanied by anaemia & splenomegaly had been apparent since early life. Episodes of jaundice were more marked during infections or after fasting & less pronounced following exposure to sunlight, was conspicuous. On investigation the following results were obtained:

Hb 11.8 g/dL

MCV 85.5 fL

MCH 29.1 pg

MCHC 34 g/dL

Retic count 5.44

Blood film shows spherical RBCs ē lack of pallor in the central area.

What is the diagnosis?

A) Anaemia of chronic diseas.

B) Sideroblastic anemia.

C) Megaloblastic anemia.

D) Hereditary spherocytosis.

18- A 47 yr old man presents ē palpitations ẃ he has had for 3 months. He feels his 'heart race' regularly. On examination his pulse is 110/min, irregularly irregular & respiratory examination is unremarkable. An ECG confirms atrial fibrillation.

What is the most appropriate next step in management?

A) Digoxin.

B) Electrical cardioversion.

C) Amiodarone.

D) Metoprolol.

E) Flecainide.

19- A 45 yr old lady has recently been diagnosed as a diabetic. Despite strict diet control, her blood sugars are running at 200 mg/l. She weighs 80 kg.

Which of the following is the best medication to start with?

A) Insulin.

B) Glibenclamide.

C) Metformin.

D) Troglitazone.

E) Gliclazide.

20- A 26 yr old woman presents ē lethargy, polyuria & nausea. She has no past medical history & is currently not taking medications. Her blood results are: sodium 135 mmol/l, potassium 4.3 mmol/l, urea 7 mmol/l, creatinine 90 µmol/l, calcium 3.2 (2.25 -2.7) mmol/l, phosphate 0.3 (0.8-8) pmol/l, Parathyroid hormone 18 (0.8-8) pmol/l.

What is the likely cause of hypercalcaemia?

A) Chronic kidney disease.

B) Hypophosphataemia.

C) Primary hyperparathyroidism.

D) 1,25 (OH) vitamin D supplementation.

E) Hypocalciuric hypophosphataemic rickets.

21- A 33 yr old female è SLE has arthralgia involving her upper limbs. She also has a butterfly facial rash & a rash on the trunk. Urine dipstick shows no proteinuria or haematuria. Her renal function is normal.

Which one of the following medications is most appropriate?

A) Methotrexate.

B) Prednisolone.

C) Azathioprine.

D) Hydroxychloroquine.

E) Cyclosporin

22- A pt has marked dizziness & unsteadiness during walking. On examination, he has a left sided Horner's syndrome & left sided weakness. There is loss of sensation to pinprick on the right side. What is the likely diagnosis?

A) Left internal capsule infarct.

B) Posterior inferior cerebellar artery occlusion.

C) Medullary infarct.

D) Multiple sclerosis.

E) Vertebral artery dissection.

23- A 50 year old man has a history of hypertension & is a smoker. He complains of visual loss. Assessment shows the presence of a right homonymous hemianopia. Which of the following structures is damaged?

A) Optic chiasm.

B) Optic radiation.

C) Left occipital lobe.

D) Right occipital lobe.

E) Temporal lobe.

24- A 58-yr-old woman had an ST-segment-elevation myocardial infarction 2 months ago. She has made a good recovery but has low mood & a poor sleep pattern ē early morning wakening. She wishes to try medication as her symptoms are affecting her ability to work.

Which is the SINGLE MOST appropriate antidepressant drug?

A) Amitriptyline.

B) Fluoxetine.

C) Lofepramine.

D) Mirtazapine.

E) Venlafaxine.

25- A 35-yr-old woman has noticed increasing weakness & numbness in her legs & arms over the past few days & today she is feeling short of breath on exertion. 6 wks ago she had diarrhoea while on holiday abroad & stool culture confirmed infection ē Campylobacter jejuni. She was treated ē ciprofloxacin & recovered fully.

Which is the SINGLE MOST likely diagnosis?

A) Drug-induced neuropathy.

B) Guillain-Barré syndrome.

C) Motor neurone disease.

D) Myasthenia gravis.

E) Multiple sclerosis.

26- A 56 yr old man has a 2 yr history of deafness affecting his right ear. He has had intermittent episodes of vertigo, tinnitus & vomiting each lasting a few hours. The whispered voice test is diminished in his right ear. You perform tuning fork tests. Which is the SINGLE MOST likely result of the tuning fork tests?

	Rinne's – conduction results	Weber's – ear localisation
A	Air > bone	Left
B	Air > bone	Right
C	Bone > air	Left
D	Bone > air	Right
E	Air same as bone	Equal

27- A 50-yr-old man has become increasingly tired & lethargic over the past 6 months & has developed erectile dysfunction. His wife comments that he looks tanned even in the winter months. His serum ferritin & transferrin levels are significantly raised, but his Hb is normal. Which is the SINGLE MOST likely diagn only.

A) Addison's disease.

B) Chronic active hepatitis.

C) Diabetes mellitus.

D) Haemochromatosis.

E) Hypothyroidism.

28- A) Adenovirus.

B) Herpes simplex virus.

C) Cytomegalovirus.

D) Human papilloma virus.

E) Echovirus.

F) Hepatitis B virus.

G) Respiratory syncytial virus.

H) Epstein-Barr virus.

I) Rotavirus.

J) Rubella virus

For each clinical condition, select the SINGLE MOST likely causative virus from the list of options.

1- Hepatocellular carcinoma.

2- Warts.

29- A 20-yr-old woman notices bright lines of light in both visual fields followed shortly afterwards by a partial loss of her vision. Her visual symptoms resolve after one hour but she has slight nausea. Which is the SINGLE MOST likely diagnosis?

A) Acute glaucoma.

B) Migraine.

C) Optic neuritis.

D) Retinal detachment.

E) Vitreous detachment.

30- A cohort study evaluated the relationship between dietary calcium supplementation & hip fractures in post-menopausal women. 100 women took calcium supplements & 100 women took placebo tablets. Over the 3 year period, 5 women had hip fractures in the calcium group & 10 women had hip fractures in the placebo group. The 95% confidence interval is 0.18 to 1.4. 10.

What is the RISK of a hip fracture in the TREATED group?

A) 0.01

B) 0.05

C) 0.1

D) 0.5

E) 1.0

What is the RISK RATIO?

A) 0.01

B) 0.05

C) 0.1

D) 0.5

E) 1.0

31- Which is the SINGLE MOST appropriate epidemiological measure to estimate the rate at ẃ the new cases of papilloma virus infection occur among students on a college campus?

A) Case fatality.

B) Incidence.

C) Median survival.

D) Mortality.

E) Prevalence.

32- MATCH EACH drug to the MOST LIKELY side effect. All four drugs must be correctly matched to score ONE mark.

A. Diclofenac

B. Hydroxychloroquine

C. Infliximab

D. Methotrexate

Side effect	Most likely causative drug
Bone marrow suppression	
Stroke	
Retinopathy	
Septicaemia	

33- A 63 yr old man ē poorly controlled hypertension, suddenly loses his vision in his left eye & his visual acuity on the left is reduced to hand movements only. Visual acuity on the right is 6/6. Fundoscopy of the left eye shows flame-shaped retinal Hge spreading out from the disc. Which is the SINGLE MOST likely diagnosis?

A) Acute glaucoma. B) Central retinal artery occlusion.

C) Central retinal vein occlusion. D) Retinal detachment.

E) Vitreous Hge.

34- A 28-year-old man has had a flu-like illness ē anorexia, nausea & fever for a week. He is jaundiced but abdominal & general examination is otherwise normal. His liver function tests are as follows (normal ranges in brackets):

Bilirubin 98 µmol/L (< 21 µmol/L)

Aspartate aminotransferase (AST) 228 IU/L (< 40 IU/L)

Alanine aminotransferase (ALT) 186 IU/L (< 40 IU/L)

Alkaline phosphatase 652 IU/L (35 – 104 IU/L)

Albumin 35 g/L (35 – 50 g/L)

Total protein 73 g/L (60 – 80 g/L)

Which is the SINGLE MOST likely diagnosis?

A) Alcoholic liver disease. B) Cholelithiasis.

C) Gilbert's syndrome. D) Hepatitis A.

E) Primary biliary cirrhosis.

Which is the SINGLE MOST appropriate SPECIFIC diagnostic test for this patient?

A) Antimitochondrial antibodies. B) Blood alcohol level.

C) Buccal smear. D) Hepatitis A IgM.

E) Ultrasound liver & gallbladder.

35- A 25 yr old woman has been infertile for 3 yrs. She has had recurrent pelvic pain due to endometriosis. Investigations in primary care are reported as follows:

CBC - normal.

Thyroid function - normal.

Sex hormone profile - normal.

Rubella serology - immune.

Day 21 progesterone – normal.

Chlamydia swab – negative.

Pelvic ultrasound – normal.

Her partner's semen analysis is reported as normal.

A referral to secondary care is agreed & she asks what is likely to happen next.

According to current guidelines, ẃ is the single most appropriate NEXT investigation?

A) Cervical cytology. B) Hysterosalpingogram.

C) Hysteroscopy. D) Laparoscopy.

E) Post-coital test

36- A 70-yr-old woman attends for her repeat prescription of 100 mcg levothyroxine daily, ẃ she has been taking for the past 30 yrs. The last record of any blood test was 6 yrs ago. She mentions a recent episode of quite severe localised back pain ẃ has now settled to a dull ache around the L3 region. She has no neurological signs.

Which is the SINGLE MOST likely diagnosis?

A) Lumbar stenosis.

B) Osteomalacia.

C) Osteomyelitis.

D) Osteoporosis.

E) Paget's disease.

37- An 80 yr old edentulous pt who lives alone & refuses meals on wheels, complains of constipation without rectal bleeding. Her weight is steady, abdominal & rectal examinations are normal & she is otherwise well.

Which is the SINGLE MOST likely diagnosis?

A) Alzheimer's disease.

B) Carcinoma of the colon.

C) Diverticular disease.

D) Hypothyroidism.

E) Poor fiber intake.

38- A 50 yr-old woman, who has recently been diagnosed ē hypertension, complains of pain in her knees. She feels tired & her memory is poor. She has lost her appetite recently & feels nauseated most of the time. Urinalysis is normal.

Which is the SINGLE MOST likely diagnosis?

A) Chronic fatigue syndrome.

B) Chronic renal failure.

C) Coeliac disease.

D) Cushing's syndrome.

E) Hyperparathyroidism.

39- For the past week, a 30 yr old woman has noticed fresh red blood on the toilet paper & experiences sharp pain around the anus when she defecates. Today she can feel a very tender lump at the anal margin.

Which is the SINGLE MOST likely diagnosis?

A) Anal fissure. B) Ischiorectal abscess.

C) Prolapsed rectal mucosa. D) Rectal carcinoma.

E) Thrombosed haemorrhoid.

40- A 35 yr old woman stopped the combined oral contraceptive pill 6 months ago because of ⇧BP. Her periods have not returned, she feels generally tired & has put on weight. A pregnancy test is negative & her FBS is 9.2 mmol/L (multiply by 18 = mg)

Which is the SINGLE MOST likely diagnosis?

A) Anaemia.

B) Chronic active hepatitis.

C) Coeliac disease.

D) Cushing's disease.

E) Hypothyroidism.

41- A) Berry aneurysm.

B) Cerebral glioma.

C) Drug induced.

D) Graves' disease.

E) Multiple sclerosis.

F) Myasthenia gravis.

G) Stroke.

For each pt described below, select the SINGLE MOST likely diagnosis from the list of options above.

1. A 27-yr-old woman who is a non-smoker, suddenly develops double vision. She had an episode of reduced visual acuity in her left eye whilst on holiday 18 months previously, for ẃ no cause was identified. She has no other significant past medical history.

2. A 35-yr-old man who is a non-smoker, suddenly develops a severe headache & double vision. His right pupil is fixed & dilated.

3. A 48-yr-old woman has transitory double vision towards the end of most days. She smokes 10 cigarettes/day. She has vitiligo & hypothyroidism.

42- Which is the SINGLE MOST appropriate treatment for a Trichophyton rubrum toe nail infection?

A) Oral fluconazole. B) Oral Griseofulvin.

C) Oral terbinafine. D) Topical Clotrimazole.

E) Topical terbinafine.

43- A 56 yr old woman ē type 2 DM has lost her appetite & developed pruritus over the past few days. On examination she is jaundiced but general & abdominal examination is otherwise normal. She takes regular metformin & simvastatin & has just finished a course of erythromycin for localised cellulitis. Her liver function tests are as follows (normal ranges in brackets):

Bilirubin 112 µmol/L (< 21 µmol/L).

Aspartate aminotransferase (AST) 56 IU/L (< 40 IU/L).

Alanine aminotransferase (ALT) 72 IU/L (< 40 IU/L).

Alkaline phosphatase 986 IU/L (35 – 104 IU/L).

Albumin 35 g/L (35 – 50 g/L).

Total protein 73 g/L (60 – 80 g/L).

Which is the SINGLE MOST LIKELY diagnosis?

A) Alcoholic liver disease. B) Drug-induced cholestasis.

C) Fatty liver disease. D) Gilbert's syndrome.

E) Primary biliary cirrhosis.

44- A 34 yr old woman has developed rash (vesicular) on her buttock over the past 2 days. It is sore to touch & she has no rash elsewhere. She says this has happened on at least 3 previous occasions & the rash is always in the same place.

Which is the SINGLE MOST likely diagnosis?

A) Chickenpox. B) Coxsackie virus infection.

C) Dermatitis herpetiformis. D) Herpes simplex.

E) Herpes zoster.

45- A 70 yr-old woman has been in long-standing poor health, ē severe DM & rheu-matoid arthritis. Her physician notes that she appears pale & orders a hematocrit, ẃ shows a result of 35%. Examination of the blood smear reveals a microcytic anemia. The physician is considering a differential diagnosis of iron deficiency anemia versus anemia of chronic disease. Which of the following laboratory determinations would be most helpful in distinguis-hing these conditions?

A) Erythrocyte: granulocyte ratio in bone marrow.

B) Presence or absence of polychromatophilic target cells.

C) Presence or absence of stippled erythrocytes.

D) Serum ferritin.

E) Serum iron.

46- A 45 yr old pt on haemodialysis for one wk has noted that his BP is more difficult to control. He reports good compliance ē his medications, ẃ include erythropoietin, ferrous sulfate, vancomycin & vit D. His BP is 180/99 mm Hg.

Which of the following is the most likely cause for the worsening control of his BP?

A) Erythropoietin. B) Ferrous sulfate.

C) Vancomycin. D) Vitamin D.

E) Uremia.

47- A 40 yr old man is brought to the emergency room by his friends. Apparently, he has ingested some unknown medication in a suicide attempt. The pt is disoriented to time. His temp 39.3 C, BP 120/85 mm Hg, HR 100/min & irregular & RR 22/min. The skin is flushed & dry. Dilated pupils & muscle twitching are also noted on physical examination. ECG reveals prolonged QRS complexes. Hepatic transaminases are normal & blood gas analysis shows a normal pH.

These findings are most likely due to intoxication by ẃ of the following substances?

A) Acetaminophen.

B) Alcohol.

C) Benzodiazepines.

D) Clonidine.

E) Monoamine oxidase inhibitors.

F) Tricyclic antidepressants.

48- A 22 yr old woman goes to the emergency department because she feels very weak & is having muscle cramping &fasciculations. Blood chemistry studies demonstrate

a plasma potassium of 1.5 mEq/L (N 3.5 -5 mEq). On questioning, she admits to chronic use of laxatives & diuretics to control her weight. Which of the following ECG changes would be most characteristic of changes related to her potassium level?

A) Increased U wave amplitude.

B) Prolongation of the P wave.

C) Shortening of the QT interval.

D) Tall, symmetric, peaked T waves.

E) Widening of the QRS complex.

49- A 29 yr old man is brought to the emergency department in a comatose state a few hours after complaining of sudden onset of excruciating headache. Neurologic examination reveals dilated pupils poorly responsive to light. A CT scan of the head without contrast demonstrates hyperdensity within the suprasellar cistern, while MRI is unremarkable. Lumbar puncture shows haemorrhagic cerebrospinal fluid.

Which of the following is the most likely diagnosis?

A) Amyloid angiopathy-related haemorrhage.

B) Cavernous sinus thrombosis.

C) Haemorrhagic infarction.

D) Pituitary apoplexy.

E) Ruptured berry aneurysm.

50- All of the following conditions can present ē spherocytosis in peripheral blood smear except:

A) ABO incompatibility.

B) Thermal injury.

C) Wilson disease.

D) Autoimmune hemolytic anemia.

E) Pneumococcal sepsis.

51- Alopecia areata is associated ē all of the following conditions except:

A) Cataract.

B) Atopy.

C) Hashimoto thyroiditis.

D) Nail dystrophy.

E) Hyperadrenalism.

52- In pt ē chest pain ẃ of the following is most suggestive of a myocardial infarction?

a) Very severe pain.

b) Sweating & vomiting.

c) Pain has lasted for over a week.

d) Pain is sharp like a knife.

53- Which of these is most likely to cause deviation of the trachea?

a) A left basal pneumonia.

B) A small right pleural effusion.

C) Previous tuberculosis of the right upper lobe.

D) Idiopathic fibrosing alveolitis.

54- Which of these features suggest that a crackling sound is more likely due to a pleural friction rub than crackles?

A) More prominent in expiration.

B) Alters ē coughing.

C) No pain over the area.

D) Clubbing.

55- Which of the following is true of a lower motor neurone lesion in the arm?

A) It leads to increased tone in the arm (hypertonia).

B) Fasciculations are never seen.

C) The reflexes are brisk. D) An ulnar nerve palsy is an example of a LMNL.

56- Which of the following is true about radial nerve palsy?

A) The radial nerve arises from the lateral cord of the brachial plexus.

B) It is associated ē sensory loss over the medial half of the hand.

C) It leads to wrist drop.

D) It can occur due to a superficial laceration over the wrist.

57- Which of the following is true about the carpal tunnel syndrome?

A) It can be caused by rheumatoid arthritis.

B) It is caused by compression of the ulna nerve.

C) It causes pain & tingling in the medial three & half digits.

D) Paraesthesia is worse during the day.

58- Which of the following is true about an intention tremor?

A) It is worse at rest. B) It is caused by Parkinson's Disease.

C) It is indicative of a cerebellar lesion.

D) Dyscalculia is a common association.

59- In the assessment of the hand function ẃ of the following is true?

A) Abduction of the thumb is supplied by spinal root T2.

B) Opposition of the thumb by opponens policis is supplied by spinal root T1.

C) Finger adduction is supplied by the median nerve.

D) Finger abduction is mediated by the palmar interossei.

60- Which of the following is true in ulna nerve palsy?

A) The ulna nerve can be affected by a fracture of the spiral groove of the humerus.

B) It gives rise to a positive phalen's sign.

C) It leads to loss of sensation over the medial half of the hand & medial one & a half digits on both palmar & dorsal aspects of the hand.

D) It supplies the biceps muscles.

61- Which of the following is true regarding the examination of the legs?

A) Sustained clonus occurs ē hypotonia.

B) Clonus can only be demonstrated at the ankle.

C) The root value of hip flexion is L4, L5.

D) The root value of toe extension is L5.

62- Which of the following is true regarding reflexes?

A) A positive babinski reflex is the same as a normal flexor response in the assessment of the plantar reflex.

B) An extensor plantar response indicates a LMNL.

C) The root value of the ankle reflex is S1.

D) The root value of the knee reflex is L1, L2.

63- Which of the following is true about the assessment of gait?

A) A stamping gait is caused by bilateral foot drop.

B) An antalgic gait is caused by a painful leg.

C) A waddling gait is sometimes called a steppage gait.

D) An apraxic gait is due to hysteria.

64- Which of the following is true in peripheral neuropathy?

A) Sensory loss is demonstrated in a stocking distribution.

B) The tone is increased bilaterally in the legs.

C) Reflexes are very brisk ē reinforcement.

D) Weakness is more marked proximally than distally.

65- Which of the following is true in spastic paraplegia?

A) Multiple Sclerosis can cause this neurological pattern.

B) Proprioceptive loss is a common feature.

C) Coordination in the legs is affected.

D) The tone is normal or flaccid.

66- When you are taking a musculoskeletal history ẃ of the following is true?

A) Drugs may be implicated in the causation of gout.

B) A history of diarrhoea is not relevant.

C) Difficulty rising from a chair is diagnostic of polymyalgic rheumatic.

D) Joint stiffness of 5 minutes duration suggests an arthropathy.

67- Which of the following is true of rheumatoid arthritis?

A) Rheumatoid factor is present in 25% of rheumatoid cases.

B) It is an example of an oligoarthropathy.

C) Anaemia is a common finding.

D) Heberden's nodes are a feature.

68- Which of the following is true about the knee joint?

A) The knee is a ball & socket joint.

B) A baker's cyst can sometimes be found anterior to the knee.

C) The patellar tap is used to demonstrate an effusion.

D) 'knock knee' deformity is due to bilateral genu varum.

69- Which of the following is true of psoriatic arthropathy?

A) The absence of plaques of psoriasis excludes the diagnosis.

B) The diagnosis can be confirmed by a blood marker.

C) Tophi can sometimes be seen over affected joints.

D) Nail pitting may give a clue to the diagnosis.

70- Which of the following is true of the spine?

A) Back pain is an uncommon complaint.

B) Schober's test is designed to quantify the flexion of the lumbar spine.

C) Ankylosing spondylitis is a cause of hypermobility of the spine.

D) Pregnancy is a cause of loss of lordosis of the lumbar spine.

71- Which of the following is true of Paget's Disease?

A) Bowing of a long bone is a characteristic feature.

B) Spinal cord compression is a common complication.

C) Heart failure is not a recognized complication.

D) Pathological fractures are not a feature.

72- Which of the following is true of facial nerve palsy?

A) Bells palsy is another term for an UMNL.

B) Ramsay Hunt Syndrome is an UMNL secondary to a Herpes Zoster infection.

C) An inability to close the eyelid on the paralysed side indicates a LMNL.

D) In Bell's Palsy the sense of taste is never affected.

73- Which of the following is true of Systemic Sclerosis?

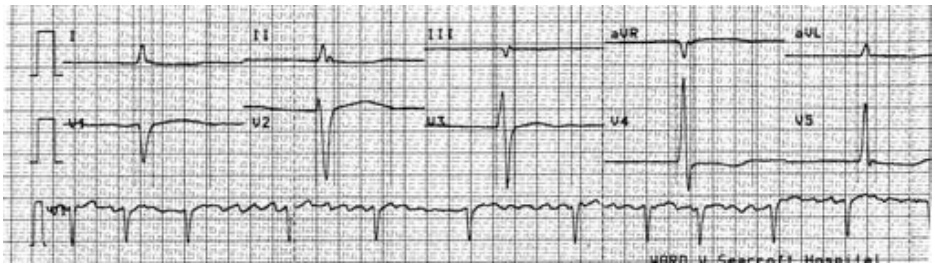
A) It affects males more than females.

B) If telangiectasia are seen this clinches the diagnosis.

C) Arachnodactyly is a feature of the disease.

D) Patients have a beaked shaped nose & waxy skin.

74- Which of the following is true about this ECG ?



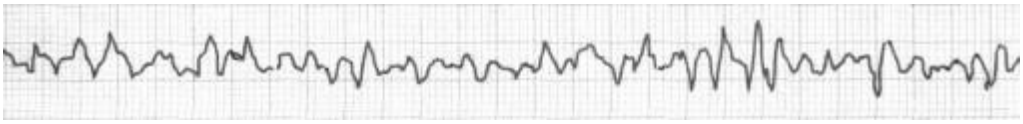
A) This is a trace of sinus rhythm ē atrial ectopics.

B) A pt ē this trace is likely to be unconscious.

C) A pt ē this trace is unlikely to have IHD.

D) A pt ē this trace may be on digoxin.

75- Which of the following is true about this ECG strip?



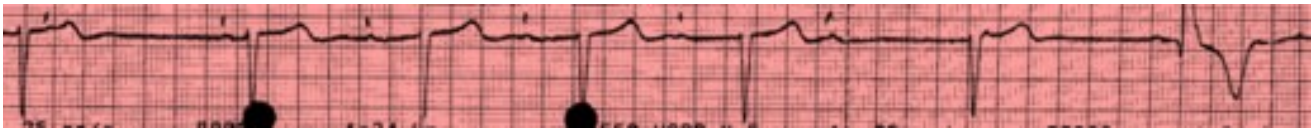
A) The pt ē this trace is like likely to be asymptomatic.

B) The most important treatment to give is adrenaline.

C) The most important treatment to give is DC cardioversion.

D) The pt should be anticoagulated as a priority.

76- Which of the following is true about this ECG strip?



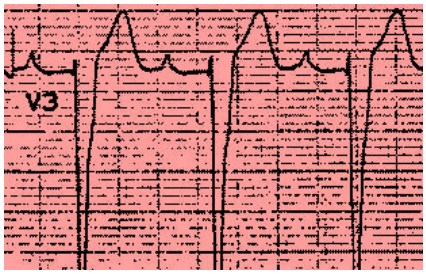
A) This is an example of the Wenkebach phenomenon.

B) This is an example of atrial fibrillation.

C) There is also coexistent anterior myocardial infarction.

D) This is an example of third degree heart block.

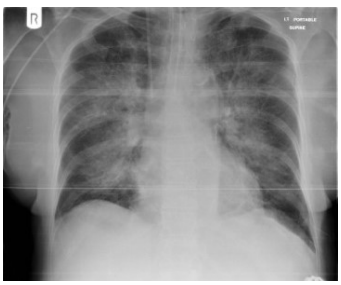
77- Which of the following is true of this ECG strip?



A) The pt is likely to be unconscious. B) The trace exhibits first degree heart block.

C) The pt may have abused cocaine. D) The trace shows right bundle branch block.

78- Which of the following is true about this CXR?



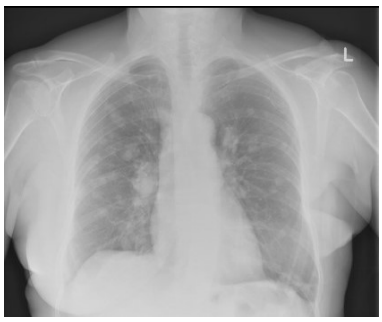
A) The X-ray film was taken in the X-ray department.

B) The X-ray shows pleural plaques.

C) There is cardiomegaly.

D) The pt is likely to be taking diuretics.

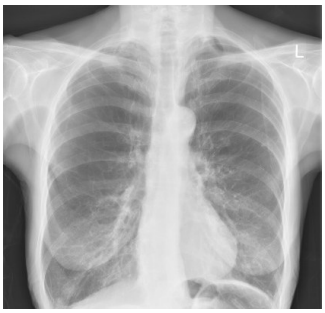
79- Which of the following is true about this CXR?



A) The patient is male. B) The X-ray shows bony metastases.

C) The X-ray shows bronchiectasis. D) The X-ray shows lung metastases.

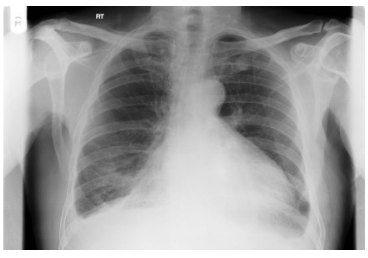
80- Which of the following is true about the CXR?



A) The pt is likely to be a smoker. B) The X-ray shows a widened mediastinum.

C) The X-ray demonstrates surgical emphysema. D) There is cardiomegaly.

81- Which of the following is true about the CXR?

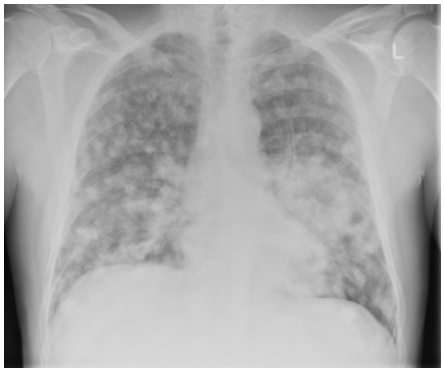


A) This is the X-ray of a very young child.

B) Air under the left diaphragm indicates a perforated viscus.

C) There are bilateral pleural effusions. D) The trachea is deviated to the left.

82- Which of the following is true about this CXR?



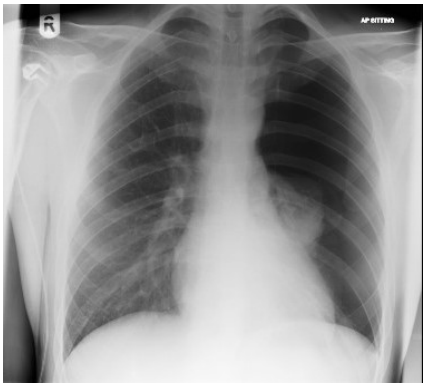
A) The bones are osteopenic.

B) The patient has lung cancer with secondary spread.

C) The patient is likely to have rheumatoid arthritis.

D) The patient has lung fibrosis.

83- Which of the following is true about this CXR?



A) The X-ray is a PA film.

B) This is an example of a cardiac aneurysm.

C) There is an absence of lung markings in the left upper lobe.

D) This is chronic obstructive airways disease ē bulla formation in the left upper lobe.

84- The highest concentration of potassium is in ?

A- Plasma

B- Isotonic saline

C- Ringer lactate

D- Darrow’s solution .

85- A 43 yr old Asian man presents ē headache& neck stiffness. CT brain is normal & a lumbar puncture is performed ē the following results of CSF: Opening pressure: 15cm, Appearance: Cloudy. Glucose: 60 mg//l. Protein: 0.7 g/l. WBCs: 100/ mm^3 (70% lymphocytes). Serum glucose 85 mg/l.

What is the most likely diagnosis?

A) Bacterial meningitis.

B) Viral meningitis.

C) Tuberculous meningitis.

D) Normal CSF result. D) Cryptococcal meningitis.

86- A 35 yr old female is admitted to hospital ē hypovolaemic shock. CT abdomen reveals a haemorrhagic lesion in the right kidney. Following surgery & biopsy this is shown to be an angiomyolipomata.

What is the most likely underlying diagnosis?

A) Neurofibromatosis.

B) Budd-Chiari syndrome.

C) Hereditary hemorrhagic telangiectasia.

D) Von Hippel-Lindau syndrome.

E) Tuberous sclerosis.

87- A 34-year-old woman is admitted to the Emergency Department following a collapse. An ECG shows a polymorphic ventricular tachycardia. Which one of the following is not associated ē ⇧risk of developing torsade de pointes?

A) Tricyclic antidepressants.

B) Subarachnoid haemorrhage.

C) Hypercalcaemia.

D) Romano-Ward syndrome. E) Hypothermia.

88- A 71 yr old woman ē no significant past medical history is investigated for lymphocytosis. She has recently lost 7kg in weight & complains of lethargy. The following blood results are obtained: Hb 9.8 g/dl. Plt 104 * 10^9/l. WBCs 70.3 * 10^9/l. Blood film: Lymphocytosis. Smudge cells seen. Four months previously her WBC count was 30.5 * 10^9/l. What is the most appropriate management?

A) Imatinib. B) Chlorambucil. C) No treatment, monitor full blood count.

D) Fludarabine, Cyclophosphamide & Rituximab.

E) Allogeneic stem cell transplantation

89- A 34 yr old man ē a past history of HIV infection presents to the Emergency De-pa-rtment ē watery diarrhoea. Cryptosporidium infection is confirmed on ZN staining. What is the most suitable management?

A) Metronidazole. B) Sulfadiazine + Pyrimethamine.

C) Supportive therapy.

D) Rifampicin + Ethambutol + Clarithromycin.

E) Co-trimoxazole.

90- A 25 yr old man is referred due to pain & swelling in his knees & ankles. On examinatIon he has a painful, erythematous rash on his legs. The following results are obtained:

- Rheumatoid factor: Negative.
- ESR: 94 mm/hr.
- CXR: Hilar lymphadenopathy.

What is the most likely outcome?

A) Improvement following a course of prednisolone.

B) Scarring and ulceration of skin. C) Spontaneous improvement.

D) Progressive arthritis. E) Renal replacement therapy in 20 yrs time.

91- A 54 yr old man presents ē a variety of physical symptoms that have been present for the past 9 yrs. Numerous investigations & review by a variety of specialties have indicated no organic basis for his symptoms. This is an example of:

A) Munchausen's syndrome. B) Hypochondrial disorder.

C) Dissociative disorder. D) Somatisation disorder.

E) Conversion disorder.

92- A 27 yr old man presents to the Emergency Department ē 2 day history of severe headache & pyrexia (38.2ºC). A CT scan of brain show petechial haemorrhages in the temporal & inferior frontal lobes. No mass. Brain parenchyma otherwise normal.

What is the most likely diagnosis?

A) Brain abscess.

B) Meningococcal meningitis.

C) Cerebral malaria.

D) Herpes simplex encephalitis.

E) New variant CJD.

93- A 25 yr old man has a renal biopsy due to worsening renal function. This reveals linear IgG deposits along the basement membrane.

What is the most likely diagnosis?

A) Systemic lupus erythematous.

B) IgA nephropathy.

C) Minimal change disease.

D) Post-streptococcal glomerulonephritis.

E) Goodpasture's syndrome

94- The serum potassium is measured in a 1000 pts taking an ACE inhibitors. The mean potassium is 4.6 mmol/l ē a standard deviation of 0.3 mmol/l.

Which one of the following statements is correct?

A) 95% of values lie between 4.5 and 4.75 mmol/l.

B) 95.4% of values lie between 4.3 and 4.9 mmol/l.

C) 99.7% of values lie between 4.0 and 5.2 mmol/l.

D) 68.3% of values lie between 4.5 and 4.75 mmol/l.

E) 68.3% of values lie between 4.3 and 4.9 mmol/l.

95- A 54 yr old farm worker presents for review. She has recently been diagnosed ē osteoarthritis of the hand but has no other past medical history of note. Despite regular paracetamol she is still experiencing considerable pain, especially around the base of both thumbs. What is the most suitable next management step?

A) Add oral diclofenac + lansoprazole.

B) Switch paracetamol for co-codamol 8/500.

C) Add topical ibuprofen.

D) Add oral ibuprofen.

E) Add oral glucosamine.

96- A 33 yr old female presents ē a vaginal discharge.

Which one of the following features is not consistent ē bacterial vaginosis?

A) Vaginal pH > 4.5

B) Thin, white homogenous discharge.

C) Strawberry cervix.

D) Clue cells on microscopy.

E) Positive whiff test.

97- Brucellosis (mark true or false)

A) Is caused by a Gram positive bacillus.

B) Causes spondylitis.

C) Is treated ē tetracycline.

D) A recognised cause if chronic depression.

E) Is contracted from unpasteurised milk.

98- Which of the following is NOT a side effect of Digoxin toxicity?

A) Bradycardia.

B) Yellow vision changes.

C) Scooping of the T segment on ECG.

D) Hypokalaemia.

E) Gynecomastia.

99- Which of the following chelating agents is recommended for acute Lead poisoning ē signs of encephalopathy?

A) Succimer.

B) Penicillamine.

C) Dimercaprol.

D) Calcium EDTA.

E) Dimercaprol + Calcium EDTA.

100- Which is true about carcinoma of the bladder:

A) Is primarily of squamous cell origin.

B) Is preferentially treated by radiation.

C) May be treated conservatively by use of intravesical agents even if it invades the bladder muscle.

D) May mimic an acute UTI ē irritability & haematuria.

E) Is preferentially treated by partial cystectomy.

MCQ ANSWERS

1- Correct answer: A) False. B) False. C) True. D) True. E) True.

The upper limit of normal for eosinophils is usually taken to be 0.4x10^9/l. The causes of eosinophilia may conveniently be divided into two groups: parasitic & nonparasitic. In general protazoal infections do not produce eosinophilia. Helminths do cause eosinophilia & the degree of eosinophilia is related to the extent of tissue invasion by the helminth. Filarial worms often cause a high eosinophilia whereas the intestinal nematodes tend to cause only a modest increase in the eosinophil count. Eosinophilic granulomatosis ē polyangiitis , also called Churg-Strauss syndrome, is a type of vasculitis that mainly affects adults aged 30 to 45. It can cause: asthma. allergic rhinitis(cold-like symptoms caused by allergies).

2- Correct answer: A) True B) False. C) False. D) True. E) False.

C. sinensis is the causative organism of oriental liver fluke disease. *A. duodenale & S. japonicum* both gain entry via penetration of intact skin by immature forms. *V. parahaemolyticus* is not uncommonly the causative organism in shellfish-associated gastroenteritis. *P. westermani* causes paragonimiasis (lung fluke). Other infectious diseases associated ē shellfish/raw fish include hepatitis A & gnathostomiasis.

3- Correct answer: A) True. B) True. C) False. D) False. E) False.

All anti-tuberculous drugs may cause anorexia, nausea & vomiting. Pyrazinamide is bactericidal & penetrates the meninges well. Its side effects include fever, liver failure & hyperuricaemia. Isoniazid is generally safe, the most common side effect of it is peripheral neuropathy, this is more common in diabetes & alcoholics. Pyridoxine should always be given to such pts. Slow acetylator status ⇧ risk of neuropathy & of lupus-like syndrome. Other side effects include psychosis, fever & hepatitis. Rifampicin can be given orally or intravenously.

4- Correct answer: A) False. B) True. C) True. D) False. E) False.

Splenectomy typically results in thrombocytosis. Heinz bodies are oxidized, denatured bits of haemoglobin found in G-6-PD deficiency for example. Special stains are required to see Heinz bodies. Asplenic pts are at particular risk of severe pneumococcal infecti-ons. They should receive Pneumovax & lifelong prophylactic penicillin. Asplenic pts also suffer more severe disease following infection ē plasmodium falciparum & haemophilus influenza.

5- Correct answer: A) False. B) False. C) False. D) True. E) False.

The use of steroids in many infections remains controversial. Consensus has been reached for some important infections. Steroids beneficial: Severe typhoid, Hib meningitis in children, Croup, Tuberculoid leprosy, Severe pneumocystis pneumonia, Tuberculous meningitis, Tuberculous pericarditis, Tuberculous pleural effusion, Type 1 lepra reaction, Katayama fever. Steroids of no benefit: Meningococcal disease, Gram negative septicemia, Herpes zoster, Cerebral malaria, Visceral leishmaniasis.

6- Correct answer: A) True. B) False. C) True. D) True. E) False

In hydatid disease the cysts are typically found in the liver & the lung. The cysts in cysticercosis may be multiple, they calcify (therefore become radio opaque) after 4-5 yrs. Nodules in onchocerciasis are less numerous & are usually found over bony prominences. There is also abundant evidence of itching.

7- Correct answer: A) True. B) False. C) True. D) False. E) True.

Young children, elderly & the immunosuppressed may fail to mount an adequate immune response. They are often tuberculin negative in the presence of active disease. In such cases the pts often become tuberculin positive during treatment. BCG vaccination usually results in a positive tuberculin test. Sometimes the tuberculin test remains negative. A strongly positive tuberculin test should always raise the possibility of active tuberculosis. Sputum negative, tuberculin negative pulmonary tuberculosis is

being increasingly diagnosed. The pt may be HIV positive. The diagnosis is based on clinical features, exposure history & CXR appearance. Characteristically in sarcoidosis the pt is tuberculin negative & Kveim positive. However, up to 30% will be tuberculin positive & up to 30% Kveim negative.

8- Correct answer: ALL False

Hookworm is a soil transmitted helminths. The infective larvae (3rd stage larvae), survive in the soil for months. They penetrate intact skin & from there migrate via lymphatics & bloodstream to the lungs. They then travel up the airways to the larynx & into the gut via the oesophagus. b. The threadworm is diagnosed by microscopy of adhesive tape previously placed perianally. Ascaris lumbricoides is sometimes complicated by pancreatitis. The eggs of Necator americanus & Ancylostoma duodenale are indistinguishable on light microscopy. Hookworm rarely, if ever, causes traveller's diarrhea.

9- Correct answer: A) True. B) True. C) True. D) False. E) True.

It is unfortunately true that breast feeding ⇧ the risk of vertical transmission of HIV. High titres of p24 & low CD4 counts also predict poor maternal outcome.

10- Correct answer: A) True. B) True. C) True. D) False. E) False.

The following may cause fever 2 wks & neutropenia: malaria, brucellosis, typhoid, disseminated tuberculosis, visceral leishmaniasis. Viral infections more characteris-tically have lymphocytosis & are often shorter than 2 wks duration. There is neutro-philia in 90% of pts ē amoebic liver abscess.

11- Correct answer: A) False. B) True. C) True. D) True. E) False.

Doxycycline is an acceptable alternative for malaria prophylaxis. It is suitable for short term use & has the additional advantage of protecting against rickettsial infections, plague & leptospirosis. Chloroquine should only be used ē caution as it reduces seizure threshold. Ciprofloxacin & other quinolones should be used ē caution in epilepsy

as they lower seizure threshold & may induce convulsions. Mefloquine is contraindicated in epileptics, in the normal population there is a 1 in 10,000 chance of serious neuropsychiatric complications. The risk is greater in epileptics.

12- Correct answer: A) True. B) False. C) True. D) True. E) False.

In Africa the ratio of male to female cases is 4:1 & most cases occur in the 20-40 yrs age group. It tends to occur at a later age in Asia & Europe. Adriamicin causes tumor regression in 20-30% of cases. Arterial embolization & hepatic resection have some success in selected patients. Hepatitis B, Hepatitis C & Aflotoxin are each associated ē the development of hepatocellular carcinoma. Presentation ē hepatomegaly, abdominal pain & weight loss is typical in endemic areas. In low incidence areas hepatocellular carcinoma usually presents in known cirrhotics. α-fetoprotein is the tumor marker.

13. Correct answer: ALL True.

The leading causes of blindness in the developing world are: cataracts, trachoma, vit. A deficiency. In the developed world senile macular degeneration & diabetes are the major causes of sight loss.

14- Correct answer: A) False. B) True. C) True. D) True. E) True.

Legionella pneumophila is a Gram negative bacterium ẃ was first identified in 1976. It is found widely in water systems & is spread by droplet inhalation. Infection may be associated ē inhalation of free-living amoebae, ē large quantities of Legionella arriving inside the amoebae. Those at increased risk include elderly men, smokers & the debilitated. Outbreaks may occur in hotels &hospitals. Many infections are asymptomatic. After 2-10 days' incubation, presentation is ē fever, rigors, headache, myalgia, cough & breathlessness. Confusion & diarrhoea also occur. Laboratory features include leucocytosis, hyponatraemia & ⇧ liver transaminases. The organism is difficult to culture & the diagnosis is usually confirmed by the detection of rising antibody titres in the

serum. It may take 2-3 wks for serology to become positive. Occasionally Legionella antigen is detected in the urine or sputum.

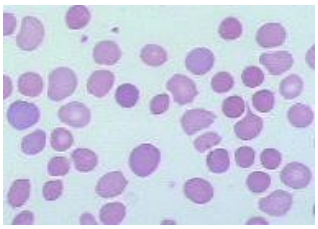
15- Correct answer: A) False. B) False. C) True. D) False. E) False.

VDRL: usually becomes positive 3-4 wks after primary infection, becomes negative about 6 months after treatment, is a marker of disease activity, if accompanied by a negative TPHA & FTA usually indicates a biological false positive. The causes of biological false positive VDRL include; mycoplasma infection, measles, chicken pox, glandular fever, hepatitis, rheumatoid arthritis, SLE, polyarteritis nodosa, malignancy.

FTA: positive in 90% of cases of primary syphilis, positive in all late cases, does not distinguish syphilis from yaws. A negative VDRL ē a positive TPHA & FTA may be due to early primary syphilis, yaws, congenital syphilis, latent, late or treated syphilis.

16- Correct answer: A) True. B) True. C) True. D) False. E) True. Causes of genital ulcers: *Sexually transmitted infections: herpes simplex, syphilis, chancroid, granuloma inguinale, lymphogranuloma venereum. *Not sexually transmitted: Behcet's disease (also mouth lesions), Pemphigus (also mouth & skin lesions), Stevens-Johnson syndrome (also mouth & skin lesions).

17- Correct answer D. Hereditary spherocytosis. Hereditary spherocytosis gene for ankyrin (cell membrane protein) has been mapped to chromosome 8 & is autosomal dominant. It presents in childhood ē jaundice & splenomegaly. Treatment is ē splenectomy.



RBCs are more spherical in hereditary spherocytosis & lack the central area of pallor.

18- Correct answer D. Metoprolol. In uncomplicated AF a β blocker should be used first line for rate control & maintenance of sinus rhythm if the pt has paroxysmal AF.

Flecainide would be a good second line option if AF wasn't adequately controlled.

19- Correct answer C. Metformin is a biguanide. It improves insulin sensitivity & is helpful especially in pts who are overweight as it does not stimulate appetites in the way that sulphonylureas do.

20- Correct answer C. The case scenario is consistent ē primary hyperparathyroidism. PTH enhances active reabsorption of Ca & Mg from distal tubules & of the kidney. As bone is degraded both Ca & Ph are released. It also greatly ⇧ the excretion of Ph, ē a net loss in plasma Ph concentration. By ⇧ the Ca: Ph ratio more Ca is therefore free in the circulation. PTH enhances the absorption of Ca in the intestine by ⇧ the production of activated vit D. PTH up-regulates the enzyme responsible for 1-α hydroxylation of 25-hydroxy vit D, converting vit D to its active form (1, 25-dihydroxy vit D). PTH stimulates bone resorption by osteoclasts.

21- Correct answer D. NSAIDs & hydroxychloroquine are used for skin involvement & arthritis. NSAIDs are used for mild disease. Hydroxychloroquine is useful for disease not controlled by NSAIDs. Steroids are used in moderate to severe disease. Immunosuppressive treatments such as azathioprine & cyclophosphamide are used typically when there is renal or cerebral disease.

22-Correct answer B. posterior inferior cerebellar artery occlusion. Also known as Wallenberg's syndrome, the signs are vertigo, ipsilateral cerebellar signs & weakness, contralateral sensory loss. There is also cranial nerve involvement causing dysphagia & dysarthria.

23- Correct answer C. Left occipital lobe. In homonymous hemianopia, the contralateral occipital lobe is affected (usually infarct).

24- Correct answer B. (Fluoxetine) SSRIs are safer in IHD than tricyclic antidepressants & fluoxetine is the first line choice.

25- Correct answer B. Guillain-Barré syndrome is an acute ascending polyneuropathy eventually affecting the respiratory muscles ẃ usually occurs following infection.

26- Correct answer A. The history suggests Ménières disease ẃ causes sensorineural deafness. Air conduction is better than bone conduction & sounds localise to the un-affected ear (left).

27- Correct answer: D) Haemochromatosis is an inherited disorder ẃ ⇧ absorption of dietary iron ẃ accumulates gradually in the liver, pancreas, skin, joints, heart or endocrine glands causing serious tissue damage. Ferritin & transferrin are raised.

28- Correct answers 1- F) (Hepatitis B). 2- D) (Human papilloma virus). Hepatocellular carcinomas is associated ē hepatitis B infection & warts are caused by human papilloma virus.

29- Correct answer B. (Migraine) Visual aura & nausea are typical of migraine ẃ can occur without a headache. Her age & the short-lived nature of the visual symptoms tends to exclude the other options.

30- Correct answers B. (0.05). Five women out of 100 had a hip fracture when taking calcium supplements. 5/100 = 0.05. & D (0.5). 5/100 for the treated group & 10/100 for the placebo group, so the ratio is 0.5

31-Correct answer B. Incidence is the term used to describe the rate of occurrence of new cases. Candidates should be familiar ē common statistical terms & definitions & understand when they should be used.

32- Correct answer

Side effect	Most likely causative drug
Bone marrow suppression	Methotrexate
Stroke	Diclofenac
Retinopathy	Hydroxychloroquine
Septicaemia	Infliximab

Diclofenac has an increased stroke risk. Methotrexate is associated ē bone marrow

suppression. Cytokine modulators such as infliximab have been associated ē infections, sometimes severe, including TB, septicemia & hepatitis B reactivation. Although GPs do not initiate these drugs, you need to be able to recognize potentially life threatening complications ẃ may present in primary care. Although retinopathy is rare, people taking long-term hydroxychloroquine should have an annual vision check.

33- Correct answer C. The history & clinical findings are typical of central retinal vein occlusion ē hypertension as the underlying risk factor.

34- Correct answers D. The history & pattern of liver function tests are consistent ē hepatitis A & the preceding history is consistent ē this. The correct diagnostic test is hepatitis A IgM (recent infection) rather than IgG. Anti-mitochondrial antibodies are usually positive in primary biliary cirrhosis.

35- Correct answer D. Laparoscopy would enable assessment of the extent of her endometriosis & any further intervention that may be required.

36- Correct answer D. A pt on replacement levothyroxine should be monitored regularly to ensure the dose is correct. Over-replacement is associated ē osteoporosis, ẃ is the most likely diagnosis in this scenario.

37- Correct answer E. Poor fibre intake. The most likely cause of this pt's constipation is dietary, there are no indicators of serious disease in her history & examination.

38- Correct answer E. The pt is most likely to have hyperparathyroidism ẃ is associated ē secondary hypertension & symptoms due to hypercalcaemia such as bone & joint pain, loss of appetite, nausea, tiredness &psychological symptoms (characterized by the classical description of 'stones, bones, abdominal groans & psychic moans).

39- Correct answer E. The history is suggestive of a thrombosed haemorrhoid. Sharp pain without the lump is more likely to be an anal fissure.

40-Correct answer D. This woman has hypertension, amenorrhoea, tiredness, weight gain & hyperglycaemia all secondary to Cushing's disease. This is a rare condition but

easily missed.

41- Correct answers 1- E. This pt has developed a nerve lesion affecting the ocular muscles after a previous episode most likely due to optic neuritis from multiple sclerosis. 2- A. A sudden severe headache in a young person associated ē a neurological deficit is most likely due to SA Hge from a Circle of Willis aneurysm (Berry aneurysm). 3- F). Fatigability affecting extraocular muscle weakness & the association ē other organ specific autoimmune disease is suggestive of myasthenia gravis.

42- Correct answer C. Terbinafine is the first line oral agent for treating T. rubrum nail infections. Fluconazole is less effective for dermatophyte infections but is sometimes used for yeast infections. Topical agents are not successful in any but the most superficial fungal nail infections.

43- Correct answer: B). The history & pattern of LFTs are consistent ē a cholestatic jaundice ē a very high alkaline phosphatase. There are many drugs ẃ can cause this adverse reaction including phenothiazines, flucloxacillin & erythromycin.

44- Correct answer: D). This recurrent vesicular rash is most likely due to herpes simplex, ẃ can occur anywhere on the body, although is most common on lips & genitals

45- Correct answer D. This is a common clinical scenario in real life. Serum ferritin is markedly ⇩ in iron deficiency anaemia & is normal to modestly ⇧ in anaemia of chronic disease. This difference makes this test very useful in this setting. The erythrocyte: granulocyte ratio in bone marrow (choice A) is slightly ⇩ in both iron deficiency anemia & anaemia of chronic disease, but may be markedly ⇧ in sideroblastic anaemia. Polychromatophilic target cells (choice B) & stippled erythrocytes (choice C) are absent in both iron deficiency anaemia & anaemia of chronic disease, but may be present in sideroblastic anemias & other iron-utilization anaemia. Serum iron (choice E) is decreased in both iron deficiency anaemia & anaemia of chronic disease, but may be markedly ⇧ in sideroblastic anaemia.

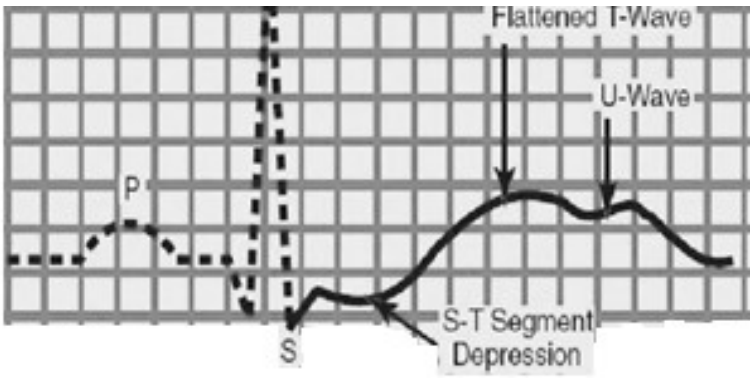
46- Correct answer A. The pt most likely has a worsening of his BP due to erythropoietin. This is seen in about 33% of dialysis pts. Vit D (choice D), iron (choice B) & vancomycin (choice C) generally do not raise BP. The pt is now on dialysis & should not be uremic (choice E).

47- Correct answer F. This pt's clinical picture is consistent ē intoxication ē tricyclic antidepressants such as amitriptyline & imipramine. Toxic effects are mediated by peripheral anticholinergic activity &"quinidine-like" action. The anticholinergic effects include mydriasis, tachycardia, impaired sweating ē flushed skin, dry mouth, constipation & muscle twitching. Quinidine-like effects (due to block of sodium channels in the heart) result in cardiac arrhythmias, especially ventricular tachyarrhythmias. In this setting, prolongation of the QRS complex is particularly important in the diagnosis. QRS width is, in fact, an even more faithful parameter of drug toxicity than serum drug levels. In severe intoxication, pt will develop seizures, severe hypotension & coma. Acetaminophen (choice A) results in liver toxicity & Liver enzymes would be elevated. Alcohol intoxication (choice B) manifests ē respiratory depression, hypothermia & coma. The manifestations of benzodiazepine intoxication (choice C) are similar to alcohol in as much as CNS depression is common to both drugs. Thus, acute benzodiazepine intoxication produces stupor, coma, & respiratory depression. The sympatholytic properties of clonidine (choice D) explain the clinical symptoms of intoxication. Clonidine overdose causes bradycardia, hypotension, meiosis, & respiratory depression. Monoamine oxidase inhibitors (choice E) represent a second-line treatment for major depression. Over-dose induces ataxia, excitement, hypertension& tachycardia. Such reactions can be precipitated by concomitant ingestion of tyramine-containing foods (as cheese & red wine).

48- Correct answer A. Both chronic laxative use & chronic diuretic use can produce hypokalaemia. Severe hypokalaemia ē K level <3 mEq/L, can markedly affect skeletal,

smooth & cardiac muscles. Skeletal muscle effects can include weakness, cramping, fasciculations, paralysis (ē risk of respiratory failure), tetany & rhabdomyolysis. Smooth muscle effects include hypotension & paralytic ileus. Cardiac muscle effects include PVCs & PACs, tachyarrhythmias & AV block. Additional ECG changes can include ST-segment depression, increased U wave amplitude & T wave amplitude less than U wave. The changes illustrated in choices B, C, D & E are characteristic of hyperkalemia.

Hypokalemia
ECG tracing has ST-segment depression, flattened T-wave, and a U-wave.



49- Correct answer E. Headache of sudden onset ("thunderclap" headache), rapid deterioration of mental status & blood in the CSF are virtually diagnostic of ruptured berry aneurysms. Note the characteristic hyperdensity on CT of the suprasellar cistern, indicating blood in the subarachnoid space. Rupture of a berry aneurysm is the most common cause of subarachnoid bleeding. Berry aneurysms develop as a result of congenital weakness at branching points of the arteries in the circle of Willis. These outpouchings tend to expand progressively, but in most cases they remain asymptomatic. Hypertension facilitates development & rupture of berry aneurysm. One third of pts recover, one third die & one third develop re-bleeding. Rapid onset of coma is an ominous sign. Amyloid angiopathy- related haemorrhage (choice A) would manifest as a cortical-based hematoma in a lobar distribution. It is due to accumulation of Aβ amyloid in blood vessel walls. Cavernous sinus thrombosis (choice B) is a rare complication of conditions leading to coagulation abnormalities, such as sepsis, antiphospholipid antibody syndrome & leukaemia. It leads to haemorrhagic infarction of large areas of hemispheric gray & white matter. Haemorrhagic infarction (choice C)

usually develops as a result of embolic occlusion of an intra-parenchymal artery. It gives rise to a hyperdense wedge-shaped area in a cortical field corresponding to a specific vascular territory. Pituitary apoplexy (choice D) refers to haemorrhage in the pituitary gland. It may occur in the setting of a large pituitary adenoma or in pregnancy. It manifests ē rapid onset of panhypopituitarism.

50- Correct answer E: Pneumococcal sepsis does not cause spherocytosis. However, clostridial septicemia ē exotoxemia can cause spherocytosis.

51- Correct answer E: Addison disease (Hypoadrenalism) is associated ē alopecia areata. Alopecia areata is also associated ē pernicious anaemia, ulcerative colitis, vitiligo, collagen vascular diseases & in some cases of Down syndrome.

52- Correct answer B: When a pt ē chest pain is very sweaty & sickly, the chances of a myocardial infarction are high.

53- Correct answer C: The trachea is usually deviated by asymmetrical pathology in the upper lobes. Tuberculosis causes asymmetrical fibrosis ẃ pulls the trachea to that side. Pleural effusions may cause tracheal deviation but only if they are large.

54- Correct answer A: Pleural friction rubs tend to predominate in expiration unlike crackles ẃ tend to be more prominent in inspiration. A pleural rub is not altered by coughing but may be associated ē pain in the region.

55- Correct answer D: An ulnar nerve palsy is an example of a LMNL. It lead to a flaccid tone (hypotonia). Fasciculations are seen occasionally. Reflexes are usually diminished or absent.

56- Correct answer C: The radial nerve arises from the posterior cord of the brachial plexus. It is associated ē sensory loss over the posterior aspect of the hand (lateral half) as well as wrist drop. A superficial laceration of the wrist can injure the median nerve but not the radial.

57- Correct answer A: The carpal tunnel is caused by compression of median nerve. It causes pain & tingling in the lateral three & half digits & this is worse during the night or morning.

58- Correct answer C: An intention tremor is worse on movement rather than at rest. There is no association ē dyscalculia.

59- Correct answer B: Abduction of the thumb is supplied by spinal root T1. Finger adduction is supplied by the ulna nerve and finger abduction is mediated by the dorsal interossei.

60- Correct answer C: It is the radial nerve that is vulnerable to injury by a fracture of the spiral groove of the humerus. The median nerve gives rise to a positive phalen's sign & it is the musculocutaneous nerve ẃ supplies the biceps muscles. Ulnar nerve injury leads to loss of sensation over the medial half of the hand & medial one & a half digits on both palmar & dorsal aspects of the hand.

61- Correct answer D: The root value of toe extension is L5. Sustained clonus is associatedē hypertonia. It can be demonstrated elsewhere such as the knee. The root value of hip flexion is L2, L3.

62- Correct answer C: The root value of the ankle reflex is S1. A positive Babinski reflex is synonymous ē an extensor plantar response & indicates an UMNL. The root value of the knee reflex is L3, L4.

63- Correct answer B: An antalgic gait is caused by a painful leg. A stamping gait is caused by sensory ataxia. The lack of sensation leads to the pt stamping their foot to ⇧ proprioceptive feedback. A steppage gait is different to a waddling gait. An apraxic gait is due to cerebrovascular disease & not hysteria.

64- Correct answer A: Sensory loss is demonstrated in a stocking distribution. Peripheral neuropathy leads to normal or decreased tone. Reflexes are diminished or absent

& reinforcing reflexes is unnecessary if brisk reflexes are obtained. If there is a motor component to the neuropathy the weakness will be distal rather than proximal.

65- Correct answer A: Multiple Sclerosis can cause this neurological pattern. In spastic paraplegic proprioceptive loss is not a feature. Coordination is similarly unaffected. The tone is increased.

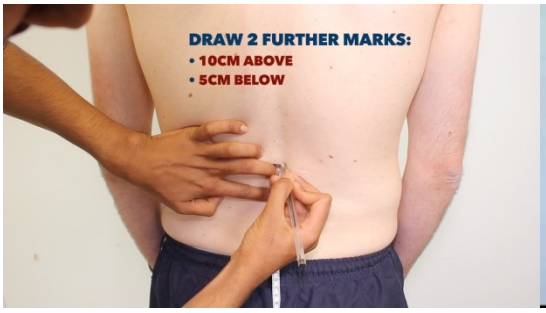
66- Correct answer A: Drugs may be implicated in the causation of gout. Drugs such as diuretics can cause gout. Difficulty rising from a chair can occur ē many musculoskeletal conditions such as arthritis. Joint stiffness of short duration is not significant.

67- Correct answer C: Anaemia is a common finding. Anaemia can be due to a number of causes including the anaemia associated ē chronic conditions. Rheumatoid factor is only present in 80% of rheumatoid cases. It is a polyarthropathy. Heberden's nodes are a feature of osteoarthritis.

68- Correct answer C: The patellar tap is used to demonstrate an effusion. The knee is a modified hinge joint. A Baker's cyst is found posterior to the knee. A 'knock knee' deformity is due to bilateral genu valgum.

69- Correct answer D: Nail pitting & onycholysis are typical features of the naily in psoriatic arthropathy. There is no blood test for psoriatic arthropathy. Tophi are seen in gout.

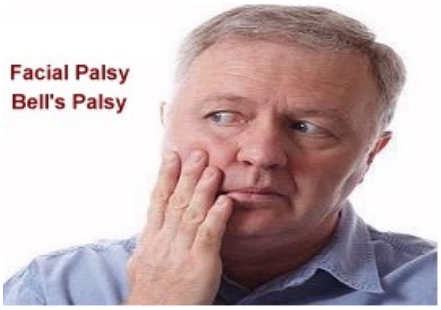
70- Correct answer B: Schobers test is designed to quantify the flexion of the lumbar spine, while the pt is in a standing position the examiner makes a mark approximately at the level of 5^{th} lumbar vertebra. Two points are marked: 5 cm below & 10 cm above this point (for a total of 15 cm distance). Then the pt is asked to touch his/her toes while keeping the knees straight. If the distance of the two points do not increa se by at least 5 cm (ē the total distance > 20 cm), then this is a sign of restriction in the lumbar flexion. This can be useful in examining a pt suspected of Ankylosing spondylitis.



Back pain is common & is one of the major reasons for sick leave in the employed. Ankylosing spondylitis causes decreased mobility of the spine. Pregnancy increases the lordosis of the lumbar spine.

71- Correct answer A: Bowing of a long bone is a characteristic feature. Spinal cord compression is a rare complication. Heart failure is a recognized complication because the highly vascular bone causes high output heart failure. The resulting bone is more fragile & prone to fracture.

72- Correct answer C: An inability to close the eyelid on the paralysed side indicates a LMNL. Bells palsy is a LMNL. Ramsay Hunt syndrome is also a LMNL secondary to Herpes Zoster infection. Sometimes taste is affected if the chorda tympani branch of the facial nerve is involved. The inability to close the eyelid on the paralysed side is known as Bell's phenomenon.



73- Correct answer D: Pts have a beaked shaped nose & waxy skin. Systemic sclerosis affects females more than males. Telangiectasia are present in the disease but can be found in other conditions so are not diagnostic. Arachnodactyly is seen in Marfan's syndrome & it is sclerodactyly ẃ is seen in Systemic Sclerosis.

74- Correct answer D: This is a trace of atrial fibrillation. It is likely that the pt is on tre-atment ē digoxin. The commonest underlying cause for atrial fibrillation is IHD.

75- Correct answer C: The most important treatment to give is DC cardioversion. This is a trace of ventricular fibrillation. This is a life-threatening condition & urgent treatment ē DC shock is mandatory.

76- Correct answer A: This is an example of Wenkebach phenomenon. It is a 2nd degree heart block & is also known as Mobitz type 1 heart block. Note the lengthening PR interval until there is no conduction of the QRS complex. A ventricular ectopic occurs as a ventricular focus compensates for the lack of atrial activity. There is no evidence of a myocardial infarction on this ECG.

77- Correct answer B. This is a trace of 1st degree heart block. The PR interval is approximately 1 large square in duration. The pt is usually asymptomatic.

78- Correct answer D. This is an X-ray of pulmonary oedema & the pt will be on diuretics to try offload fluid. The pt has had a portable taken & there is an ETT suggesting that this pt is on ITU. Pulmonary oedema is usually associated ē cardiomegaly but in this instance the heart is normal size. The fact that the heart is normal sized & the pt is on ITU suggests an acute episode of pulmonary oedema.

79- Correct answer D: This X-ray shows breast cancer ē lung metastases. The pt is fem-ale & the right breast shadow is seen but not the left. This indicates that the pt has had a mastectomy (most likely) for breast cancer. The multiple shadows in the lung substance show lung metastasis.

80- Correct answer A: The pt (female) is likely to be a smoker. This is an X-ray of chron-ic obstrutive pulmonary disease. It is highly likely to have been a smoker.

81- Correct answer C: There are bilateral pleural effusions

This is X-ray of heart failure, there is cardiomegaly & bilateral pleural effusions. The X-ray is of an adult.

82- Correct answer B: The pt has lung cancer ē secondary spread. This is an X-ray of bronchogenic cancer ē widespread metastatic lung spread. The primary cancer is in

the left lung adjacent to the heart border.

83- Correct answer C: There is an absence of lung markings in the left upper lobe. This is an X-ray of a pneumothorax, ẃ is evidenced by the lack of lung markings in the left upper lobe. This gives the lung a deep black appearance compared to the opposite side. The collapsed lung is a knuckle shaped shadow adjacent to the heart border ẃ could be mistaken for a cardiac aneurysm or bronchial neoplasm unless the film is studied carfuely.

84- Correct answer D. Darrow's solution ẃ is a mixture of potassium chloride, sodium chloride & sodium lactate; used in fluid therapy to repair a potassium deficit. also called lactated potassium saline injection.

85- Correct answer B. The CSF lymphocytosis combined ē a glucose > half of serum level points towards a viral meningitis. TB meningitis is associated ē a low CSF glucose The Ziehl-Neelsen stain is only 20% sensitive in the detection of tuberculous meningitis and therefore PCR is sometimes used (sensitivity = 75%). *mumps is unusual in being associated ē a low glucose level in a proportion of cases. A low glucose may also be seen in herpes encephalitis.

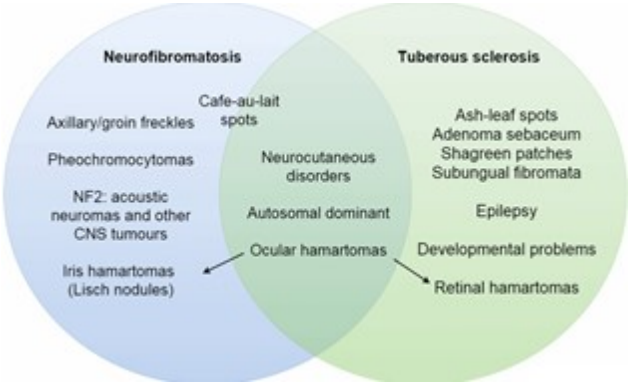
86- Correct answer E. Tuberous sclerosis is a genetic condition of autosomal dominant inheritance. Like neurofibromatosis, the majority of features seen in Tuberous sclerosis are neuro-cutaneous.

Cutaneous features of tuberous sclerosis

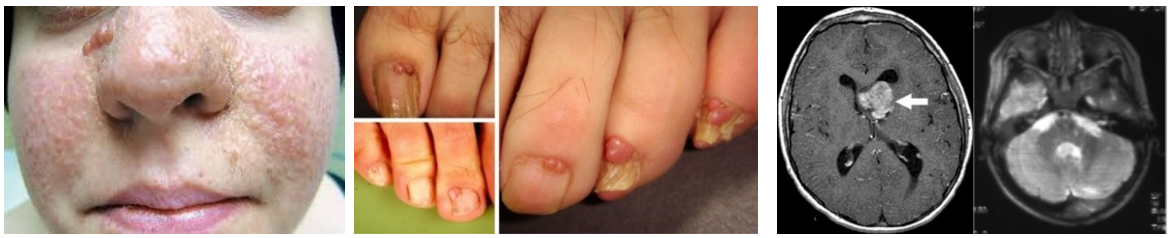
- Depigmented 'ash-leaf' spots ẃ fluoresce under UV light.
- Roughened patches of skin over lumbar spine (Shagreen patches).
- Adenoma sebaceum (angiofibromas): butterfly distribution over nose.
- Fibromata beneath nails (subungual fibromata).
- Café-au-lait spots* may be seen.

Neurological features of tuberous sclerosis

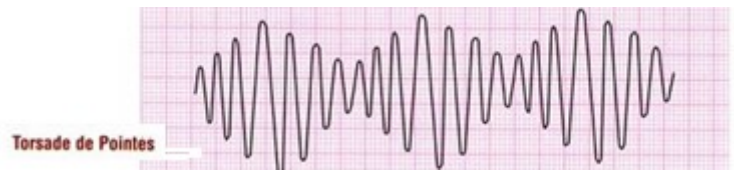
- Developmental delay. Epilepsy (infantile spasms or partial).
- Intellectual impairment.
- Also Retinal hamartomas: dense white areas on retina (phakomata).
- Rhabdomyomas of the heart.
- Gliomatous changes can occur in the brain lesions.
- Polycystic kidneys, renal angiomyolipomata.
- Lymphangioleiomyomatosis: multiple lung cysts.



Comparison of neurofibromatosis and tuberous sclerosis. Note that whilst they are both autosomal dominant neurocutaneous disorders there is little overlap.



87- Correct answer C. Hypocalcaemia, not hypercalcaemia, causes prolongation of the QT interval & hence may predispose to the development of torsade de pointes. It is a specific form of polymorphic VT in pts ē a long QT interval, characterized by rapid, irregular QRS complexes, ẃ appear to be twisting around the ECG baseline. This arrhythmia may cease spontaneously or degenerate into ventricular fibrillation



88- Correct answer D. This pt has CLL. The lymphocyte doubling time is< 6 mont-hs, the pt has some evidence of marrow failure & also has systemic symptoms. She should therefore be treated & of the options given a combination of fludarabine, cyclophosphamide & rituximab (FCR) is the most appropriate treatment. Chlorambucil used to be the first-line treatment of choice but studies have shown it not to be as effective as FCR. As ē many haematological cancers such pts are often entered into randomised trials.

Indications for treatment of CLL include:

- Progressive marrow failure: the development or worsening of anaemia &/or thrombocytopenia.
- Massive (>10 cm) or progressive lymphadenopathy.
- Massive (>6 cm) or progressive splenomegaly.
- Progressive lymphocytosis: > 50% ⇧ over 2 months or lymphocyte doubling time < 6 months.
- Systemic symptoms: weight loss > 10% in previous 6 months, fever >38ºC for > 2 weeks, extreme fatigue, night sweats.
- Autoimmune cytopaenias e.g. ITP.

Management of CLL:

- Pts who have no indications for treatment are monitored ē regular blood counts.

Fludarabine, Cyclophosphamide & Rituximab (FCR) has now emerged as the initial treatment of choice for the majority of pts.

89- Correct answer C. Supportive therapy is the mainstay of treatment in Cryptosporidium diarrhea. Diarrhea is common in pts ē HIV. This may be due to the effects of the virus itself (HIV enteritis) or opportunistic infections. Possible causes include; Cryptosporidium + other protozoa (most common), Cytomegalovirus, *Mycobacterium avium intracellular,* Giardia. Cryptosporidium is an intracellular protozoa & has an in-

cubation period of 7 days. Presentation is very variable, ranging from mild to severe diarrhoea. A modified Ziehl-Neelsen stain (acid-fast stain) of the stool may reveal the characteristic red cysts of Cryptosporidium. Treatment is difficult, ē the mainstay of management being supportive therapy.

90- Correct answer C. The majority of pts ē sarcoidosis get better without treatment. This man has an acute form of sarcoidosis. There are no indications for steroid therapy & his symptoms will resolve spontaneously in the majority of cases.

Sarcoidosis is a multisystem disorder of unknown etiology characterized by non-caseating granulomas. It is more common in young adults & in people of African descent. Sarcoidosis remits without treatment in approximately two-thirds of people. Factors associated ē poor prognosis include: insidious onset, symptoms > 6 months. Absence of erythema Nodosum. Extrapulmonary manifestations: e.g. splenomegaly. CXR: stage III-IV features. Black people.

91- Correct answer D. Somatisation disorder is the correct answer as the pt is concerned about persistent for the past 9 years.

* Hypochondrial disorder: is the persistent belief in the presence of an underlying serious disease, e.g. cancer. Pt refuses to accept reassurance or negative test results.

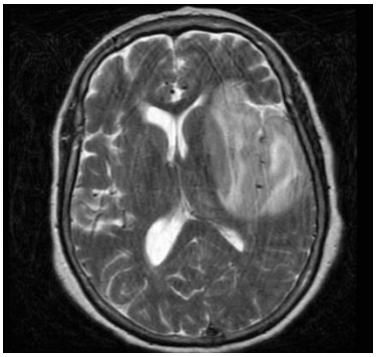
*Conversion disorder: typically involves loss of motor or sensory function. the pt doesn't consciously feign the symptoms or seek material gain.

*Dissociative disorder: process of 'separating off' certain memories from normal consciousness.

*Munchausen's syndrome: intentional production of physical or psychological symptoms ē the intention of financial or other gain.

92- Correct answer D. CT head showing temporal lobe changes - think herpes simplex encephalitis. HSV encephalitis is a common topic in the exam. The virus characteristically affects the temporal lobes - questions may give the result of imaging or

describe temporal lobe signs e.g. aphasia.



The above MRI of a pt ē HSV encephalitis show hyperintensity of the affected white matter & cortex in the medial temporal lobes & insular cortex.

Features of HSV encephalitis: fever, headache, psychiatric symptoms, seizures, vomiting. Focal features e.g. aphasia.

Pathophysiology of HSV encephalitis: HSV-1 responsible for 95% of cases in adults. typically affects temp-oral & inferior frontal lobes

Investigation of HSV encephalitis: CSF: lymphocytosis, elevated protein. PCR for HSV. CT: medial temporal & inferior frontal changes (e.g. petechial haemorrhages) but it is normal in one 1/3 of pts. 'The MRI is better'. EEG changes: lateralised periodic discharges at 2 Hz.

Treatment of HSV encephalitis: intravenous acyclovir.

93- Correct answer E. Goodpasture's syndrome is rare condition associated ē both pulmonary haemorrhage & rapidly progressive glomerulonephritis. It is caused by anti-glomerular basement membrane antibodies against type IV collagen. It is more common in men (sex ratio 2:1) & has a bimodal age distribution (peaks in 20-30 & 60-70 age bracket). It is associated ē HLA DR2.

Features of Good pasture's syndrome: pulmonary haemorrhage followed by rapidly progressive glomerulonephritis. Factors ẃ ⇧ likelihood of pulmonary haemorrhage include: smoking, lower respiratory tract infection, pulmonary oedema, inhalation of hydrocarbons & young males.

Investigations of Good pasture's syndrome: renal biopsy: linear IgG deposits along basement membrane. Raised transfer factor secondary to pulmonary haemorrhages. Management of Good pasture's syndrome: plasma exchange (plasmaphoresis). Steroids. Cyclophosphamide

94- Correct answer E. We know that 68.3% of values of a normally distributed variable lie within 1 SD of the mean. This means the range is 4.3 to 4.9 mmol/l.

Normal distribution: also known as the Gaussian or 'bell-shaped' distribution. It is characterized by:

- Symmetrical i.e. Mean = mode = median.
- 68.3% of values lie within 1 SD of the mean.
- 95.4% of values lie within 2 SD of the mean.
- 99.7% of values lie within 3 SD of the mean.
- Within 1.96 SD of the mean lie 95% of the sample values.
- The range of the mean - (1.96 *SD) to the mean + (1.96 * SD) is called the 95% confidence interval, i.e. If a repeat sample of 100 observations are taken from the same group 95 of them would be expected to lie in that range.

The standard deviation is a measure of how much dispersion exists from the mean. SD = square root (variance).

95- Correct answer C. NICE published guidelines on the management of osteoarthritis in 2014. all pts should be offered help ē weight loss, given advice about local muscle strengthening exercises & general aerobic fitness. paracetamol & topical NSAIDs are 1st -line analgesics. Topical NSAIDs are indicated only for OA of the knee or hand. 2nd -line treatment is oral NSAIDs/COX-2 inhibitors, opioids, capsaicin cream & intra-articular corticosteroids. A proton pump inhibitor should be co-prescribed ē NSAIDs & COX-2 inhibitors. These drugs should be avoided if the pt takes aspirin. The non-pharmacolo- gical treatment options include supports & braces, TENS & shock ab-

sorbing in soles or shoes if conservative methods fail then refer for consideration of joint replacement.

What is the role of glucosamine? it is normal constituent of glycosaminoglycans in car-tilage & synovial fluid. Glucosamine in knee osteoarthritis reported significant short-term symptomatic benefits including significantly reduced joint space narrow-ing & improved pain scores.

96- Correct answer C. A strawberry cervix is associated ē Trichomonas viginalis.

Bacterial vaginosis describes an overgrowth of predominately anaerobic organisms such as Gardnerella vaginalis. This leads to a consequent fall in lactic acid producing aerobic lactobacilli resulting in a raised vaginal pH. Whilst BV is not a sexually trans-mitted infection it is seen almost exclusively in sexually active women. BV may be asymptoma-tic in 50% or associated ē vaginal discharge: 'fishy', offensive.

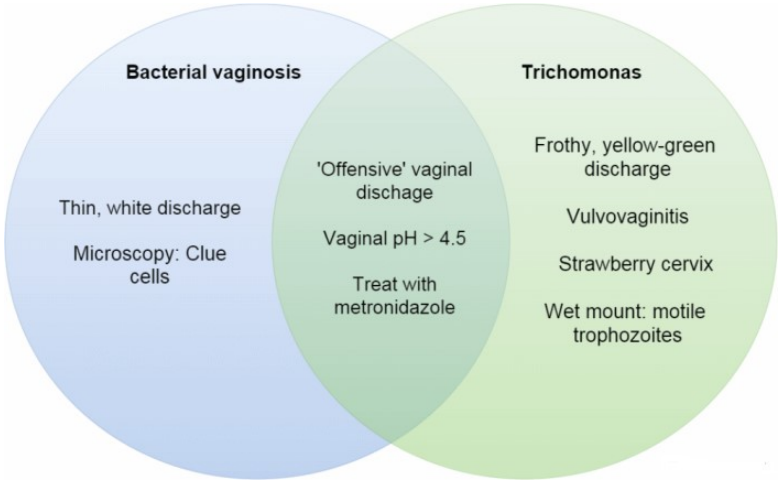
For diagnosis of BV 3 of the following 4 points should be present (Amsel's criteria BV).

1-Thin, white homogenous discharge.

2- Clue cells on microscopy: stippled vaginal epithelial cells.

3- Vaginal pH > 4.5

4- Positive whiff test (addition of potassium hydroxide results in fishy odour).



Bacterial vaginosis in pregnancy results in an increased risk of preterm labour, low birth weight and chorioamnionitis, late miscarriage. It was previously taught that oral metronidazole should be avoided in the 1st TM & topical clindamycin used instead.

Recent guidelines however recommend that oral metronidazole is used throughout pregnancy.

97-Correct answers: A) False. B) True. C) True. D) True. E) True.

The causative organism is a Gram negative bacillus: Brucella abortus (from cows), Brucella suis (from pigs) and Brucella militensis (from goats). Transmission is by oral ingestion of unpasteurised dairy produce. Inhalation of organisms is also an important mode of transmission amongst those dealing ē livestock. The incubation period is 1-3 wks but may be much longer. The disease may present non-specifically & some complications may arise months after infection. It is commonly present ē; fever malaise, sweating, body ache, positive exposure history. The complications of brucellosis include; spondylitis, orchitis, arthritis, endocarditis, depression, meningoencephalitis.

Diagnosis: Blood culture, PCR or Brucella.

Treatment: Doxycycline plus an aminoglycoside for 4 wks & then doxycycline plus rifampicin for a further 8 wks.

98- Correct answer D. Despite the number of pts who come in taking Digoxin, it is important to remember that this medication comes ē a large range of side effects. Bradycardia is a common effect due to the parasympathetic activity of Digoxin. (Note: This is also the reason it works as a second-line agent for rate control of Atrial Fibrillation.) Yellow, halo-like vision changes (think Van Gogh's 'Starry Night') are a more rare, but classic finding. The "scooped" ST segment is also a classic finding, commonly seen on ECGs – I recommend looking this up if you are not familiar ē the appearance of this finding. Gynecomastia is rare side effect of Digoxin. Finally, Hyperkalemia (Not Hypokalaemia) occurs due to Digoxin's primary effect on the Na-K ATPase Pump, blocking Na from leaving & K from entering the cell. It is also important to know that Hypokalaemia can ⇧ digoxin's toxicity by enhancing its binding to the Na-K ATPase Pump.

99- Correct answer E. Succimer is the agent of choice for asymptomatic, mild Lead poisoning (45-70 mcg/dL in children, 70-100 mcg/dL in adults) because it is available PO & has a low side effect profile. Penicillamine is used predominately for the treatment of Wilson's Disease (Copper chelation) & is no longer used in Lead toxicity due to its significant side effect. For severe toxicity ē signs of encephalopathy, Dimercaprol (previously known as BAL; British Anti-Lewisite) is given IM followed by Calcium EDTA via continuous infusion to combine to chelate Lead from the brain & body, respectively. Dosages are as follows:

Succimer: 10 mg/ kg PO Q 8H x 5 days, followed by 10 mg/kg Q 12H for 14 days.

Dimercaprol: 4 mg/kg IM Q 4H x 5 days.

Calcium EDTA: 1500 mg/m2 IV Q 24H via continuous infusion x 5 days (started 4 hours after Dimercaprol).

100- Correct answer D. Carcinoma of the bladder is primarily of transitional cell origin, arising from the transitional epithelium that lines the bladder. It may be confused ē acute UTI by producing urgency, frequency & haematuria. Bladder carcinoma may be treated conservatively using intravesical agents if the tumour is intraepithelial in origin & does not invade through the basement membrane. Neither radiation nor chemotherapy is the treatment of choice for disease that invades the muscle of the bladder. Partial cystectomy may be chosen only when the disease is focal & there are no mucosal changes in other parts of the bladder.

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