

Medicine

Final year case templates

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Acute Flaccid Paralysis

PC – B/L lower limb weakness [duration]

HPC-

- Onset – sudden/ gradual
- Progression of the weakness- rapid or slow, ascending, proximal / distal
- Any sensory loss- sensory level, numbness, tingling
- Bladder & bowel incontinence
- Cord compression
 - Low back pain
 - Weakness of the legs
 - Sensory loss below the compression, numbness
 - Urinary symptoms-hesitancy, frequency, painless retention
 - Bowel symptoms - constipation
 - Exclude causes of cord compression if back pain present
 - a. If onset is chronic
 - Gradual onset
 - History of Breast, lung, prostate CA
 - Severe bone pain
 - Nocturnal bone pain
 - Not responding to analgesia
 - 1. Myeloma –
 - ✓ Back pain
 - ✓ Recurrent infections, easy bruising
 - ✓ Symptoms of anaemia like lethargy, SOB, palpitations
 - ✓ Nocturia, polyuria
 - 2. 1ry tumours –
 - ✓ radicular pain at the level of obstruction which increase with laughing, cough, straining, sneezing
 - 3. Spinal TB-
 - ✓ low grade fever, night sweats, LOA
 - ✓ Previous history of TB, contact history of TB
 - 4. Exclude syringomyelia
 - ✓ Upper limb pain exacerbated by exertion or coughing- typical
 - ✓ Painless upper limb burns due to sensory loss (spinothalamic sensory loss : pain and temperature)
 - ✓ Trophic changes in upper limbs
 - ✓ Difficulty in walking
 - 5. Exclude Motor neuron disease
 - ✓ Dysarthria, dysphagia, nasal regurgitation – cranial nerve involvement
 - b. If it is acute onset
 - 1. Hx of trauma – when, how
 - 2. Epidural haemorrhage/haematoma -
 - ✓ Trauma,
 - ✓ Bleeding disorders
 - ✓ On anticoagulant therapy
 - ✓ Liver disease
 - 3. Acute epidural abscess-
 - ✓ Debilitated patient with DM
 - ✓ Liver failure, renal failure
 - ✓ IV drug abuse
 - ✓ Alcoholic
 - ✓ Very severe pain & tenderness over the area
 - ✓ Pyrexia, malaise, LOA
 - ✓ Rigidity over neck & spinal column

Differential Diagnoses

GBS

Cord compression

Cauda equina syndrome

Transverse myelitis

Channelopathies

4. Cervical spondylosis (vertebral degenerative changes that occur during ageing or due to trauma
 - ✓ Sharp pain worsen with cough
 - ✓ Radiating to shoulders or downward
 - ✓ Feeling of stiffness
 - ✓ Parastheasia, numbness & tingling
 - ✓ Along nerve root distribution
5. Myelopathy
 - ✓ Paraparesis or quadripareisis
 - ✓ LMN feature at the level of lesion
 - ✓ UMN features below

- GBS

Symptoms

- ✓ Acute onset
- ✓ Difficulty in standing up from sitting position or climbing stairs(proximal muscle weakness), unable to walk
- ✓ Initially weakness of legs, symmetrical
- ✓ Progresses upwards & may be weakness of all 4 limbs
- ✓ Rapidly progressive- usually 4 weeks
- ✓ Distal parastheasia, tingling, burning sensation of extremities

Complications

- ✓ Autonomic symptoms
 - Incontinence or retention of urine & stools
 - Dizziness from sitting up – postural hypotension
 - Nocturnal diarrhea
- ✓ Dyspnoea, tightness of chest, DIB – respiratory muscle involvement
- ✓ Diplopia, drooling of saliva - cranial nerve involvement 3, 4, 6, 7
- ✓ Lower cranial nerve weakness - difficulty handling secretions and maintaining an airway

Aetiology

- ✓ Hx of respiratory infection(Mycoplasma, EBV, CMV, Varicella zoster) or blood & mucous diarrhea (Campylobacter jejuni) 1 – 3 weeks ago
- ✓ Hx of rabies or influenza vaccine

- Poliomyelitis(In children)

- ✓ asymmetrical weakness
- ✓ Vaccination against polio

- Paralytic rabies

- ✓ History of animal bite
- ✓ Fever, agitation, abnormal behavior
- ✓ Headache, malaise

- Cauda equina syndrome

- ✓ High lesion
 - Pain over thigh, buttocks & perineum
 - Back pain
 - Leg weakness

- ✓ Low lesion
 - Pain in thigh buttock & perineum
 - Sexual dysfunction
 - Sphincter dysfunction of bladder & bowel (urinary retention, constipation)
- Transverse myelitis
 - ✓ Bladder & bowel symptoms - incontinence
 - ✓ History of viral infection – chicken pox, HIV
 - ✓ History of CTD, SLE
 - ✓ Radiation
- Channelopathies
 - ✓ Previous attacks-Periodic paralysis
 - ✓ After heavy carbohydrate meal
 - ✓ Trigger events
 - Potassium excretion - severe sweating (climbing mountain)
 - High temperature
 - Excitement
 - ✓ Notices the symptoms on next day
 - ✓ Difficulty in speech, swallowing & breathing
 - ✓ Rapid improvement in young patients

SHx

- Housing conditions
- Sexual promiscuity (transverse myelitis)

Examination

- Dyspnoeic, catheterized, cardiac monitor
- Febrile
- In pain
- Conscious

Disease	GBS	Transverse myelitis	Cord compression	Poliomyelitis
Cranial nerves	External ophthalmoplegia in Millar fisher syndrome B/L vii nerve palsy Bulbar weakness	Normal	Normal	Normal
Muscle wasting	Absent			
Tone	Flaccid	Flaccid	Initially flaccid Later spastic	
Power	Symmetrically ↓	↓	↓	Asymmetrical weakness
Reflex	Areflexic		Exaggerated	
Plantar reflex	Down	Up	Up	Down
Sensory	Intact	Sensory level	Sensory level	
Sphincter function	Normal/impaired	Impaired	Impaired	Normal
Cerebellum	(+) ataxia	Normal	Normal	Normal

- Cord compression
 - Determine the level of compression- sensory level
 - Initially flaccid then spastic tone
 - Cervical spondylosis
 - Tenderness, crepitus over neck
 - Radiculopathy
 - Sensory- impairment over dermatome distribution
 - Motor – muscle wasting, weakness
 - Reflexes – impaired
 - Trophic changes
 - Dry scaly skin
 - Myelopathy
 - UMN signs below level
 - Sensory level of impairment
 - Sphincter tone disturb
 - Spinal cord tumour
 - kyphosis
 - Look for 1ry site – breast, lung, kidney, prostate
 - Tenderness over spine (commonly thoracic)
 - Epidural abscess
 - Febrile
 - Tachycardia
 - Neck rigidity
 - Spinal rigidity
 - TB
 - Febrile
 - Wasted
 - Kyphosis
 - Bony tenderness & gibbus

- GBS
 - General
 - Dyspnoeic
 - Respiratory
 - Single breath count
 - Neck muscle weakness- ask to raise the head against resistance
 - Increase RR
 - Reduced chest expansion
 - CNS
 - Gait
 - Cranial nerves- 3, 4, 6, 7
 - Motor-
 - Power reduced
 - Tone reduced
 - Reflexes absent
 - Sensory
 - Distal numbness
 - Few sensory signs
 - Cerebellar signs
 - Ataxia- Miller- fisher syndrome (**Miller fisher Xn – Ataxia, Areflexia, Ophthalmoplegia**)
 - Abdomen
 - Distended bladder
 - DRE – sphincter tone

- Cauda equina syndrome
 - LL wasting
 - Motor
 - Power reduced in muscles of foot- dorsi flexion
 - Sensory
 - Saddle anesthesia
 - Sensory deficit over inner calf
 - Reflexes
 - Increase ankle jerk
 - Brisk knee reflexes
 - Abdomen – bladder distension, DRE to assess sphincter tone

Investigation

- Acute cord compression is an medical emergency (146pg in Emergency medicine)
 - FBC & blood picture
 - BU & SE
 - CSF – protein elevated
 - Epidural abscess
 - ✓ CXR
 - ✓ Blood culture- often +ve
 - Spinal TB
 - ✓ Xray – collapsed vertebrae
 - ✓ MRI- epidural mass, para spinal soft tissue swelling
 - Haematoma – MRI
- GBS (emergency medicine 153, 154pg)
 - CSF – raised protein, normal cell count

Management

- Cord compression (146pg in emergency medicine)
 - Conservative MX
 - ✓ Analgesia
 - ✓ Cervical collar
 - ✓ Traction
 - Surgery
 - ✓ To prevent progression
 - ✓ Indications
 - Progressive neurological deficit
 - Intractable pain
 - ✓ Foraminotomy
 - ✓ Laminectomy
- Spinal cord tumour
 - Radiotherapy
 - Surgical decompression if rapidly deteriorate
 - Dexamethazone
 - Pain relief

- Epidural abscess
 - Urgent Decompression laminectomy
 - Abscess drainage
 - Antibiotics for several weeks
 - Spinal TB
 - Anti TB drugs for 9 months
 - Surgical decompression
 - Hematoma
 - Urgent decompression
 - After correcting coagulation defects
-  Long term management - physiotherapy
- GBS
 - Mainly clinical diagnosis
 - ✓ Nerve Conduction Study – slow conduction / conduction block
 - ✓ LP – CSF shows PROTEIN CELLULAR DISSOCIATION (Positive 10-14 days after the onset)
 - Raised protein 2 – 3 g/l (normal 40mg/dl)
 - Normal cell count
 - Management
 1. Monitoring
 - Monitoring bed
 - Monitor for complications
 - Respiratory muscle paralysis
 - Respirometer (Measure forced vital capacity)
 - ✓ >75ml/Kg – normal
 - ✓ <20ml/Kg – ICU admission needed
 - ✓ <15ml/Kg – Intubate & ventilate
 - Single breath count : >25 → Normal
 - Assess neck muscle weakness
 - RR, Pulse oxymetry (But changes occur at very late stage)
 - Autonomic instability
 - wide fluctuation in blood pressure, postural hypotension, and cardiac dysrhythmias
 - So monitor PR, BP, Cardiac monitoring
 - ✓ 4 hourly in progressive stage (1st 4 weeks)
 - ✓ 6 hourly in plateau stage
 - Specific management
 - Plasmapheresis
 - IVIg - 0.4g /kg/day x 5 days
 - Steroid no benefit

- Supportive care
 - Pain relief – pains are self-limited and often respond to standard analgesics
 - Fluid
 - Nutrition
 - Bladder & bowel care
 - Prevention of bed sores
 - SC heparin prophylaxis for DVT
- Long term management – Physiotherapy & rehabilitation

Prognosis

- Recovery begins (with or without) treatment between several days & 6 weeks from onset
- Approximately 85% of patients with GBS achieve a full functional recovery within several months to a year
- Improvement towards independent mobility is gradual over many months but may be incomplete
- 15% patients die or are left disabled
- Between 5 and 10% of patients with typical GBS have one or more late relapses; such cases are then classified as chronic inflammatory demyelinating polyneuropathy (CIDP)

Discussion

➤ Cord compression

- Acute or chronic
- Initially flaccid paralysis, later become spastic
- Causes of cord compression
 - Spinal cord neoplasms
 - Disc & vertebral lesions
 - Chronic degenerative
 - Trauma
 - Inflammatory
 - Epidural abscess
 - Tuberculosis
 - Granuloma
 - Vertebral neoplasms
 - Metastases
 - Myeloma
 - Epidural haemorrhage

Table 21.47 Causes of spinal cord compression

Spinal cord neoplasms
Disc and vertebral lesions:
Chronic degenerative
Trauma
Inflammatory:
Epidural abscess
Tuberculosis
Granuloma
Vertebral neoplasms:
Metastases
Myeloma
Epidural haemorrhage/haematoma
Rarities
Paget's disease, scoliosis and vertebral anomalies
Epithelial, endothelial and parasitic cysts
Aneurysmal bone cyst
Vertebral angioma
Haematomyelia, arachnoiditis
Osteoporosis with fracture
Cord arteriovenous malformation

➤ Other causes which produce similar presentation

- Syringomyelia
- Motor neuron disease

➤ Syringomyelia

- A fluid filled cavity in cervical or thoracic spinal cord
- Expanding cavity destroys spinothalamic neurones, anterior horn cells, lateral cortico spinal tract
- Spinothalamic sensory loss – loss of pain & temperature
- Trophic changes

- Cervical syrinx
 - Loss of UL reflexes
 - Muscle wasting of hand & forearm
 - Initially spastic
 - Neuropathic joints- trophic skin changes(scars, nail dystrophy) & ulcers

➤ Motor neurone disease

- Degeneration of both upper & lower motor neurone in spinal cord, cranial nerve nuclei in cortex
- Progressive muscular atrophy
 - Wasting begins from small muscles of hand
 - Fasciculation
 - No pain, muscle cramps
- Amyotrophic lateral sclerosis
 - Lateral cortico-spinal tract
 - Muscle atrophy – wasting
 - Spastic
 - LMN signs
 - Fasciculation
- Progressive bulbar & pseudo bulbar palsy
 - Mixed UMN & LMN signs in lower cranial nerves
- Primary lateral sclerosis
 - Rare
 - Confined to UMN

➤ GBS

- Acute inflammatory demyelinating polyneuropathy
- Self limiting
- Picture
 - Rapid progressive onset
 - Plateau
 - Recovery
- Causes
 - Paralysis following infection
 - ✓ *Campylobacter jejuni* - severe GBS
 - ✓ Virus – CMV, EBV, VZV, HIV
 - ✓ Vaccines - Rabies, influenza
 - ✓ 40 % no cause
- Infective organisms induce antibody response against peripheral nerves
- Pathogenesis – Molecular mimicry

Shared antigens between pathogen & surface glycolipids of peripheral nerves.

Immune mediated inflammatory polyradiculo-neuropathy

The target epitopes – Myelin, Axonal membrane, Cerebellum, Cranial nerve nuclei (3,4,6,7), Dorsal route ganglion.

- Other neurological involvement
 - Cerebellum
 - Cranial nerves 3, 4, 6 dorsal root ganglia
 - Miller – fisher syndrome
 - ✓ Ataxia
 - ✓ Ophthalmoplegia
 - ✓ Areflexia
- Distal limb weakness or distal numbness
- Ascends proximally – days to 6 weeks
- Areflexia, sensory symptoms, few sensory signs
- 50 % facial weakness
- Severe
 - Respiratory & bulbar involvement
 - Need ventilation if vital capacity drops to 1L(15ml/kg) or below
 - No signs of dyspnoea
- Protein – cellular dissociation
- NCS –slow conduction velocities or conduction block (MCQ)
- Changes best seen after 10 – 14 days
- GBS unlikely
 - Marked asymmetry of signs
 - Sensory level
 - Persistent bladder, bowel dysfunction
 - Fever at onset
 - CSF cells >50
- High dose IV IG within first 2 weeks reduce duration & severity of paralysis
- Screen for IgA deficiency prior to Ig
 - Severe allergy reaction to IgG
 - Angina or MI can be precipitated by Ig

➤ **Cauda equina syndrome**

- Collection of lumbar sacral roots
- Control movements of thighs, sphincter tone
- B/L flaccid LL weakness
- 2 types
 - High lesions
 - Low lesions
- High –
 - Both UMN & LMN lesion features
 - Pain over thigh, buttock, perineum
- Low
 - S1, S2,S3 affects
 - Only LMN lesion
 - AJ, KJ variable
 - Sphincter dysfunctions- urine retention
 - sexual dysfunction
 - Pain in thigh ,buttock, perineum
 - Saddle anaesthesia – diagnostic

Syringomyelia

The following are typical signs of a substantial cervical syrinx

- Areas of dissociated sensory loss, i.e. spinothalamic loss without loss of light touch. Bizarre patterns are seen.
- Loss of upper limb reflexes.
- Muscle wasting in the hand and forearm.
- Spastic paraparesis – initially mild.
- Neuropathic joints, trophic skin changes (scars, nail dystrophy) and ulcers.
- Brainstem signs – as the syrinx extends into the brainstem (syringobulbia) there is
 - Tongue atrophy
 - Fasciculation
 - Bulbar palsy
 - Nystagmus, Horner's syndrome
 - Hearing loss and impairment of facial sensation.

Blood and mucus diarrhoea.

Age, gender, occupation

DD

1. Inflammatory bowel disease (Ulcerative colitis, Crohn's disease)
2. Amoebic dysentery / Amoebic colitis
3. Bacillary dysentery
4. Diverticulitis
5. Colonic carcinoma

HPC

- Onset
- Frequency
- Duration
- Whether nocturnal
- Nature of stools – steatorrhoea
- Associated features
 - ✓ Abdominal pain
 - ✓ Nausea, vomiting
 - ✓ fever
 - ✓ Loss of appetite
 - ✓ Loss of weight
 - ✓ Malaise, lethargy
 - ✓ Urgency, tenesmus
- Complications
 - ✓ Anaemic features
 - ✓ Features of malabsorption – Nutritional deficiencies, Steatorrhoea
 - Vit. A deficiency - Night blindness, keratosis
 - Vit. K deficiency – Bleeding tendency
 - Vit. D deficiency – Osteomalacia
 - ✓ Dehydration and electrolyte imbalance
 - ✓ Weight loss

❖ Features of IBD

- Colicky abd. Pain or discomfort
- Associated with LOW, LOA, N, V, malaise, lethargy, low grade fever
- Acute or insidious onset
- If insidious onset
 - PHx of recurrences with multiple hospital admissions
 - How and when the diagnosis was made
 - Ix and Mx done up to now
 - SE of medications
 - Hx of surgery
 - Hx of hospital admissions for emergencies – Peritonitis, intestinal obstruction

- Whether nocturnal (**UC**)
- Urgency, tenesmus, faecal incontinence (**UC with rectal involvement**)
- Passing of blood and mucus w/o stools (**UC**)
- Steatorrhoea (**with SI involvement in CD**)
- Other associated features
 - Painful red eye
 - Joint pain
 - Back ache
 - Skin rashes
 - Hx of gall stones, renal stones
 - Hx of liver disease
- Risk factors
 - Hx of smoking – **increase CD but reduce UC**
 - High fat and high sugar diet
 - Good domestic hygiene - **CD**
 - FHx of similar disease
 - PSHx of appendectomy - **increase CD but reduce UC**
- Complications
 - ✓ Obstructive features – stricture
 - ✓ Peritonitis - Intestinal perforations in **CD**
Toxic megacolon in **UC**
 - ✓ Perianal , ischiorectal abscesses
 - ✓ Anorectal fistula
 - ✓ Enteric fistula (faecaluria, faecal vaginal discharge)
 - ✓ Haemorrhoids

} **CD**

❖ Features of Amoebic dysentery /amoebic colitis

- Gradual onset
- For several weeks
- Initially mild intermittent diarrhoea → Blood and mucus diarrhoea
- (Rarely can present as acute onset blood and mucus diarrhoea)
- Abdominal pain
- Fever (10- 30%)
- LOW , LOA, headache
- Poor hygiene, Hx of contaminated food ingestion and hx of toddy consumption.
- Complications
 - Obstructive features –Stricture from chronic infection, Amoeboma causing obstruction or intussusception
 - Severe haemorrhage
 - Amoebic liver abscess – high swinging fever, right hypochondrial pain, malaise

❖ **Features of bacillary dysentery**

- Sudden onset – 24 to 48 hours after the ingestion
- Frequent small volume stools with blood and mucus
- Colicky abd. pain
- Poor hygiene with faeco-oral transmission

❖ **Features of diverticulitis**

- Pain in left iliac fossa
- Fever
- Constipation
- Complications – obstructions, strictures, intestinal perforations

❖ **Features of colonic CA**

- Altered bowel habits
- Abdominal pain
- LOA, LOW
- Faecal incontinence, tenesmus, spurious diarrhea
- Risk factors
 - Low fibre, high fat, high protein diet
 - FHx of colorectal CA and colonic polyps
 - FHx of gastric, breast, endometrial, ovarian, biliary, urinary tract and small intestinal CA

DHx

- Steroids – Cushinoid appearance, proximal myopathy, 2ry DM, osteoporosis
- Cyclosporin - Headache, hypertension, renal impairment, hepatic impairment, GI disturbances
- Sulphasalazine – GI sym., headache, myalgia, arthralgia, agranulocytosis
- Azathioprine – myalgia, arthralgia, malaise, dizziness, GI sym., hair loss, liver impairment

SHx

- Income and occupation (whether a food handler – Amoebic and bacillary dysentery carrier)
- Source of food and water – cleanliness in food handling
- Hygiene – type of toilet and cleanliness
- Level of education and pt's knowledge about the disease (As IBD is a chronic disease)

Examination

- Built – wasted (**Colonic CA**)
- Febrile
- Signs of dehydration
- Signs of anaemia and nutritional deficiency
- Clubbing (**Colonic CA, IBD**)
- Aphthous ulcers in mouth - **CD**
- Red eye
- Joint tenderness and tenderness over the spine
- Erythema nodosum
- Pyoderma gangrenosum

More common in CD

Abdominal Ex

- Tenderness
- Guarding , rigidity – **Acute diverticulitis**
- Masses (**intestinal obstructions, intussusception in IBD and colonic CA**)

DRE

- Anal tags, fissures, fistulas, abscesses, haemorrhoids - **CD**
- Contact bleeding -**UC**

Investigations

FBC

- Leukocytosis - Amoebic dysentery , Bacillary dysentery, Diverticulitis, IBD
- Iron deficient microcytic hypochromic anaemia – right colonic carcinoma, IBD
- Normocytic normochromic anaemia – IBD (anaemia of chronic disease)

ESR /CRP

- Infections, diverticulitis, IBD

Stool full report, stool smears and stool culture

- Pus cells +
- Culture on SS agar, Mc Conkey agar, Selenite broth
- Trophozoites and cysts of entamoeba histolytica +

Colonoscopy

- Aphoid ulcers (superficial ulcers in mild stage)
Cobble stone appearance, Mainly right sided colon and ileum(enteroscopy needed)
Transmural inflammation – **CD**
- Mainly left sided mucosal inflammation - **UC**
- Polyps and tumors – **Colorectal CA**
- Diverticulae - **Diverticulitis**
- Ulceration with normal mucosa in intervening areas and flask shaped ulcer with overhanging/ undermined edges in microscopy – **Amoebic dysentery**
- Ulcers with inflamed intervening mucosa – **Bacillary dysentery**

Serum albumin

- Low in severe **CD**

Serology

- Shigella antibodies
- pANCA antibodies – Positive in **UC** and negative in **CD**

Barium studies

- limited value with the availability of colonoscopy
- Helpful in imaging in the presence of an obstruction

Plain abdominal x – ray

- **In toxic megacolon** – Dilated, thin walled colon with a diameter >5cm
Gas filled and contains mucosal islands

Management

A. Ulcerative colitis

Induction of remission – *In a severe attack of UC*

- **IV corticosteroids** 100mg 6/H with oral aminosalicylates oral
- IV cyclosporine
- IV infliximab (TNF α /tumor necrosis factor antibody)

Maintenance of remission

- **Sulphasalazine** (an aminosalicylate)
- 6 Mercaptopurine
- Mesalamine
- Azathioprine

Surgical Mx

- Sx - subtotal colectomy with end ileostomy or ileorectal anastomosis
- Indications
 - Fulminant acute attack with – Failure of medical Rx, toxic dilatation, haemorrhage, perforation
 - Chronic disease with – Incomplete response to medical Rx, excessive steroid requirement, non compliance with medication and risk of CA

B. Crohn's disease

Induction of remission

- **IV corticosteroids or oral prednisolone**
- Cessation of smoking
- Low fat, low linoleic acid containing diet
- Oral steroids + azathioprine or mercaptopurine

Maintenance of remission

- **Aminosalicylates**
- Azathioprine, 6 Mercaptopurine, Mycophenolate mofetil

For glucocorticosteroid resistance

- Methotrexate
- IV cyclosporine
- Infliximab

Perianal disease

- Ciprofloxacin + Metronidazole

Control diarrhoea

- Loperamide, Codeine

Surgical Mx

- Indications –
 - Failure of medical therapy
 - Complications like toxic dilatation, obstruction, perforation, abscesses, enterocutaneous fistula
 - Failure to thrive in children
- Sx
 - Surgical resection with end to end anastomosis or end ileostomy

C. Amoebic dysentery

Tissue amoebicides – Metronidazole

- ✓ For amoebic colitis and liver abscess

Luminal amoebicides – Diloxanide, Paramomycin

- ✓ To clear the bowels from parasites after treating the tissue invasion

D. Bacillary dysentery

Rehydration
Antibiotics – Amoxicillin, Co trimoxazole

- More sensitive to - **Ciprofloxacin**, Azithromycin, Aminoglycosides, Cefuroxime

E. Diverticulitis

Mild – Oral Cephalosporin / Metronidazole
If severe – Bowel rest , IV fluids, Antibiotics (Metronidazole , Gentamycin /Cephalosporin)

Surgery –

If complicated with perforations, fistula, obstruction, massive haemorrhage

F. Colorectal CA

Surgical resection with end to end anastomosis

Discussion

A. What is diarrhoea

Is the passage of loose stools 3 or more times per day. Each stool is loose and takes the shape of the container. It is due to a disease of the small intestine and leads to fluid and electrolyte loss.

Stool weight is 250g/ day.

B. What is chronic diarrhea

Diarrhoea for > 2 weeks

C. What are the genetic factors for IBD

- IBD 1 – Chromosome 16q 12 NOD 2 gene (CARD 15) gene
 - Associated with a frame shift mutation
- IBD 2 - Chromosome 12q 13 - 15
- IBD 3 - Chromosome 6p
- IBD 4 - Chromosome 14 q

D. Definition of a severe attack of UC

Disease severity

Disease severity can be graded as:

- 1 mild – rectal bleeding or diarrhoea with four or fewer motions per day and the absence of systemic signs of disease;
- 2 moderate – more than four motions per day but no systemic signs of illness;
- 3 severe – more than four motions a day together with one or more signs of systemic illness: fever over 37.5°C, tachycardia more than 90 min⁻¹, hypoalbuminaemia less than 30 g l⁻¹, weight loss more than 3 kg.

E. Role of probiotics used in IBD

Probiotics = Live micro-organisms which compose the enteric micro flora when ingested.

Commonly used strains – Lactobacilli, Bifidobacteria, non-pathogenic E.coli

Germ free animals are susceptible to GI infections and inflammation.

As regulatory signals between bacterial flora and intestinal epithelial cells maintain mucosal integrity.

Therefore with the use of probiotics the GI mucosal integrity is maintained.

Thus probiotics are used in preventing the onset of inflammation and maintaining remission.

F. Extraintestinal manifestations of IBD

- **Eyes** – Uveitis, episcleritis, conjunctivitis
- **Joints (Commonest)** – Peripheral arthropathy, arthralgia, ankylosing spondylitis, inflammatory back pain
- **Skin** – erythema nodosum, pyoderma gangrenosum
- **Liver and biliary tree** – sclerosing cholangitis – **More in UC**
 - fatty liver
- **Nephrolithiasis** – In CD only (5% – 10%)
- **Gall stones** - In CD only (15% – 30%)
- **Venous thrombosis** - More in UC

Above manifestations occur in both UC and CD, but more common in CD. (except for above mentioned)

Summary box 65.4

Complications of UC

Acute

- Toxic dilatation
- Perforation
- Haemorrhage

Chronic

- Cancer
- Extra-alimentary manifestations: skin lesions, eye problems, liver disease

Summary box 65.7

Differences between UC and CD

- UC affects the colon; CD can affect any part of the gastrointestinal tract, but particularly the small and large bowel
- UC is a mucosal disease whereas CD affects the full thickness of the bowel wall
- UC produces confluent disease in the colon and rectum whereas CD is characterised by skip lesions
- CD more commonly causes stricturing and fistulation
- Granulomas may be found on histology in CD but not in UC
- CD is often associated with perianal disease whereas this is unusual in UC
- CD affecting the terminal ileum may produce symptoms mimicking appendicitis, but this does not occur in UC
- Resection of the colon and rectum cures the patient with UC, whereas recurrence is common after resection in CD

G. About bacillary dysentery

- Organisms – *Shigella dysenteriae* -> *Shigella shigae*
Shigella schmitzii
Shigella flexneri
Shigella sonnei
- Faecal oral transmission
- Low infective dose
- Mainly affects small intestine

H. About amoebic dysentery

- Organism – *Entamoeba histolytica*
- Transmission occurs via cysts in the faecal oral route through contaminated food.
- Invasion of wall of colon is by trophozoites.
- Mainly affects large intestine
- 4- 10 % with amoebic colitis are asymptomatic carriers.
- Extracolonic spread of amoebiasis occur via blood. Eg: amoebic liver abscess

I. How to prepare a pt for colonoscopy

- Avoid iron containing food/ drugs for 1/52 prior to the investigation
- Stop clopidogrel for 2/52
- Low fibre diet on the 3 consecutive days prior to the investigation
- On the day of bowel preparation – light diet for breakfast and lunch
- Bowel preparation with polyethylene glycol (An osmotic laxative)
- Clear liquids only since bowel preparation is started
- Fasting for 6 hours prior to the investigation
- Informed written consent

J. What is IBS (irritable bowel syndrome)

- Recurrent abdominal pain or discomfort (>3 / day), for at least 3 days/ month, in the last 3 months associated with 2 or more of the following;
 - Improvement with defecation
 - Onset associated with a change in frequency of stools (>3/ day or <3/day)
 - Onset associated with a change in form/ appearance of stools
- **Types of IBS**
 - IBS with constipation
 - IBS with diarrhoea
 - Mixed IBS
 - Unsubtyped IBS
- **Diagnostic criteria in IBS**
 - Rome III

Mx of IBS

❖ IBS with diarrhoea

- Dietary modifications – Avoid legumes and excess fibre
- Loperamide 2-8mg
- Codeine phosphate 30-90mg
- Amitriptyline
- Alosetron

❖ **IBS with constipation**

- Dietary modifications – Increase roughage
- Lactulose
- Tegaserod
- Lubiprostone

❖ **Other drugs used in IBS**

✓ **Anti spasmatics**

- Mebeverine
- Pepermint oil

✓ **Antidepressants**

- Amitriptylline
- Fluoxetine

✓ **Relaxation therapy**

Ascites / Generalised oedema

HISTORY

Name:

Age:

Sex:

Occupation:

Presenting Complaint: Generalized Body swelling

History Of Presenting Complain:

Differential diagnoses

1. Cirrhosis/chronic liver disease
2. Congestive cardiac failure
3. Nephrotic syndrome
4. Malabsorption
5. Hypothyroidism

1. Presenting Complain
 - For how long?
 - Gradual onset or sudden onset
 - Sites involved
 - Diurnal variation : Heart failure(Ankle swelling towards evening)
 - Associated Symptoms
 - Any precipitating factors
2. Questions to exclude other differential Diagnoses

- Congestive Cardiac Failure
 - Orthopnoea
 - PND
 - SOB (LVF)
- Nocturnal cough
 - Oedema – Ankle oedema towards evening
 - Liver Congestion → Right Hypochondrial Pain
 - Intestinal Congestion → Severe LOA

 **IN CCF ANKLE OEDEMA IS THE COMMONEST PRESENTATION. IF ABDOMINAL DISTENSION IS PRESENT, IT'S THE END STAGE**

- Nephrotic Syndrome
 - Nephrotic → Hypoalbuminaemia → Equal distribution of oedema
 - **Periorbital oedema in the morning**
 - **Frothy urine**
 - Reduction or increase of **UOP → CRF**
 - Past history of any kind of renal disorder(DM,SLE)
- Exclude Malabsorption
 - Steatorrhoea
 - Weight loss
 - Anaemic features (Lethargy, SOB, palpitations)
 - Peripheral neuropathy
- Exclude hypothyroidism
 - Hair loss, tiredness, hoarse voice, dry skin, cold intolerance, constipation, menorrhagia, weight gain, proximal muscle weakness

3. Establish the most probable diagnosis

- Features to support diagnosis of chronic liver disease

 To develop oedema in liver disease, it should have persisted for >6 months. Because albumin takes 6 months of its T½ to reduce.

- Abdominal distension > Ankle oedema (Portal hypertension in addition to hypoalbuminaemia)
 - Jaundice
 - Confusion, Inverted sleep pattern
 - Bleeding tendency : haematemesis/melaena
 - Pigmentation & skin bruising
 - Wasting & LOA
- Whether it's compensated or decompensated
 - Portal hypertension, ascites, Oesophageal & gastric varices & splenomegaly favors decompensation
 - Whether it is stable disease or gradually worsening

4. Assess complication

- Jaundice – Poor uptake, conjugation, excretion → Hepatocellular jaundice
- Ascites & hepato-renal syndrome (due to PHT +/- Hypoalbuminaemia)
- Bleeding tendency
 - ↓ synthesis of clotting factors 2,7,9,10 (Vit K dependant) & 5,6,12,13 (Vit K non dependant)
 - Abnormal clotting factors – Dysfibrrogenaemia
 - Defective platelet function
 - Reduce platelet count (Less production from bone marrow & sequestration in spleen)
- Endocrine and metabolic disturbances
 - Hypoglycaemia
 - Hypocholesterolaemia
 - Pathological fractures : Osteomalacia/osteoporosis (impaired active vit-D₃ production)
 - Hyponadism (↓ oestrogen catabolism and ↓testosterone production : Impotence, testicular atrophy, loss of libido)
 - Altered drug metabolism : drug toxicity
- Hepatic encephalopathy
 - Toxic substances from the gut cause direct damage (eg : NH₃) or act as false neurotransmitter
 - EEG changes
 - Inverted sleep pattern
 - Confusion, drowsiness, convulsions & coma
 - Precipitating factors : ↑ protein load (diet & GI bleed), Electrolyte imbalance (Dehydration, starvation, diuretics & paracentesis), Drugs (Sedatives, hepato toxic drugs), Alcohol binges, Infection (SBP), Constipation
- Hepato-renal syndrome : Renal impairment due to pre-renal failure due to liver cell destruction
Vasodilatation → Reduced renal blood flow → Reduced GFR → Pre renal failure

5. Assess the management of the disease and it's complications

- When did it diagnose ?
- Number of hospital admissions due to complications such as haematemesis, ascitis
- Interventions done : Banding for oesophageal varices
- Constipation

- Dietary control : low protein/low salt diet

6. Aetiology of Chronic liver disease

- Alcohol
 - Commonest cause
 - CAGE questions for addiction

Two "yes" responses indicate that the possibility of alcoholism should be investigated further. The questionnaire asks the following questions:

1. Have you ever felt you needed to Cut down on your drinking?
2. Have people Annoyed you by criticizing your drinking?
3. Have you ever felt Guilty about drinking?
4. Have you ever felt you needed a drink first thing in the morning (Eye-opener) to steady your nerves or to get rid of a hangover?

- Chronic HBV or HCV
 - Hx of hepatitis
 - Blood transfusions, sexual promiscuous behavior, IV drug abuse, Prostitution
- Autoimmune
 - Past Hx and FHx of autoimmune diseases such as **Thyroid disease, Vitiligo, Type I DM**
- NASH (Non-alcoholic steatohepatitis)
 - Past hx of uncontrolled DM
 - Obesity
 - Family Hx
 - Drugs like Tamoxifen
- Metabolic
 - Haemochromatosis
 - Wilson's disease : Tremor, Dysarthria, involuntary movements & eventually dementia, abnormal behavior & movement)
 - Alpha 1 antitrypsin deficiency
- Drugs & toxins
 - Methotrexate, INAH, Anti-psychotics, Methyl dopa
 - Ayurvedic treatment
- Miscellaneous – Biliary cirrhosis
- Cryptogenic

❖ If patient have only ascites

- Malignancy – LOA, LOW, Fever, altered bowel habits
- TB peritonitis – Chronic cough, haemoptysis, night sweating, contact history
- Pancreatic ascites
 - Severe epigastric pain radiating to back
 - Relieve with leaning forward
 - History of DM

- Alcohol, viral infection – mumps, gallstones

Past medical history

Past surgical history

Drug history

Family history

Social history

- Family support
- Occupation
- Social relationships
- Monthly income
- Abstinence from ALCOHOL

EXAMINATION

General

Wasted, thin limbs

Lying uncomfortably with distended abdomen

Signs of chronic liver disease

Icterus

Bilateral parotid enlargement (evidence of chronic alcohol consumption)

Loss of body hair : axillary hair

Spider naevi (portal hypertension)

Bilateral painful gynaecomastia

Dry skin

Palmer erythema

Deputyrens contractures (Alcoholic liver disease)

Testicular atrophy

Ankle oedema

High fever (ongoing infection → hepatic encephalopathy)

Pallor

Hands – Leukonychia, hepatic flaps, clubbing

Hyper pigmented skin, bruises, tattoos, scratches

Cyanosis

Facial puffiness – Periorbital oedema, generalized oedema to suggest CRF

Mask like face, obese, thyroid goiter, bradycardia, slow relaxing reflexes (Hypothyroidism)

Abdomen

Grossly distended

Caput medusa

Dilated veins – Check for direction of flow

Signs of previous peritoneal tap

Splenomegaly >5cm below the costal margin

Hepatomegaly in alcoholic liver disease (In ♀ liver span 7cm, in ♂ 10.5 cm. +/- 2-3cm considered as abnormal)

Ascites – Shifting dullness, fluid thrill

Testicular atrophy

Hepatic bruit (Alcoholic hepatitis & 1ry or 2ry liver CA ; may also seen on alcoholic cirrhosis)

Cardiovascular system

Cardiac failure – Displaced apex beat, gallop rhythm.

Respiratory system

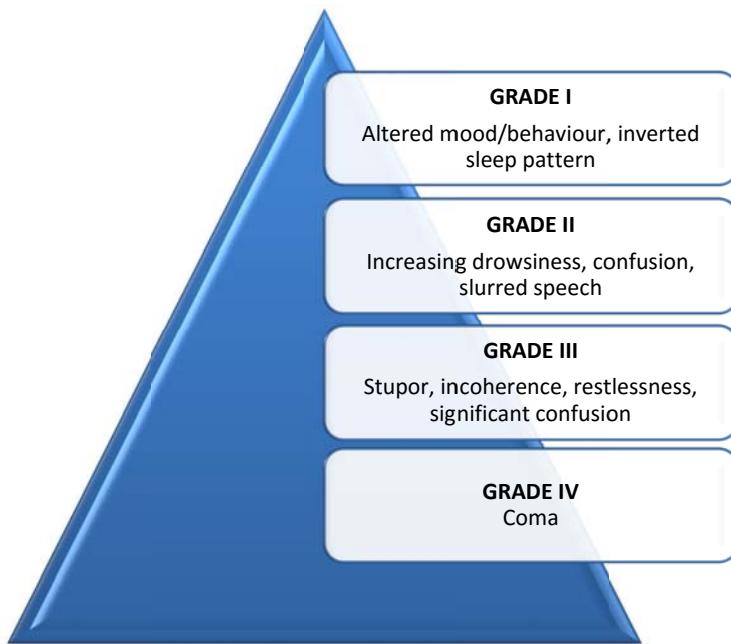
CNS

- Hepatic encephalopathy features
 - Drowsiness, confusion
 - Constructional apraxia : Unable to draw a 5 pointed star & unable to arrange a group of numbers in an ascending order
 - Flapping tremor
 - GCS



Hepatic encephalopathy

As the liver fails, nitrogenous waste(as ammonia) builds up in the circulation & passes to the brain, where astrocytes clear it (by processes involving the conversion of glutamate to glutamine) This excess glutamine causes an osmotic imbalance & a shift of fluid into these cells hence cerebral oedema.



Abnormal behavior & disease

movements suggest Wilson's

SUMMARY

PROBLEM LIST

- Decompensated/compensated due to (eg : alcohol/infection)
- Aetiology – Alcohol, Viral HBV, Wilson's
- Complications – Varices, bleeding tendency, jaundice, pulmonary hypertension
- Social problems/economical problems

INVESTIGATIONS

Severity & complications

- Liver function
 - S. Albumin < 28 g/L
 - PT : Prolonged
- Liver biochemistry
 - Depend on the severity
 - Decompensate disease → all biochemistry is deranged
 - ALP ↑
 - ALT & AST both are ↑
 - ALT/AST ratio is reversed in Established Cirrhosis, Alcoholic hepatitis, or dengue hepatitis
- FBC : Platelet count (↓ due to hypersplenism)
- Serum electrolytes
 - Low sodium indicates severe liver disease due to a defect in free water clearance or to excess diuretic therapy
- Serum creatinine
 - An elevated concentration >130 µmol/L is a marker of worse prognosis
- OGD – To detect evidence of portal hypertension

To detect Aetiology/Type

- Serum α-fetoprotein
 - If >400ng/mL is strongly suggestive of the presence of hepatocellular carcinoma
- Serum autoantibodies – Autoimmune hepatitis
- Viral markers – Viral hepatitis
- Serum immunoglobulins – Viral hepatitis
- Iron indices(TIBC) & s. ferritin – Hereditary haemochromatosis
- 24 hour urine copper & ceruloplasmin levels (Wilson's disease)
- α-1 antitrypsin levels – Cystic fibrosis

Imaging (USS/CT/MRI) : MRI has replace the need of biopsy

- USS

- Changes in size & shape of the liver
- Fatty change & fibrosis produce a diffuse increased echogenicity
- In established cirrhosis there may be marginal nodularity of the liver surface and distortion of the arterial vascular architecture
- The patency of the portal and hepatic veins can be evaluated
- Useful in detecting hepatocellular carcinoma
- Elastography is being used in diagnosis and follow up to avoid liver biopsy

- CT Scan
 - Hepatosplenomegaly, and dilated collaterals in chronic liver disease
 - Arterial phase-contrast-enhanced scans are useful in the detection of hepatocellular carcinoma

- Endoscopy
 - To detect and treat varices & portal hypertensive gastropathy
 - Colonoscopy is occasionally performed for colopathy

- MRI scan
 - Useful in diagnosing of benign tumours such as haemangiomas
 - MR angiography can demonstrate the vascular anatomy and MR cholangiography to image biliary tree

- Liver biopsy
 - Necessary to confirm the severity and type of liver disease
 - The core of liver often fragments and sampling errors may occur in macronodular cirrhosis
 - Special stains are required for iron & copper, and various immunocytochemical stains can identify viruses, bile ducts and angiogenic structures
 - Chemical measurement of iron and copper is necessary to confirm diagnosis of iron overload or Wilson's disease
 - Adequate samples in terms of length and number of complete portal tracts are necessary for diagnosis and for staging/grading of chronic viral hepatitis

MANAGEMENT

OVERVIEW

1. **Treat/avoid cause if possible**
 - a. Abstain from alcohol
 - b. Anti viral drugs for HBV
 - c. Venesection for haemochromatosis
 - d. Penicillamine for Wilson's disease

2. **Treat decompensation**
 - a. Liver failure
 - b. Portal hypertension

3. **Detect / prevent complications / follow up**
 - a. Clinical presentation
 - b. LFT, PT, FBC, Creatinine, electrolytes – 3m
 - c. US abdomen & alpha-feto protein – 6 m
 - d. OGD – 12 m

4. Liver transplantation

2. Treat for decompensation

Management of liver failure

[A] Treat encephalopathy

1. Management of an unconscious patient is appropriate
 - Nurse in semi-prone position
 - NG tube
 - Bladder, bowel & skin care
2. Correct/avoid risk factors
 - Avoid sedatives, diuretics & paracentesis
 - Reduce risk of GI bleeding : PPI
 - Antibiotics if evidence of infection
3. Reduce protein load and gut bacterial flora
 - Metranidazole 400mg po tds
 - Lactulose till bowel opening then 20 ml tds
 - Can use bowel washes and enemas. But there's risk of GI bleeding
 - Restrict oral protein intake during acute HE. Then start 20mg/day until recover from HE. Then increase slowly. 40mg/day → 60 mg/day
4. L-orthinine – L – aspartate IV (expensive)
5. IV mannitol in cerebral oedema

[B] Correct bleeding tendency

Vitamin K IM
FFP/Fresh blood
Platelet concentrates

[c] Nutrition

2000 cal/day (10% dextrose IV)
Vitamin and mineral supplements

[D] Management of ascites

When a patient with portal hypertension presents with ascites

- If there's evidence of encephalopathy
 - No active treatment as it will worsen HE.
 - Except, if there's acute distress
 - Severe abdominal pain
 - Respiratory embarrassment
- ↓
- Do limited paracentesis – 500 ml

- If no evidence of encephalopathy
 1. Restrict salt intake : 5g/day
 2. Spironolactone (Aldosterone antagonist) : Ascites is a hyperaldosterone state
 - 25 mg bd → double the dose every 2-3 days
 - Maximum dose 200mg bd
 3. Add loop diuretic – Frusemide/amiloride
 - Frudemide 40mg/day to 80mg bd
 4. Monitor : weight, abdominal girth, UOP + s. creatinine and electrolytes + look for early evidence of encephalopathy.

If no response → bad prognosis

5. Paracentesis : 5L/day or more if intra-vascular volume can be maintained.
Eg : Salt free albumin – repeated paracentesis often necessary (8g of 20% human albumin for each 1L removed ; 1 bottle 50ml = 10g per bottle; contains 200g/L)
6. Spontaneous bacterial peritonitis
 - If a pt with ascites develops fever and/or abdominal pain → probably SBP
 - Aspirate ascitic fluid (full report/culture)
 - >500 WBC/ml and/or >250 N'phil/ml → Diagnostic of SBP without culture
 - Treat with IV antibiotics
 - Ceftriaxone 1g/tds for 7 days or
 - Norfloxacin 400 mg/daily

A diagnostic aspiration of 10-20ml of fluid should be obtained and the following performed

1. Cell count
Neutrophil count $>250/\text{mm}^3$ is indicative of an underlying SBP
2. Gram stain & culture
For bacteria and acid fast bacilli
3. Protein
A high serum – ascitic fluid albumin gradient $>11\text{ g/dl}$ suggest portal hypertension, and a low gradient $< 11 \text{ g/dl}$ is associated with abnormalities of the peritoneum
Eg : Inflammation, infections, neoplasia
4. Cytology – For malignant cells
5. Amylase – To exclude pancreatitis

Spontaneous bacterial peritonitis

About 8 %

- Organisms gain access to the peritoneum by haematogenous spread
- Most are E.coli, Klebsiella or enterococci

3. Detect or treat complications / follow up

1. Progression of the disease
Monitor the child pugh score – clinically
Do relevant investigations
Monitor for other complication
2. Oesophageal varices
1st visit → Endoscopy → Detect varices
Positive → Annually endoscopy + appropriate treatment
Negative → 2-3 yearly endoscopy
3. Hepatocellular carcinoma
 - Alpha feto protein – non specific
 - Increase : suggest CA
 - Nil : can't exclude CA
 - High risk patients
 - Hep B, C infections
 - Haemochromatosis
 - Follow up
 - With USS abdomen
 - High risk groups : 3 monthly
 - Others : 6 monthly
 - Why USS frequently
 - Detect CA > 2cm
 - To detect CA early, which is suitable for local treatment – increase prognosis
 - Why not CT? It gives more detail
 - High radiation and high cost
 - Can detect 1 cm CA, But management is conservative till 2 cm
 - So it's less useful
 - Treatment modalities
 - Till 2 cm → Conservative management
 - 2-5cm → Need treatment
 - Best are transplant or lobectomy
 - But hear,
 1. Alcohol injection – 100% injection
 - Useful for single lesion
 - Tumour will be necrosed
 2. TACE
 - Trans arterial chemo embolisation
 - Radio ablation to surrounding area
 - But after TACE – some surrounding tumour can regrow
 - So need to follow up with alcohol injection
 3. Local resection
 - Problems already reduce functioning liver cells
 - Increase risk of bleeding

4. Liver Transplantation

Indications

1. Acute liver disease – Fulminant hepatic failure of any cause, including acute viral hepatitis
2. Chronic liver disease

All patients with end-stage(Child's grade C) Cirrhosis

1. Primary biliary cirrhosis

When their serum bilirubin is persistently $> 100 \mu\text{mol/L}$ or symptoms such as itching are intolerable.

2. Chronic hepatitis B

3. Chronic hepatitis C

- Most common indication

4. Autoimmune hepatitis

In patients who have failed to respond to medical treatment or have major side effects for corticosteroid therapy. But can recur

5. Alcoholic liver disease

Well motivated patients who have abstained from alcohol for 6 months will be eligible.

6. Primary metabolic disorders

Examples are Wilson's disease, hereditary haemochromatosis and α -1 antitrypsin deficiency

7. Other

Sclerosing cholangitis

Contraindications

Absolute contraindications

- Active sepsis outside the hepatobiliary tree
- Malignancy outside the liver
- Liver metastases (Except neuroendocrine)
- Patient is not psychologically committed

Relative Contraindication

- Extensive splanchnic venous thrombosis
- Aged 65 years or over
- Hepatocellular carcinoma
 - Recurrence rate is high unless there are fewer than 3 small ($< 3\text{cm}$) lesions, or a solitary nodule of $< 5\text{cm}$

Rejection

• Acute or cellular rejection

- Is usually seen 5-10 days post transplant

• Chronic ductopenic refection

- Is seen from 6 weeks to 9 months post transplant, with disappearing bile ducts (vanishing bile duct syndrome , VBDS) and an arteriopathy with narrowing and occlusion of the arteries.
- Early ductopenic rejection may rarely be reversed by immunosuppression, but often requires transplantation

- **Graft Versus Host disease** – Extremely rare

Prognosis

Elective liver transplantation in low risk patients has a 90% 1 year survival. 5 year survival are as high as 70-85%.

DISCUSSION

Prognosis of cirrhosis

Child-pugh score

3 investigations

1. S. Bilirubin
2. S. Protein
3. PT/INR

2 clinical features

4. Ascites
5. Encephalopathy

Score	1	2	3
S. bilirubin (mg/dl)	<2	2-3	>3
S. albumin (g/l)	>35	28-35	<28
PT (sec. pr) / INR	<4 / <1.7	4-6 / 1.7-2.3	>6 / >2.3
Ascites	None	Mild	Marked
Encephalopathy	None	Mild	Marked

- Score <7 = Child's grade A, survival 15 - 20 yrs
- 7-9 = Ch grade B, for liver transplantation evaluation
- >9 = Child's Grade C, survival < 1yr

This is an imperfect scoring system in term of prognosis

1. It does not include PORTAL HT
 - i. Reduce platelets
 - ii. USS – mild splenomegaly, dilated portal vein > 1 cm

- iii. Oesophageal varices
- 2. Hepatorenal syndrome
 - Pre renal type renal failure due to renal hypoperfusion
 - Detected by S.creatinine level
- 3. Dilutional hyponatremia
 - Activated rennin – Angiotensin – Aldosterone system
 - Na and H₂O retention. But more H₂O than Na⁺
 - DDs – SIADH
 - But cirrhotics can get SIADH following an infection
 - Eg : LRTI

✓ In SIADH :	Serum Osmolality ↓	Urine Osmolality ↑
✓ Dilutional hyponatremia :	Serum Osmolality ↓	Urine Osmolality ↓
 - How to manage
 - ✓ Dilutional hyponatremia - Restrict fluid intake 1-1.5 L/ day
 - ✓ SIADH – 3 % NaCl

How to advise a patient with cirrhosis

- It is a chronic liver problem
- Part of liver damaged and replaced by scarred tissue
- But you need 25% of liver to survive. It can regenerate and come to a compensate state.
- We can stop the damage or slower the progression by eliminating the cause
 - o Eg : Hep B/C – Medication
 - o Haemochroatosis – venesection
 - o Wilson's- penicliiamine
 - o Alcoholic – Stop alcohol
 - o Auto immune – Immunosuppressive therapy
- But as it is chronic disease cant do anything to damaged part
- Can develop complication at any time
- Can have complete cure with liver transplant
- Till then you have to come to the clinic for follow up : Complication and to monitor the progression

Complications and effects of cirrhosis

- Portal hypertension
- Variceal haemorrhage
- Ascites
- Portosystemic encephalopathy
- Porto-pulmonary hypertension
- Hepato-pulmonary syndrome
- Primary hepato cellular carcinoma

Portal Hypertension

Portal vein is formed by the union of **Superior mesenteric and splenic veins**. The pressure within it is normally 5-8 mmHg with only a small gradient across the liver to the hepatic vein in which blood is returned to the heart via inferior vena cava.

Causes of portal hypertension

Prehepatic	Posthepatic
Portal vein thrombosis	Budd-Chiari syndrome
Intrahepatic	Veno-occlusive disease
Cirrhosis	Right heart failure (rare)
Hepatitis (alcoholic) Idiopathic non-cirrhotic portal hypertension	Constrictive pericarditis
Schistosomiasis Partial nodular transformation Congenital hepatic fibrosis Myelosclerosis (extramedullary haemopoiesis)	
Granulomata	

Classification

1. **Prehepatic** – Due to blockage of the portal vein before the liver
2. **Intrahepatic** - Due to distortion of the liver architecture, which can be pre-sinusoidal (eg: in schistosomiasis) or postsinusoidal (eg : in cirrhosis)
3. **Posthepatic** –Due to venous blockage outside the liver (rare)

As portal pressure rises above 10-12 mmHg, the compliant venous system dilates and collaterals occur within the systemic venous system

1. Gastro-oesophageal junction
2. Rectum
3. Left renal vein
4. Diaphragm
5. Retroperitoneum
6. Anterior abdominal wall via the umbilical vein.

The collaterals at the gastro-oesophageal junction (Varices) are superficial in position and tend to rupture

Porto-systemic anastomoses at other sites seldom give rise to symptoms

Rectal varices

The microvasculature of the gut becomes congested giving rise to portal hypertensive gastropathy and colopathy, in which there is **punctuate erythema** & sometimes **erosions**, which can bleed.

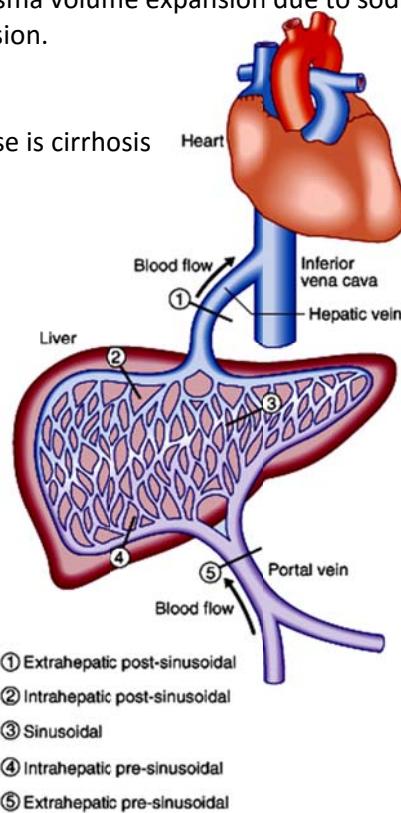
Pathophysiology

- Portal vasculature resistance is increased in chronic liver disease
- During liver injury, stellate cells are activated and transform into myofibroblasts
- Contraction of these activated cells contributes to abnormal blood flow patterns and increased resistance to blood flow.
- In addition the balance of fibrogenic and fibrolytic factors is shifted towards fibrogenesis.
- This increased resistance leads to portal hypertension and opening of portosystemic anastomoses in both pre-cirrhotic and cirrhotic livers.
- Neoangiogenesis also take place. Patients with cirrhosis have hyperdynamic circulation.
 - This is thought to be due to release of mediators, such as nitric oxide and glucagon, which leads to peripheral and splanchnic vasodilatation.

This effect is followed by plasma volume expansion due to sodium retention, and this has a significant effect in maintaining portal hypertension.

Causes

The commonest cause is cirrhosis



Pre-hepatic causes

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- Extrahepatic blockage is due to portal vein thrombosis

Some cases are due to some cases are due to portal vein occlusion secondary to congenital portal venous abnormalities or neonatal sepsis of the umbilical vein.

- Inherited defects causing prothrombotic conditions, e.g. factor V Leiden.
- Patients usually present with bleeding, often at a younger age. They have normal liver function and, because of this, their prognosis is good.

Investigations

- USS with Doppler imaging
- CT
- MR angiography

Treatment

- Usually repeated endoscopic therapy
- Non selective beta blockers
- Splenectomy is only performed if there is isolated splenic vein thrombosis
- Anticoagulation
 - Prevents further thrombosis, and does not increase the risk of bleeding
 - It is used when there is a high risk of recurrent thrombosis.

Intra-hepatic causes

Although cirrhosis is the most common intra hepatic cause of portal hypertension

- Non-cirrhotic portal hypertension
 - Mild portal tract fibrosis
- Schistosomiasis with extensive pipe-stem fibrosis

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- Commonest cause, but is confined to endemic areas like Egypt and Brazil
- Other
 - Congenital hepatic fibrosis
 - Nodular regenerative hyperplasia
 - Partial nodular transformation

Post-hepatic causes

- Prolonged severe heart failure with tricuspid incompetence
- Constrictive pericarditis
- The Budd-Chiari syndrome

Clinical features

Often asymptomatic

Only clinical evidence is splenomegaly

Clinical features of chronic liver disease are usually present and may include

- Haematemesis or melena from rupture of gastro oesophageal varices or portal hypertensive gastropathy
- Ascites
- Encephalopathy
- Breathlessness due to porto-pulmonary hypertension or hepatopulmonary syndrome (rare)

Variceal haemorrhage

- Approximately 90% of patients with cirrhosis will develop gastro-oesophageal varices, over 10 years but only 1/3 of these will bleed from them
- Bleeding is likely to occur
 - With large varices
 - Red signs on varices (diagnosed at UGIE)
 - Severe liver disease

Management

- 1. Active bleeding episode**
- 2. Prevention of re-bleeding**
- 3. Prophylactic measures to prevent the 1st haemorrhage**

Prognosis depends on the severity of the underlying liver disease.

1. Initial management of acute variceal bleeding

Emergency medicine notes – Attached at the end of this document

Resuscitation

- Assess the general condition of the patient
 - Pulse, BP, GCS
- Insert an IV line and obtain blood for
 - Grouping & DT
 - Hb

- PT/INR
 - BU/SE, S. Creatinine
 - Liver biochemistry
 - Blood cultures
- Restore blood volume with plasma expanders or if possible, blood transfusion.
Prompt correction of hypovolaemia is necessary in patients with cirrhosis as their baroreceptor reflexes are diminished.
- Ascitic tap
- Monitor for alcohol withdrawal. Give IV Thiamine 100mg daily
- Start antibiotics prophylactically -3G cephalosporins
 - Cefotaxime

Urgent UGIE

- Endoscopy should be performed to confirm the diagnosis of varices.
- It also excludes bleeding from other sites(eg: Gastric ulceration) or portal hypertensive (or congestive) gastropathy.
- Propranolol is the best treatment for this gastropathy

Injection sclerotherapy or variceal banding

- Scerosing agent that may arrest bleeding by producing vessel thrombosis.
- A needle is passed down the biopsy channel of the endoscope and sclerosing agent is injected into the varices.
- Alternatively, banded by mounting a band on the tip of the endoscope, sucking the varix just into the end of the scope and dislodging the band over the varix using a trip-wire mechanism.
- **Acute variceal sclerotherapy and banding are the treatment of choice ; they arrest bleeding in 80% of cases & reduce early re-bleeding.**

Other measures available

1. Vasoconstrictor therapy

The aim of vasoconstrictor agents is to restrict portal inflow by splanchnic arterial circulation.

- Terlipressin

This is only vasoconstrictor shown to reduce mortality

- 2mg 6/H
- Reducing 1mg 4/H after 48 hours
- It should not be given to patients with IHD
- The patients will complain of abdominal colic, will defecate and have facial pallor owing to the generalized vasoconstriction.

- Somatostatin

- This drug has few side effects
- Infusion of 250-500 μ g/hr appears to reduce bleeding, but has no effect on mortality
- Used if there are contraindications to terlipressin

2. Balloon tamponade

● This procedure is used mainly to control bleeding if endoscopic therapy or vasoconstrictor therapy has failed or is contraindicated or if there is exsanguinating haemorrhage.

- The tube should be left in place for up to 12 hours and removed in the endoscopy room prior to the endoscopic procedure.

- The usual tube is a four –lumen Sengstaken-Blakemore.
- The tube is passed into the stomach and the gastric balloon is inflated with air and pulled back.
- The oesophageal balloon should be inflated only if bleeding is not controlled by the gastric balloon alone.
- This technique is successful in up to 90% of patients and is very useful in the first few hours of bleeding. However,

Complications

- Aspiration pneumonia
- Oesophageal rupture
- Mucosal ulceration,

Additional management of acute episode

- Measures to prevent encephalopathy
 - Portosystemic encephalopathy (PSE) can be precipitated by a large bleed (since blood contains protein)
- Nursing
 - Patients require HDU/ICU care
 - Kept NBM until bleeding has stopped
- Sucralfate 1g 4 times daily given to reduce oesophageal ulceration following endoscopic therapy.

Management of an acute re-bleed

- Re-bleeding occurs in 20% - 30% within 5 days after a single session of therapeutic endoscopy. The source of bleeding should be established by endoscopy.
- It is sometimes due to a sclerotherapy induced ulcer or slippage of a ligation band.
- Management starts with repeat endoscopic therapy – once only to control re-bleeding (further sessions of sclerotherapy or banding are not advisable).

Transjugular intrahepatic portacaval shunt (TIPS)

TIPS is used in cases where the bleeding cannot be stopped after two sessions of endoscopic therapy within 5 days.
In this technique,

- A guide wire is passed from the jugular vein into the liver and an expandable metal shunt is forced over it into the liver substance to form a channel between the systemic and portal venous systems.
- It reduces the hepatic sinusoidal and portal vein pressure by creating a total shunt, but without the risks of general anaesthesia and major surgery.
- TIPS is useful in the short term.
- But recurrent portal hypertension owing to stent stenosis or thrombosis occurs.
- Collaterals arising from the splenic or portal veins can be selectively embolized.

Emergency surgery

- This is used when other measures fail or if TIPS is not available and, particularly, if the bleeding is from

gastric fundal varices.

- **Oesophageal transection and ligation of the feeding vessels** to the bleeding varices is the most common surgical technique.
- Acute portosystemic shunt surgery is infrequently performed

2. Prevention of recurrent variceal bleeding

- Following an episode of variceal bleeding, the risk of recurrence is 60-80% over a 2-year period with an approximate mortality of 20% per episode.

Long-term measures

Non-selective beta-blockade - Oral propranolol

Portal inflow is reduced by two mechanisms

1. By a decrease in cardiac output.
2. By the blockade of β_2 vasodilator receptors on the splanchnic arteries, leaving an unopposed vasoconstrictor effect.

As effective as sclerotherapy and ligation.

It is the treatment of first choice.

Endoscopic treatment

- The use of repeated courses of banding at 2-weekly intervals leads to obliteration of the varices.
- Follow-up endoscopy with ablation should be performed.
- Banding is superior to sclerotherapy.

Transjugular portosystemic stent shunt

- These reduce re-bleeding rates compared to endoscopic techniques but do not improve survival, and increase encephalopathy.

Devascularization procedures including oesophageal transection do not produce encephalopathy, and can be used when there is splanchnic venous thrombosis.

Liver transplantation is the best option when there is poor liver function.

3. Prophylactic measures

- Patients with cirrhosis and varices, who have not bled, should be prescribed non-selective beta-blockers (e.g. propranolol).
- This reduces the chances of upper GI bleeding, may increase survival and is cost-effective.
- If there are contraindications or intolerance, variceal banding is an option.
- Beta blockers do not prevent development of varices.

Ascites

Ascites is the presence of fluid within the peritoneal cavity and is a common complication of cirrhosis.

The pathogenesis of the development of ascites in liver disease is controversial, but is probably secondary

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to renal sodium and water retention.

Several factors are involved.

- *Sodium and water retention*
 - As a result of peripheral arterial vasodilatation and consequent reduction in the effective blood volume. Nitric oxide has been postulated as the putative vasodilator, although other substances (e.g. atrial natriuretic peptide and prostaglandins) may be involved.
 - Activation of sympathetic nervous system and the rennin-angiotensin system
- *Portal hypertension* exerts a local hydrostatic pressure and leads to increased hepatic and splanchnic production of lymph and transudation of fluid into the peritoneal cavity.
- *Low serum albumin* (a consequence of poor synthetic liver function)

In patients with ascites, urine sodium excretion rarely exceeds 5 mmol in 24 hours. Loss of sodium from extrarenal sites accounts for approximately 30 mmol in 24 hours.

The normal daily dietary sodium intake may vary between 120 and 200 mmol, resulting in a positive sodium balance of approximately 90-170mmol in 24 hours (**equivalent to 600-1300 mL of fluid retained**).

The serum-ascites albumin gradient

High serum-ascites albumin gradient (>11 g/dl)

- Portal hypertension (Eg : Hepatic cirrhosis)
- Hepatic outflow obstruction
- Budd-chiari syndrome
- Hepatic veno-occlusive disease
- Cardiac ascites
- Tricuspid regurgitation
- Constrictive pericarditis
- Right heart failure

Low serum-ascites albumin gradient (<11g/dl)

- Peritoneal carcinomatosis
- Peritoneal TB
- Pancreatitis
- Nephrotic syndrome

Causes of ascites divided according to the type of ascitic fluid	
Straw-coloured	Chylous
Malignancy (most common cause)	Obstruction of main lymphatic duct (e.g. by carcinoma) - chylomicrons are present
Cirrhosis	Cirrhosis
Tuberculosis	Haemorrhagic
Following infra-abdominal perforation - any bacteria may be found (e.g. <i>E. coli</i>)	Malignancy
Spontaneous in cirrhotics	Ruptured ectopic pregnancy
Hepatic vein obstruction (Budd-Chiari syndrome)	Abdominal trauma
protein level high in fluid	Acute pancreatitis
Chronic pancreatitis	
Congestive cardiac failure	
Constrictive pericarditis	
Meigs' syndrome (ovarian tumour)	
Hypoproteinaemia, (e.g. nephrotic syndrome)	

Renal Failure (Hepato renal syndrome)

- The hepatorenal syndrome occurs typically in a patient with advanced cirrhosis, portal hypertension with

jaundice and ascites.

- The urine output is low with a low urinary sodium concentration, a maintained capacity to concentrate urine (i.e. tubular function is intact) and almost normal renal histology.
- The renal failure is described as 'functional'. It is sometimes precipitated by over vigorous diuretic therapy, NSAIDs, diarrhoea or paracentesis, and infection particularly spontaneous bacterial peritonitis.
- The mechanism is similar to that producing ascites.
- Diuretic therapy should be stopped and intravascular hypovolaemia corrected, preferably with albumin.
- Terlipressin or noradrenaline with IV albumin improves the renal function in 1/3 of patients.
- Liver transplantation is the best option.

TYPES OF CIRRHOSIS

- **Alcoholic cirrhosis**
- **Primary biliary cirrhosis**
- **Secondary biliary cirrhosis**
- **Hereditary haemochromatosis**
- **Wilson's disease (progressive hepato-lenticular degeneration)**
- **Alpha-1 antitrypsin deficiency**

Hereditary haemachromatosis

- Hereditary haemachromatosis is an inherited disease characterized by excess iron deposition in various organs leading to eventual fibrosis and functional organ failure.

Wilson's disease (progressive hepato-lenticular degeneration)

- Dietary copper is normally absorbed from the stomach and upper small intestine. It is transported to the liver loosely bound to albumin. Here it is incorporated into apoceruloplasmin forming ceruloplasmin, a glycoprotein synthesized in liver, and secreted into the blood. The remaining copper is normally excreted in bile and excreted in faeces.
- Wilson's disease is a very rare inborn error of copper metabolism that results in copper deposition in various organs, including the liver, the basal ganglia of the brain and the cornea.
- It is potentially treatable and **all young patients with liver disease must be screened for this condition.**

Investigations

- **Serum copper and ceruloplasmin** are usually reduced but can be normal.
- **Urinary copper** is usually increased 100-1000 μ g in 24 hours (1.6-16 μ mol);
Normal levels < 40 μ g (0.6 μ mol)
- **Liver biopsy**
The diagnosis depends on measurement of the amount of the copper in the liver (>250 μ g/g dry weight), although high levels of copper are also found in the liver in chronic cholestasis.
- **Haemolysis and anaemia** may present

- **Genetic analysis** – is limited but selected axons are screened according to population group. ATP7B gene mutation.

Treatment

- Lifetime treatment with penicillamine, 1-1.5 g daily, is effective in chelating copper

Alpha 1 antitrypsin deficiency

- A deficiency of alpha 1 anti trypsin is sometimes associated with liver disease and pulmonary emphysema.
- Alpha 1 antitrypsin deficiency is inherited as an autosomal dominant.
- How this causes liver disease is uncertain. It is postulated that the failure of secretion of the abnormal protein leads to an accumulation in the liver, causing liver damage.

NON ALCOHOLIC FATTY LIVER DISEASE

Fatty liver can progress into cirrhosis in up to 30% of patients after 20 yrs. 30% of that cirrhotics will develop hepatocellular carcinoma.

Spectrum of NAFLD

1. Fatty liver
2. NASH
3. NASH with fibrosis and cirrhosis

Classification

Primary

- Part of metabolic syndrome

Secondary

- Drugs like tamoxifen, amiodarone
- TPN

Histopathological features of NASH

- Ballooning degeneration
- Perisinusoidal fibrosis
- Mallory's hyaline

Aetiology

- Insulin resistance
- Genetic predisposition

Examination

- Obese
- BMI>25
- Abdominal girth in males >90 cm, in females >80cm
- Acanthosis nigricans

Investigations

- USS – Bright liver/fatty liver
- Biochemical abnormalities
 - Moderately elevated SGPT, SGOT

- Serum bilirubin normal
 - Gilberts syndrome
 - ALP – Normal
 - Gamma GT – Normal or elevated
- When to biopsy
 - Routine biopsy is not recommended
 - Liver biopsy is the gold standard to assess the severity.

Predictors of fibrosis

- **Age > 45**
- **AST/ALT ratio > 1**
- **Obesity**
- **Diabetes mellitus**

Management

[A] Dealing with risk factors

- NIDDM
- Obesity
- Hypertriglyceridaemia
 - Statins
 - Fibrates
 - Fish oils
 - NASH patients do not have an increased risk of liver damage with statins compared with patients normal LFTs.

[B] Life style modification

- Exercise
- Reduced fat intake
- Reduce weight
- Abstinence from alcohol

[C] Pharmacological Management

- Vitamin E,C – Antioxidants
- Metformin – Increased sensitivity to the insulin at peripheral tissues.
- Pioglitazone/Rosiglitazone – Insulin sensitizer
- Urso deoxycholic acid – Hepatoprotectant
- Hypertension – Losartan

[D] Look for other components of metabolic syndrome

ALCOHOLIC LIVER DISEASE

Alcoholic liver disease

- Micronodular cirrhosis (<3cm)
- Liver involved uniformly

Safe limit of Alcohol

- 14 Units a week for males

- 7 units a week for females
- One wine glass → 1 unit

Alcoholic hepatitis

- Can be acute onset in otherwise healthy
- Hepatomegaly & jaundice
- SGOT>SGPT
- Gamma GT elevated
- Blood picture – Macrocytosis

Abdominal distension - Tutorial

Causes (5FT)

F – fluid (ascitis)
F – aences }
F – latus
F – at
F – etus
T – umour

Common medical pathology is ascitis – confirm by abdominal examination for FF

Ascitis definition

- Pathological
- Accumulation of free fluid
- In the peritoneal cavity

Ascitis classification – based on serum ascitic albumin gradient (s. Alb – ascitic Alb)/ SAAG

SAAG > 11g/L	SAAG <11g/L
Portohypertensive ascitis	Non portohypertensive ascitis
Similar to transudate	Exudates
Causes - Portal vein thrombosis	Causes – tumours – Iry/Irry
Cirrhosis	Irry bacterial peritonitis (following rupture of diverticulae/ appendicitis)
Budd chiari syndrome	Chronic peritoneal TB
RA - Restrictive cardiomyopathy	pancreatitis
Constrictive pericarditis	NS

Hx

Age

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Onset

Features of decompensated cirrhosis

- 1) Icterus
- 2) Ankle oedema
- 3) Ascitis
- 4) Hepatic encephalopathy – altered sleep pattern, hospital stay with LOC
- 5) UGI bleeding – melaena, haematemesis

Aetiology – alcohol use – CAGE

NASH – Diabetes mellitus, dyslipidemia, Hx of IHD/stroke, obesity

Chronic viral hepatitis – blood Tx, RTA, surgery, promiscuous behavior, IV Rx use

AI disorders – type I DM, vitiligo, premature graying

Haemochromatosis – pigmentation, cardiomyopathy, DM

Drugs – anti epileptics, anti psychotics, anti TB

Portal vein thrombosis – secondary to cirrhosis

Thrombotic tendency – DVT –

PE –

High coagulation – APLS (recurrent abortions)

Mode of delivery, how long hospital stay, umbilical sepsis

RA – features of heart failure, chest pain

TB – contact history, past history, chronic cough, low grade evening fever, LOA, LOW

Ilry BP – fever, ill patient (UNLIKELY FOR LONG CASE)

Ex

Build

Dyspnoeic

Icterus, pigmented, spider naevi – over the drainage site of the SVC, anterior chest and back, bleeding patches,
Hands – leuconychia, palmar erythema, hepatic flaps, excoriations - itching

ABD – symmetrical distension

Caput medusa – blood flow away from umbilicus

In SVC obstruction blood flow is downwards

In IVC obstruction blood flow is upwards

Spider naevi

Palpable liver – in macronodular cirrhosis (haemochromatosis), hepatoma

Free fluid – flank dullness with shifting dullness → horse shoe dullness → fluid thrill

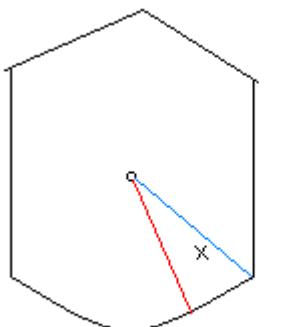
CVS – raised JVP, pericardial rub

RS – apical fibrosis, tracheal deviation

Discussion

How would you investigate this patient?

Confirm type of ascitis as well as exclude certain causes – ascitic fluid analysis



Red line – umbilicus to mid inguinal point (structure underlying is inferior epigastric artery – need to avoid)

Blue line is safe, Macburney's point can be used

Why left side? Sigmoid colon is freely mobile with its wide mesentery, less risk of puncture, hard stools → indentation

R/S – caecum – retroperitoneal and fixed → risk of rupture

Liquid stools – easy leaking

Ascitic full report – cell count, protein, sugar

Gram stain and culture

TB PCR

Cytology – malignant cells

2) USS of abdomen – cirrhosis, portal vein thrombosis, hepatic vein thrombosis (Budd chiari Xn), tumours

How would you manage his patient?

Based on grading of ascitis

Grade I – only seen on USS - 1

Grade II – clinically seen, non tense – 1+ 2

Grade III – tense - 1+2+3 +/- 4

- 1) Salt restriction - <2g/day (1/3rd of a table spoon with top diced)

Avoid high salt foods – dry fish, processed meats, jadi, king coconut

2) Diuretics

Start with spironolactone – 100mg → max 400mg/ day (200mg bd)

Add frusemide – at a ratio of 100: 40 – to maintain K balance (40-160mg)

3) Large volume paracentesis (LVP)

Remove around 5L

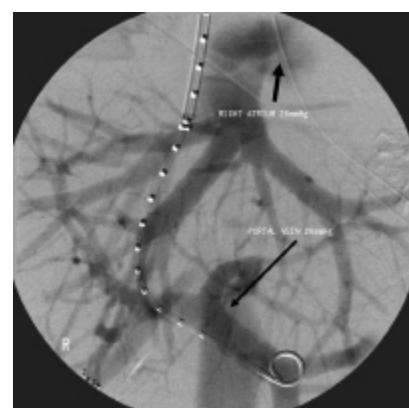
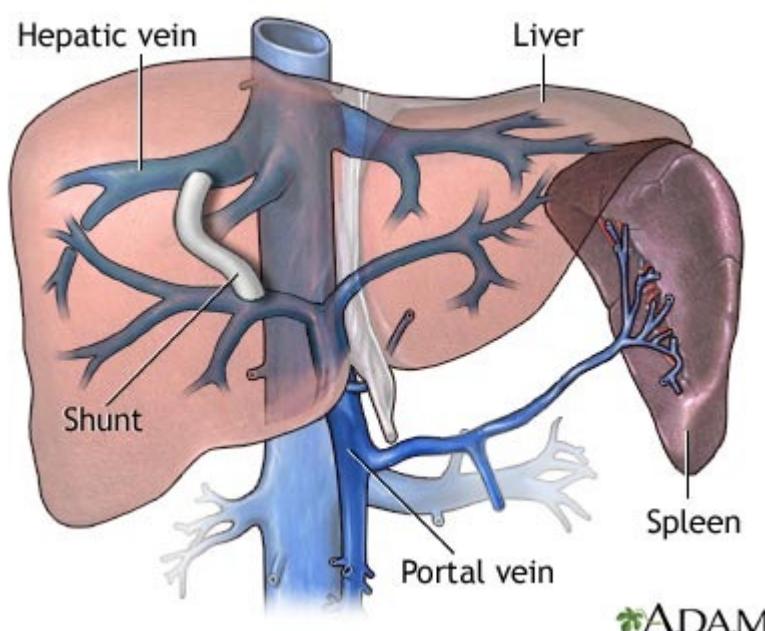
For each litre of fluid → 8g of albumin infused

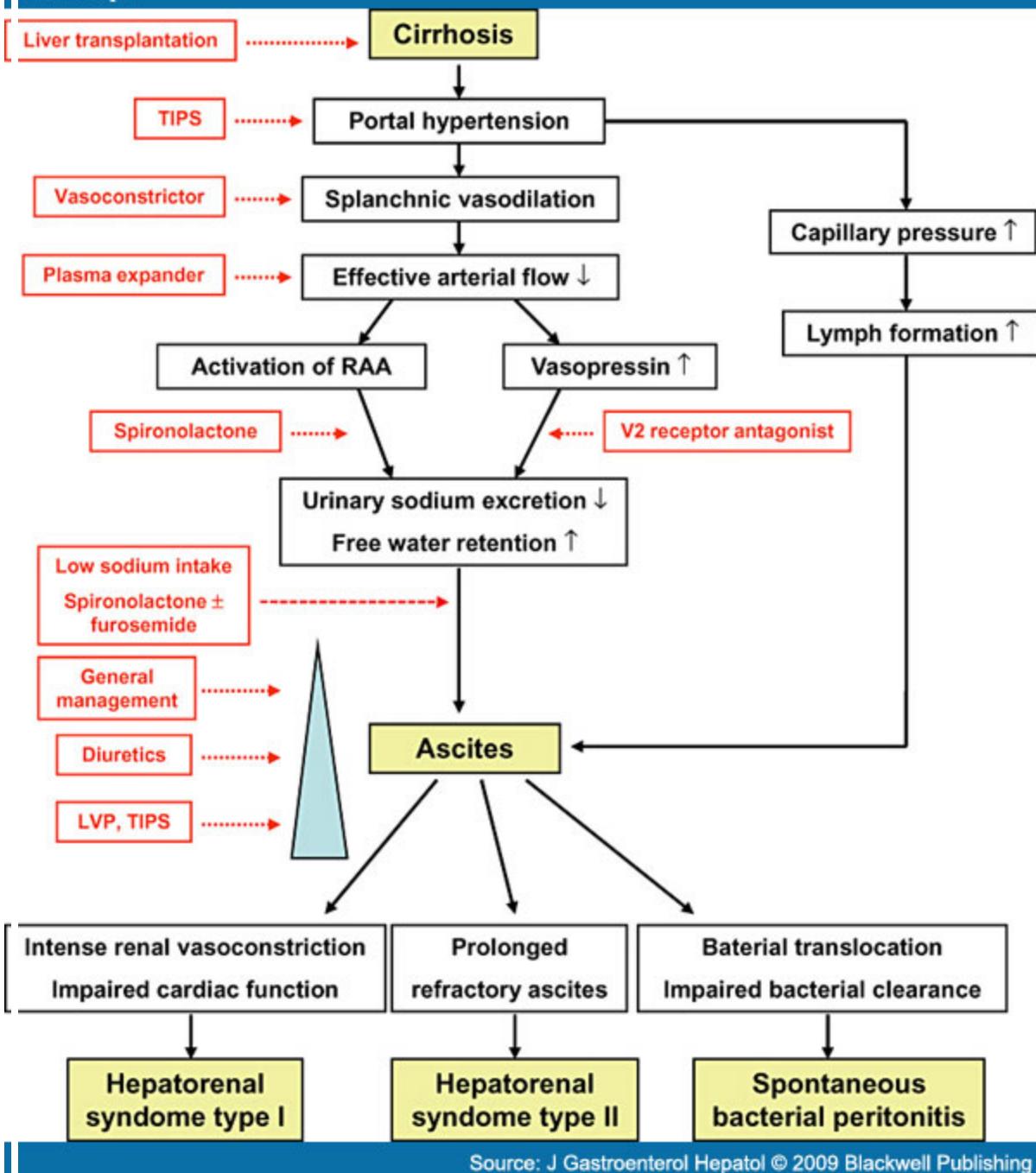
Human albumin 20% - 200g/L, 1 bottle 50ml = 10g per bottle

Need to infuse 4 bottles for the 5L

1 bottle cost – 10,000/-

4) Compensated cirrhosis with refractory ascitis → TIPS (transjugular intrahepatic portosystemic shunt)





Source: J Gastroenterol Hepatol © 2009 Blackwell Publishing

The development of portal hypertension (PHT) is the first step toward fluid retention in the setting of cirrhosis. Patients with cirrhosis but without PHT do not develop ascites or edema [7]. A portal pressure >12 mmHg appears to be required for fluid retention [7,8]; on the other hand, ascites will usually disappear if portal pressure is reduced below 12 mmHg, eg, after a surgical or radiologic portosystemic shunt [9]. Sinusoidal hypertension appears to be required for fluid retention to occur; presinusoidal portal hypertension, as in portal vein thrombosis, does not result in ascites formation in the absence of another predisposing factor.

PHT leads to profound changes in the splanchnic circulation. Although it was formerly thought that PHT was due solely to a mechanical obstruction to portal flow, data from animal models

provide evidence for a component of increased portal venous inflow as a consequence of splanchnic arterial vasodilation

Management of Upper GI haemorrhage

Causes :

- Gastric/duodenal ulcers or erosions (NSAIDs, H.pylori infection, smoking, alcohol)
- Oesophageal varices (Portal HT)
- Mallory weiss syndrome (Repeated vomiting)
- Malignancy (Hx of dysphagia & weight loss)

Clinical features

- Haematemesis – Fresh or altered blood
- Melena (Take 4-6 hours) – Black, sticky & smelly stools
- Epigastric pain & tenderness
- Evidence of portal hypertension
- Evidence of circulatory volume loss
- Angina

Investigations

- Blood for grouping & DT
- Urgent endoscopy
- FBC
- U & E – Blood uria raised
- Erect CXR (air under the diaphragm)
- LFTs, coagulation profile, blood glucose, ECG

General management

- Give high flow O₂
- Insert 2 wide bore cannula
- Monitor pulse,BP, half an hourly
- Insert NG tube and keep nil orally
- Cross match at least 4 units
- IV N.saline infusion
- Give PPI, **Omeprazole 80mg IV** followed by 8mg/hour as an infusion for 72 years (\downarrow the risk of re-bleeding)
- Alternatively, give **ranitidine 50mg in 20 ml of normal saline IV (over 2 minutes) stat and 6 hourly OR cimetidine 200mg stat and 6 hourly OR Pantoprazole 40mg IV daily**
- If haemodynamically unstable → Give rapid infusion of colloids/plasma substitutes or expanders until blood is available. Give blood with minimal delay.

If the pt is exanguinating, uncross-matched O negative blood may be given to avoid delay. (**Save patients blood for cross matching before the transfusion**)

- If the patient is having a major bleed, insert a central line and monitor CVP

- Monitor UOP, a haemodynamically stable patient should maintain a UOP of >30ml/hour. A urinary catheter may be required.
- Watch for signs of fluid overload - ↑ JVP, ↑ CVP, Pulmonary oedema, peripheral oedema
- If coagulation abnormality is suspected, transfuse **FFP & give Vit-K 5-10mg IV**. If the patient has an absolute indication for warfarin (eg : Prosthetic valve), correct clotting with FFP and use a smaller (0.5-1mg IV) dose of vitamin K if required.
- If platelet count is below 50,000/mm³, transfuse platelets 6-12 units
- Further management will depend on the underlying cause as detected during endoscopy. For the specific management of bleeding due to gastro-esophageal varices.

Bleeding from gastro-oesophageal varices

The following measures should be taken in addition to the steps given under general management

- Give **Metoclopramide 20 mg IV stat**
- Give **Vasopressin infusion** (Constrict venules and ↓ portal pressure) **120 units to 250ml of 5% dextrose**, give **50ml of this solution over 15 minutes & continue 50ml hourly for 12 hours**
OR
Give **Terlipressin 2mg IV stat** followed by **1-2mg IV every 4-6 hours upto 72 hours (Contraindicated in IHD)**
- Give infusion of nitrates to reduce cardiac side effects of vasopressin. Use either GTN 50mg in 50ml of 5% dextrose at the rate of 2-20ml per hour
OR
ISDN 25mg in 50ml of 5% dextrose at the rate of 2-10ml per hour (maintain SBP > 90 mmHg). **If vasopressin is not administered, do not give nitrates alone.**
- As an alternative to vasopressin give **Octreotide 100µg IV (somatostatin analogue) stat** followed by **continuous infusion of 25-50µg per hour**. (dilute 500µg of octreotide in normal saline for injection /infusion)
NB : A nitrate infusion is not required with octreotide
- If there is evidence of chronic liver disease give neomycin, metronidazole(P.O 200mg 8/H), lactulose, thiamin.
- Start prophylactic antibiotics as for SBP with oral norfloxacin 400mg 12 hourly.
- If bleeding continues despite above measures, insert a Sengstaken-Blakemore tube and surgical assistance.
- Refer to a gastroenterologist for injection sclerotherapy or band ligation.

Hypertension

History

- Assessment of hypertensive state
- Symptoms suggestive of 2ry HT
- Symptoms suggestive of organ damage
- Identify risk factors for cardiovascular disease
- Identify concurrent diseases

PC:

- Uncomplicated essential HT – asymptomatic and identified during routine checkup.
- Can present with other diseases- DM
- Can present with complications – CVA , HF , IHD, RF

HPC:

- Duration
- First episode
 - When and how was it first diagnosed
 - What were the symptoms
 - BP reading if can remember
 - What was the initial treatment
- Previous BP readings
- Was BP under control
- Regular clinic visits
- Investigations and treatment that the patient had undergone up to now.

To find the aetiology of the HT

Age → young – 2ndry HT is more likely (hypertensives <35 Yrs considered as young hypertensives)

→ Old age – more likely essential HT

Renal

- Chronic pyelonephritis
 - Recurrent UTI with loin pain, pyrexia, rigors
 - Hx of childhood UTI
- Acute nephritic Xn
 - Haematuria
 - Oliguria
 - Oedema
 - Hx of recent throat infection or skin sepsis
- Adult PCKD
 - Haematuria
 - Acute onset episodes of loin pain
 - FHx of PCKD or sub-arachnoid haemorrhage

- Chronic kidney disease
 - Malaise lethargy ,LOA , insomnia
 - Polyuria , nocturia , oedema
 - Itching ,nausea , vomiting
 - Anaemic symptoms , bone pain

Endocrine and metabolic

- **Phaeochromocytoma**
 - Episodic headache, sweating and palpitations
 - Flushing
 - Weight loss
- **Conn's syndrome (1st hyperaldosteronism)**
 - Associated proximal muscle weakness (difficulty in climbing stairs, getting up from squatting position)
 - Fatigue (due to low K⁺)
 - Muscle cramps
 - Polyuria
- **Cushing's syndrome**
 - Weight gain, hair growth, acne, easy bruising, amenorrhoea, poor libido
- **Thyrotoxicosis**
 - Weight loss despite increased appetite
 - Irritability, tremor, heat intolerance
- **Acromegaly**

Drugs

- OCP, steroids, MAO inhibitors

To find out risk factors for essential HT

- High salt intake
- Heavy alcohol consumption
- Sedentary life style, lack of exercise, stress
- High fat diet

To find out target organ damage

- cardiovascular
 - ✓ CCF : exertional dyspnea, orthopnoea, PND, ankle oedema, RHC pain
 - ✓ IHD : Chest pain, MI, past Hx of IHD
- Blood vessels
 - ✓ Intermittent claudication, rest pain, gangrene
 - ✓ Ulcers
- CNS
 - ✓ Stroke , TIA
 - ✓ Dementia (due to multiple infarcts)
 - ✓ Transient blindness (due to retinopathy)
 - ✓ Blurring of vision
 - ✓ Headache (malignant HT)

- Kidney
 - Features of CRF
 - ✓ Nocturia, polyuria, itching, pigmentation, symptoms of anaemia, frothy urine, bone pain, oedema
- Previous hospital admissions due to high BP

PMHx

- DM, hyperlipidaemia, sexual dysfunction

PSHx

- Renal calculi

Drug Hx

- Any anti hypertensives
- Drug compliance
- Clinic follow up

FHx

- HT in first degree relatives (HT in <50 Yrs), endocrine diseases, renal diseases, DM, dyslipidaemia

Social Hx

- Smoking, alcohol, exercise

Examination

General

- Weight, height, BMI
- General appearance
- Pallor
- Hyperpigmentation, scratch marks, half & half nails (CRF)
- Features of Cushings: cushinoid faces, bruising, truncal obesity, thin skin, hirsuitism, purple striae in abdomen
- Acromegaly: large face, Prognathism, spade like hand, prominent supra-orbital ridge, interdental separation
- Hyperthyroidism: tremor , warm peripheries, eye signs , goitre
- Stigmata of neurofibromatosis: Café-au-lait spots, neurofibroma palpable
- Ankle oedema

CVS

- Pulse : Rate, rhythm, volume, character
- All peripheral pulses
- Radio-femoral delay (Coarctation of aorta)
- BP
- JVP :elevated/ not
- Precordium
 - ✓ Apex – shifted, heaving

Measurement of BP

- ✓ Avoid tobacco, caffeine 30 min before
- ✓ Should be seated quite room for ~ 5min
- ✓ Avoid tight sleeves
- ✓ Arm muscles relaxed & forearm supported with cubital fossa at heart level
- ✓ Cuff size; to cover 2/3 of arm
- ✓ Inflate rapidly 30mm higher than disappearance of pulse
- ✓ Sys BP : Korotkoff sounds appear
- ✓ Dias BP: sounds disappear (phase V)
- ✓ Average of 2 or more readings
- ✓ Verify BP in contra-lateral arm
- ✓ Heart failure – gallop rhythm (sinus tachycardia + 3rd heart sound)

RS

- Fine end inspiratory crepitations all over the lung fields / pulmonary oedema

Abdomen

- Tender hepatomegaly (in CCF)
- Palpable kidneys (PCKD)
- Renal artery bruits (renal artery stenosis)

CNS

- Higher functions, fundoscopy
- evidence of CVA, TIA

Investigations

General

- UFR : red cells, casts, protein
 - If no RBC in UFR → Request to look for dysmorphic RBC in urine (Nephritic Syndrome)
- BU & SE
 - BU increase in renal failure
 - Low K⁺ in Conn's syndrome
- S. Cr : increase in renal failure
- Fasting blood sugar
 - Increase in DM, Cushing's, acromegaly, phaeochromocytoma
- Lipid profile
- ECG
 - LVH
 - Past MI
 - Recent MI

Specific Ix

- Resting plasma catecholamines
 - 24 hr urinary VMA
 - CT scan abdomen } Phaeochromocytoma
-
- 24 hr urinary free cortisol
 - Low dose dexamethasone suppression test }
 - Oral glucose suppression test → Acromegaly }
 - Elevated plasma aldosterone levels
 - That are not suppressed with 0.9% saline infusion (2 L over 4 hours) or fludrocortisone administration.
 - Suppressed plasma renin activity }
 - USS abdomen → PCKD }
 - Renal duplex scan }
 - Renal angiography } Renal artery stenosis
 - CXR }
 - Aortography } Coarctation of aorta

- Renal biopsy → if renal pathology is suspected
- TSH, T₃, T₄ → hyperthyroidism

Ix to detect complications

- CXR: cardiomegaly, HF
- 2D ECHO: LV function
- 24 hr urinary protein
- Microalbuminuria
- USS abdomen
- S. Creatinine
- Serum uric acid level

Management

Table 1: New definition and classification of blood pressure levels (mmHg).

Category	Systolic	Diastolic
Normal	<120	<80
Pre-hypertension	120 - 139	80 - 89
Grade 1 hypertension (mild).	140 - 159	90 - 99
Grade 2 hypertension (moderate)	160 - 179	100 - 109
Grade 3 hypertension (severe)	≥180	≥110
Isolated systolic hypertension	≥140	<90

- When a patient's sys & diastolic BPs fall into different categories, higher category should apply
- Obtain average of 2 or more readings in 2 or more visits
- A sys. BP 140 – 159 or dias. BP 90 – 99 should be confirmed within 8 weeks
- Consistently elevated BP > 160/100 requires further evaluation

Important

- HT accounts for 10% of cardiovascular deaths.
- Decision to commence antihypertensive depend on
 - ✓ Grade of HT
 - ✓ Presence of risk factors
 - ✓ Presence of target organ damage
 - ✓ Associated clinical conditions

Blood pressure	Other risk factors & disease history		
Grades	No risk factors	1-2 risk factors	3 /> risk factors or TOD or DM or ACC
Grade 1 SBP 140-159 DBP 90-99	Low risk Life style mod. 6-12m	Med risk Life style mod. 3-6 m	High risk Life style mod. Drug therapy
Grade 2 SBP 160-179 DBP 100-109	Med risk Life style mod. 3-6 m	Med risk Life style mod. 3-6 m	High risk Life style mod. Drug therapy
Grade 3 SBP >180 DBP > 110	High risk Life style mod. Drug therapy	High risk Life style mod. Drug therapy	High risk Life style mod. Drug therapy

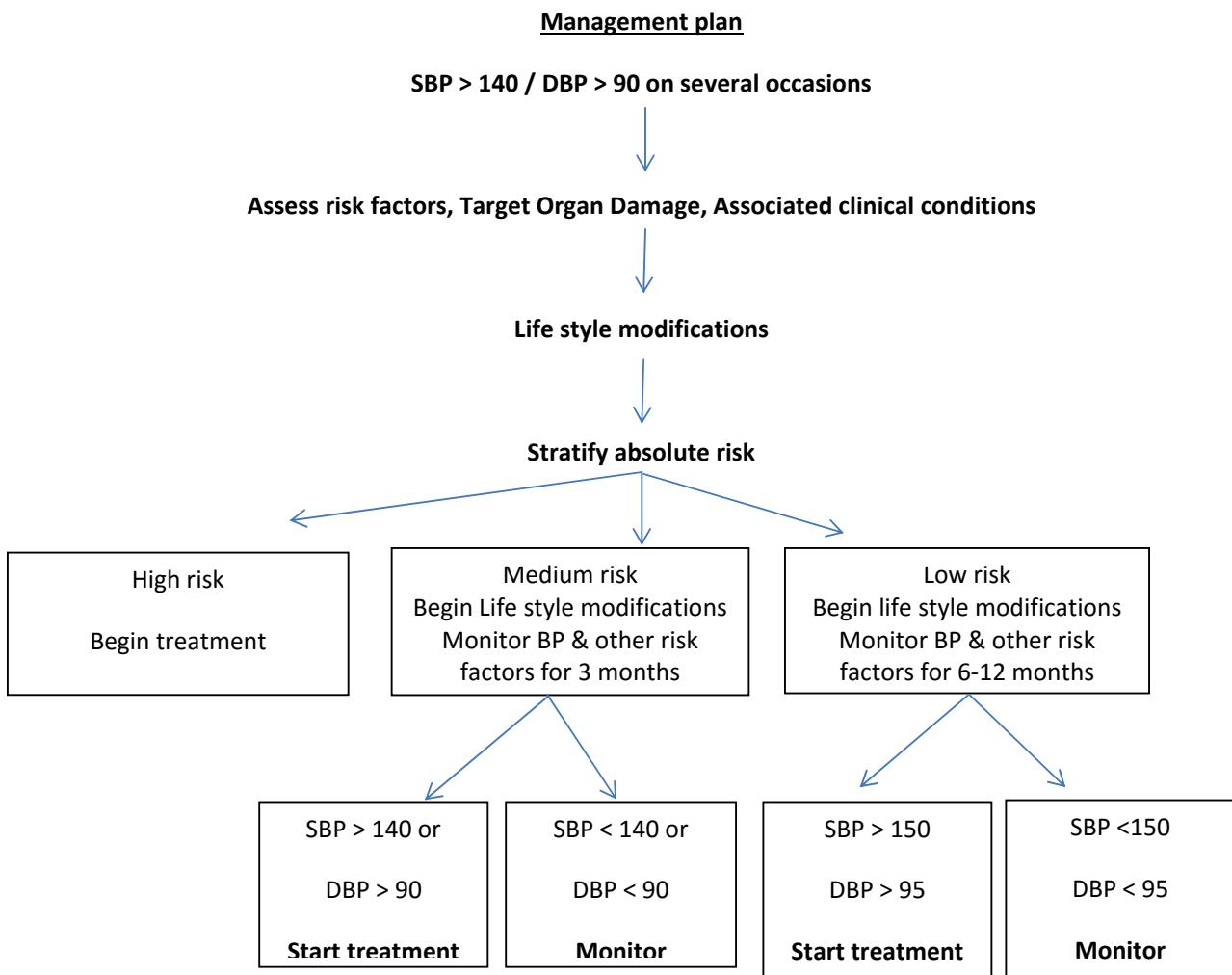
Risk factors for Cardio-vascular disease

Factors used for risk stratification

- ✓ Men >55, Females >65
- ✓ Smoking
- ✓ Total cholesterol > 6.5mmol/l (250mg/dl)
- ✓ Diabetes
- ✓ F/H/O premature cv disease

Other factors adversely influencing prognosis

- ✓ Reduce HDL cholesterol
- ✓ Raised LDL cholesterol
- ✓ Micro-albuminuria in DM
- ✓ Impaired Glucose Tolerance Test
- ✓ Obesity
- ✓ Sedentary lifestyle
- ✓ Raised fibrinogen
- ✓ High risk socioeconomic group
- ✓ High risk ethnic group
- ✓ High risk geographic group



Non pharmacological treatment

- Weight reduction – BMI < 25
- Low fat and saturated fat diet
- Low sodium diet
- Limited alcohol consumption (<21units/wk for men and < 14u /wk for women)
- Exercise (at least 30 min)
- Stop smoking

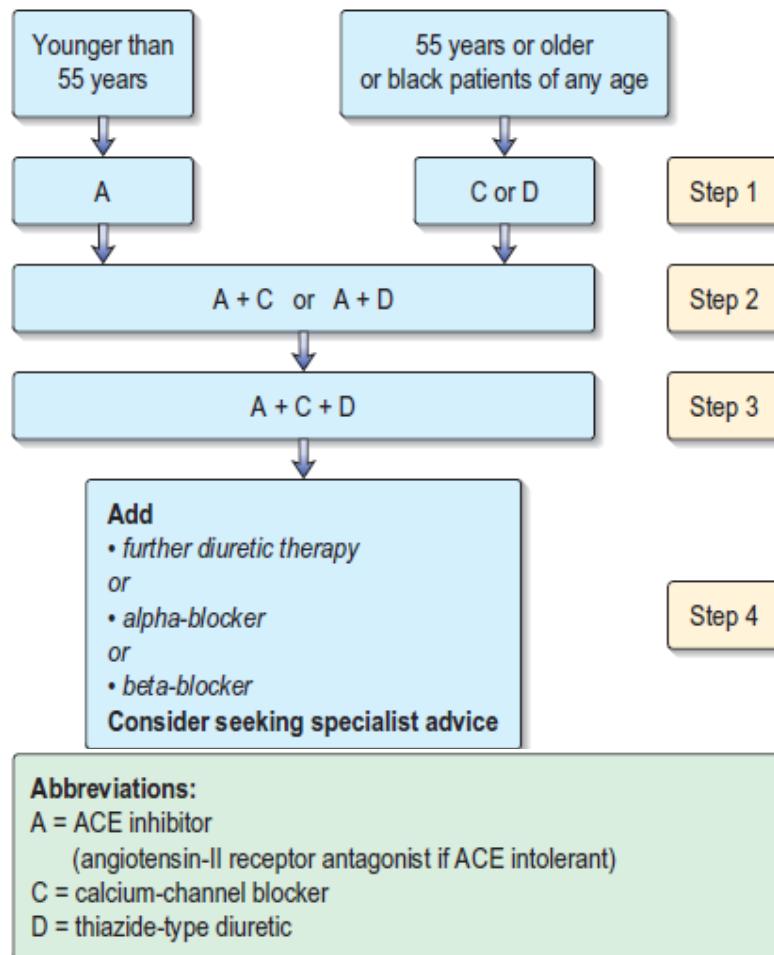
Pharmacological therapy

Principles of using anti hypertensive treatment

- Anti hypertensives are started in patients with sustained systolic blood pressure (BP) ≥ 160 mmHg, or sustained diastolic BP ≥ 100 mmHg.
 - Decide on treatment in patients with
 - ✓ Sustained **systolic** blood pressure between **140 and 159 mmHg**
 - ✓ Or sustained **diastolic** BP between **90 and 99 mmHg**
 - ✓ According to the **presence or absence of target organ damage** or a 10-year cardiovascular disease risk $> 20\%$.
 - In patients with diabetes mellitus, start antihypertensive drug therapy if sustained systolic BP ≥ 140 mmHg, or diastolic BP is ≥ 90 mmHg.
 - Start with the lowest dose. If not controlled increase the dose provided no side effects.
 - If side effects are common with high dose add a low dose second drug.
 - If no effect or poor tolerability of the low dose first drug change into different class.
 - Use long acting
 - ✓ Increased compliance
 - ✓ For 24 hr BP control
- **Target blood pressures**
- ✓ **Uncomplicated HT < 140 / 85**
 - ✓ **Diabetes, Renal failure, Heart failure < 130 / 80**
 - ✓ **Renal failure with proteinuria > 1g/ 24 hrs < 125 / 75**
- Lowering of the
 - SBP by 10 – 12 mmHg
 - DBP by 5 - 6 mmHg
 - Reduce the relative risk of stroke by 40%
 - Reduce the coronary disease by 15%
- Most patients will require combined treatment.

High-Risk Conditions With Compelling Indication*	Recommended Drugs					
	Diuretic	β -Blocker	ACE Inhibitor	ARB	CCB	Aldosterone Antagonist
Heart failure	•	•	•	•	•	•
Post-myocardial infarction		•	•			•
High coronary disease risk	•	•	•	•		
Diabetes	•	•	•	•	•	
Chronic kidney disease			•	•		
Recurrent stroke prevention	•		•			

Choosing drugs for patients newly diagnosed with HPT



ACE inhibitors (captopril, enalapril, lisinopril)

- Dilate capacitance and resistance vessels.
- Act mainly on Angiotensin sensitive vascular beds in heart, kidney and brain.
- Indications: CCF, LVF, HT, after MI, diabetic nephropathy
- Contraindications: B/L renal artery stenosis, pregnancy
- Cautions : Aortic stenosis, PVD or generalized atherosclerosis, renal impairment
- SE : dry cough, hyperkalaemia, hypotension(first dose),angioedema

Angiotensin receptor blockers

Losartan / Valsartan / Candesartan

- Better side effects profile - useful in those who develop cough with ACEIs
- Usually given orally once daily
- Theoretically more effective & beneficial than ACEIs

CCB

- Indications : Angina, elderly, HT, PVD
- CI : 2nd and 3rd degree heart block
- Cautions : CCF
- Two groups
 - Dihydropyridines (DHP): Nifedipine, Felodipine, Amlodipine, Nimodipine
 - Non dihydropyridines: Verapamil, Diltiazem
 - (Heart rate lowering agents)
- Selectivity between heart & vascular smooth muscle varies
- Dihydropyridine
 - Vasodilator effect mainly on resist. vessels
 - A/E: flushing, headache, ankle swelling, reflex tachycardia, variation in BP (short act.)
 - Duration of action varies
 - Short acting nifedipine – not recommended
 - Amlodipine / longer acting nifedipine– prefer
- Verapamil
 - Highly negatively inotropic (reduce CO)
 - Should not be used with beta blockers
 - SE : constipation

Diuretics

- Indications: HF, elderly, HT
- CI : GOUT
- Cautions: dyslipidaemia, sexually active males

Beta blockers

- β -1 receptor → control heart rate (located mainly in the heart and in the kidneys)
- β -2 receptor → vasoconstriction (located mainly in the lungs, gastrointestinal tract, liver, uterus, vascular smooth muscle, and skeletal muscle)
- Non-selective β (1&2) blockers: Propranolol, Sotalol
- Selective β -1 blockers → Atenolol, Metoprolol
- Non-selective β blockage + α -1 blockage → Labetalol, Carvedilol
- Indication: Angina, after MI, tachyarrhythmia
- Possible indications : HF, DM, Pregnancy
- CI: asthma, COAD, heart block
- Cautions: PVD, dyslipidaemia, athletics
- Indication: Angina, after MI, tachyarrhythmia
- Possible indications : HF, DM
- CI: asthma, COAD, heart block
- Cautions: PVD, dyslipidaemia, athletics

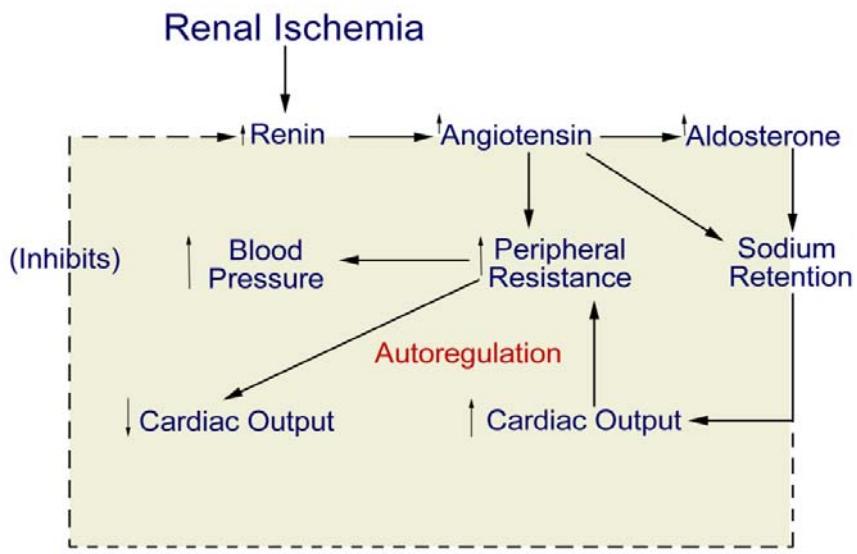
Alpha blockers

- Alpha 1 adreno-receptor blocker (spares alpha 2 receptor) – Prazosin
- Prostatic hypertrophy
- Possible Indications: glucose intolerance, dyslipidaemia
- Cautions: orthostatic HT

2ry Hypertension

Reno vascular disease

- Disease affecting blood vessels of kidney
→ Arterial narrowing → Reduce renal blood flow



Causes

1) Atherosclerosis → 2/3

- >60 years
- Men > Women
- Affects proximal 1/3 of main renal artery
- Important cause of ESRD
- With hypertension → increased mortality

2) Fibromuscular dysplasia → 1/3

- < 40 yrs
- Women > Men
- Affects distal 2/3 & branches of renal arteries
- Curable** cause of severe hypertension



Fig. 13.124 Digital subtraction angiography, showing typical unilateral atheromatous renal artery stenosis with post-stenotic dilatation (arrow).

Medical Mx

Antihypertensive drug therapy

- All classes of antihypertensives are used

- ACE inhibitors & ARBs

- Most effective

- Minimizes ischaemia-induced rise in angiotensin

- Decreases blood flow through stenotic kidney

If single kidney or bilateral reno-vascular disease → BP falls rapidly → sudden deterioration in renal function

- Reverses on stopping drug

- Increase in s.creatinine up to 35% above baseline acceptable

- Not a reason to withhold ACEI/ARB unless hyperkalaemia develops

- Beta-blockers

- Diuretics with/without ACE inhibitors

- Calcium channel blockers

Control other risk factors for atherosclerosis

- Stop smoking
- Dietary modification
- Statins
- Aspirin

Fibromuscular dysplasia

- Percutaneous transluminal renal angioplasty (PTRA) – better for sub-total occlusion, fibromuscular, unilateral disease
- PTRA With stenting – best option
- Surgical revascularisation
 - ✓ Cure in 80%
 - ✓ Morbidity low
 - ✓ BUT results not significantly better than with renal angioplasty

Atherosclerotic disease

- Complication → cholesterol embolization
- Treatment is surgical revascularisation
- Cure or improvement in 80-90%
- Peri-operative mortality <5%

Hypertensive Retinopathy

- Grade 1 : Tortuosity of retinal arteries with increased reflectiveness. (Silver wiring)
- Grade 2 : Grade 1 + Appearance of arteriovenous nipping (produced when thickened retinal arteries pass over the retinal vein).
- Grade 3 : Grade 2 + flame shape haemorrhages and soft ("cotton wool ") exudates actually due to small infarcts.
- Grade 4 : Grade 3 + papilloedema

Grade 3 and 4 are diagnostic of malignant HT.



Fig. 13.123 Fundus showing hypertensive changes:
Grade 4 retinopathy with papilloedema, haemorrhages and exudates.

Malignant HT

- Malignant or accelerated hypertension occurs when blood pressure rises rapidly and is considered with severe hypertension
- Diastolic blood pressure > 120 mmHg with acute micro-vascular damage.
- The characteristic histological change is fibrinoid necrosis of the vessel wall.
- If not treated it may lead to death from progressive renal failure, heart failure, aortic dissection or stroke.
- The changes in the renal circulation result in rapidly progressive renal failure, proteinuria and haematuria.
- There is also a high risk of cerebral oedema and haemorrhage with resultant hypertensive encephalopathy.

Mx

- Bed rest
- Monitor BP $\frac{1}{2}$ hourly
- Catheterise the patient
- Insert IV cannula

Aim is to reduce DBP to 100 mmHg over 24hrs.

Most patients can be managed with oral therapy.

If there is no LVF, give a beta blocker (Labetolol 200mg PO or Atenolol 50 mg PO)

Give frusemide 40 – 80mg IV

IF LVF is a problem give sodium nitroprusside 0.3-10mcg/kg/min IV as an infusion or a low dose ACEI orally.
(Avoid sublingual nifedipine)

If BP is uncontrolled with beta blockers add a low dose ACEI orally or Nifedipine.

Hypertensive encephalopathy

- **Cerebral oedema with uncontrolled hypertension.**
- Clinical features: focal neurological signs, seizures, coma

Mx

- Strict bed rest.
- Catheterise the patient.
- Insert lv cannula
- Correct electrolyte imbalances
- Give frusemide 40 – 80 mg IV
- Reduce DBP to 100mmHg over 1-2 hrs.
- give sodium nitroprusside 0.3-10mcg/kg/min IV as an infusion
- If BP is still not controlled give IV labetolol 50mg IV over 2 min. Repeat every 10 min till the BP is controlled or total of 200mg is given.

Caution: Never use sublingual nifedipine or centrally acting agents.

Patient Factors Affecting Antihypertensive Drug Choice

The choice between the drugs is to a large degree determined by the characteristics of the patient being prescribed for, the drugs' side-effects, and cost. Most drugs have other uses; sometimes the presence of other symptoms can warrant the use of one particular antihypertensive. Examples include:

- **Age** can affect choice of medications. Current UK guidelines suggest starting patients over the age of 55 years first on calcium channel blockers or thiazide diuretics.
- **Anxiety** may be improved with the use of beta blockers.
- **Asthmatics** have been reported to have worsening symptoms when using beta blockers.
- **Benign prostatic hyperplasia** may be improved with the use of an alpha blocker.
- **Diabetes**. The ace inhibitors and angiotensin receptor blockers have been shown to prevent the renal and retinal complications of diabetes mellitus.
- **Gout** may be worsened by diuretics, while losartan reduces serum urate.
- **Kidney stones** may be improved with the use of thiazide-type diuretics
- **Heart block** β-blockers and nondihydropyridine calcium channel blockers should not be used in patients with heart block greater than first degree.
- **Heart failure** may be worsened with non-dihydropyridine calcium channel blockers, the alpha blocker doxazosin, and the alpha-2 agonists moxonidine and clonidine. Whereas β-blockers, diuretics, ACE inhibitors, angiotensin receptor blockers, and aldosterone receptor antagonists have been shown to improve outcome.
- **Pregnancy**. Although α-methyldopa is generally regarded as a first-line agent, labetalol and metoprolol are also acceptable. Atenolol has been associated with intrauterine growth retardation, as well as decreased placental growth and weight when prescribed during pregnancy. Ace inhibitors and angiotensin II receptor blockers (ARBs)are contraindicated in women who are or who intend to become pregnant.
- Tremor may warrant the use of beta blockers.

Asiri Gamage (ME/2006/034) Batch 19

Joint pain with skin rash (systemic lupus erythematosus)

Presentations of SLE

1st time - joint pain with skin rash

Painful red eye

PUO

Flare up of the disease – in a diagnosed patient

Differential diagnosis

SLE

Rheumatoid arthritis

Psoriatic arthritis

Still's disease

HPC

Describe the onset and progression of presenting symptoms

1st time presentation: exclude

Rheumatoid arthritis	<ul style="list-style-type: none">B/L symmetrical small joints of hands with DIPJ sparing – painful swelling with morning stiffness >1hr, improves with activityDeformed joints, impaired hand powerEye – scleritis – severe eye pain, red eye
Psoriatic arthritis	<ul style="list-style-type: none">scaly rash over scalp line & extensors –preceding joint symptomsasymmetric joint involvement, DIPJ commonly involvednail changes
Ankylosing spondylitis	<ul style="list-style-type: none">Commonly in malesPain in one/both buttocks (sacroilitis)Lower back pain and stiffness - ↓ with exercise, ↑ by restChest pain (costochondritis)Uveitis – severe eye pain with photophobia
Still's disease / Adult onset JIA	<ul style="list-style-type: none">Salmon pink maculopapular rash at the height of feverHigh swinging early evening feverHx since childhood, RARE in adultsOligoarthritis - ≤ 4

Diagnosed patient:

- ▢ Onset of initial symptoms
- ▢ When and where the diagnosis of SLE was made
- ▢ Initial investigations done and their results – ESR, ANA, RF, anti ds-DNA, skin biopsy
- ▢ Initial management
- ▢ No of relapses – precipitating factors → OCP,HRT
Sun exposure
Rx – methyldopa, hydralazine, Penicillamine,
procainamide (anti-arrhythmic),INAH
Drug withdrawal
Pregnancy (esp. postpartum) , stress

Disease manifestations in Chronological order ($\geq 50\%$ incidence in bold)

System	Manifestations
General	Fever , marked malaise, fatigue
Eye	Episcleritis – mild eye pain, red Conjunctivitis – painless red eye, tearing Optic neuritis – reducing VA, eye pain with movement, poor colour vision, central scotomas
Arthritis	Symmetrical small joint arthralgia, early morning stiffness for $>1\text{hr}$, \downarrow by exercise slight soft tissue swelling w/o joint deformity
Skin	Malar rash on face, discoid rash – face and scalp (lead to alopecia), photosensitive rashes, oral ulcers, vasculitis – finger tips and nail folds, Raynaud's – pale & numb → painful finger tips → blackish discolouration and loss of digits, worse with cold rash over palms and soles, pigmentation
♥	Chest pain relieved on leaning forward - Pericarditis, pericardial effusion Myocarditis – arrhythmia (chest pain, syncope, palpitations) APLS – arterial and venous thrombosis – CAD – chest pain on exertion, Hx of MI PVD – claudication site and what distance, DVT – pain and swelling of LL after immobility
Lung	Pleurisy and pleural effusion – pleuritic type chest pain Shrinking lung syndrome , pulmonary fibrosis– progressive DIB , lung tightness Intrapulmonary haemorrhage – haemoptysis
Renal	Proteinuria/frothy urine Glomerulonephritis – haematuria, hypertension, oliguria ESKD – polyuria, pruritus, intractable hiccups,
CNS	Migraine, fits Altered behavior, depression, psychosis – CEREBRAL LUPUS Peripheral /cranial neuropathy – focal weakness, diplopia, deviation of mouth Strokes – hemiplegia (APLS and infarcts due to vasculitis), encephalopathy
Haematological	Anaemia with tea colour urine - AIHA Recurrent infections - \downarrow WBCC, lymphopenia Bleeding tendency - \downarrow platelets
abdomen	Abdominal pain (small bowel infarcts and perforations, renal vein thrombosis)
Muscles	Myalgia (but myopathy is $<5\%$)
Reproductive	Recurrent pregnancy loss (APLS)

Treatment – what, response, S/E

- ✓ NSAIDs - peptic ulcer disease
- ✓ Chloroquine, hydroxychloroquine – visual disturbances – eye checkup (VA) – before starting & annually
- ✓ Corticosteroids (prednisolone) – S/E
- ✓ Methotrexate – pancytopenia, cirrhosis, acute interstitial pneumonitis
Monitoring of FBC, LFT, RFT (2weekly for 6 weeks → monthly)

- ✓ Cyclophosphamide pulses - haemorrhagic cystitis – haematuria, suprapubic pain, LUT symptoms
Infertility – male – azoospermia female – amenorrhoea
Marrow suppression
- ✓ Azathioprine – pancytopenia
- ✓ Alendronate – weekly white tablet , GORD

Functional status: ADL – using toilet, dressing, bathing, mobility

Occupation

Recreational activities

FHx – AI disorders

SHx – education level, knowledge about disease and prognosis

Accepted disease/in denial, depression symptoms

Effect on other family members, family support

Nearest rehabilitation hospital, mode of transport



Discoid rash



Livedo reticularis

Examination

GE –

- ✓ Build – thin, obese (steroid S/E)
- ✓ Alopecia
- ✓ Pallor – anaemia of CD, AIHA
- ✓ Eye - Icterus ,Red eye,Dry eyes – secondary sjogrens disease
Cataract (steroids)
- ✓ **Febrile**
- ✓ **Malar rash, discoid rash**
- ✓ Mouth – oral ulcers
- ✓ Lymphadenopathy
- ✓ Purpura, urticaria, palmar plantar rash, pigmentation
- ✓ Hands – Raynaud's, nail fold vasculitis
- ✓ Oedema – AGN, NS, CCF

Steroid S/E

Musculoskeletal – inspection – mild swelling

Tender

Movements, effusions – N/L



CVS – pulse – regular/not

BP - ↑

JVP - ↑

Cardiomegaly, parasternal heave

Auscultation – Pericardial effusion – muffled S1, S2

Loud P2

murmurs – MS, MR (non infective endocarditis of MV – Libman sacks Xn)

AR

Pericarditis – pericardial rub

Respiratory sys – pleural effusion

Pulmonary fibrosis - ↓ chest expansion, RR ↑, tracheal deviation

Fine basal crepts – CCF

Abdomen – Hepatomegaly

Moderate splenomegaly

Renal A. bruit



NS – fundi – retinal haemorrhages, hard exudates (cytoid bodies)



Cranial nerves

cerebellar signs – ataxia(gait)

hemiplegia, peripheral neuropathy

SUMMARY

--- year old lady presenting with ---PC--- (mention as to fulfill the diagnostic criteria). She is a diagnosed patient with SLE since ---duration---- now presenting in her ---no.--- relapse precipitated by -----. She is on ----- with these ---S/E. she has/ hasn't a Hx of severe lupus with ---renal, cerebral, CVS manifestations. O/E positive findings

Problem list

Acute medical → SLE relapse

Complications – ARF, pleural effusion etc

Chronic medical → SLE

Subfertility

Poor drug compliance/ clinic followup

Social – family disputes, occupation issues, financial

Psychological - depression

Discussion

How will you diagnose SLE?

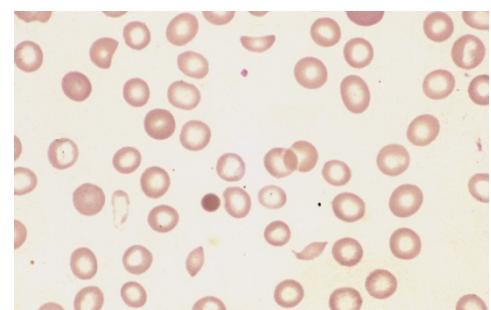
- It's a clinical diagnosis
- Presence of 4 out of 11 criteria at any given time during the course of the disease is diagnostic. (ACR classification)

- 1) **M** – malar rash – fixed erythema, flat/ raised, over the malar eminences
- 2) **I** – immunological – anti dsDNA, anti- Sm and/or APL
- 3) **R** – renal – proteinuria > 0.5g/dL or 3+ or cellular casts
- 4) **A** – arthritis – non erosive arthritis involving ≥2 peripheral joints, characterized by tenderness, swelling or effusion
- 5) **N** – neurologic disorder – seizures/ psychosis w/o other cause
- 6) **D** – discoid rash
- 7) **A** – ANA ↑
- 8) **S** – serositis – pleuritis/pericarditis documented by ECG/rub/evidence of pericardial effusion
- 9) **H** – haematological – HA/ WBCC<4000/ μ L / lymphopenia < 1500/ μ L / Plt < 100,000/ μ L
- 10) **O** – oral ulcers
- 11) **P** - photosensitivity

How will you manage this patient?

Ix

- 1) To confirm diagnosis –
 - ESR ↑
 - CRP – normal unless superimposed infection
 - FBC and blood picture – pancytopenia, HA(fragmented rbc)
 - ANA – (+) in 95% (also ↑ in pregnancy, RA, malaria, pneumonia)
 - Anti ds-DNA – specific for SLE, (+) ve in 50%
 - RF – (+)ve in 25%, require a titre>128 to be (+)



2) Assess extent of target organ involvement

Renal	UFR – RC cast, dysmorphic RC 24hr proteinuria/ urine protein:creatinine ratio Creatinine clearance(CRF), BUN, SE Renal imaging
Lungs , 	CXR, ECG, echo (if murmur)
Liver	LFT
Skin	Biopsy – (+)ve lupus band test Bx taken from normal non sun exposed skin Eg: buttocks Immunofluorescence – IgG and complement deposits at dermo-epidermal junc.
CNS (if indicated)	CT brain – infarcts and haemorrhage MRI – lesions in the white matter

3) Assess disease activity

ANA titre - ↑↑
C3, C4 - ↓↓

Signify active disease
Ascending trend in ANA & descending trend in C3,C4 herald renal lupus

4) Identify subsets

Anti phospholipid syndrome → check 1) lupus anticoagulant
2) Anti β2 glycoprotein Ab
3) anti-cardiolipin Ab

Renal lupus → kidney bx

General

Educate regarding disease – 1) chronic inflammatory condition with a remitting and relapsing nature
2) Due to formation of Abs that act against your own tissue
3) Need long term treatment
4) Reassurance – serious complications rare hence normal life expectancy

Advise to reduce CVS risk factors

- Control hypertension
- Control hyperlipidemia – diet and exercise
- Stop smoking and passive exposure

Avoid excessive sun exposure and OCP (precipitants)

Treat joint pain - simple analgesics (PCM, NSAIDs)

DMARDs – hydroxychloroquine (if not responding to NSAIDs, reduce frequency of SLE Flares)

Thrombotic events – start on anticoagulants – Aspirin,

Warfarin lifelong if previous thrombotic episodes

Acute thrombosis - LMWH

Induction of remission in acute relapse

Prednisolone **1mg/Kg/day for 6weeks** or IV methylprednisolone pulses treatment

Tailed off following remission/ maintained on low dose/EOD steroid

Other immunosuppressant Rx indicated— renal lupus, cerebral or CVS involvement
Requiring high doses of steroids → leading to S/E

Criteria for a remission

- Absence of clinical symptoms?
- Proteinuria < 0.5g/dL
- ANA and anti-ds DNA – N/L

Treatment of acute complications

Renal lupus - classified according to histology following renal bx

Class I – minimal mesangial	- no treatment
Class II – mesangial proliferative	- steroids if RBC in urine
Class III – focal proliferative	
Class IV – diffuse proliferative	
Class V – membranous	
Class VI – advanced sclerosing	

Induce remission – steroids & IV pulses of cyclophosphamide
Maintain remission – azathioprine & mycophenolate mofetil
Mx of CRF, may require renal transplantation

Lupus nephritis Mx

IV cyclophosphamide pulse - D1 750mg

Next 3 days 1g/day → Discharge on D4 with oral prednisolone

R/V at clinic in 1month with ESR – prednisolone titrated according to ESR

Repeat cyclophosphamide pulse treatment – monthly x 6months → 3 monthly x 18months

CNS -

Prevention of drug S/E

1) Osteoporosis – Alendronate

Advice on taking

- White tablet taken weekly (on Sunday)
 - Early morning soon after rising on **an empty stomach**
 - Take with full glass of plain water only
 - Remain upright for 30min
- S/E - GORD

Drug	S/E	Advice
Cyclophosphamide	Haemorrhagic cystitis Infertility	Adequate hydration before & 24-48hrs after taking Rx Can be permanent Sperm storage prior to Rx
Mycophenolate mofetil	Pancytopenia N,V,D	FBC – every wk/ for 4weeks 2x month for 2/12 → monthly in 1 st year
Hydroxychloroquine	Retinal damage – may be irreversible Alopecia, skin and hair discolouration	Eye check up – before starting and annually
Azathioprine	Pancytopenia, hypersensitivity, liver toxicity	FBC weekly for 4weeks → every 3 monthly

Follow up

- Monthly clinic follow up
- Monitoring – ESR and CRP monthly
- 2D echo –

If she wants to get pregnant how will you advise?

- Pregnancy is not contraindicated unless severe(renal , cerebral or CVS lupus)
- Concerns → need to continue usual treatment and achieve remission before pregnancy
 - Until then contraception – barrier methods
 - Risk of recurrent miscarriages – anti- PL syndrome
 - Risk of exacerbation – esp. postpartum
- Early booking visit, need to control hypertension

SLE pathophysiology? (Davidson pg 856)

Immunologically mediated tissue damage via 2 mechanisms

- 1) Direct type II hypersensitivity – Ab mediated cytotoxicity Eg: brain damage & abortion
- 2) Type III hypersensitivity – immune complex and complement mediated (renal & vascular lesions)

How do you get pulmonary hypertension?

- 1) Pulmonary vasculitis
- 2) Hypoxia and fibrosis from interstitial lung disease
- 3) thromboembolic disease

What is anti phospholipid syndrome

Thrombophilic state where there is Ab formation against (-)vly charged phospholipids

Features – recurrent miscarriage and recurrent arterial/venous thrombosis

Chorea, migraine, epilepsy, MI, stroke, multi-infarct dementia

Valvular heart disease, adrenal haemorrhage

Livedo reticularis

Ix – ESR, ANA – N/L

↓ Plt.

(+) coombs test

Diagnosis - ELISA

- 1) Lupus anticoagulant
- 2) anti-cardiolipin Ab (diagnostic)
- 3) IgG, IgM antiphospholipid Ab
- 4) anti β 2 glycoprotein

Back pain

Age, Name

Present as:-

- Already diagnosed
- Initial presentation

Presenting complaint:- Back pain and duration

History Presenting Complaint:-

- Pain
- Onset
- Site
- Duration
- Frequency
- Character
- Radiation – to leg (sciatica) , radiation across to abdomen
- Progression- pain at rest /persist during sleep
- Aggravating factors
- Relieving factors
- Associated factors- urinary incontinence , LOA, documented LOW
- Progression of the pain

If previously diagnosed

- Initial diagnosis → When, where, by whom diagnosis was made, what were the symptoms then.
- What investigations initially done, what were the drugs given, how the disease symptoms controlled.

Differential Diagnosis

❖ **Non mechanical back pain → In the spine → inflammatory → Non infective**

- **Seronegative spondyloarthropathies**
 - Has familial counterpart HLA-B27 gene
 - Inflammatory Type arthritis. Pain increase at rest, Reduces on movement, Increase stiffness in the morning
 - Back pain main contribution by Ankylosing spondylitis
- 1. **Ankylosing spondylitis**
 - Usually affect adult male
 - Pain in one or both buttocks and low back pain and relieved by exercise
 - Lumbar stiffness, Typically worse in the morning and relieved by exercise

- **Non spinal complications of Ankylosing spondylitis**
 - Uveitis→Severe eye pain, Photophobia, Blurred vision
 - Costochondritis→Anterior chest pain
 - Costovertebral joint involvement causes Recurrent respiratory infections due to reduction of chest expansion

2. Other inflammatory conditions Seronegative Spondyloarthropathies

- Psoriatic arthritis→Skin patches, Nail changes, Small joint involvement DIP involved (like in osteoarthritis)
- Inflammatory bowel disease→Blood and mucus diarrhea, oral ulcers, anal tags
- Reactive arthritis→associate with urethritis, balanitis, Planter fascitis, Achilis tendinitis

❖ Non mechanical back pain→ In the spine→Non infective→SLE

- Inflammatory type arthritis.
- Other features of SLE like Oral ulcers, photosensitive skin rashes, hair loss

❖ Non mechanical back pain→In the spine→Infective→Specific(TB)

- Night sweats or cough
- Malaise, fever, Pain
- Limitation of movement of spine (TB cause a Discitis)
- Hx of pulmonary TB

❖ Non mechanical back pain→In the spine→Infective→Non specific→

- Acute osteomyelitis
 - Fever
 - Immunocompromised patients eg:-Diabetes mellitus

❖ Non mechanical back pain→In the spine→Neoplasm→Benign

❖ Non mechanical back pain→In the spine→Neoplasm→Malignant→primary→ Rare

❖ Non mechanical back pain→In the spine→Neoplasm→Malignant→secondary

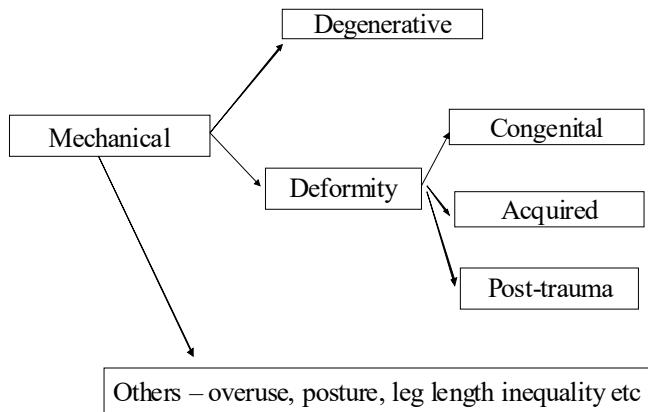
- Patient is unwell
- With severe unrelenting pain
- Often localize to a particular area of spine
- There may be a past history of primary tumour: Bronchus, Breast, Thyroid, Prostate, Kidney , GIT
- Pain may occur with a sudden onset pathological fracture by a collapsed vertebra
- Rarely Paraplegia is a presenting feature (B/L LL numbness)
 - 2ndry deposits
 - Prostatic involvement→ retention, hesitancy, Poor stream
 - Thyroid involvement
 - Breast→any lumps, previous operations
 - Bronchus→chronic cough, haemoptysis , pleuritic type chest pain

- **Multiple Myeloma**
 - Presentation over 60 years
 - Causing pancytopenia
 - Recurrent infections → Urinary tract infections, Chest infections (especially streptococcus pneumonia)
 - Anaemia → Lethargy, faintness, shortness of breath on exertion
 - Bleeding manifestations → Epistaxis, Gum bleeding, Easy bruising
 - Hypercalcaemia → Constipation, Polyuria, Polydipsia
 - Hyperviscosity
 - Pain and swelling of limb—DVT
 - Venous claudication
 - Hemi-sensory loss/One side weakness → stroke
 - SOB and Haemoptysis → Pulmonary embolism
 - Headache and dizziness
 - Blurred vision
 - Pruritus following hot baths
 - Cord compression or cauda equina – B/L LL weakness , numbness
 - Acute renal failure → Oliguria, Anorexia,
 - Chronic renal failure → Polyuria, Polydipsia, Uraemic symptoms
 - Amyloidosis → Carpal tunnel syndrome, Diarrhoea
 - Unilateral limb swelling-malignant infiltration → Lymphatic/venous block by Rectal, prostate malignancy

- ❖ Non mechanical back pain → Outside the spine → Gyn, Pancreas, Peptic ulcer disease, Renal, GB
 - **Visceral pain**
 - **Penetrating peptic ulcer**
 - Epigastric pain which radiates to back
 - Pain relieved by food and antacid
 - **Ca of pancreas**
 - Boring pain in the back
 - Unrelenting pain
 - History of anorexia and weight loss
 - **Ca of the rectum**
 - Per rectal bleeding
 - Lower back pain with sciatica (Invasion of sacrum and the sacral plexus)

 - **Vascular**
 - Dissection of Aortic aneurysm
 - Gives a severe tearing type pain interscapular,
 - Pain associated with chest pain
 - Usually patient is in shock
 - Hx of aortic aneurysm, Myocardial infarction (can cause aneurysm form)

- Renal
 - Carcinoma of the Kidney
 - Haematuria
 - Ureteric colic
 - Pain radiates from loin to groin and is severe
 - Unable to get in to a comfortable position
 - Inflammatory disease of kidney
 - Upper lumbar back pain
 - Feverish with rigors
 - Complains of frequency and dysuria
- Gynaecology
 - Usually associate with pelvic discomfort
 - Patient also complain of dysmenorrhoea, Menorrhagia, Post menopausal bleeding



- ❖ Mechanical
 - Pain → Increase with movement, Relief with rest
- ❖ Mechanical → Degenerative
 - Osteoarthritis
 - Usually present in older patients
 - Arthritis of large joints, asymmetrical involvement, small joint involvement (DIP joints)
 - Pain made worse on movements, Relieved by rest
 - Sudden onset of pain radiating down the back of the leg (Sciatica)
 - Neurological symptoms may be present : weakness of limbs, bladder symptoms

❖ Metabolic

- Osteoporosis
 - Commonest in post-menopausal woman, Bone pain, Pathological fractures present
- Osteomalacia
 - Adults with a history of gastrectomy, Anticonvulsant therapy, Steatorrhoea
 - Cushing's syndrome
 - Long term steroid therapy

❖ Mechanical→Deformity→congenital

- Spondylolisthesis
 - Low lumbar back pain
 - Worst on standing
 - May not present until late childhood or early adult life

❖ Mechanical→Deformity→Acquired

- Lumbar spondylosis
 - Episodic mechanical spinal pain
 - Progressive stiffening
 - Facet joint pain
 - Spinal stenosis features
- Spondylolisthesis
 - Cause features of acute disc prolapse→with or without nerve root irritation
- Spinal and root canal stenosis
 - Cause neurogenic claudication→Pain at first step of walk.
 - Pain and parasthesiae in a root distribution brought by walking and relieved with climbing steps and rest.

❖ Mechanical→Deformity→Post trauma

- Clear history of trauma, Road traffic accidents, fall from height

PMHx

Hypertension, DM, Hyperlipidaemia, Epilepsy

SHx

- Occupation
- No of family members
- Income
- Effect on Activities of daily living - House environment stairs, Toilet, well

Examination

General examination

- Febrile(Osteomyelitis, Infection)
- Emaciated(neoplasms)
- Pale(Chronic disease)
- He is in pain
- Icteric(Pancreatic CA, Porta hepatis involvement)
- Puffy face(CRF)
- Gum bleeding, Epistaxis(MM)
- Hands
 - Half half nails(CRF)
- Limbs
 - Echymosis, bruises, purpura(MM)
 - Oedema(CRF)

Inspection of spine

- Gross deformities of spinal cord→Kyphosis, scoliosis, Lumbar lordosis
- Curvature of the spine (loss of curvature if large area is affected)
- Any trauma, abrasions

Palpation

- Swelling, redness, tenderness, Reduce movements
- Movements→flexion, Extension, lateral flexion, Rotation
- Gibbus→due to vertebral collapse in Tuberculosis
- Spondylolisthesis→Inspection Kyphosis, spina bifida
- Palpation—A step may be palpable in the line of the spinous process with a skin crease below.
(L5 slip on S1 usually)
- Or less commonly L4 slip on L5
- Occasionally neurological signs

Disc prolapsed

- Marked scoliosis and muscle spasm, straight leg raising test positive

Spinal cord stenosis

SLRT +ve or negative with the degree of limitation
(Straight leg raising Test)

Ankylosing Spondylitis

- Stiff spine→Lateral flexion and forward flexion restriction
- Shober's test
- In advanced cases cannot raise head
- Check eyes

Nervous system

- Sensory
- Motor

Breast examination

Respiratory examination

- Effusion → malignancy
- Healed/active TB . Active TB bronchial breathing, Reduced Vocal fremitus and Vocal Resonance
- Lung collapse → Tracheal deviation to affected side, Reduce Vocal fremitus and Vocal resonance, Dull on percussion

Abdominal examination

- Liver, spleen , any other masses , kidney, bladder, para-aortic LN
- **No hepatosplenomegaly in multiple myeloma**
- Pelvic lumps → Uterine, ovarian
- Groin :Testicular lumps
- DRE → Rectal CA, Enlarged, hard nodular prostate with obliterated median groove
- Vaginal examination → Fibroids, PID, Endometriosis, Uterovaginal prolapse

CVS

- Arrhythmias(Calcium increase)

Discussion

Investigations

1. X ray of spine → Postero-anterior view, Lateral view
 - Ankylosing spondylitis
 - Ealiest sign → Blurring of upper and lower vertebral arms of thoroco-lumbar (Lateral chest x ray)
 - Syndesmophytes
 - Bamboo spine → Sacroiliac fuse, costovertebral fuse
 - Metastatic deposits – large lytic lesions
 - pedicular erosions(only in mets)
 - Normal disc space
 - Prostatic CA – osteosclerotic lesions
 - TB spine – wedge fractures
 - disc space narrowing
 - sclerosis near the discs
 - paravertebral ascess (cold abscess)
 - Lumbar spondylosis → Bone become sclerotic and osteophytes form around the rim of vertebral end plate to produce schmorls node on X ray

2. Infection

FBC

- Increase WBC → Osteomyelitis,
- Pancytopenia, anaemia (in malignancy)
- Increase ESR → TB, metastasis, Myeloma, Ankylosing spondylitis
- Normal ESR → referred pain (aneurism, pancreatic neoplasm, pancreatitis)
- Increase CRP → Infection

3. Blood picture

- Bicytopenia, pancytopenia, rouleaux formation

4. Renal involvement → Urea and electrolyte

5. Liver function test

ALP increase → Ca of pancreas, Paget's disease, Osteomalacia, metastatic deposits

ALP is usually normal in multiple myeloma

Find out the suspected primary tumour

1. Chest X ray

Suspected primary tumour-Bronchial ca

2. Skeletal survey – for MM

- multiple small , lytic lesions in ribs, pelvic bone ,angle of jaw, skull(pepper pot skull)

3. Serum protein electrophoresis → look for monoclonal bands (in MM)

4. Urine Bence Jones protein (MM)

5. PSA-Prostate specific antigen in Prostate CA

6. High S. Calcium- Malignancy, Myeloma

USS

Aortic aneurysm, Renal lesions, Uterine lesions

CT scan

Pancreatic lesions, Aortic lesions

MRI

Spinal cord lesions-Disc lesions, spinal cord tumors, Increase spinal compression

CT myelogram

Management

Infection

- Treat infection with antibiotics
- Pain → NSAIDS, O.tramadol

Lumbar spondylosis

- Orthopaedic assessment
- Needs careful monitoring during growth spurt

Disc prolapse

- Bed rest → Advice a short period 2-3 days bed rest
- Lying flat for a lower disc but semi reclining for a high lumbar disc
- Prescribe analgesia and muscle relaxants
- X ray guided epidural or nerve root canal injection by a pain specialist
- Physiotherapy - once the pain is tolerable, encourage to mobilize
- Referral to a surgeon For a possible microdisectomy or hemilaminectomy (If pain persists and is severe for more than 6-10 weeks or if the disc is central)

Ankylosing spondylitis

- -Exercises → Morning exercises aim to maintain spinal mobility, posture, chest expansion
- -Pain control → an evening dose of slow releasing NSAIDs
- -Peripheral arthritis and enthesitis -Managed with NSAIDs or local steroid injections
- -Peripheral arthritis → Sulfasalazine or methotrexate
- -In severe disease → TNF-alpha

Psoriatic arthritis

- Pain - Analgesics or NSAIDS (But occasionally they can lessens the skin lesion)
- Local synovitis → Responds to intra-articular corticosteroid injections
- Slows the joint damage → Sulfasalazine
- Severe disease → Methotrexate or cyclosporin given because they control both skin lesion and arthritis
- Severe skin and joint disease → Anti TNF alpha agents → eg:-entanercept
- Corticosteroids should avoid, why?
 - Destabilize the skin disease

Enteropathic arthritis

- Inflammatory bowel disease need to be treated
- Arthritis→NSAIDS
- If monoarthritis→best treated by intra articular corticosteroids
- Sulfasalazine→prescribed both bowel and joint disease
- TNF-alpha blocking→effective in Crohn's disease but not in ulcerative colitis
- Remission of joint disease occur with the remission of Ulcerative colitis or after total colectomy.
- But in Chron's even after remission of IBD→arthritis remain

Reactive arthritis

- Treat the infection→antibiotics
- Pain- Local corticosteroids injections, NSAIDS
- Relapsing cases→sulfasalazine or methotrexate
- TNF alpha blocking agents→in sever disease

Multiple Myeloma

Treatment

Supportive therapy

1. Anaemia corrected→Blood transfusion required, Erythropoietin helpful
2. Infection→antibiotics
3. Bone pain-radiotherapy, NSAIDS(be aware of renal involvement)
4. Pathological fractures→orthopedic surgeon

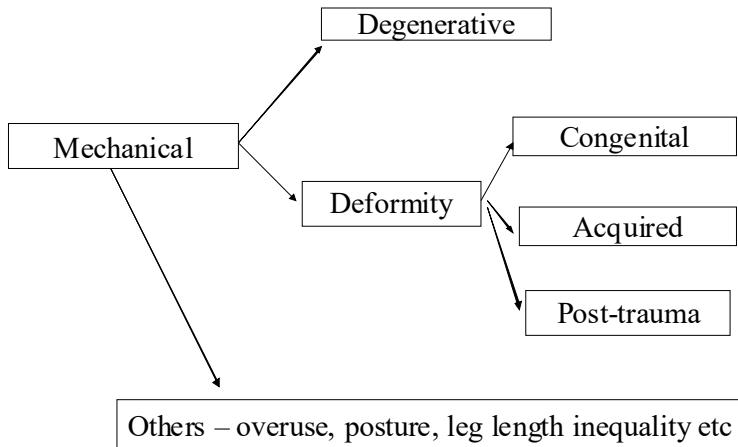
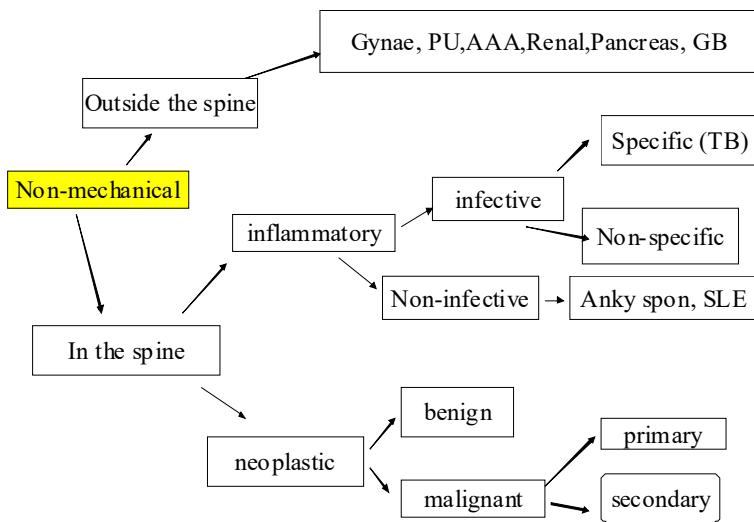
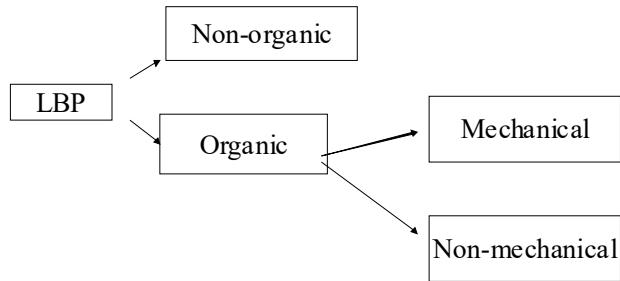
Specific treatment - chemotherapy

1. Bisphosphonates→zoledronate or clodronate which inhibit osteoclastic activity (It reduces progression of bone disease)
2. High dose Melphalan→improved the duration of remission
Auto-transplantation→improved duration of remission

1. What are the red flag signs of back pain?

- a. starts before the age of 20 or after 50 years
- b. Is persistent and a serious cause is suspected
- c. Is **worse at night** or in the morning, when inflammatory arthritis(eg:- ankylosing spondylitis) infection or a spinal tumour may be the cause
- d. Is associated with a systemic illness, fever or weight loss
- e. Is associated with neurological signs or symptoms

Non-traumatic back pain



Multiple myeloma

- Malignant neoplasm of plasma cells → Abnormal plasma cells accumulate in the bone marrow → secrete immunoglobulin fragments (paraproteineamia)
- Characterised by
 - ↑ malignant plasma cells in BM
 - Monoclonal proteins in serum & urine
 - Lytic skeletal lesions

Epidemiology

- 98% → >40yrs
- Peak at 7th decade
- Survival time – few weeks to 2 years

Pathological basis

1. Tissue infiltration
2. Paraproteineamia
3. Impaired immunity

MM → Malignant plasma cells → Secretes more osteoclastic factors → Form little holes on bone → Lytic lesion appearance on x-ray → fragile bones → Disc collapse → Nerve root compression → Backache

Clinical features

- Hypercalcaemia
- Renal impairment (due to paraproteineamia) – Polydypsia, polyuria, LOA, Vomiting, Constipation, Mental disturbances
- Abnormal bleeding tendency, due to
 - Myeloma proteins interfering with
 - Coagulation factors
 - Platelets
 - Thrombocytopenia (in advanced disease)
- Anaemia (Tissue infiltration)
- Bone involvement (Tissue infiltration) – Bone pain, Pathological fractures
- Recurrent infections (Reduced antibody production, despite of abnormal production of plasma cells & neutropenia due to BM infiltration)
- Hyperviscosity Xn due to abnormal increase of monoclonal antibodies.
- Primary amyloidosis (Macroglossia, CTS, diarrhea)

Diagnosis of MM

1. Monoclonal proteins in serum/urine M band
2. IgG in 2/3, IgA in 1/3
3. >30% of plasma cells in the BM
4. Osteolytic lesions/generalized rarefaction of bone – Osteoclast activating factor
5. Urine Bence Jone Proteins – in 2/3 of cases

Investigations

- FBC - Neutropenia & thrombocytopenia in an advanced disease
- Blood picture
 - Normocytic normochromic anaemia
 - Prominent rouleaux formation
 - Leucoerythroblastic blood picture

- ESR ↑
- ↑ S. Ca
- ALP – Normal except in fractures
- ↓Albumin in advanced disease with ↑ total serum proteins
- Cryoglobulineamia
- Urine – BJP, ↑ Uric acid
- Xray skull - lateral

Treatment

1. Supportive
 - a. Renal failure
 - i. Rehydrate & treat underlying causes
 - ii. Dialysis
 - b. Bone disease & hypercalcaemia
 - i. Bisphosphonates (Pamidronate) –Inhibits osteoclastic activity → Reduce progression of the disease
 - c. Compression paraplegia
 - i. Decompression laminectomy or irradiation
 - ii. Corticosteroid therapy
 - d. Anaemia – Blood transfusions
 - e. Bleeding (caused by paraproteins interfering with coagulation) → Repeated plasmapheresis
 - f. Infections
 - i. Prophylactic immunoglobulins
 - ii. Broad spectrum antibiotics & antifungals
2. Specific
 - a. Chemotherapy
 - i. Melphalan (Oral alkylating agent. In elderly combine with prednisolone)
 - ii. Allopurinol
 - iii. Thalidomide
 - iv. Velcade – Proteosome inhibitor
 - v. Bisphosphonates
 - With chemotherapy →↑ cell breakdown → Pt should have to drink at least 3L/day of water to flush out toxic substances
 - b. Bone marrow transplantation

Causes of renal impairment in MM

Causes for leucoerythroblastic blood picture

1. Bone marrow invasion by a tumour
2. Tumour arising from BM
3. Infections – TB(Miliary)
4. Severe sepsis
5. Severe haemolysis (G6PD deficiency)
6. Severe haemorrhage
7. DIC
8. Osteopetrosis
9. Multiple myeloma
10. Myelofibrosis

Medical emergencies in MM

1. Hypercalcaemia
2. Cord compression
3. Renal failure
4. Hyperviscosity

Chest Pain [IHD & CCF]

PC- Chest pain (duration)

HPC-

- ❖ Details of chest pain
 - At what time & what he was doing when chest pain occur
 - Onset (Sudden/Gradual)
 - Nature (Tightening in Cardiac causes)
 - Site (Retro sternal in MI, If pleuritis only on the site of inflammation)
 - Duration (>20mins = MI, <20mins = Angina)
 - Severity (Impending death in cardiac causes)
 - Radiation (Left arm, Neck, Jaw in cardiac causes)
 - Associated factors (Sweating, SOB, Syncope, Palpitations, Vomiting, Faintishness, Nausea in cardiac causes)
 - Exacerbating factors (Heavy meals, Exercise, Psychological stress, Cold weather)
 - Relieving factors (Resting/lying down, GTN)

- IHD
 - Retro sternal, tightening type
 - Radiates to neck, jaw, arm
 - Sob, palpitations
- Stable angina
 - Sudden onset progressive
 - Chest pain for <20min.
 - Following exertion
 - Relieved by rest, GTN
- Unstable angina
 - Duration > 20 min
 - Not relieved by resting, GTN
 - Can't predict the pain
 - Reduced exercise tolerance
- MI
 - New onset chest pain
 - Pain at rest
 - Deteriorating chest pain
 - Retro sternal chest pain > 20 min.
 - Tightening type
 - Radiation to arm, jaw, hand
 - Associated with sweating, palpitations, vomiting, faintishness, SOB, weakness
 - Not relieved by sublingual GTN

Differential diagnoses

- IHD
- Aortic dissection
- Pulmonary embolism
- Pneumonia
- GORD
- Musculoskeletal
- Pericarditis

Complicated IHD with CCF,

LVF

- Symptoms - Breathlessness, Orthopnoea, PND, pink frothy sputum
- Signs – Fine end inspiratory crepts, Gallop rhythm, Pulses alternans.

RVF

- Symptoms – Fatigue, Anorexia, Abdominal distension, Ankle swelling.
- Signs – Elevated JVP, Tender hepatomegaly, Pleural effusions

- ❖ Exclude other differential diagnoses
- Aortic dissection
 - Sudden severe tearing type chest pain
 - Central pain
 - Radiates to arm, back
 - Dizziness, numbness, pain, coldness of arm
 - Transient weakness of the part of the body
- Pulmonary embolism
 - Sudden onset
 - Pleuritic type chest pain
 - Tachypnoea, haemoptysis
 - Previous hx of DVT, long term immobilization following surgery
- Pneumonia
 - Pleuritic pain
 - Aggravated with breathing, cough
 - Productive cough
 - Fever
 - Wheezing
 - Haemoptysis
- GORD
 - Retrosternal burning pain
 - At night or bending forward
 - Belching, burping, heart burn, regurgitation of food
 - Cough due to laryngeal irritation
 - Risk factors- dairy products, fatty meals, chocolate, coffee, smoking, alcohol, NSAIDs
- Muscular skeletal
 - History of trauma, exercise ,fever
 - Aggravated by deep breathing, movement & touching
 - Exact site of pain & tenderness
- Pericarditis
 - Diffuse stabbing pain
 - Aggravated by deep breathing & movements
 - Relieved by leaning forward
 - dyspnoea
- Psychological
 - Anxiety
 - Depression
 - Family problems
 - Social problems

❖ ASK for **risk factors** of IHD

- DM
- HT
- Hyperlipidaemia
- OCP
- Smoking
- Alcohol
- Sedentary life style - lack of exercises, High fat diet
- Previous hx / Fhx of IHD
- Psychological stresses

❖ Management up to now

❖ Similar previous episodes

❖ If present,

- When
- How many episodes
- What happened
- Hospital admissions
- Drugs
- Duration of the drugs

PMHx – Anaemia, hypo/ hyperthyroidism

PSHx – underwent any coronary interventions

DHx – as mention above

FHx – IHD, DM, Hypercholesterolemia

SHx – occupation, exercise, lifestyle, psychological aspect

Examination –

- Ill looking, sweaty, cold peripheries
- Patient is in pain
- Febrile [pneumonia ,pericarditis, pulmonary embolism]
- obese
- Pale - In MI, anaemia
- Cyanosis - LVF
- Goiter [hypo/ hyperthyroidism]
- Xanthelesma, xanthoma, corneal arcus [hyper cholesterolemia]
- Skin rash [herpes zoster]
- B/L pitting ankle oedema

CVS Examination

- Inspection : Dyspnoea (pulmonary oedema due to LHF), Patient is haemodynamically stable ?
- Pulse : Unequal radial pulses in aortic dissection, Check peripheral pulses(PVD & aortic dissection)
Irregularly irregular pulse in AF
Tachycardia
- BP : Low in aortic dissection, Postural drop in MI
- JVP : Prominent 'a' wave in Right heart failure
- Precordium : Look for apex location and character(heaving)
- Auscultation ; Loud 1st HS → MS or tachycardia
Loud 2nd HS → Pulmonary HT
Gallop rhythm

Respiratory Examination

- Inspection: Reduced chest movements
- Palpation: vocal fremitus reduced (pneumothorax), Increased in consolidation(pneumonia)
- Percussion : dull(Consolidation), Hyperresonant(pneumothorax)
- Auscultation : Coarse Crepitations(Pneumonia), Bilateral fine end inspiratory crepitations all over the lung(if resolving it's basal) in pulmonary oedema

Abdominal Examination

- Palpation : Features of acute abdomen such as severe guarding, rigidity & severe diffuse tenderness as a result of perforated peptic ulcer or acute pancreatitis
- Percussion : Flank dullness due to bleeding in perforated peptic ulcer
Absent liver dullness(due to leakage of air from perforated ulcer)
- Rectal examination : Malaena(Perforated peptic ulcer)

Nervous system

- Consciousness (GCS)
- Speech
- Evidence of focal signs
- Hemiparesis

Investigation

- To confirm the diagnosis of MI
 - Urgent bed side ECG : ST segment elevation(STEMI), T inversion, New onset LBBB
 - Cardiac enzymes : Troponin I and Troponin T (peak at 12-24hrs and remain elevated upto 7 days)

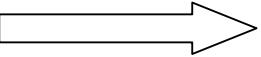
For Angina

- ✓ ECG
 - Normal between attacks
 - Pathological Q waves- old MI
 - LVH
 - LBBB
 - During an attack
 - Transient ST depression
 - T inversion
- ✓ Exercise ECG
 - ST depression > 1mm- myocardial ischemia
- ✓ Echo
 - Assess ventricular wall involvement
 - Ventricular function
- ✓ Coronary angiography
 - In selected pts when diagnosis is unclear
 - If interventional procedure is planned

For Unstable Angina

- ✓ ECG
 - ST depression
 - T inversion
- ✓ Cardiac enzymes – troponin I, T are normal

MI

- ✓ ECG
 - ST elevation 
 - New LBBB
 - Non ST elevation
- ✓ Cardiac enzymes normal initially
 - Elevated after 9- 12 hours
 - Troponin I, T
 - CK- MB- less specific
- ✓ FBC - Anaemia
- ✓ FBS
- ✓ CXR – PA (If heart failure is present)
- ✓ Lipid profile
- ✓ 2D Echocardiogram (before discharge)
 - Ejection fraction
 - Hypokinetic areas
 - Valvular defects

Anterior	V3- V5
Antero septal	V1 – V3
Lateral	V4- V6, aVI , L1
Inferior	L2,L3, aVf
R/ventricle	V4R
Posterior	V1,V2 tall & wide T & R waves, slight ST depression V5, V6 ST elevation

Aortic dissection

- ✓ ECG – normal or ST/ T non specific changes
- ✓ CXR- widened mediastinum

Acute pericarditis

- ✓ ECG – saddle shape ST elevation, low voltage complexes if pericardial effusion

Pulmonary embolism

- ✓ ECG-
 - L1- deep s
 - L3- Q wave, T inversion
 - RBBB, R/ axis deviation
- ✓ ABG
 - Normal
 - lowPaO₂
 - low - normal PaCO₂ – suggestive
- ✓ CXR
 - Wedge shape infarcts
 - Dilated proximal pulmonary arteries
 - Focal oligaemia

MANAGEMENT

ANGINA

- ✓ Patient education
 - Nature of illness
 - Good prognosis
- ✓ Manage coexisting conditions
 - Diabetes
 - Ht
 - Anaemia
 - Hypothyroidism
- ✓ Exclude risk factors
 - Smoking
 - Hypercholesterolemia
 - Obesity
- ❖ Medical management
 - Nitrates
 - Short acting – SL/spray GTN
 - Long acting – ISDN (bd, tds) ISMN (once daily)
 - Beta blockers
 - Atenolol
 - Metoprolol
 - CCB
 - Verapamil
 - Diltiazem
 - Amlodipine
 - Nicorandil
 - When others Cl
- ❖ General management
 - Aspirin 75mg- 325 mg
 - Lipid- statins, dietary modifications
 - Ht management
 - Life- style changes- smoking, exercise
- ❖ Surgical
 - Angioplasty (PTCA)
 - Angioplasty & stenting
 - Coronary artery bypass grafting

Issues in MI

- Anti platelets
- Pain relief
- Specific treatment
- Other acute therapy

Acute coronary syndromes

ST elevation MI –

- General mx
- A medical emergency
- High flow oxygen via face mask
- Aspirin 300mg tablet to chew & swallow + Clopidogrel 300mg stat
- Statins- atorvastatin 20 mg stat
- Gain IV access
- Attach to ECG monitor BP, PR,RR,sPO2

- Pain relief
 - IV Morphine 2.5- 5mg slowly
 - Repeat morphine every 5 min until pain relieved
- IV Metoclopramide 10 mg
- Sub lingual GTN or 10 – 200 microgram/min infusion
- Beta blockers
 - Metoprolol 5 mg IV repeat in every 5 min up to maximum 15 mg
- Specific
 - Thrombolysis
 - Streptokinase
 - Tissue plasminogen activator
 - Tenecteplase (TNKase)
 - Reteplase
- ✓ Sterptokinase
 - Within 12 hours of onset
 - When ECG shows 1 or more of,
 - ST elevation > 1mm in limb leads
 - ST elevation > 2 mm in two adjacent chest leads
 - New LBBB
 - 1.5 million units in 100 ml of N/saline infusion over 1 hour
 - SK contains in a glass vial in powder form
 - Should be dissolved gently to avoid frothing(frothing → more allergic reaction)
 - Patient should be in monitoring bed with a cardiac monitor
- Low dose ACEI (enalapril or captopril)
- Look for complications
 - Cardiac arrest
 - Tachyarrhythmias
 - Heart block
 - Pulmonary oedema
 - Cardiogenic shock

NON ST elevation MI-

- General mx
- Aspirin 300 mg followed by maintenance dose of 75mg
- Clopidogrel 300 mg followed by maintenance dose of 75mg oral
- Metoprolol 25 mg oral bd, verapamil 80 mg/ diltiazem 60mg if unable to take beta blockers
- Statins- atorvastatin 20 mg stat
- low dose ACEI
- Specific treatment
 - (Fractionated heparin)LMWH 1 mg / kg sc bd 3 days
 - No need to monitor APTT. Doesn't cause thrombocytopenia
 - If not available unfractionated heparin IV infusion 70 u/kg bolus & 5u/kg/hr for 2- 5 days
 - After 6 hours of unfractionated heparin do APTT
 - If APTT is raised reduce the dose, if low increase the dose
 - Cause thrombocytopenia
 - Glycoprotein2B/3A inhibitors
 - Absiximab

- ❖ Day 1- strict bed rest + NBM + catheterize
- ❖ Day 2- Can sit on bed + liquids, initiate with oral sips + toilet onto a bed pan
- ❖ Day 3 – Can sit on a chair near the bed + semi liquid diet + toilet onto a bed pan
- ❖ Day 4 – can walk around the bed + Semi solid diet + Go to toilet on a wheel chair
- ❖ Day 5 – can walk to toilet + solid diet but small amounts + discharge
- ❖ After discharge can walk around house for few min and gradually increase
- ❖ 2 weeks rest
- ❖ 3 weeks avoid heavy work & driving heavy vehicles
- ❖ 2 weeks avoid sexual activities. Then 1st become the passive partner.

Aortic dissection

- Strict bed rest
- 2 large bore IV cannulae
- Blood for FBC, BU/SE, cross match & coagulation profile
- Pain relief-slow IV morphine
- IV metoclopramide 10 mg
- Monitor BP, PR, UOP
- Catheterize the patient
- Keep NBM
- Strict BP control
 - Keep SBP 100 – 110
 - Labetalol 50 mg IV over 2 min or
 - Atenolol IV 5 – 10 mg slowly or
 - CCB

Pericarditis

- Stop oral anticoagulants
- NSAIDs – oral ibuprofen 400mg 8 hourly with PPI [omeprazole 20 =-40mg orally]
- Treat underlying cause like infection
- Prednisolone 40mg oral If no response to NSAIDs after 48 hours

Pulmonary embolism

- High flow oxygen
- Pain relief – NSAIDs
- Monitor sPO2
- Gain IV access- colloid if BP is low
- Anti coagulants
 - Heparin for 5-6 days
 - LMWH 1.5 mg/kg sc
 - Unfractionated heparin 100units/kg loading dose
 - Warfarin after confirm diagnosis
 - 5mg/daily adult

Discussion

- ❖ Angina- only ischemia
- ❖ MI- cardiac muscle death due to ischemia
 - STEMI- Full thickness of muscle death
 - nonSTEMI – Sub endocardial infarction. Inner 1/3 – 1/2 of myocardial death
- ❖ causes for IHD
 - obstructed coronary blood flow
 - atheroma
 - thrombus
 - spasm
 - emboli
 - stenosis
 - low oxygenated blood
 - anaemia
 - hypotension
 - increase demand
 - thyrotoxicosis
 - AS
 - Hypertension
- ❖ Symptomatic when lumen reduced < 70%, < 90 % symptoms at rest
- ❖ Risk factors

Non modifiable	Modifiable	
Age	Smoking	Heavy alcohol
Male sex	DM	OCP
+ve family hx in 1 st degree relatives <50 yrs	HT	Workstress
Genetics	Hyperlipidemia	
	Lack of exercise	
	Obesity	

- ❖ Types of angina
 - Exertional angina
 - Decubitus angina - when lying down
 - Nocturnal angina - at night. Provoked by vivid dreams, due to vaso-spasm
 - Variant angina - at rest , due to artery spasm, ST elevation,
- ❖ MI
 - Due to thrombosis on a pre existing plaque
 - Silent in elderly & DM
 - Diagnosis
 - 2 of
 - History suggestive of MI
 - ECG changes
 - Cardiac enzymes

- Complications of MI

Acute	Late
Arrhythmia	Thrombo embolism
Cardiac failure	Tamponade
Cardiogenic shock	Septal defects
Pericarditis	MR
Myocardial rupture	Post MI syndrome
	Left ventricular aneurysm

❖ What are the signs of reperfusion ?

- ✓ Reduce pain
- ✓ At least 15% reduction in the ST elevation in worst leads
- ✓ Wash-out phenomenon
- ✓ Reperfusion arrhythmia
 - Sinus bradycardia
 - Accelerated idioventricular rhythm(Wide QRS complex, regular rhythm, rate 60–100 beats/min, is common and usually benign; if it causes hypotension, treat with atropine 0.6 mg IV.)

❖ What are the signs you look for in the 2nd day ward round after full thickness MI?

- ✓ Pericardial effusion
- ✓ Pericardial rub
- ✓ Pulse , BP

❖ When you are giving SK the patient developed hypotension. What are the causes?

- ✓ Anaphylaxis to SK
- ✓ Bleeding due to SK
- ✓ LVF
- ✓ RVF
- ✓ Ongoing ischaemia

❖ How do you manage acute LVF?

Basic measures

- ✓ Sit upright
- ✓ High oxygen (face mask, CPAP)
- ✓ IV cannula
- ✓ IV loop diuretics - frusemide 40mg (vasodilatation diuresis)
- ✓ IV opiates - morphine 2.5 – 5mg(reduce anxiety and preload)
- ✓ Buccal or sublingual nitrates(reduce preload and after load)
- ✓ Frusemide Can be repeated
- ✓ If no improvement
 - SBP <90 Inotropes
 - Dopamine IV (high dose)
 - Dobutamine IV
 - SBP > 110mmHg
 - Glyceryl nitrates infusion

Restrict fluids

❖ Mx of acute RVF

❖ Complications of acute MI

VENTRICULAR ARRHYTHMIA – VF, VT, SVT, Accelerated idioventricular rhythm , bradyarrhythmia and heart block

MECHANICAL COMPLICATIONS Ventricular septal rupture and acute mitral regurgitation due to papillary muscle ischemia/infarct develop during the first week following MI and are characterized by sudden onset of CHF and new systolic murmur. Echocardiography with Doppler can confirm presence of these complications.

CONGESTIVE CARDIAC FAILURE

VENTRICULAR ANEURYSM Localized “bulge” of LV chamber due to infarcted myocardium. *True aneurysms* consist of scar tissue and do not rupture. However, complications include CHF, ventricular arrhythmias, and thrombus formation. Typically, ECG shows persistent ST-segment elevation, _2 weeks after initial infarct; aneurysm is confirmed by echocardiography and by left ventriculography. The presence of thrombus within the aneurysm, or a large aneurysmal segment due to anterior MI, warrants oral anticoagulation with warfarin for 3–6 months.

RECURRENT ANGINA Usually associated with transient ST-T wave changes; signals high incidence of reinfarction; when it occurs in early post-MI period (_2 weeks), proceed directly to coronary arteriography.

DRESSELER’S SYNDROME an autoimmune response to cardiac damage occurring 2-10 weeks(late in the recovery phase) post-infarct . Anti-myocardial antibodies are formed. Recurrences are common. Can also have pleural effusions.

- ❖ Advice before discharge
 - Life style modification – stop smoking , healthy diet. Regular exercise
- ❖ Post MI drug therapy
 - Reduce mortality over the following years
 - Aspirin 75-100mg/day
 - β blockers to maintain HR <60 b.p.m.
 - ACE inhibitors
 - Lipid lowering agents
 - (long acting nitrates; if there is residual angina

Acute coronary syndrome decisions

High risk patients for progression to MI or death require urgent coronary angiography

- Patients with recurrent or persistent angina with ST changes ≥ 2mm or deep T wave changes
- Clinical signs of heart failure or haemodynamic instability
- Life threatening arrhythmias (VF, VT)

should have early (<72 hours) coronary angiography and interventions

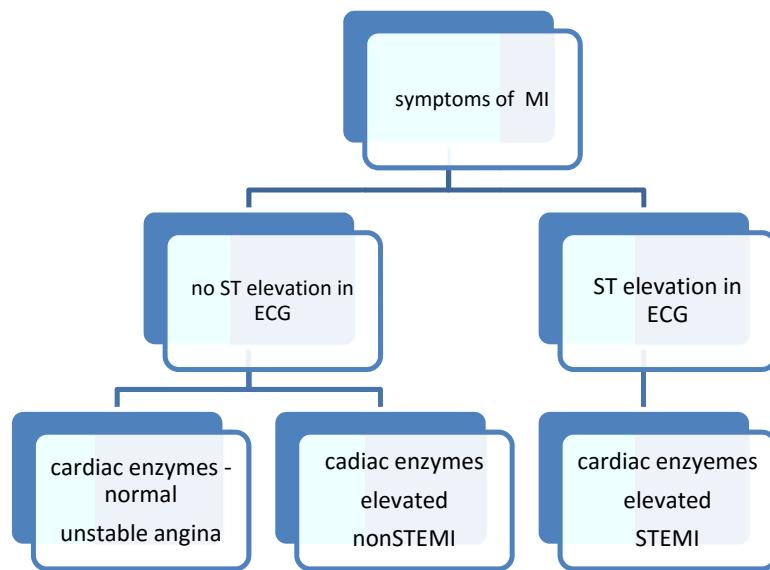
- immediate or high risk TIMI or GRACE scores,
- elevated troponin,
- dynamic ST or T wave changes,
- diabetes mellitus,
- renal dysfunction,
- reduced left ventricular function,
- early post infarction angina,
- previous MI,
- PCI within 6 months or
- previous CABG

- ❖ TIMI risk score in acute coronary syndromes
 - Age > 65
 - More than three CAD risk factors (HT, Lipids, F/H/O, DM, Smoking)
 - Known coronary artery disease (> 50% stenosis in previous coronary angio)
 - Aspirin use in the last 7 days
 - Severe angina (more than 2 episodes of rest pain during last 24 hours)
 - ST elevation in ECG (Horizontal ST depression or Transient ST elevation > 1mm)
 - Elevated cardiac markers (CK-MB / Trop. T)

- ❖ The surgical options
 - Angioplasty;
 - Angioplasty and stenting

Coronary artery bypass grafting (Triple vessel)

- ❖ Unstable angina
 - Accelerating angina
 - New onset angina
 - Progressive angina



- ❖ Drugs used in IHD
 - Morphine
 - Reduce pain
 - Reduce anxiety
 - Vasodilation- low pre load & after load
 - Nitrates
 - Reduce venous return: reduce intra-cardiac diastolic pressure
 - Vasodilatation: reduce left ventricular impedance to emptying
 - GTN ,ISDN, ISMN- headache, tachycardia, palpitations
 - Relax coronary arteries

- CCB
 - Block voltage gated Ca channels
 - Relax coronary vessels
 - Peripheral vasodilatation
 - Reduce force of ventricular contraction
 - Reduce HR (non-dihydropiridine Ca B)
 - Verapamil, Amlodipine, Diltiazem
 - Dihydropyridines- nifedipine, amlodipine
 - Reflex tachycardia, Flushing, headache
 - Non dihydropyridine
 - Verapamil- not used with beta blockers cause bradycardia, constipation
 - Diltiazem – no reflex tachycardia
- Nicorandil
 - a potassium channel activator; both arterial and venous dilators
 - Not used as a first line drug.
 - When others are contraindicated / refractory angina
- Beta blockers
 - Reduce heart rate
 - Reduce force of ventricular contraction
 - Reduce myocardial O₂ demand esp. on exertion
 - Proven benefit in 2ry prevention
 - Beta blockers
 - Selective (β_1): Atenolol, Metoprolol
- ACEI
 - Reduce pre load, after load
 - Limit progression of HF
 - A/E- dry cough, hyperkalemia
 - Avoid in renal artery stenosis, pregnancy
 - Captopril, enalapril, lisinopril
- ARB
 - Losartan, valsartan
 - No dry cough
- Statins
 - Atorvastatin, lovastatin, simvastatin
 - Inhibit cholesterol synthesis
 - Stabilize the plaque , doesn't rupture
 - Cl in pregnancy & breast feeding
- Anti platelet drugs
 - Aspirin
 - Inhibit COX enzyme
 - Cause GI bleeding
 - Continue throughout the life time 75mg daily
 - Clopidogrel
 - ADP receptor inhibitor
 - More effective
 - Continue 9 months (75mg daily)

- Glycoprotein 2b/3a antagonist
 - Inhibit platelets aggregation
 - Cause thrombocytopenia
- Streptokinase
 - Convert plasminogen to plasmin
 - Rapid administration may cause hypotension- stop infusion .wait till BP pick up & continue
 - Bleeding tendency
 - urticaria

Contraindications for Streptokinase therapy

- Active internal bleeding
- Suspected aortic dissection
- Recent head trauma within last 3 weeks
- Intracranial neoplasm
- Previous haemorrhagic stroke at any time
- Ischaemic stroke within the previous 1 year
- Allergy to SK
- Trauma and surgery within past 2 weeks
- Prior exposure to SK (esp. previous 6-9 months) – Relative CI
- Pregnancy or postpartum – Relative CI

DIABETES MELLITUS

- DD**
- DM
 - DI
 - CRF
 - DIURETICS

PRESENTATION

- Polyuria
- Polydipsia
- Weight loss

} Acute

As a complication or sub-acute presentation

- Skin infection - cellulitis
- Lack of energy
- Visual blurring
- Pruritus vulvae
- Balanitis
- PVD, MI
- Impotence
- Tingling and numbness of the feet
- Reduced visual acuity or retinopathy detected by an optician

Secondary problem in another long case (commonest)

Already diagnosed patient

- Diagnosis - Incidental, due to any symptoms/infections, medical check ups
- How, When, How worse (Initial FBS level & presence of complications)
- Rx since then/changes up to now-eg:-change over to oral hypoglycaemic drugs to insulin
- Oral hypoglycemic
 - What previously, what now
 - Metformin (large panadol size), glibenclamide(rice grain size),glitazone
 - S/E & compliance
- Insulin-
 - Soluble(clear), isophane(milky), mixtard
 - Knowledge about identification of expired insulin
 - What type/why
 - Advices regarding-use, storage-1st compartment
 - Injection technique-pen-90° subcutaneous-45°
 - Rotation of sites
 - Relation b/w meals- half hour before injection
 - Insulin storage – fridge
 - From where he gets the insulin
 - What's the practice
 - S/E-weight gain
 - Compliance/defaulted/Why
- Glycemic control – how frequently clinic follow up, glucometer and home testing
FBS monthly done, last FBS – done when, HbA1c – done last

Hypoglycemic attacks- *Nervousness, sweating, intense hunger, trembling, weakness, palpitations, and often have trouble speaking.*

Hyperglycemic attacks- *frequent urination (polyuria) and thirst, fatigue and lethargy, nausea, vomiting, abdominal pain, fruity odor to breath, rapid, deep breathing, muscle stiffness or aching, coma*

- When, after what incident
- How they were managed
- Hospital admissions due to complications

Complications up to now

Micro-vascular (since when)

- Retinopathy
 - Blurred vision
 - Reduced visual acuity
 - Diplopia
 - Painful red eyes
 - Ophthalmologist referral (slit lamp examination)
 - Laser treatments
 - Cataract-diagnosed, Sx done, how frequently, retinal eye scan, last eye referral,
- Nephropathy
 - Frothy urine
 - Urine albumin levels
 - Polyuria
 - CRF
- Neuropathy
 - Symmetrical sensory poly-neuropathy
 - Numbness
 - Glove and stocking (Legs > Arms)
 - Walking on cotton wool (Later)
 - Acute painful neuropathy
 - Burning/crawling pain over anterior thigh, dorsum of foot, shin, worse in the night
 - Due to sudden improvement in glycemic control
 - Spontaneously resolve within 30-12 months if good glycaemic control
 - Autonomic neuropathy
 - CVS - Postural dizziness, gustatory sweating
 - GIT - Nocturnal watery diarrhea, fullness after meals/intractable vomiting (gastroparesis)
 - GU - Incontinence, incomplete bladder emptying, urgency
 - Sexual - Impotence
 - Diabetic amyotrophy – Painful wasting of quadriceps or deltoid(tenderness over the quadriceps)
 - Knee reflexes diminished or absent
 - Associated with poor glycaemic control
 - Resolves with good control
 - Non healing ulcers at pressure points, poor wound healing
 - Neuropathic Arthropathy – Charcot foot, claw foot
 - Mononeuritis multiplex
 - 3,6 nerves, 7-bell's palsy-squints, facial palsies
 - Common peroneal nerve - Foot drop
 - Lateral cutaneous nerve of thigh - Sudden root pain
 - Carpal tunnel syndrome
 - Dermopathy
 - Necrotic black patches over the shins

- Macrovascular
 - Coronary vascular disease
 - Exertional angina – grade of exertion (following heavy meal/cold weather)
 - PHx of Acute coronary syndrome
 - Heart failure – SOB, PND, Orthopnoea, B/L ankle oedema
 - Coronary interventions, heparin/streptokinase given, cardiology referral, Echo
 - Cerebro Vascular Accidents
 - Acute onset hemisensory loss/ hemiparesis, slurred speech, blurring of vision transient (TIA)
 - Stroke – physiotherapy, surgical intervention
 - PVD – Intermittent claudication – at calf, at a distance of....., worse on going uphill
Rest pain, amputations, duplex scan of LL
- Metabolic
 - Hypoglycemia
 - Hyperglycemia Hx of previous hospital admissions due to diabetic emergencies
 - Ketoacidosis Symptoms experienced by the patient
 - Lactic acidosis
 - Hyper osmolar state
- Infections
 - Skin
 - Boils
 - Cellulitis
 - Impetigo
 - Carbuncle
 - Candidiasis of skin, nail, oral, interdigital - painful itching red colour wet skin lesion opposing skin folds
 - Conjunctivitis
 - GU
 - Balanitis, vaginitis - Foul smelling vaginal discharge
 - UTI
 - Respiratory
 - TB

PMHx- Renal problems, hyperlipidemia, on treatment/not
Hypertension, on treatment/not, last BP
Auto Immune disorders – Thyroiditis, vitiligo, pernicious anaemia
PCOS, chronic pancreatitis – episodes of epigastric pain

PSHx- Amputations, infections, wound toilet, pain radiating to back, heavy alcohol

DHx- – Thiazide, atypical antipsychotics – secondary DM
 β blockers – worsen glucose intolerance & mask hypoglycemia
 Lithium – diabetes insipidus, OCP
 Allergy

Diet Hx-Controlled/not

On what basis
 Content of food/amounts/snacks

Equal amounts at fixed intervals for main meals, in between snacks

Restriction of CHO – amount of rice/meal

Avoid refined sugar, sugary food

Dried fruits, cereals – wheat flour products, beet root, pumpkin, nuts – cashew, peanuts

Starchy foods – long grain rice, pasta, chick pea



Lean meats – skinless chicken, small fish
 Avoid beef, pork, tuna (kelavallo), seer fish (Thora), prawns, cuttle fish
 Fruits – high fibre, low sugar – plantains, papaw, wood apple
 Avoid overripe fruits, apple, grapes, mango
 Moderate – fatty foods, take away
FHx- DM in 1st degree relatives
 Complications – retinopathy, nephropathy – high risk, stage of disease
 MODY – young onset type II DM, AI diseases, unexplained death
 CV disease
SHx- Level of education
 Occupation
 Income
 Glucometer at home
 Who administer insulin at home
 Storage
 Sedentary life style, exercise
 Family support

Examination

General

- BMI
- Features of hyperlipidemia - Xanthelesma, xanthoma, vitiligo, oral thrush



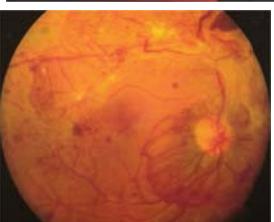
SKIN

- Infection, candida, wounds, diabetic dermopathy
- Amputations
- Nape of the neck & axilla - acanthosis nigricans



EYES

- Conjunctivitis
- Cataract
- Fundus
 - Non proliferative (Annual Ophthalmology referral)
 - Microaneurisms(dot)
 - Haemorrhage(blot)
 - Hard exudate(lipid deposit)
 - Pre proliferative (Non-urgent Ophthalmology referral)
 - Cotton wool spots
 - Venous beading
 - Proliferative (Urgent Ophthalmology referral & lazar therapy)
 - New vessels
 - Retinal subhyaloid haemorrhage
 - Advanced retinopathy (Urgent Ophthalmology referral & lazar therapy. But much vision already lost)
 - Retinal fibrosis
 - Retinal detachment
 - Maculopathy (Ophthalmology referral soon)
 - Hard exudates within one width of macula





Claw foot



Diabetic dermopathy



Diabetic cheiroarthropathy-
limited joint mobility

NERVOUS SYSTEM

- Cranial nerves- 5, 3, 6 (3 rd nerve-complete ptosis with intact pupillary reflex)
- Visual acuity
- CVA features
- Sensory
 - Two point discrimination
 - Joint position sense (proprioception)
 - Pain-deep before superficial
 - Temperature
- Glove and stocking type
- Motor- reflexes (diminished or reduced)

HANDS

- Small muscle wasting
- CTS
- Trigger finger
- Diabetic cheiroarthropathy-limited joint mobility causing painless stiffness in the hands (elicit the prayer sign)

FEET

- Ulcers
- Charcot's joints
- small muscle wasting
- Callous formation
- Skin lesions - Necrobiosis lipoidica
- Thigh muscle wasting
- Low or absent reflexes

INSULIN INJECTION SITES

- Lipohypertrophy
- Pigmentation

ABDOMEN-

- Hepatomegaly - fatty liver
- Distended bladder – autonomic neuropathy
- Renal Artery bruit

CVS

- BP-postural drop
- Pulse-irregularly irregular(AF)
- Resting tachycardia

- Peripheral pulses
- Microangiopathic cardiomyopathy
- Cardiomegaly
- Carotid bruit

RESPIRATORY SYSTEM

- Infections like pneumonia, TB, bronchiectasis

DISCUSSION

Investigations to diagnose

Criteria for the diagnosis

- Fasting plasma glucose $\geq 126\text{mg/dl}$ (7mmol/l)
- RBS $\geq 200\text{mg/dl}$ (11.1mmol/l)

- ✓ One abnormal value is diagnostic if symptomatic
- ✓ Two values if asymptomatic

- OGTT
 - Fasting $\geq 126 \rightarrow \text{DM}$
 - 2 hour value
 - $\geq 200 \rightarrow \text{DM}$
 - 140 – 199 $\rightarrow \text{Impaired glucose tolerance (Pre diabetes, same risks for CVD as DM, No risk of microvascular complications)}$

Preparation for OGTT

- 3 days unrestricted CHO diet
- 3 days of normal activity
- No medication on day of test
- No smoking during the test
- 8-12 hours fasting
- Seated and resting during the test

Procedure

- Adults 75g anhydrous or 82.5 monohydrate glucose
- Dissolve in 300ml of water
- Drink over 5min
- Samples taken 10 min before and 2 hrs after the glucose load

<140 =normal

140-199=IGT

>200 =DM

Baseline blood tests for newly diagnosed patient

- Serum electrolyte
- Serum creatinine
- Lipid profile
- Urine protein
- Urine micro-albumin

Monitor the patient already on Rx

- HbA_{1c}
- Fructosamine

Other initial Ix at diagnosis

- i. lipid profile – if high; dietary advice + statin after LFT, USS – abdomen
Repeat every 6 months
- ii. UFR & Urine micro-albumin
- iii. LFT
- iv. Eye referral, feet Examination

Management

Manage acute problem Eg:- UTI

- CBS
- Other Ix according to problem – UFR – proteinuria, few Red cells (balanitis)
- Change to insulin if on OHG, dose according to blood sugar level
- Monitor CBS bd/tds
- Diabetic diet
- Definitive treatment for acute problem Eg: Antibiotics

Manage if Emergency

- DKA
- HONK
- Hypoglycemia
- Lactic acidosis

Long term management

- Patient education
- Dietary modifications
- Life style modifications
- Drug therapy
 - Oral hypoglycaemics
 - Insulin
- Follow up
- Screening for complications
- Management of complications
- **Important aspects of patient education**
 - Educate about the disease – Pathophysiology of the disease in simple terms
 - Discuss the dietary and life style modifications
 - Educate on the complications of diabetes and their prevention-especially foot care
 - Discuss the important aspects of the management and the importance of compliance to treatment
 - Discuss with the patient on insulin therapy
- Follow up

Mx plan

- 1) Pt. education
 - Lifelong condition, pathophysiology of the disease (simplified)
 - Good Glycemic control ↗ almost normal life
- 2) Life style modification
- 3) Drug treatment
- 4) Follow up
- 5) Mx complications
- 6) Acute Mx of emergency – Hypoglycemia
 - DKA
 - HONK

What are the important dietary recommendations of diet and lifestyle modifications in a DM patient?

- General Recommendations
 - Find out his normal diet – 24hr dietary recall/food diaries (few days/ 1 week)
 - Calculate his BMR – energy expenditure based on activity
 - Determine Daily calorie intake based on BMR
 - Eg:- Standard 70kg male with moderate intensity activity – 2500cal.
 - Should take a balanced diet comprising of,
- Carbohydrates
 - 45-60% of total caloric requirement
 - Avoid refined sugar based products-confectionary, cakes, biscuits
 - More starchy, high fiber containing food-
 - Soluble- beneficial in glycaemic and lipid metabolism
 - Insoluble -satiety & GI health
 - Unpolished red rice(B_{12} ,fiber), basmathi, suwandel, thai rice, rathu kekulu-OK
 - Samba rice-discourage
 - Foods with low glycemic index-

Food	Glycemic index
Chick peas	31
lentils	42
Navy beans	43
Split beans	55
White rice	80
White`bread	100
potatoes	121

- Encourage artificial sweeteners
- Eat moderate amounts of fruits and many recommended vegetables
- Fat
 - <30% of total calorie intake
 - Limit - fat/oil in cooking, fried foods (cutlet, potato chips, parata), processed meats (ham, bacon), high-fat snacks(devilled cashew)
 - Encourage – low fat dairy products, lean meat(meat with low fat - chicken)
 - Saturated and trans-unsaturated fat < 10% of TEI
 - Polyunsaturated fat < 10% of TEI
 - Eat fish 1-2/week (contains omega3 FA, Fish oil supplements not recommended) = baking & grilling very good
 - Cis -monounsaturated fat 10-20% of TEI (olive oil, avocado)
 - Dietary cholesterol 300 mg/d
 - Limit coconut intake, use thin milk rather than thick milk
- Protein
 - 10-20% energy intake
 - Milk, egg, soy, fish, meat
 - Normal protein diet
 - Vitamins and antioxidants
 - Best taken as fruit and vegetables
 - 5 portions per day
 - No evidence for use of supplements



- Alcohol
 - Not forbidden
 - Energy content
 - May cause delayed hypoglycaemia in those on Insulin
- Salt
 - <6 g per day
 - Lower in hypertension
- Exercise
 - Requirement: 30min of moderate intensity activity minimum of 5days/week
Eg:- brisk walking, climbing stairs, cycling
 - Integrate exercise as much as possible into the daily routine
Eg:- use staircase instead of the elevator
 - If going by bus get down 1 halt before the stop and walk
 - Walk around workplace during breaks
 - Join in outdoor play with children
 - Take up hobby with exercise – dancing, swimming
 - Weekend sports
 - Adequate exercise intensity should achieve $HR = age + 100$
 - Aerobic exercise required for weight loss (anaerobic – will not reduce weight. Only ↑ tone of the muscles)
- Life Style modification
 - Stop smoking
 - Reduce alcohol intake
 - ✓ High calorie
 - ✓ Increase appetite → increase body weight
 - ✓ Hypoglycemia – Take with food
 - Weight loss
 - Maintain BMI 18-23 – calculate target weight = $23 \times height^2$
 - ↓ Calorie intake by 500cal than required amount
 - Increase energy expenditure
 - Achieve maximum of 0.5-1kg weight t loss per week (5-10% reduction in 1st 6 months)
 - Abdominal girth <90cm in males & <80cm in females, waist: hip ratio = 1
- **What else you need to advice on diet?**
 - Contents of diet
 - Quantity should be small and equal in each diet
 - Gap between diets should be equal
 - 3 main meals and 2 snacks in between
- **Initial pharmacological management of a pt with DM**
 - Just after the diagnosis oral hypoglycemic should be started preferably metformin concurrently with dietary and lifestyle modifications
 - If patient does not respond to that → combination therapy should be started

- Characteristics of new oral hypoglycemic

Drug class and mechanism	Example	Adverse Effects
Biguanides <ul style="list-style-type: none"> ↓ Gluconeogenesis ↑ Peripheral sensitivity to glucose 	Metformin	<ul style="list-style-type: none"> Risk of lactic acidosis Anorexia, epigastric discomfort and diarrhoea Cl in pt with renal or liver failure S. creatinine $\geq 150 \mu\text{mol/L}$ (1.9mg/dl) → STOP NO hypoglycemia or weight gain
Sulphonylureas <ul style="list-style-type: none"> Promote secretion of stored insulin by β cells Enhances the peripheral action on liver, muscle, adipose Reduce gluconeogenesis 	<ul style="list-style-type: none"> Tolbutamide(tds) – Preferable in elderly (Cl in liver disease) Glibenclamide (Once a day Rx (Cl in renal disease) Gliclazide (expensive) – Intermediate half life → once a day Rx (Cl in liver impairment) Glipizide – Once a day Rx (Cl in renal impairment) Chlorpropamide – Very long half life (Cl in renal impairment & elderly) 	<ul style="list-style-type: none"> Weight gain hypoglycemia
Thiazolidindions (Glitazones) Reduces peripheral insulin resistance Used alone or in combination Monitor liver functions	<ul style="list-style-type: none"> Pioglitazone Rosiglitazone 	<ul style="list-style-type: none"> Hepatotoxicity Weight gain Water retention and aggravation of heart failure Anaemia Osteoporosis
Alpha glucosidase inhibitors <ul style="list-style-type: none"> Reduce absorption of CHO 	<ul style="list-style-type: none"> Acarbose 	Flatulence, bloating and diarrhoea

INSULIN THERAPY

- HbA1c $> 8\%$
- Pt. with CVS risk and HbA1c $> 7\%$
- Type I DM
- DKA

Insulin types and regimens

- Ultra short acting
 - Should be injected immediately before eating
 - Clear appearance
 - Ultra short acting insulin analogues - Insulin lispro, Insulin aspart, insulin glulisine
 - Produced using recombinant technology. Similar to human insulin
 - Starts to act in 5 to 15 minutes, peaks in 90 minutes, lasts 3 hours
- Short acting
 - Clear appearance
 - Should be injected half an hour before a meal
 - Drug name- Insulin neutral/soluble insulin(regular) -Actrapid™



- Intermediate acting
 - Does not need to be injected with a meal
 - **Cloudy** in appearance
 - Needs to be gently shaken before every use
 - Isophane – protamine suspension
 - Lente – Zn suspension
 - Mixtard insulin – 30% soluble + 70% NPH/isophane
 - Onset 1½ hours, peak 4-12 hours, duration 16-24 hours
- Premixed insulin/Biphasic insulin
 - This type of insulin combines intermediate- and short-acting insulin
 - 30% insulin neutral/soluble(regular) & 70% isophane
 - Often taken twice a day before meals – 2/3 in morning, 1/3 in the evening
 - It should be taken 10 minutes to 30 minutes before eating
- Long acting(basal insulin)
 - Clear in appearance
 - Does not need to be injected with a meal, often taken at bed time
 - insulin glargine, insulin detemir
 - Starts to act about 2 hours after taking and can last 20 to 24 hours



Insulin regimes - commonly – soluble insulin before 3 main meals + intermediate single dose before bed

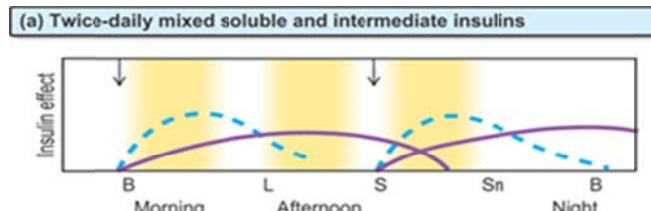
Based on CHO content of the meal Eg:- 1U of soluble per 20g of CHO (thin)

1U per 5g (obese)

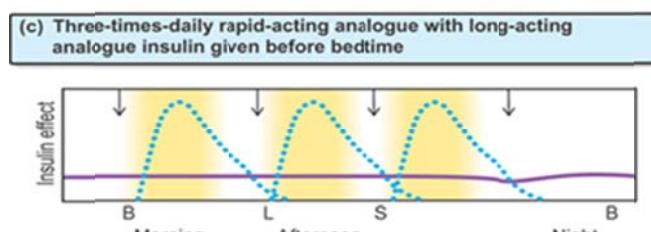
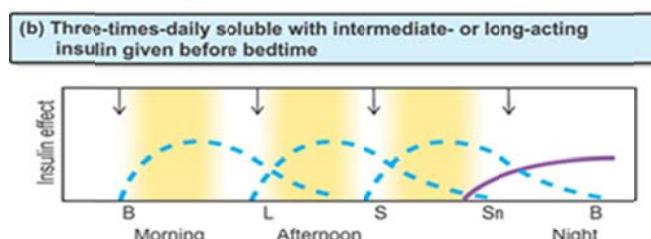
Total daily dose – type II – 1-1.2U/Kg obese – 0.4-0.8U/Kg

Ambulant Pt. starting on insulin – Mixtard 8 units twice daily

Dose – 4U daily increment



If any patient needs insulin > 100 Units →
Indicates reduce compliance or insulin resistance



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Insulin resistance – required insulin dose >200U

Features of resistance – obesity

Acanthosis nigricans

Insulin Abs +

Insulin antagonist hormone – growth hormone, cortisol, thyroxin, glucagon

Target – HbA1c – 6.1 if arterial disease < 6.5%

FBS <110

PPBS - <160mg/dL (9mmol/L)

- **How will you follow up this patient**

- See the patient in the clinic(monthly)
- FBS-monthly HbA_{1c}-3 monthly
- BP-every 3 months (target 130/80). If high microalbuminuria → start ACEI/ARB2
- If obese Weight and BMI in each visit
- Lipid profile – 6 monthly, target LDL - <70mg/dL total CH
- Assess for complications – urine micro albumin – annually
- Eye referral – every 2yrs if no prb.
- Asses the glyeamic control of the patient
 - Self monitoring of glucose
 - FBS-only gives the point of glyeamic control
 - HbA_{1c}-gives the estimation of glucose over the preceding 3 months
- Asses the complications
 - HX and Ex,Ix-lipid profile, UFR, micro-albuminuria
- Asses the drug therapy and compliance
- Asses the complications of medication
- Compare with the following management targets

Parameter	Target
Blood glucose	<130/80
FBS	Between 90 and 130(ideal around 100)
HbA _{1c}	<7%
Total cholesterol(mmol/l)	<4
LDL cholesterol(mmol/l)	<2

- **Addition/ modification therapy**

- When there's a failure to achieve a good glyeamic control (HbA_{1c}>7%) after 3 months of therapy
- Asses the compliance and adherence to dietary and life style modifications
- Addition is done with sulphonylureas
- Insulin therapy is considered if the HbA_{1c} is extremely high or if there is poor response to treatment with combination therapy of oral hypoglyceamics.
- Insulin
 - Is initiated following consultation with a senior physician
 - Start at a low dose and adjust the insulin dose based on FBS and PPBS values
 - Insulin can be started as concurrent therapy with oral hypoglycemic drugs

- **Advices to a patient who is on insulin therapy**

- Tell the patient the reason for starting insulin
- Advice on where to obtain insulin and insulin injection devices
- The most commonly used device in insulin pen.
- There's a plain syringe 29G needle and calibrated up to 1000 of insulin
- Storage of insulin-in the refrigerator(middle compartment)

- Before injection have a wash. Check the insulin bottle (regular insulin is colourless and other preparations are turbid)
- Gently roll the bottle in your palms
- Don't use surgical spirit to clean the area
- Demonstrate the technique
- Look for lipoatrophic areas and lipohypertrophic areas and avoid using the same site
- Syringes can be re-used if the same person using it. Dispose the sharps in to the sharp bin.
- Have your meals 30 min before the insulin injection
- Educate the patient on complications of insulin therapy. e.g.: hypoglycemic attacks, weight gain, increased appetite

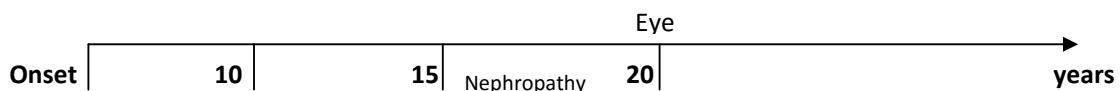
Causes for poor Glycemic control

- 1) Drug compliance
- 2) Dietary control
- 3) Subclinical infection
- 4) Inadequate insulin dose
- 5) Storage problem – insulin pen should not be stored in fridge
- 6) Incorrect insulin preparation
- 7) Incorrect technique
- 8) Insulin injecting to same site
- 9) Insulin resistance

• **Initial assessment of complications**

category	investigations
Diabetes control	FBS, HbA _{1c}
Micro-vascular complications and RF	UFR, micro-albuminuria Eye referral
Macro-vascular	Lipid profile
Foot complications	examination

• **How to assess for complications and manage complications**



complication	Ix and Mx
Retinopathy	<ul style="list-style-type: none"> • Screening • Arrange for an eye referral annually • Non proliferative - Glycemic control and risk factor modification, annual ophthalmology referral • Pre proliferative –Non urgent referral to ophthalmologist • Proliferative – Urgent ophthalmology referral and laser photocoagulation • Maculopathy – Ophthalmology referral soon
Nephropathy	<ul style="list-style-type: none"> • Screening-monitor proteinuria-annualy, S.creatinine - every 6 months • Rx UTI • Improve lipid profile – LDL< 100 TG<150 • Intensify IHD Mx • Aggressive reduction in BP(target BP-130/80-ACE1,ARB2) • Improve glycemic control • Avoid Glibenclamide, nephro-toxic Rx (NSAIDs) • Insulin dose reduction – with deterioration of renal functions • If established renal disease-Dialysis <p>e. GFR = $(140 - \text{age}) \times \text{BW}$ s. Creatinine $\times 72$</p>
Neuropathy	<p>Management of painful neuropathy-</p> <ul style="list-style-type: none"> • Strict glycemic control • Anticonvulsants - gabapentin, carbamazepine, TCA • Opioids <p>Autonomic</p> <ul style="list-style-type: none"> • Postural hypotension-Fludrocortisone • Gastro paresis-dopamine antagonists, loperamide for diarrhea • Nocturnal diarrhea-AB(SI bacterial growth) • Erectile dysfunction-sildenafil

Causes for recent onset hypertension in long standing DM

- 1) CRF – complication
- 2) Renal artery stenosis – atheroma formation

Causes for chronic non healing ulcer

- 1) Neuropathy
- 2) PVD
- 3) Infection

Causes for Postural hypotension

- 1) Autonomic neuropathy
- 2) CRF
- 3) Rx – anti hypertensives Eg:- Nitrates

Management of diabetic foot

- Patient education
 - Prevention is better than cure
 - Avoid walking barefoot
 - Use proper well fitting shoes
 - Wash your feet everyday and moisturize the skin if dry & cut toe nails regularly

Management of acute conditions

Hypoglycemia – severity – Mild - < 60mg/dL

Moderate <45mg/dL

Severe <30mg/dL

Mx – Mild – oral sugar drink

Moderate – severe → 50% glucose 25cc / 50cc → flush with N/saline to prevent sclerosis

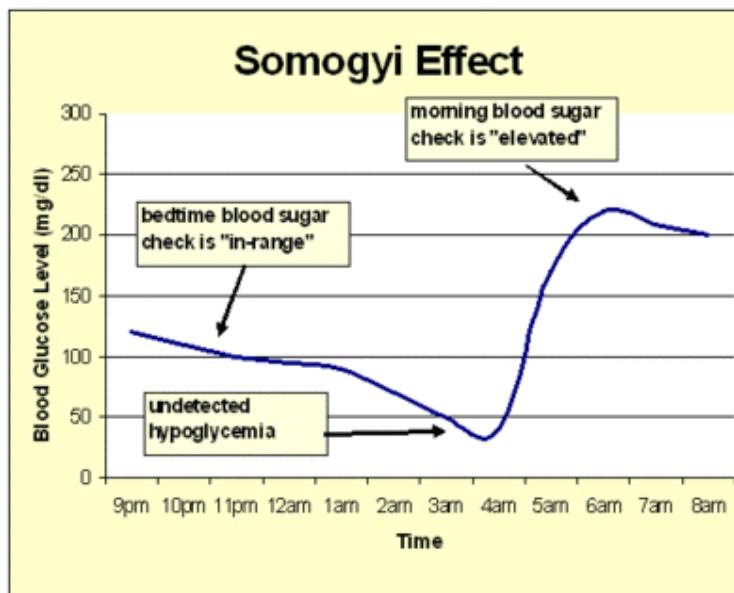
Causes for recurrent hypoglycemia

- 1) Renal failure → failure to excrete insulin
- 2) Not on adequate diet/ meals delayed after taking the drug
- 3) Excessive exercise
- 4) OHG with long half life- Glibenclamide, kothala hibutu, bitter gourd – glucose lowering agents
- 5) Unrecognized low renal threshold for glucose – Treatment based on urine sugar → excessive dosing
- 6) Endocrine causes – pituitary / adrenal insufficiency.
Can lead to ‘Hypoglycemic unawareness’ – disappearance of adrenergic response

Somogyi effect – Morning hyperglycemia following nocturnal hypoglycemia

Due to release of counter-regulatory hormones

Mx – Reduce evening insulin dose



Dawn effect – Morning hyperglycemia in the absence of nocturnal hypoglycemia

Due to waning insulin levels & surge in growth hormone

Mx – increase insulin dose

DKA

Causes- precipitated by infection, dehydration, MI, surgery, trauma, poor compliance with insulin Tx

- Clinical Features-
 - General weakness, malaise and dehydration over 1-2 days
 - Polyuria, polydipsia
 - Hyperventilation-met acidosis, Ketotic breath
 - Severe abdominal pain and vomiting
 - Confusion and coma
 - Look for signs of precipitating illness

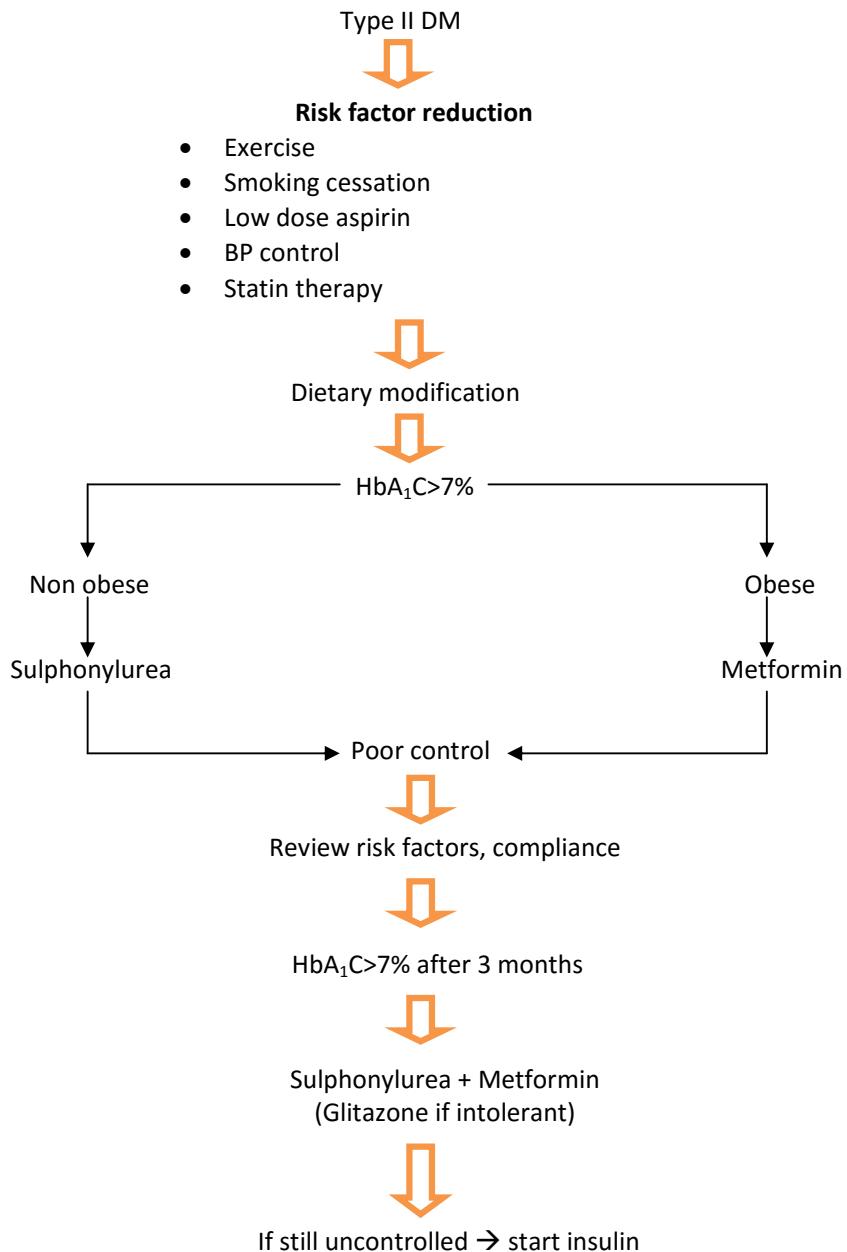
- Why does it happen?
Pt lacks insulin, extracellular glucose can't enter cells → intracellular hypoglycemia
Other mechanisms activate → FA break down by glycogen, cortisol
FA → acetyl co A (can't enter KREBS) → ketone bodies (β hydroxybutyrate, acetoacetate, acetone)

<u>Problems</u>	
Hyperglycemia	-RBS>300
Ketonemia	-ward test
Acidosis	-ABG

- How do you manage?
 - **Investigations**
 - Blood glucose (may not be very high compared to HONK)
 - FBC (evidence of an infection)
 - U&E – Serum K
 - ABG – Metabolic acidosis
 - Urine – ketone bodies
 - ECG – Silent MI
 - Blood & urine cultures
 - CXR
 - Gain IV access
 - **Hydrate** the pt by using N/S or hartmann
 - 1L stat (Do not add K^+ to this bag)
 - 1L over 1 hour
 - 1L over 2 hours
 - 1L over 4 hours
 - 1L over 6 hours
 - Add KCL to each litre of N.saline depending on serum K^+ as given in the table

SERUM K^+ (MMOL/L)	KCL (MMOL)	15% KCL
< 3.0	40	20
3.1 – 4.0	30	15
4.1 – 4.9	20	10
>5	NO K^+	-
 - **Insulin administration** (IM/IV/Not given SC) – Preferably via an infusion pump. If not available consider IM
 - Soluble insulin IV 6 units bolus (0.1unit/kg/hr). Then 6 units/hour infusion
OR
20 units IM stat followed by 6 units IM hourly
 - Continue until urine ketone bodies cleared
 - Ultimate goal is to correct insulin not glucose level
 - When glucose <180mg/dl(10-12mmol/L) change infusion to 5% dextrose
 - **Monitoring**
 - UOP, Pulse, BP
 - Monitor CBS hourly
 - Monitor ABG & serum K^+ 2-4 hourly
 - Don't administer K^+ . if K^+ level 4.5-6 administer KCl 10ml/hr.
 - Adjust KCl concentration depending on results of 2 hourly K^+ monitoring

- Acidosis → auto corrected
 - If very severe pH < 7, give IV HCO₃ 8.4%
- Once stable able to eat and drink, start soluble insulin SC 4 divided doses daily regime (0.5-1U/kg/24hour) 30 to 60 minutes before stopping the IV insulin infusion.
- Rx the cause of DKA
- DVT prophylaxis with SC LMW heparin or 5000 units of UFH 8 hourly for 48 hours
- ⊕ When treating DKA → β hydroxybutyrate converts to acetone → urine ward test shows worsening of DKA
(Urine ward test only detects acetone & acetoacetate)
- SEE HONK MANAGEMENT ON EMERGENCY MEDICINE PAGE 176
- Management summary of type II DM



දියවැඩියා රෝගීත්තේ ආහාර පෙනෙ ප්‍රමුණු

1. පෙන යෙන් ආහාරවලින් දියවැඩියා වැළැනීම් පිටපා ප්‍රතිඵල.

සියලුම පැණිරය, පිනි, ගකුරු, පිරිස එක

පැහැ රසයන් යාදා ලද ආහාර එක

වොපි, ගස්ත්, රෘගුලිලි, තලංගු, මසකට්, උපිවර්ග, රෘලංපත්, වොක්ලට්, පැණිරය ඉයින්තම්, ජුම් එක, පැරිමල්වි, එල් එක, පිමිල් එල්, පැණිරය එල්, එක, පැහැ රස යෙදු පෙනු ප්‍රාප්ත, තැව්ලි, ග්ල්බෝස්, පැණිරය එශකට් එක, ඇප්ස්ට්‍රූම්, වින්ස්ට්‍රූම්, ගෝල්ට්‍රූම්, නොර්ලිස්ප්, විච්, මාල්ටින්, විච්චෝල්ට් යනාදිය)

පෙනු ඇත්තා අත්තාපි, දුරියන්, ටුල, මරකා, මිදි, අලිපෙර, පැංඡුජ්වින්

2. පෙනන පදනම් ආහාර වර්ග සිමා කළයුතු තොළුවේ.

සියලුම පළ වර්ග - මුදුණුවැන්න, තොළුණාල, තම්පාල, සිවිති, ගංඛන්, තෙනු මුදුණාලා

පිළියාඟා අස්ථි එළඹලු වර්ග - ගෝංටි, මුළුරුල්, දබල, වම්බෙළු, බැවක්කා, එලංඩු, තැක්කාලී, ගෝංටි, එක්කාලී, රාඛු, නොශක්කාලී, තරවිල, තුව, පෙනුලා, ටුටෙනාලු, සිමිජ්ජා, තට්ටෙකා, මුදුණාලා, මුදුණාලා, රුදුදුනු, ගඟ.

නේ, ගෝංටි (පැහැ රසයන් තොර-පික්කා, බුඩිල්, පාලපිටි

මාලු, කරපල, භාල්මූපියන්, වින්තර පුදුම්, තුළුබහු වර්ග, අව්‍යාරු, විනාඩිරි

පෙන යෙන් ආහාර වර්ග පිළිත ප්‍රමාණයකින් ගත ප්‍රභාස.

උජා වර්ග - බත්, ඉදිනාරු, ගැසප, පිවිවු යනාදිය
තිරිගු පාන, පැන් ගක්ක්, රැඳි, ඉදිනාරු

ඇරෙක්ස් - පිවිවු, තලප යනාදිය

දුරු - ගක්කේ, ඉඩලී, එක්කි
අල එක - අංතාපල්, තලප, මැංඡලාක්කා, ගහල, හිට අල, කුරට්, ඉන්නල, දන්දල
පරිප්ප, මුදුණාලා, තෙනු, ගෝංටිපිටි, තෙනු, දුරු

පිටි පිළිත පෙනු ඇත එළඹලු වර්ග - අල ගෙයෙල්, ගොය් ඇත ගොය් අල, දෙල්

මෙද ඇධික ආහාර - තරන් පස්, උරු පස්, යහ එමින් යාදා ලද ආහාර, ඇඟු පස් ඇත වෙනත්
ස්ථාන එක, වින්තර ගත අල, ඔවුන්, ගැඹු ගෙල් වර්ග

පැහැ රස ගොයුදු පෙනු ඇතුළු, ප්‍රාප්ත - රට දෙකි, අදාම්, අදික, මල්දාවීම්

පෙනු - ගෙයෙල්

දියවැඩියා රෝගීයෙකුට යෝගීත ආහාර විවිධාරුව

රුධියන

- සේ හෝ ගෝංටි සිංහ පෙනු පෙනු 01 ත්
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- පැහැ රසයන් තොර පෙනු ඇතුළු ප්‍රාප්ත 01 ත්

ලංද ආහාරය

- 1/2 පාන් පෙනු ඇත්තේ

- හෝ ඉදිනාරු ගොඩ 04 ත් හෝ අංතා, 6 ත්

- හෝ ගැසප ගොඩ ප්‍රාප්ත ප්‍රාප්තයේ 02 ත් හෝ

- අංතා ප්‍රාප්තයේ 03 ත්

- හෝ 2/3 පිවිවු ගැඹු ඇත්තේ

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ඡේ තෝරා සොයුම් නිවැස පෙන්පා 01 අ
පිහි තෝරා තැංකුමීති
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රිඛ්‍රනයක් යෙය.
- ඇතුරුපය
ඡේ තෝරා ගුම් 30 අ තෝර ප්‍රාග්‍රහණයේ තෙවියෙන් තැංකුමීති
පිහි තෝර අන්‍යාද තෝර දැමිලුන් ගෙවියෙන් තාමයක් තෝර දැමිලු
ඇත් තෙවියෙන් වර්ග එවැනි එවැනි එකක්
තෝර ලදවාප නිවැස තෝරා 01 අ (පැහැ පිහි තැංකුමීති)
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ඡේ තෝරා මින් පෙන් පෙන (පිහි තෝර තැංකුමීති
පැහැ රජයෙන් තොර විස්තරාත්මක 02 අ).
- රාම් ආහාර
ඡේ තෝර ඩඩා දුන් උපදෙස් පිළිපිටින්න.

එන් තෝර නිවැස තෝරා ප්‍රාග්‍රහණයේ ප්‍රාග්‍රහණය තෝරා තෝරා ප්‍රාග්‍රහණය (ම දේ 200
ක) ප්‍රමාණයකි.

ඬාමාත්‍ය උපදෙස් බලන්න.

ආහාර තුවමාරුව -

පාන් යන බත් වෙළුවට ගෙනුම් වෙනත්

පිහි දේ තෝර තෝරා ප්‍රාග්‍රහණය ප්‍රාග්‍රහණය තෝර තෝරා ප්‍රාග්‍රහණය තෝර තෝරා ප්‍රාග්‍රහණය.

1/2 පාන් පෙන දෙකක්
4" ප්‍රාග්‍රහණය තෝර තෝරා ප්‍රාග්‍රහණය
පුරවන දේ තෝර තෝරා ප්‍රාග්‍රහණය තෝර තෝරා ප්‍රාග්‍රහණය
තෝර තෝරා ප්‍රාග්‍රහණය තෝර තෝරා ප්‍රාග්‍රහණය
තෝර තෝරා ප්‍රාග්‍රහණය තෝර තෝරා ප්‍රාග්‍රහණය
2" පිටු තෝර තෝරා ප්‍රාග්‍රහණය තෝර තෝරා ප්‍රාග්‍රහණය
තම්බන දේ තෝර තෝරා ප්‍රාග්‍රහණය තෝර තෝරා ප්‍රාග්‍රහණය
තම්බන දේ තෝර තෝරා ප්‍රාග්‍රහණය තෝර තෝරා ප්‍රාග්‍රහණය

වෙනත් - ඉස්සන්, පැඳුන්න, පාමිචියෙන් යන දේල්න්
විධි යන දේල්න් එකතු

4. ඬාමාත්‍ය උපදෙස් -

අධික ගෙදී යෙහි ආහාරයැනිම සුදුසුව.
පරු රාන් දුද රාන්වෑම වනා සුදුසුව
අරක්කන් යන පළා වර්ග ගෙදී අධික ආහාර වේ
රඟ කැඳුව තාල (අධික පාන් දේ අදින්පර, ආර්ථ වැනි ආහාර)
පාහින දේ භාල් යන එකින් පාන් දේ ආහාරවලට වනා සුදුසුව.
තැංකුමීති දේ වෙනත් අනිතරය.
තරක් එස් . උරාරු එස් යන එස් විවෘතයෙන් ම පිළා තැංපුදාය.
පැලතුරු දුෂ්‍ර විමාන වනා ගෙවී කැම සුදුසුව.
සෙව්ව තෙලට වනා එලාදු තෙල සුදුසුව වේ

තාද රෝග , අධික රුධිර පිරිනාය එකාග්‍ර හා අක්‍රා, එර්ග ඇති දියවැවිය වෝගින්ට අහන
සාදන් ආහාර රිඛ්‍රනයා වෙනත් තිරිම් පිළිවා ගැනීය.

යෙහි නිවැස් ගෙන්න එවැනි පිහි ගොඩන් දුවුරිම ජ්‍යා ස්ථානයය,
අනුදිය දැමිලු, ඇශ්‍ර පන ගැනීම් පිම ගැං, එවැනි දුවුරිම ජ්‍යා ස්ථානයය
වෙන් නිවැස් ගොඩන් ගොඩන් දුවුරිම ජ්‍යා ස්ථානයය ගැං ගැං.

දියවැඩියා රෝගීන්ගේ ආහාර සඳහා උපදෙස්

පහත සඳහා ආහාර මගින් සම්පූර්ණයෙන්ම වැඩකි සිටිය යුතුයි.

- ❖ සියලුම පැහැර සහ පැහැර කොඳ ඉදෑ රුකුවේලු
 සිනි, සිනුද් ය අනෙකුත් පැහැර විරශ, මිපැනි, රුධිදී, වෙශ්, හේත්, තලුදී, මසකරි, පුවිත විරශ, විවුරුත්, පැනි රාජ තියකරි, අයිස්කුම්, රුන්කරි, මෝද්රිචි කිරි විරශ (උඟ, නෙය්ලෝද්රි, ටිවා, හෝට්ලිස්, චිච්ලිට්)
- ❖ පත් පිටි, සහළු පිටි, දුරක්කයේ පිටි වැඩින් සාදන විරශ
 (උඟ : පාන්, රෝග්ල්, ඩිනිඩ්, මාබුන්, ඉදිනාජ්‍ර, අර්ථ, රෝට්, පිටුපු)
- ❖ සියලුම වත් වැඩ සෙල්
 (උඟ : පොල්කර්, විළවින සෙල්, ඩිලිටියෙල්, සන්ට මේද්, බිටර්, මායින්)
- ❖ සෙල් සහිත ආහාර
 සිර්තර නිත්තු පැහැර සහළු විවිධ සාදන විත් සාදන ඉදෑ ආහාර
 (උඟ : කොයේරය්, නැම් වේිකන්)

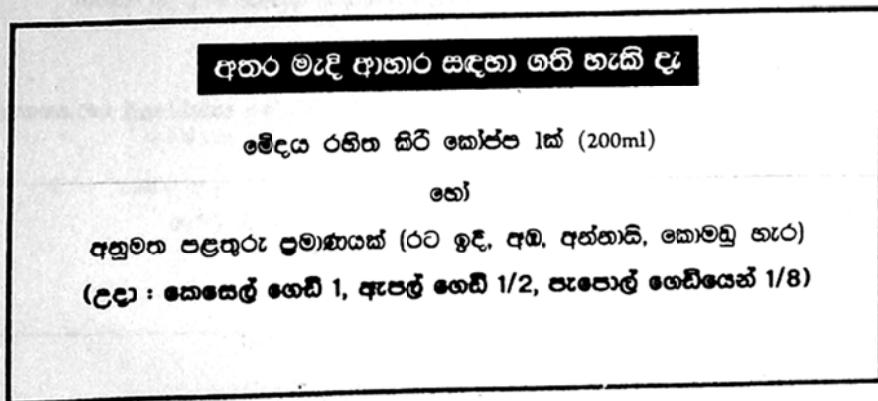
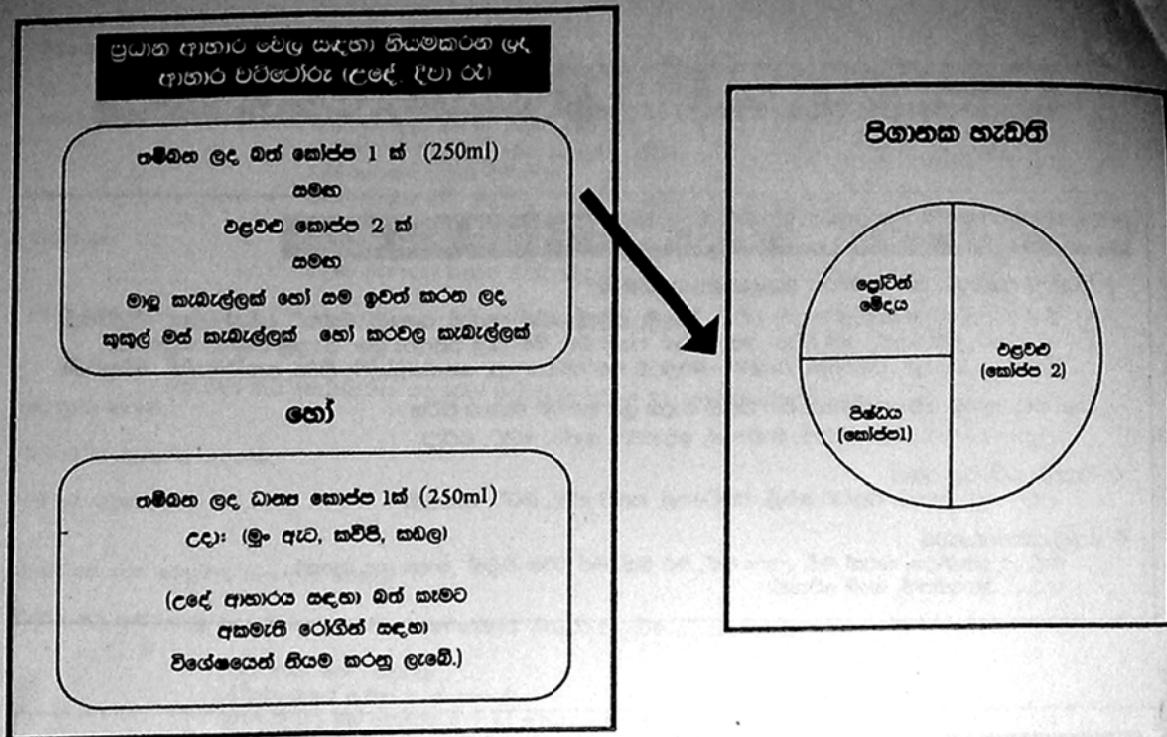
සීමිත ප්‍රමාණයකින් ගත සැකි ආහාර

- ❖ දුඩාන ආහාර වේල් සඳහා පිළිසිය / කාබිඩ්සිලේඩ් ලෙස යහු භාජි ආහාර
 1. සහළු (උඟ, දිය ඇට්, රුමිනු සහළු හම් මිඩාන් පුදුසුය.)
- 2. අලවත් සහ පිටි ගෙනිය සීමිත විළවින වත්
 (උඟ ආරකාපල්, මහල, මයියෙන්දුනා, ඉත්තල, කිරි අල, ඩිට්, විටටිකානා, කොස්, දෙල්, අන් කොසෙල්)
 බ්‍රහ්ම (කඩිල, මුංඡල, කුඩිල)
- ❖ අතර මද ආහාර වේල් සඳහා ගතහැකි ආහාර
 1. (පළුදුරා, රුට් ඉඩ්, අන්නායි, අඩි, පැනිලකාමුඩ් හැර) විනෑම පළුදුරා විරශ
 2. මේදය රහිත කිරි.

බහුල වශයෙන් ගත හැකි ආහාර

විවිධ බිජ සහ කොදී ලබාගත හැකි ආහාර

1. සියලුම පෘෂ්ඨය
 (ගෙෂු කොල, ගමිරා, මුදුනුවන්නා, කිවිගි, කංකුං, කඹදුලිරුංගා)
 2. අඟ විරශ ගරු සියලුම විළවින විරශ
 (අභිජල්ලා, පොලුගැන්, අඩි, මලුගුලී, කොයේල මුව, කොහිල, තක්කාලී, ගෝව්, ලිංක්ස්, පොලුගැන් කර්මිල, අඩි, මුරසාගා, රුඩුවනු, වෛශ්‍යා, විමිඩු, මැ, දුමිල, පැක්ල, එළුවෙකාපු, තැංකිර්, එළුවනු අදිය.
- ❖ පෙරේන් පෘෂ්ඨයක් ලෙස ගතහැකි ආහාර
 (කරවු, සෙකා ඕප්පි, ගැලුම්දේශ්කි, සිංහර පුදු මුදය, සම රහිත ගුණුලු මැඟ, මාඟ, පරිජ්පා, ගැඹු)



මත දුරක්ෂ වි ඇති ආකාරයට තැබුරු විගාර ප්‍රමාණයක් සින්න ප්‍රභාව ආහාර වේළැ තැනක් ගැනීමට
වහා තැබුරු මැ ප්‍රමාණයකින් ඇත්ත නැත් වේළැ තැනක් ගැනීමෙන් දැවඩියා රෝහිස්සේ උස්සාගා
සින් මෙටිම පාදනය සිරිල වහා පහසුවේ.

7.00 a.m. - 8.a.m	උදේ ආකාරය (ප්‍රධාන ආහාර වේළැ)
10.00 a.m.	කෙරී කැම වේළ
12.30 p.m. - 1.30 p.m.	ද්‍රව්‍ය ආකාර වේළ
4.00 a.m.	කෙරී කැම වේළ
7.00 p.m. - 8.00 p.m.	රාඩ්‍රි ආකාර වේළ
10.00 p.m.	කෙරී කැම වේළ

ବ୍ୟାଦିତିକ ପ୍ରଦୂଷ. ଉତ୍ତର ପରାମର୍ଶ ଏହା ଲକ୍ଷ ବୈଚିଳ୍ପିକୁ ଦା ରତ୍ନ ଉପ ଧ୍ୟାନିରେ ଉଦ୍‌ଦିତ.

ଅରଜୁବ

ଅର୍ଥାତ୍ ପଦ୍ମାଲୀ ଏବଂ ପଦ୍ମାଲୀ

ଫଳିତ କେତେଟିବ୍ୟାପରେ ଉଚ୍ଚ ଅଧିକତମିତିରେ ଦେଖାଯାଇଛି ।

ಕರ್ನಾಟಕ

ଅକ୍ଷୁତ ହେଁ ପାପ ହେଁ
ଦିନ ଲେଖାତି ତିଥି କୁ ଯେବେ ତିଥି
ପିଲିତ ମୁହଁରୁ ଉଚ୍ଛି ଲିଙ୍ଗ
ଦେବାଳୀର ଦୂରୁ ଯନ୍ତ୍ରଣା
କିମା, ଏକିନ୍ ପରାମର୍ଶ କରା
ଦୂଷପର, ଦୈତ୍ୟରୁ ଏକିନ୍
ମାରୁ ଦିନରିତିର ବୀଷମିର
ଦୂର୍ଯ୍ୟାଳୀର ଦୂର୍ଧ୍ୱ ଦିନିର
ପରିଭିତ୍ତ ଦଳ ହାତି ଲି.
ଦିଲ୍ଲି, ଏକିନ୍ ଦୂର୍ମିଳ ଦୂର୍ଯ୍ୟ
ଦୂର୍ଧ୍ୱ ଲିଙ୍ଗ ବିନିନ୍ଦନ.



ମାର୍ଗଦୟ ଦିର୍ଘଲେନ ଯାତ କାହା ଚାଲି ପାଏ କୁଳବନୀ
ରଥୀ ଗନ୍ଧି.

ଓଡ଼ିଆ ଲେଖକ

- රුදුම්වන් ඉවත පා ඇත.
 - (නෙකුණෙයි සොලුම්විටරේප් එම්බ් දැක්වම්හි සහ ඉ අල් හරර, සිගරවී වූ තිහැරින් හිඹා තව දුරටත් සෙයක්වනාය යේ.)
 - මූදල් ගරවල් අයි මේය ඇස්.
 - ප්‍රස් ගැලුපෙන රාවහන් ඇස්.
 - ඉරයි තිහර වෙනත් කොර, එක්ම කඩුලය එට සභුලය දුමා වශී වෙළුවය තබා නොහැරි. (එන් හරඳු තැබාගැනීම්හි අයි වහ පිහිනා පාදුලය් යට කොවිනයි රැසිර ඩිවිනය අසිජ් ගොලර්.)
 - රැසිර සිංහ පමුණු පාදුනයි යටත වේ.

ලොඛවරයා ඇවගුස වන්නේ කවර මොනොයද?

କାନ୍ତିମାର୍ଗ ପାଇଁ ଆମାରିଲାମାରିଲା

- ଧୂର୍ବାଳ୍ୟକ ପ୍ଲଟ ତିଥି ପାଇଁ ଛୁଟିଲା
 - ଧୂର୍ବାଳ୍ୟକ ହେବେ ନିଯମ ଦିଲା ଛୁଟିଲା
 - ପାନ୍ଦୁଳେ ଶିଖାମ ଲାଗୁବିଳାଦ୍ୱାରା ନିର୍ମିତ ହେବେ କାହାର ପାଇଁ ହେବେ କାହାର କାରିବାକ ଅଣିଲା
 - ଗାଈର କିରଣାଳୀ ବିନ୍ଦୁ ଲାଗୁବିଲାବୁଲା ଧାର୍ଯ୍ୟକିଳିକ ଲେଇଦୁଇବି, ରିଯ ଲାକର କିରଣାଳୀଙ୍କ ପାଇଁ କାହାର ପାଇଁ ଲାଗୁବିଲା

- සිංහල තාවය හෝ වේද්‍යාච්‍රා යෙත හෝ ආකෘතියේ ගැනීයයි ඇති විට
 - ඉදිමාවුවින් ඇති වශි වේද්‍යාච්‍රා හෝ පිරිප්‍රේමිය හෝ පැද රුන් එමක හෝ ඇති විට
 - ධපු ප්‍රතිඵල වෙළු මත ආවැළි ජ්‍යෙෂ්ඨාච්‍රා හෝ රජ පිළිස් ද්‍රා ආවැළි ද්‍රාච්‍රා හෝ ප්‍රමුඛ දැනුගත විට

କବିତାମ ପିରଗଲେ ମେହିର ରତ୍ନଯାତ୍ର ଦୃଶ୍ୟବନ୍ଧ ଆଚାର୍ଯ୍ୟମ ଅନେହିମ
ଚିତ୍ତବୀ ଲାଦୁ ରୂପ ଭଲା ଗନ୍ଧନ.

ପରି ଲେଖ ଦାନ୍ତି କିମ୍ବା କିମ୍ବା ଅଛି କାହାର ଦ୍ୱାରା କିମ୍ବା କିମ୍ବା କାହାରଙ୍କ ଦ୍ୱାରା ଉପରୁକ୍ତ ଦୟାବଳୀ ପାଇଲା ଏବଂ ଏବଂ ଏବଂ କାହାରଙ୍କ ଦ୍ୱାରା ଉପରୁକ୍ତ ଦୟାବଳୀ ପାଇଲା ଏବଂ ଏବଂ

ମତକ ରବୀ ଗନ୍ଧୀ !

ବିଭିନ୍ନ କାର୍ଯ୍ୟଙ୍କ ପାଇଁ ଏହାର ଅଧିକାରୀ ଦ୍ୱାରା ଉପରେ ଥିଲୁଛି ଏହାର ପାଇଁ ଏହାର ଅଧିକାରୀ ଦ୍ୱାରା ଉପରେ ଥିଲୁଛି



මෙන්න සිතුව එයත පණිවිධයක්

କବି କିରେଣ୍ଟ ପା ମୁଖଭୂକ ଦୟାତ୍ମିକର ଧର୍ମନିକରଣପାଇଁ ମୁଲାଯ
ପାହାନ୍ତର ଫର୍ମିଲୋଗ୍ରେ କିମ୍ବା ପା ଜପିର ଦିନ୍ଦ୍ରିୟ

୧୯୫

ക്രാന്റെ

ପ୍ରାଚୀକା

ପ୍ରକାଶକ ମେଳି.

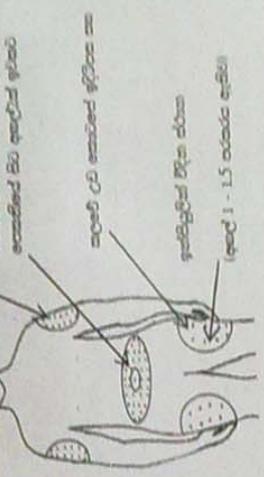
වෙත පැහැදිලි සංස්කරණ වලදී පොකුණ හෝ වෘත්තියෙන් සිටින වූ

(සිංහල මෙහෙයුමේ) පැහැදිලි සංස්කරණ වලදී පොකුණ හෝ වෘත්තියෙන් සිටින වූ



ඇංග්‍රීස් අනුව
Eye diagram

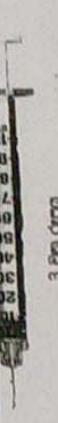
වෘත්තියෙන් සිටින වූ



සිංහල අනුව
Eye diagram

වෘත්තියෙන් සිටින වූ

අභ්‍යන්තර තුනක් නිසා මෙයි මෙයි එම මෙයි එම මෙයි එම මෙයි එම මෙයි

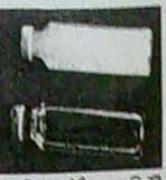


1. තුනක් නිසා මෙයි එම මෙයි එම මෙයි එම මෙයි එම මෙයි එම මෙයි

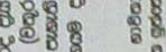
අභ්‍යන්තර තුනක් නිසා මෙයි එම මෙයි එම මෙයි එම මෙයි එම මෙයි



2. තුනක් නිසා මෙයි එම මෙයි එම මෙයි එම මෙයි එම මෙයි

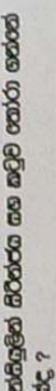


3. තුනක් නිසා මෙයි

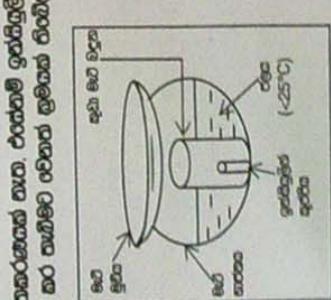


4. තුනක් නිසා මෙයි

අභ්‍යන්තර තුනක් නිසා මෙයි එම මෙයි එම මෙයි එම මෙයි

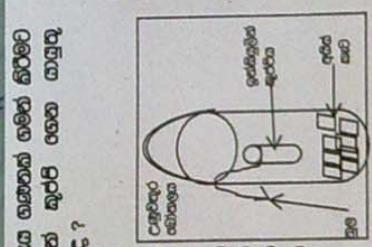


5. තුනක් නිසා මෙයි



වෘත්තියෙන් සිටින වූ

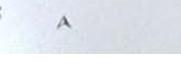
1. තුනක් නිසා මෙයි එම මෙයි එම මෙයි එම මෙයි එම මෙයි එම මෙයි එම මෙයි
2. තුනක් නිසා මෙයි එම මෙයි එම මෙයි එම මෙයි එම මෙයි එම මෙයි
3. තුනක් නිසා මෙයි එම මෙයි එම මෙයි එම මෙයි එම මෙයි
4. තුනක් නිසා මෙයි එම මෙයි එම මෙයි එම මෙයි එම මෙයි
5. තුනක් නිසා මෙයි
6. තුනක් නිසා මෙයි



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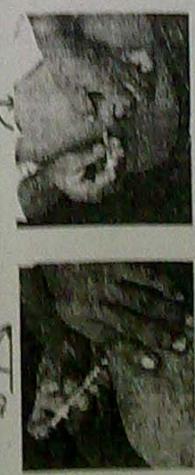
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STROKE

HISTORY

Age : >65 years

Sex : Male>Female

Presentation

- Onset : Sudden
- Face, arm and leg weakness
- Altered level of consciousness (Cortical stroke)
- Facial weakness, double vision, Facial numbness
- Difficulty in talking, dysphagia, nasal regurgitation (Bulbar cranial nerve palsies)
- Loss of balance/ataxia (Cerebellar)

History of presenting complain

1. Explain the presenting complain
 - What was he doing at the time of stroke
 - Duration of symptoms
 - Loss of consciousness or fainted (with duration)
 - Type of weakness or paralysis (Face/arm/leg/speech)
 - Progression of symptoms
 - Worsening of symptoms (progressing stroke)
 - No change (completed stroke –deficits have reached maximum usually within 6 hrs)
 - Minor stroke (Pt recovers without significant deficit within a week)
 - Disappearance of symptoms within 24 hrs(TIA)
 - Associated symptoms - Severe headache , vomiting , seizures
 - What happened after the stroke
 - Movement – Paralysis
 - Sensation
 - Consciousness
 - Speech : Expression, Understanding
 - Vision – homonymous hemianopia
 - Giddiness, vertigo, vomiting, headache
 - Sudden death
2. Differential diagnosis
 - Cerebral tumor
 - Chronic headache , vomiting , focal signs , seizures
 - Features of raised ICP(headache when getting out of bed , headache changing with posture/when bending forward , increasing with LSCS)
 - Followed by gradual onset hemiplegia
 - Cerebral abscess
 - Fever
 - Aetiology : ear discharge, skull fractures, IE(congenital heart disease)
 - Symptoms mentioned in cerebral tumour

- Head injury
 - H_x of fall , assault
 - Nasal or ENT bleeding
 - Rhinorrhoea : CSF leakage through the nose (Base of the skull fracture)
- Encephalitis - Fever , drowsiness , headache, Altered behavior
- Epilepsy (todd's paralysis) - Past history of seizures
- Migraine
 - H_x of aura (blurring of vision , Zig Zag lines , flashing lights, paralytic migraine)
 - Past H_x of migraine

3. Risk factors/Aetiology

- Disease related - HT, DM, Hypercholesterolemia, IHD, Cardiac arrhythmia(AF), Rheumatic valvular heart disease, Bleeding disorder, Polycythaemia, Past MI/Stroke
- Life Style – Smoking, Alcohol excess, Physical inactivity, Diet

4. What are the functional difficulties patient is experiencing?

Activities of daily living

Past Medical history

- Previous similar type episodes
- Intermittent claudication, rest pain

Past surgical history

- Recent surgeries

Drug history

- Anticoagulants
- Anti-platelet medications

Family history

- CVA , DM, MI, HPT, Family Hx of PCKD → Berry aneurysm → Risk of SAH

Social history

- Occupation
- Income
- Impact on the family , psychological level
- Family support available
- Social supports available
- Accessibility to physiotherapy
- Smoking/Alcohol
- Diet

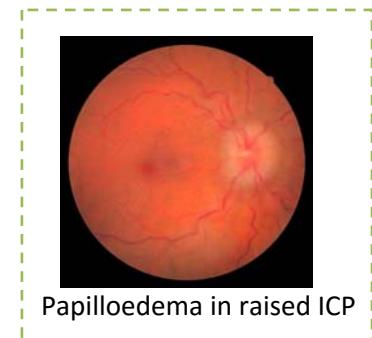
EXAMINATION

General

- GCS (or check AVPU)
- Built
- Neck stiffness / Kernig's sign (SAH)
- Plethora (PRV)
- Xanthalesma
- Peripheral stigmata of IE
- Ankle oedema
- Peripheral stigmata of limb infarction : Gangrenous areas (PRV)
- Pressure sores

CNS

- Higher functions
- All cranial nerves, motor, sensor , cerebellar
- Fundoscopy (Hypertensive and diabetic changes, Raised ICP)
 - Anterior circulation disturbance signs
 - Hemiparesis/hemisensory symptoms
 - Visual field defects (Homonymous hemianopia)
 - Cortical signs (Aphasia, Apraxia)
 - Large cortical stroke (Altered consciousness, Raised ICP, Seizures)
 - Vertibro-basillar territory
 - Occipital lobe(Homonymous hemianopia)
 - Cerebellar signs
 - Brain stem (Cranial nerves, Long tract signs, Bilateral signs +/-)
 - Lacunar stroke
 - Hemiparesis/hemisensory symptoms
 - Dysarthria
 - No cortical signs (Aphasia, Apraxia)
 - No features of large cortical stroke



CVS

- ✓ All peripheral pulses, rate, rhythm (AF), character
- ✓ Carotid bruits
- ✓ BP
- ✓ Apex – site, nature
- ✓ Gallop rhythm in cardiac failure
- ✓ Murmurs

RES

- ✓ Signs of LRTI (Orthostatic pneumonia)

ABDOMEN

- ✓ Hepato-splenomegaly (PRV)
- ✓ Balatable kidney (PCKD)

Finally..... Comment about

- Pathology – Haemorrhagic or Infarcted
- Site
- Stroke territory
- Type
 - TIA
 - Minor stroke
 - Progressing stroke
 - Completed stroke
- Risk factors
- Functional state

INVESTIGATION

DIAGNOSIS OF STROKE IS CLINICAL

- Distinguish between haemorrhage and ischaemia
 - ✓ Non Contrast CT : Infarctions may not seen early. But useful to exclude haemorrhage.
 - ✓ MRI
- RBS
- Find out the cause for the stroke
 - ✓ FBC (Polycythaemia, Infection, Thrombophilia)
 - ✓ ECG (AF)
 - ✓ PT/INR
 - ✓ ESR (Vasculitis)
 - ✓ VDRL (Syphilitic screening - Aneurysm)
 - ✓ Carotid Doppler (Carotid artery stenosis)
- To assess the risk factors
 - ✓ Lipid profile
 - ✓ FBS
 - ✓ Chest X-Ray (Hypertensive changes)
 - ✓ Angiography
- Exclude other DDs
 - ✓ CRP (Infection)

Risk Factors	
Modifiable	Non Modifiable
• HT	• Sex (Males)
• DM	• Age (>65Yrs)
• Hyperlipidaemia	• Family Hx (1 st degree relatives)
• Smoking	• Carotid artery stenosis
• Alcohol	

MANAGEMENT

- General Care
 - ✓ ABC (Management of unconscious patient)
 - ✓ Oxygen via face mask
 - ✓ Assessment of swallowing, Nutrition, Bladder & Bowel
 - ✓ Check BP & look for source of emboli
- Control BP
 - ✓ Treat after 7-10 days
 - ✓ Treat early if only SBP>220 & DBP>120, Hypertensive emergencies(MI, LVF, Aortic dissection, Encephalopathy) & pre-existing hypertension
 - ✓ Fall of BP → Aggravate ischaemia in penumbra due to loss of auto regulation
 - ✓ Early antihypertensive gives rise to extension of infarct
- Fluids
 - ✓ Oral/NG tube/IV 0.9% saline
 - ✓ Avoid IV glucose unless hypoglycaemic (No Dextrose. Its neurotoxic in ischaemic time & it'll cause cerebral oedema)
 - ✓ Avoid hypovolaemia(Aggravate ischaemia) & Hypervolaemia(Aggravate cerebral oedema)
- Manage cerebral oedema
 - ✓ Avoid hypervolaemia & Hyperglycaemia
 - ✓ IV mannitol to reduce cerebral oedema
 - ✓ Steroids no use
- Thrombolysis (*Only for ischaemic stroke*)
 - ✓ rt-PA – within 3hrs (Now upto 4.5hrs) : 0.9mg/kg (Maximum of 90mg/day)... 10% of total dose as initial IV bolus over 1 minute and remainder over 1 hour)
 - ✓ Early use of Aspirin (Within 48 hrs) → Reduces the incidence of further infarction following thrombo-embolic stroke
 - ✓ NO USE OF HEPARIN
- Management in a stroke unit is essential
 - ✓ Multidisciplinary stroke team : Doctors, Nurses, Physiotherapists, Occupational therapist, Speech therapists, Social workers, Mental health workers
- Rehabilitation(should be commenced from Day 1)
 - ✓ Team approach
 - ✓ Restoration of patients to previous physical, mental & social capacity
 - ✓ Get the active participation of the patients & the care givers
- Secondary prevention of stroke (prevent recurrences)
 - ✓ Life style modification
 - Diet
 - Exercise (30-60 min exercise, 4-6 times/week)
 - Increase physical activity
 - Quit smoking

- ✓ Management of risk factors
 - Hypertension
 - Heart diseases
 - Diabetes
 - Hyperlipidaemia
 - Treat Polycythaemia
 - Carotid artery stenosis >70% at the side of infarction → Carotid artery surgery
- ✓ Drug treatment
 - Aspirin (75mg daily)
 - Dipyridamole (200mg bd), Clopidogrel
 - Warfarin (For cardio embolic stroke – in valvular heart diseases, AF, intracardiac thrombus following MI)

Management of haemorrhagic stroke

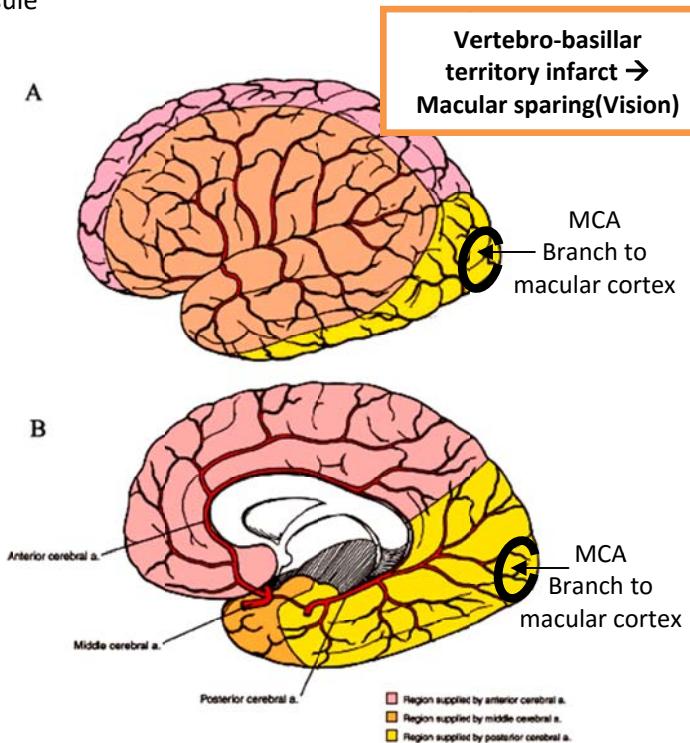
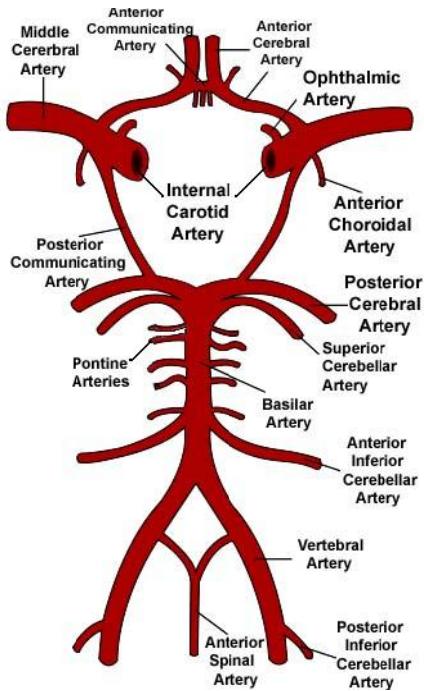
- General care
- No specific treatment
- No benefit in giving factor VII A
- Surgeries usually not done
- Indications for surgery : Cerebellar haemorrhage and Large cortical haematoma

TIA

- Symptoms lasts <24 hrs
- Mini stroke
- Usually due to micro-emboli
- Usually the infarct is controlled by auto regulation
- Secondary to valvular disease, MI, AF, Cardiac mural thrombi, total high red cell volume)
- Hemiparesis
- Aphasia
- Amaurosis fugax (sudden transient loss of vision in one eye due to passage of emboli in retinal arteries.
It is often the 1st clinical evidence of internal carotid artery stenosis)

DISCUSSION

- What are the affected territories?
 - Middle cerebral artery stroke – Arm weakness>Leg
 - Anterior cerebral artery stroke – Leg weakness>Arm
 - Arms = Legs → Internal capsule

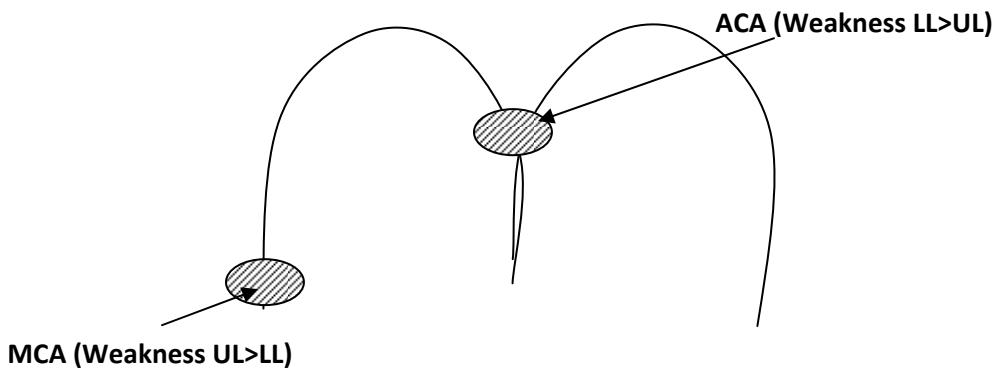


- What is ischaemic penumbra
 - Compromised, Salvageable, Therapeutic window of opportunity
- What is lacunar infarct?
 - Small infarct(<1.5cm²) seen on MRI or at autopsy
 - It is more common at the caudate, putamen, thalamus and the internal capsule.
 - Eg : Pure sensory strokes
Sudden uni-lateral ataxia
Sudden dysarthria
Clumsy hands
- What is Borderzone(Watershed) Infarct?
 - Multiple cortical infarcts that follow prolonged periods of very low perfusion.
 - Occur in the areas supplied by the anterior, middle & posterior cerebral arteries.
 - Cortical visual loss, Memory loss & intellectual impairment are typical.
 - Severe cases → Persistent vegetative state or minimal conscious state develops.
- Which blood vessel causes the stroke in internal capsule?
Thrombo-embolism of middle cerebral artery

- Features of brain stem infarction

Clinical Features	Structures involved
Hemiparesis or tetraparesis	Corticospinal infarcts
Sensory loss	Medial leminiscus & Spinothalamic tracts
Diplopia	Occulomotor system
Facial numbness	5 th Nerve nuclei
Facial weakness(LMN weakness)	7 th Nerve nucleus
Nystagmus, vertigo	Vestibular connections
Dysphagia, Dysarthria	9 th & 10 th Cranial nerves
Dysarthria, Ataxia, Hiccups & Vomiting	Brain stem & cerebellar connections
Horner's syndrome	Sympathetic fibres
Altered consciousness	Reticular formation

- What is the prognosis after TIA?
 - 30% of them will have a stroke. Among that 30% 1/3 of them will have a stroke within the 1st year.
 - 15% have suffered a myocardial infarct
 - TIA in anterior cerebral circulation carries more serious prognosis than one in the posterior circulation
- What is the prognosis after stroke?
 - 25% die within 1st two years
 - Around 30% of this group die in the 1st month
- Features of a cortical lesion
 1. Face, arm, leg weakness (Extensive cortical involvement)
 2. Localised lesion – Differential deficit



3. Cortical sensory loss
 - a. 2 point discrimination
 - b. 3 point discrimination (Steriognosis)

4. Inattention

a. Sensory

- i. Touch both hands separately → Patient will feel
- ii. Touch both hands simultaneously → Patient will ignore the site opposite to the lesion

b. Visual

- i. Examiner should stand behind the patient.
- ii. Examiner moves his index fingers separately in-front of the patient's eyes from medial to postero-laterally → Pt can visualize both fingers
- iii. Examiner moves index fingers in both hands from medial to postero-lateral in-front of the patients both eyes → Patient can't see finger at the affected side

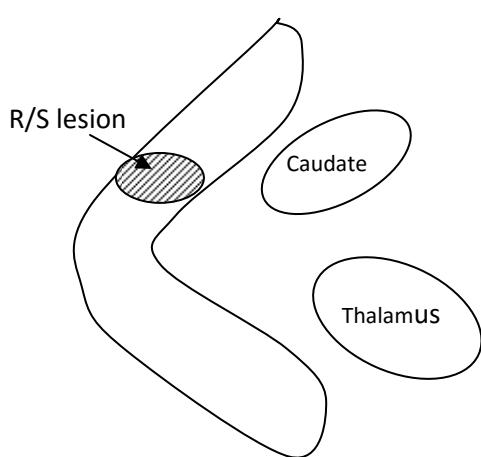
5. Dysphasia – Speech (When dominant lobe affected)

6. Non dominant lobe – Apraxia → Unable to do complex motor activity (Dressing)

7. Gaze palsy

- a. Cortical → Gaze towards the normal side of the body
- b. Pontine → Gaze towards the weak side of the body

Internal capsule lesion



In the internal capsule nerves move as a bundle

- R/S lesion
 - L/S hemiparesis, Face, arm, leg
 - UMN type
 - Diffuse hemiparesis : Can be pure motor or sensory
 - * No cranial nerve involvement
 - * Only crude sensations are lost (touch)

R/S Mid-brain lesion

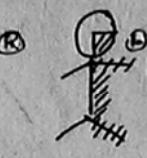
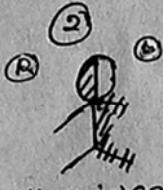
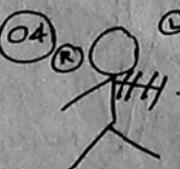
- Cranial Nerve 3,4 involvement on R/S (LMN type)
- L/S hemiparesis
- L/S UMN type facial nerve palsy
- +/- Cerebellar lesion

R/S Pontine lesion

- R/S CN 5,6,7,8 Involvement
- R/S LMN type facial nerve palsy
- Gaze palsy – Eyes deviated to the weak side of the body
- L/S hemiparesis

R/S Medulla lesion

- R/S 9,10,11,12,CN LMN type involvement
- No facial palsy
- R/S Hemiparesis

Examination Limb	of a Patient with weakness	Examination sequence
①	 <p>contralateral CR/S) cerebral hemisphere contralateral CR/S) IC lesion Nodysphasia Hemiplegia → contralateral CR/S) Midbrain lesion - contralateral C- 8th nerve CR/S .), body (3rd & 4th Nerves starts from midbrain) * 4th Nerve decussate after emerging), It gives the posterior of the the superior oblique of the at the side of limb weakness ,</p>	<p>consciousness impaired visual field defect Dysphasia</p> <p>Higher functions: - Alert - consciousness - Speech + Dysphasia</p> <p>• Cranial nerve Ex - Visual field (corneal) - 3rd Nerve (Mid brain) - Facial nerve (Pons) - 9th, 10th, 12th - Below gives weakness (pons damage ↳ looks at weak limb side)</p>
②		
③	 <p>Hemiplegia</p> <p>Left sided Pontine lesion.</p> <p>conjugate gaze deviation towards the weak limbs.</p> <p>Facial Nerve LMN Weakness C-R/S.</p>	<p>• Discrimination sense (cortex)</p> <p>• Proprioception</p> <p>• Pain and temperature</p>
④		
⑤	 <p>Hemiplegia</p> <p>R/S corticob ortex</p> <p>R/S Medullary lesion, (Take it as motor nerves still not crossed the sides),</p> <p>L/S spinol lesion.</p> <p>R/S cortical lesion</p> <p>L/S spinol lesion</p> <p>visual field defect Discriminatory sensory loss,</p> <p>Pain temp loss on L/S</p> <p>Proprioception loss R/S</p> <p>R/S palate and tongue weakness</p> <p>R/S horner's Xn.</p> <p>Pain temp loss over R/S.</p> <p>Proprioception loss other L/S.</p> <p>L/S horner's Xn</p> <p>visual field defect Dysphasia (dominant hemisphere) Discrimination sensory deficit</p> <p>visual field defect Dysphasia Discrimination sensory deficit</p>	<p>• Examination sequence</p> <p>• Higher functions: - Alert - consciousness - Speech + Dysphasia</p> <p>• Cranial nerve Ex - Visual field (corneal) - 3rd Nerve (Mid brain) - Facial nerve (Pons) - 9th, 10th, 12th - Below gives weakness (pons damage ↳ looks at weak limb side)</p> <p>• Discrimination sense (cortex)</p> <p>• Proprioception</p> <p>• Pain and temperature</p>
⑥		

Q6

Bilateral Pontine lesion → Only vertical gaze retains.
Facial movements loss.
↓
Locked in syn.

Q7

Bilateral Medullum lesion → Retained facial movements.
No tongue, palate or speech.
Bilateral cervical spine lesion C1-C3 → Ventilation support required
C4 bilateral → Diaphragmatic respiration

Q8

Bilateral cortical lesion } Discriminatory sensation intact
Pain & temperature intact
Frontal incontinence
Bilateral Thalamic spin lesion (CT1-L1) → Sensory level or loss of all sensation
Hypotonia of micturition or acute urinary retention

Q9

Medullary lesion.
CB below arm fibre decussation above leg fibre decussation. } Weakness of palmar and tongue on the side of the arm weakness.

MB - 3rd & 4th
pons - 6th - 8th
medulla - 9th - 12th

Thalamus
Medulla
OI
AMN
Dorsal column
141

Site of lesion	Disorder	R	L
Frontal, either	Intellectual impairment Personality change Urinary incontinence Monoparesis or hemiparesis		
Frontal, left	Broca's aphasia		
Temporo-parietal, left	Acalculia Alexia Agraphia Wernicke's aphasia Right-left disorientation Homonymous field defect		
Temporal, right	Confusional states Failure to recognize faces Homonymous field defect		
Parietal, either	Contralateral sensory loss or neglect Agraphaesthesia Homonymous field defect		
Parietal, right	Dressing apraxia Failure to recognize faces		
Parietal, left	Limb apraxia		
Occipital/occipitoparietal	Visual field defects Visuospatial defects Disturbances of visual recognition		

Fig. 21.2 Principal features of destructive cortical lesions in a right-handed individual.

Brainstem infarction

This causes complex signs depending on the relationship of the infarct to cranial nerve nuclei, long tracts and brainstem connections (Table 21.27).

- *The lateral medullary syndrome* (posterior inferior cerebellar artery (PICA) thrombosis and Wallenberg's syndrome) is a common example of brainstem infarction presenting as acute vertigo with cerebellar and other signs (Table 21.28 and Fig. 21.22). It follows thromboembolism in the PICA or its branches, vertebral artery thromboembolism or dissection. Features depend on the precise structures damaged.
- *Coma* follows damage to the brainstem reticular activating system.
- *The locked-in syndrome* is caused by upper brainstem infarction (p. 1126).
- *Pseudobulbar palsy* (p. 1110) can follow lower brainstem infarction.

Table 21.27 Features of brainstem infarction

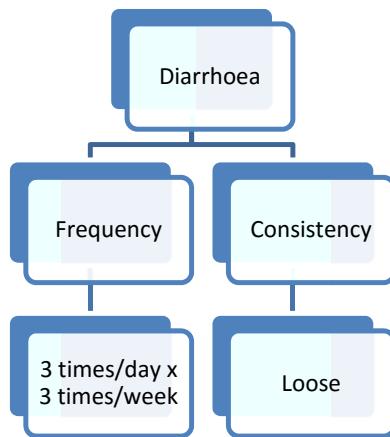
Clinical feature	Structure involved
Hemiparesis or tetraparesis	Corticospinal tracts
Sensory loss	Medial lemniscus and spinothalamic tracts
Diplopia	Oculomotor system
Facial numbness	Vth nerve nuclei
Facial weakness	VIIth nerve nucleus
Nystagmus, vertigo	Vestibular connections
Dysphagia, dysarthria	IXth and Xth nerve nuclei
Dysarthria, ataxia, hiccups, vomiting	Brainstem and cerebellar connections
Horner's syndrome	Sympathetic fibres
Coma, altered consciousness	Reticular formation

Table 21.28 Clinical signs in the lateral medullary syndrome (PICA thrombosis)

Ipsilateral	Contralateral
Facial numbness (Vth)	Spinothalamic sensory loss
Diplopia (VIth)	Hemiparesis (mild, unusual)
Nystagmus	
Ataxia (cerebellar)	
Horner's syndrome	
IXth and Xth nerve lesions	

Tutorial on Chronic Diarrhoea

Diarrhoea



Chronic diarrhoea

Diarrhea persisting for more than one month

Differential Diagnoses

- Infective causes
 - Bacterial overgrowth
 - Autonomic Neuropathy (Eg : DM) → Atonic bowel → Bacterial overgrowth
 - Blind loops created by GI surgeries (Eg : Gastrectomy → Bacterial Overgrowth)
 - Viral
 - CMV
 - HIV
 - HSV
 - Protozoal
 - Giardia
- Inflammatory bowel disease
 - Ulcerative colitis
 - Crohn's disease
- Metabolic
 - Diabetes mellitus
 - Thyrotoxicosis
- Neoplastic
 - Benign
 - Polyps – Tubulo-villous adenoma
 - Malignant – Colo-rectal Carcinoma
- Malabsorption
 - Chronic pancreatitis
 - Coeliac disease
- Iatrogenic
 - Drug induced – Metformin, PPI

History

- Duration
- Describe the diarrhea
- Ask about the normal bowel habits
- Compare the change
- Ask about **Red flag signs**
 - Age
 - Personal & family history of malignancies
 - Significant weight loss
 - Blood in stools
 - Rectal symptoms
 - Urgency
 - Tenesmus
 - Bleeding per rectum
 - Fresh bleeding
- Stools mixed with mucous – Pathology in large bowel
- Steatorrhoea
- Nocturnal diarrhea → Organic disorder
- Obstructive features

Social History

- Type of the toilet
- Sanitation

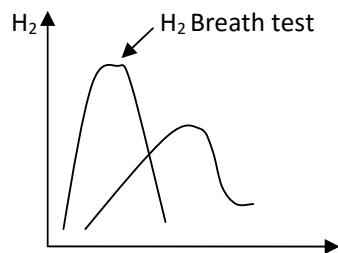
Examination

- Nutritional deficiencies
 - Weight
 - Height
 - BMI
 - Signs of nutritional deficiencies
- IBD
 - Eyes – Iritis
 - Finger clubbing
 - Scratches
- Abdomen
 - Distended – Nutritional hypoalbuminaemia
 - Scaphoid abdomen
 - Surgical scars
 - Features of liver secondaries

Investigations

- Stool full report
 - Amoeba, Ova, Cysts
- FBC + Blood picture (Anaemia)
 - Macrocyes
 - B_{12} deficiency – In terminal ileum resection
 - ↑ WBC – Active infection
 - Thrombocytosis (In any inflammatory disease)
- Blood urea - ↓ UOP
- Serum electrolytes – Dehydration

- Abdominal X-Ray in alcoholic
 - Look for **Tropical chronic calcification of pancreas (TCCP)**
- Bacterial overgrowth
 - H₂ breath test
 - Give lactulose



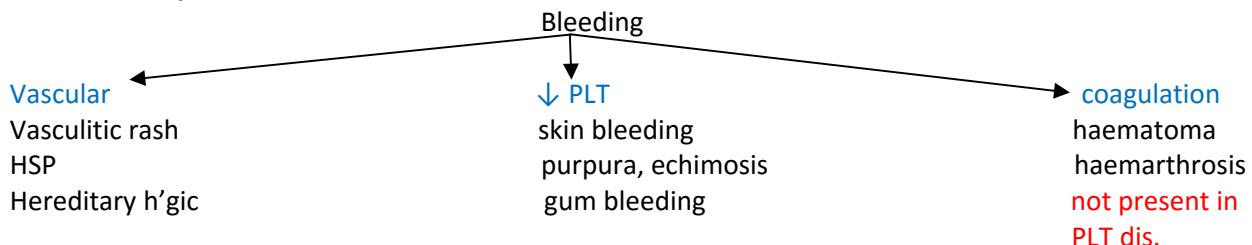
- Endoscopy – Nasojejunal tube
- Colonoscopy & Biopsy
- CT scan abdomen

Bleeding tendency

Presents as

- Spontaneous bleeding
- Bleeding following mild trauma
- Persistent bleeding after Sx
- Skin bleeding
 - Petechiae, purpura, echymosis

Involves multiple sites



Low PLT

1. PLT number defect
 - BM (production)
 - Spleen (destroy)
2. PLT functional defect
 - Drugs – Aspirin, Clopidogrel
3. Excessive PLT consumption -Excessive intra vascular coagulation
 - HUS
 - TTP (neurological symptoms, renal failure)
 - DIC

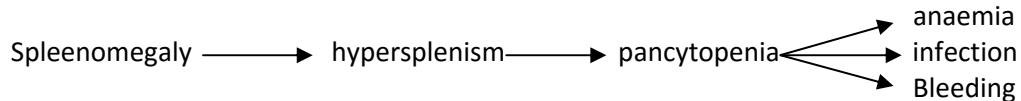
BM disorders

1. Malfunction of the precursor cells
 - Aplastic anaemia- pale + bleeding
2. Replace by other cells (infiltration) → organomegaly + lymphadenopathy
 - Lymphoma (lymphocytes)
 - Leukaemia (malignant blood cells)
 - Myelofibrosis (fibrosis)
 - MM (plasma cells) → no organomegally; back pain, bone pain
3. BM dysplasia – factory is not working properly
4. Infection (when infection ↓ plt get NL)
 - Transient dengue
 - HIV
 - IMN (palatal petechiae)

Hypersplenism

- Causes for massive splenomegaly
 - CML
 - Myelofibrosis
 - Chronic malaria
 - Leishmaniasis
 - Gauchers Xn

- Moderate splenomegaly
 - Infection – EBV, IE, TB, Malaria
 - Portal HT - liver cirrhosis
 - Hematological – HA, CML, Lymphoma
 - CT disorders – RA, SLE
 - Others – sarcoidosis, IgM anti body def



4. Excessive consumption of PLT

- DIC
 - Acute – after Sx, Abortion, Sepsis
 - Chronic – malignancy, old age
- TTP (Thrombotic thrombocytopenic purpura)
- HUS

Fever with bleeding

DD

1. Lymphoma
2. Leukaemia
3. Infection
 - Dengue
 - HIV
 - IMN
 - Malaria
 - IE
 - TB
4. DIC
5. TTP
6. HUS

P/C

- Pathognomonic features of above mentioned diseases
- Fever
- Bleeding
 - Spontaneous bleeding
 - Bleeding following mild trauma
 - Persistent bleeding after surgery
 - Skin bleeding
 - Petechiae, purpura, echymosis

DD	Symptoms	Signs
Lymphoma	Lymphadenopathy Fever , LOW, night sweats pruritus, lethargy Alcohol induced LN pain	LN-enlarged, painless, non tender, rubbery, superficial LN Mainly cervical Axillary Inguinal Cachexic Anaemic Fx Spleno/ hepatomegaly
Leukaemia CML <ul style="list-style-type: none">• BM infiltration• Splenomegaly	Mostly chronic & insidious LOW, tiredness, fever, sweats, Fx of gout (excessive formation→ excess breakdown → purine) Bleeding Abd discomfort (splenic enlargement)	Massive splenomegaly Hepatomegaly Anaemic Fx bruising
Infection		
Dengue	Immune suppression	
HIV	Persistent / recurrent infection Persistent generalized LN AIDS	
IMN	Fever, sore throat, LOA, malaise	Lymphadenopathy Palatal petichiae Splenomegaly Fx of hepatitis Fx of haemolysis –icterus
Malaria	Classic periodic fever(tertian)+ rigors Headache, malaise, myalgia, anorexia	Anaemia Jaundice Hepatosplenomegaly
IE	Septic – fever, rigors Cardiac – chest pain, palpitation Emolic – immune Risk factors	Peripheral signs Anaemia , clubbing, splenomegaly, Fx of heart failure, murmurs Emolic
TB	Chronic cough, haemoptysis Night sweats, LOW Mantoux test	Cachexic
TTP	Fever Fluctuating CNS signs (fits, hemiparesis, LOC, loss of vision) Microangiopathic haemolytic anaemia- jaundice Mucosal bleeding Renal failure- ↓UOP, uraemic symptoms	Febrile Focal neuro signs Icterus Purpuric patches

HUS	Hx of febrile illness Hx of gastroenteritis, URTI Bleeding ARF MAHA - jaundice	
DIC	Acute – after Sx, Abortion, Sepsis (SIRS) Chronic – malignancy, old age Hx of extensive bleeding/ bruising ARF	Fx of SIRS Temp>38 c or <36 c HR >90 RR> 20 WBC <4000 or >12000 bleeding

Thrombotic thrombocytopenic purpura (TTP)

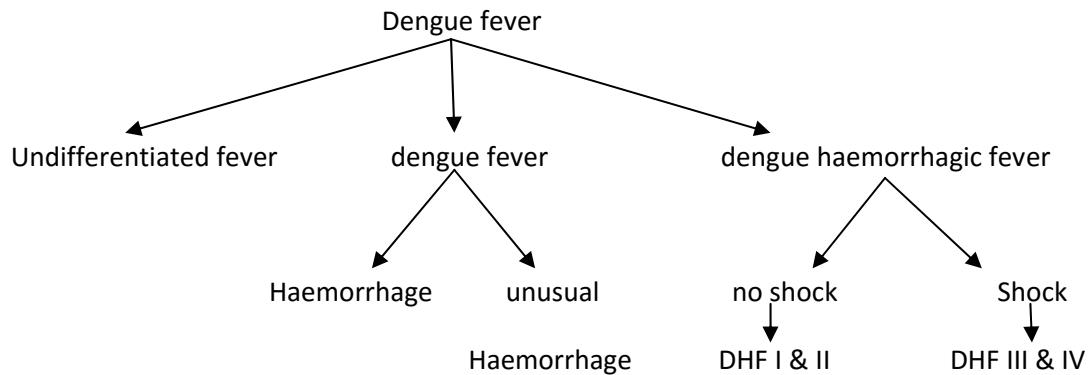
- Platelet consumption leads to profound thrombocytopenia.
- There is a characteristic symptom complex of
 - florid purpura
 - Fever
 - fluctuating cerebral dysfunction
 - haemolytic anaemia with red cell fragmentation
 - renal failure.
- The coagulation screen is usually normal.
- Lactic dehydrogenase (LDH) levels are markedly raised as a result of haemolysis.
- TTP arises due to endothelial damage and microvascular thrombosis. This occurs due to a reduction in
- ADAMTS 13 (A Disintegrin-like and Metalloproteinase domain with Thrombospondin-type motifs), a protease which is normally responsible for VWF degradation. ADAMTS 13 is needed to break down ultra large von Willebrand factor multimers (UL VWFMs) into smaller haemostatically active fragments that interact with platelets.
- Reduction in ADAMTS 13 results in the adhesion and aggregation of platelets to UL VWFMs and multiorgan microthrombi.
- Secondary causes of acute TTP include pregnancy, oral contraceptives, SLE, infection and drug treatment,
- including the use of ticlopidine and clopidogrel.

Treatment

- Plasma exchange as the mainstay of treatment. It provides a source of ADAMTS 13 and removes associated autoantibody in acute TTP.
- Cryoprecipitate and Solvent-Detergent FFP (fresh frozen plasma) both contain ADAMTS 13.
- Pulsed intravenous methylprednisolone is given acutely.
- Rituximab is also used as a primary treatment.
- Disease activity is monitored by measuring the platelet count and serum LDH.
- Platelet concentrates are contraindicated.
- The untreated condition has a mortality of up to 90%.

Dengue

Hallmark of dengue fever is plasma leakage



DF

Febrile phase	Recovery phase
---------------	----------------

DHF

Febrile phase	Leaking phase	Recovery phase
3 – 5 days	48 hrs	

Undifferentiated febrile illness & classical DF Mx → as other viral fever with symptomatic Rx

DF & DHF febrile phase is similar → closely monitor to identify DHF

DHF - 3 stages

- Febrile phase
- Critical phase
- Convalescent phase

Phase	Symptoms	Signs	Lab
Febrile	High fever 2-7 days Facial flushing, skin erythema, arthralgia, myalgia, headache, N, V, In some pts, sore throat, injected pharynx, conjunctival injection, diarrhea	Tender hepatomegaly (suggestive of DHF)	Leucopenia (WBC<5000) Mild thrombocytopenia (<150,000) PLT < 100,000 indicate entry to critical phase
Critical phase (onset of plasma leakage)	Usually around 5-6 th day Last for 48 hrs Above features + Petechiae, echymosis, purpura Bleeding from mucosa, injection sites	Bleeding manifestation (not a must) +ve Hess test Ascites, pleural effusion	Plt <100,000 Evidence of plasma leakage ↑PCV> 20%rise from baseline PCV (M- 40 , F-36) USS – FF CXR (right lateral decubitus film)– Effusion ↓S. Alb <3.5g/dl Non fasting S. Cholesterol <100mg/dl
Recovery phase (Re-absorption of extravasated fluid)	Last 2-5 days Improve general well being & appetite	Convalescent rash Generalized itching Haemodynamic stability Bradycardia (in some pts) diuresis	Stabilization of HCT (even ↓due to reabsorption of extravasated fluid) ↑WBC, ↑PLT

Symptoms of Shock

- ▶ **Sweating**
- ▶ **Abdominal pain**
- ▶ **Persistent vomiting**
- ▶ **Restlessness / altered conscious level**
- ▶ **Postural dizziness**
- ▶ **Decreased urine output (<0.5 ml/kg/hour)**

Signs of Shock

- ▶ **Cold extremities**
- ▶ **Prolonged capillary refill time >2 seconds**
- ▶ **Unexplained tachycardia**
- ▶ **Tender hepatomegaly >2 cm**
- ▶ **Increasing diastolic pressure**
- ▶ **Narrowing of pulse pressure ≤ 20 mmHg**
- ▶ **Postural drop ≥ 20 mmHg of systolic blood pressure**
- ▶ **Hypotension (from patient's baseline)**

Diagnosis at OPD level

- DD of pts with acute onset fever+ ≥2 of the following
- Headache – retro orbital pain
- Myalgia/ arthralgia
- Rash (diffuse, erythematous, macular)
- Haemoragic manifestations (petechiae, +Hesses test)
- Leucopenia (<5000/mm³)
- Rising HCT of 5-10%
- PLT ≤150,000

Criteria for admission

PLT<100,000 +

Following warning signs

Abdominal pain or tenderness

Persisting vomiting

Signs of plasma leakage: pleural effusion, ascites

Mucosal bleeding

Liver enlargement

↑HCT with a rapid ↓of PLT

Other pts who need admission even without above criteria

Pregnant

Elderly

Obese pts

Pts with other co morbidities; DM, CRF,IHD

Pts with other social circumstances

Mx of those who don't need admission

- Adequate oral fluid intake(around 2500ml/24hrs) ; ORS, king coconut water, other fruit juices, kanji, soup
Exclude red & brown drinks(confusion with haematemesis)
- Physical rest
- Tepid sponging for fever
- PCM (not exceeding 2tab 6hrly)
- Anti emetics
- Avoid all NSAIDS & steroids
- FBC – done at least the 3rd day of the illness (done on the 1st day in preg, CRF pts)

Immediate admission if

- Clinically deterioration with settling o fever
- Inability to tolerate oral fluids
- Severe abdominal pain
- Cold & clammy extremities
- Lethargy, irritability or restless
- Bleeding tendency
- No UOP for 6 hrs

Mx of inward pts

- DHF I – No spontaneous bleeding, No shock
- DHF II – spontaneous bleeding + No shock
- DHF III – compensated shock
 - Tachycardia
 - Narrow pulse pressure
 - <25- suggestive
 - <20 – worried
 - Cold peripheries
 - Cold line – demarcation
 - Low volume pulse
 - CRFT < 2sec
 - UOP <0.5ml/kg/hr
- DHF IV – profound shock
 - Uncompensated
 - BP un-recordable
 - No pulse

In a patient who arrives from home or transferred from another institution and found to be in shock on admission, every effort should be taken to find out how much fluid was given during the preceding 12-24 hours. This is because the critical phase would have started 12-24 hours prior to the detection of shock in such a patient. This fluid amount should be subtracted from M+5% and only the balance amount of fluid should be given for the next 24 hours.

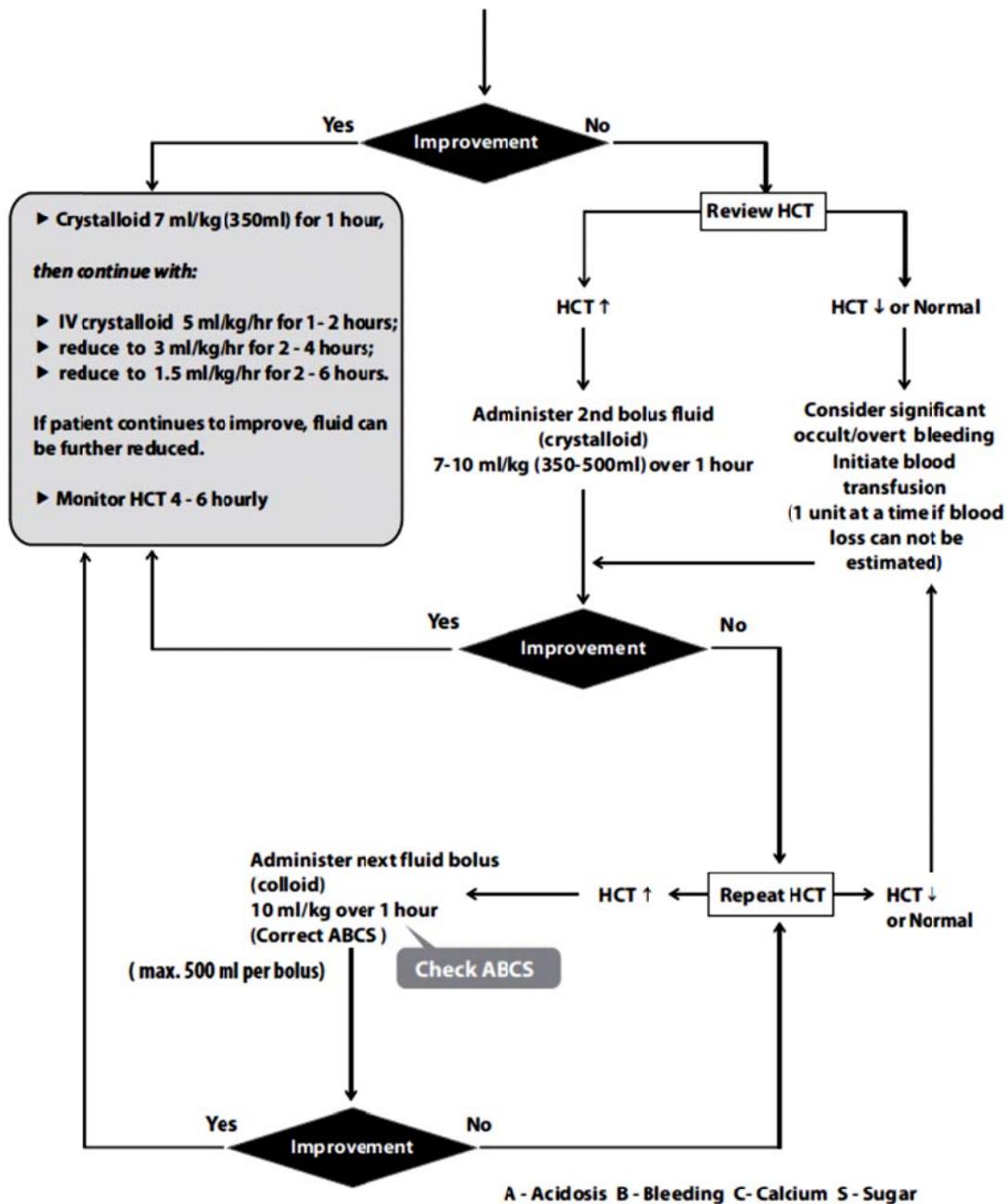
► Hence, it is important for all transferred patients from smaller hospitals to have this information clearly mentioned in the Transfer Forms

	Monitoring	Management
If the pt is clinically stable on admission & suspecting DF/ DHF	<ul style="list-style-type: none"> • QHT 4 hrly • Watch for evidence of bleeding ; meleana, bleeding PV • Assess vital signs • FBC on admission & daily 	<ul style="list-style-type: none"> • Similar to OPD Mx except additional IV fluid • Pts unable to take oral ,D,V • Total (IV + Oral)- 2500ml/24hr • (2ml/kg/hr up to max. wt of 50 kg) • If V, D, + ↑accordingly • Over hydration doesn't prevent shock in critical phase, but cause fluid overload
When PLT < 100,000 (use monitoring chart) – to detect entering critical phase	<ul style="list-style-type: none"> • QHT 4 hrly • PR, BP, RR, CRFT – 4hrly • Fluid balance (in detailed) <ul style="list-style-type: none"> ◦ intake with type & route of fluid – 6 hrly ◦ Op urine/vomitus – 6 hrly ◦ FBC daily ◦ HCT – twice daily 	<ul style="list-style-type: none"> • 18 G cannula • Start slow IV infusion of Hartmanns/n. saline to keep the vein open.(1000ml can give over 24hrs) • Total (IV + Oral)- 2500ml/24hr (unless pt is having V or D)
When the pt enter critical phase – plasma leakage See monitoring chart 2	<ul style="list-style-type: none"> • Vital parameters – hrly • Fluid balance – 3hrly • HCT – 6hrly 	<ul style="list-style-type: none"> • TFR=maintenance + 5% deficit(over 48 hrs) both IV & Oral <ul style="list-style-type: none"> ◦ 1st 10 kg - 100ml ◦ 2nd 10 kg - 50ml ◦ From 20kg & above up to 50kg - 50ml * 5% deficit = 50ml/kg (up to 50Kg) • If BW<50kg- IBW • Use N/ Saline or Hartmann;s • Orally; electrolyte solutions, - king coconut, fruit juices, ORS, kanji • Drinking plain water actively discouraged <p>If pt is stable M+5 spread over 48hrs Volume not given in uniform rate. Just sufficient to maintain an effective circulation Start at a slow rate1-1.5ml/kg/hr ↑in a step wise pattern ↑of HCT ↓UOP<0.5ml/kg/hr</p>
If there is evidence of shock	<ul style="list-style-type: none"> • Vital parameters – every 15min (until pt is haem. Stable) • HCT – during fluid resuscitation immediately before & after each fluid bolus • & then 2-4hrly • If not responding to adequate fluid resuscitation, liver failure, renal failure Check <ul style="list-style-type: none"> ◦ liver profile ◦ blood sugar ◦ S.Ca²⁺ ◦ SE ◦ S.Creatinine ◦ Clotting profile 	

SHOCK WITH NARROW PULSE PRESSURE & HYPOTENSION

Fluid resuscitation with isotonic crystalloid 7- 10 ml/kg (350-500ml)* over 1 hour

(Try to obtain a haematocrit before fluid resuscitation)

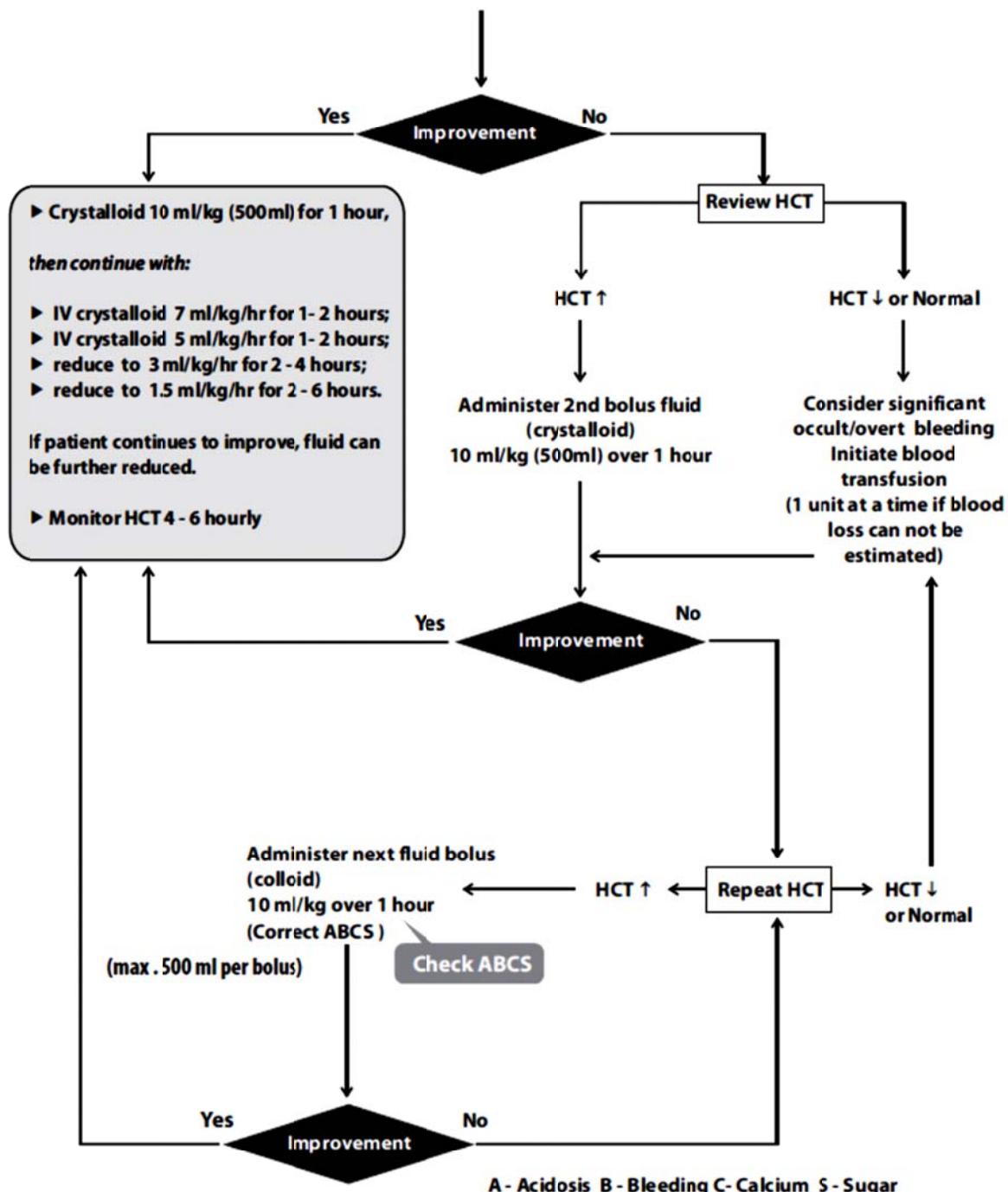


* In the elderly and in patients with heart disease & renal disease consider using lower infusion rates.

PROFOUND SHOCK (UN-RECORDABLE BLOOD PRESSURE)

Fluid resuscitation with 10 ml/kg (500ml) isotonic crystalloid over 15 minutes

(Try to obtain a haematocrit before fluid resuscitation)



Fluid overloaded patient

Too much IV + oral fluid

Hypotension & moderately high HCT due to dehydration → mis-diagnosis of shock

Fluid overloading should be treated according to the haemodynamic status + HCT

- Fx of shock } start bolus of colloid(dextran 40/ hetastarch)
- Pulm. Oedema } 10ml/kg/hr
- High HCT } in the midway of the bolus – Frusemide 1mg/kg
- If pt in shock } Immediate transfusion of blood (until blood is available bolus of colloid 300-400 ml)
NL/↓HCT } Frusemide 1mg/kg
- If pt haemodynamically } restrict fluid
Stable } monitor carefully
- High HCT } pt will go in to poly uric phase & HCT will settle within hrs
- patient is haemodynamically stable and normal or low HCT
 - fluid should be restricted and patient should be monitored carefully, the patient is likely to improve within hours.
 - The most probable reason for low hematocrit is haemodilution.
 - If the patient develops features of pulmonary oedema, frusemide 0.5 mg/kg should be given intravenously.

Fluid for Resuscitation

Crystalloids:

Normal saline or Hartmann's solution, should be used for initial fluid resuscitation

Colloids:

Only hyper-oncotic colloids are effective. They are used only as boluses of 10 ml/kg/hour. Dextran 40 or Hetastarch (6% starch solution) can be used :

- ✓ In patients who present in shock and fluid overload
- ✓ In patients whose shock does not respond to two boluses of crystalloids with rising HCT or still high HCT
- ✓ In patients who are being treated for shock, and has high HCT and whose fluid quota (M+5%) is nearing completion

As dextran can sometimes interfere with cross matching, blood should be drawn for grouping and cross matching before starting on dextran.

The maximum amount of dextran for 24 hours is 3 boluses of 500 ml/hour (10 ml/kg/hour).

The maximum of Tetra starch is 5 boluses of 500 ml/hour (10 ml/kg/hour) in 24 hours.

Colloids should not be used in a dehydrated patient who presents with shock and high HCT, until the hydration is corrected with crystalloid.

If the patient is not responding to two boluses of crystalloid, contributory causes for shock other than plasma leakage should be considered. These are,

- ✓ **Acidosis**-check venous blood gas (if present, check liver and renal profiles)
- ✓ **Bleeding**- check HCT
- ✓ **Calcium** and other electrolytes (sodium and potassium) - check serum
- ✓ **Sugar**-check random capillary blood sugar
- It is important to correct these conditions as quickly as possible. Therefore empirical treatment with 10% calcium gluconate 10 ml over 10 minutes.
- I.V. calcium gluconate may be used in patients who show evidence of myocarditis as well, as hypocalcaemia is common in DHF grade I.V. patients and calcium may improve the myocardial contractility in such patients.
- If the patient is clinically acidotic one dose of 8.4% sodium bicarbonate 50 ml may be given empirically if blood gas cannot be assessed.
- Correct the blood glucose if it is less than 60 mg/dl

Indications for Blood Transfusion

Significant bleeding in DHF is

- ✓ Due to DIC
- ✓ Liver failure which occurs as a consequence of prolonged shock causing multi-organ dysfunction.
- ✓ Bleeding, during the early phase of DHF, usually due to drugs, such as NSAIDS.
- If there is significant overt bleeding (e.g. haematemesis, mleana, bleeding per vagina etc.) of more than 6-8 ml/kg body weight, blood transfusion is necessary.
- However, bleeding could be concealed. Suspect significant occult bleeding in the following situations and transfuse blood:
 - ✓ Haematocrit not as high as expected for the degree of shock to be explained by plasma leakage alone. (Hypotensive shock with low or normal HCT)
 - ✓ A drop in HCT without clinical improvement despite adequate fluid replacement (40-60 ml/kg).
 - ✓ Severe metabolic acidosis and end-organ dysfunction despite adequate fluid replacement.
(haemoglobin level may remain normal initially despite significant blood loss.)
- 5 ml/kg of packed red cells or 10 ml/kg of whole blood can be given at a time.
- HCT is expected to rise by 5 points (e.g. from 30 to 35) with this amount of blood.

Criteria before discharge from hospital.

- ✓ No fever for at least 24 hours without the usage of antipyretic drugs
- ✓ At least two days have lapsed after recovery from shock
- ✓ Good general condition with improving appetite
- ✓ Normal HCT at baseline value or around 38 - 40 % when baseline value is not known
- ✓ No distress from pleural effusions or ascites
- ✓ When platelet count has risen above 50,000 /mm³
- ✓ No other complications

DIC

Uncontrolled activation of the pathways leading to coexistent microthrombosis & bleeding

Causes

- Sepsis is the commonest cause
- Falciparum malaria
- Malignancy
- Liver failure
- Obstetric emergencies
- Snake bite

Clinical Fx

- Predominant Fx – the underlying condition
- Bleeding tendency
- Extensive bruising
- Mucosal bleeding
- Bleeding from vena puncture sites
- (intravascular haemolysis, consumption of PLT, activation of thrombolysis)

Ix

- FBC – anaemia, thrombocytopenia
- APTT/PT – prolong
- FDP ↑
- serum fibrin ↓
- blood picture – RBC fragments from haemolysis
- BU/SE
- LFT
- Blood culture

Mx

- IV access
- High flow O₂
- Catheterize – monitor fluid balance
- Maintain blood volume with transfusions of fresh whole blood(or packed cells & NL saline)
- If there is active bleeding / APTT↑ more than twice NL – give FFP(15ml/kg) or cryoprecipitate
- Consider PLT transfusion if <50,000/mm³
- Continue to monitor FBC, coagulation, FDP
- Consider administering cryoprecipitate, if plasma fibrinogen is <500ml/L
- Consider plasma exchange in severe cases
- Treat the underlying cause

Acromegaly

Pt presents with,

1/3 – changes in appearance

1/4 – headache or visual field defects

Remainders - Δ made by an alert observer in another clinic

Hx – start the Hx from the beginning,

When did it start?

How & when did u noticed?

First abnormality?

Ask other symptoms of acromegaly

- ↑ size of hands & feet
- Coarsening of facial features
- ↑ sweating
- Tiredness
- Obstructive sleep apnoea- due to soft tissue swelling in larynx
- Wt gain
- Amenorrhoea/ oligomenorrhoea-in women
- Galactorrhea
- Impotence/ poor libido
- Deep voice, goiter
- Breathlessness
- Pain/ tingling in hands
- Muscle weakness, joint pains
- Features of CTS

Symptoms of hypopituitarism +/- local mass effects – due to pituitary tumour

Tiredness, malaise- ↓TSH/ACTH
Slow thinking & movements,
Cold intolerance,dry skin
& hair- ↓TSH
Loss of libido & 2ry sexual hair,
Amenorrhoea- ↓LH/FSH

hypothalamus- altered appetite
obesity
thirst
precocious puberty
somnolence
ventricular-hydrocephalus → headache
Cavernous sinus- cranial N palsies(3rd,4th,6th)
Bones & meninges-headache

Ix done/not? What are the findings?

Has taken any Rx/ not?

Has it been successful?

Ask about complications-

- ✓ DM (20%), impaired glucose tolerance (40%)- coz GH is counter regulatory to insulin
- ✓ Vascular- ↑BP ,LVH , cardiomyopathy , ↑risk of IHD
- ✓ CA- ↑risk of colonic polyps, colonic CA-PR bleeding

SHx- Occupation

Effect on life

Psychological impact

Examination

Prominent supra orbital ridge

Prognathism

Inter-dental separation

Large tongue (macroglossia)

Hirsutism

Thick greasy skin

Spade like hands & feet

Features of heart failure- oedema

CVS Ex- ↑BP

Signs of HF

Abd Ex- hepatomegaly (heart failure)

CNS Ex- signs of CTS

CN- visual field defects , 3rd,4th,6th nerve palsies

Discussion

Acromegaly- caused by excessive production of GH

GH excess → gigantism in children
→ Acromegaly in adults

Due to a pituitary tumour in almost all cases (>99%)

Hyperplasia due to GHRH excess – very rare

Ectopic production of GHRH eg- from a carcinoid tumour- rare

Incidence- 3-4 million / yr

Prevalence- 40-60 /million

M: F -1:1

5% associated with MEN 1

Physiology of GH-

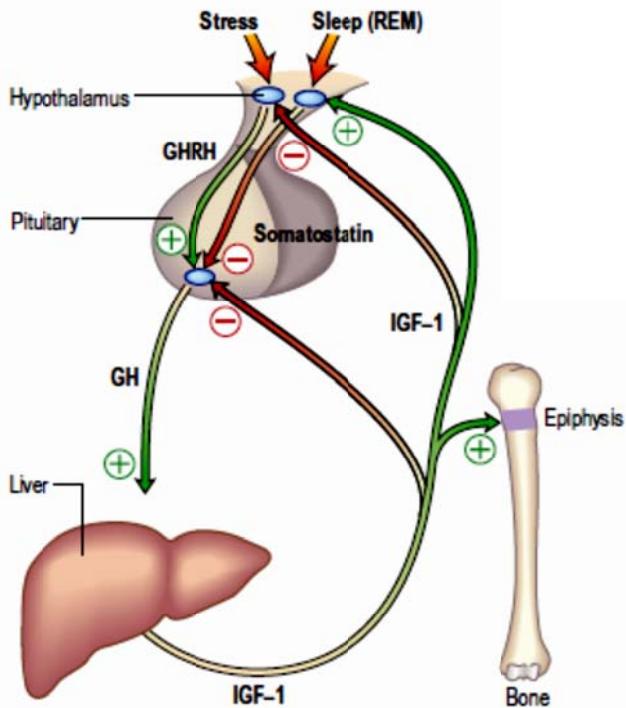


Fig. 18.9 The control of growth hormone (GH) and insulin-like growth factor-1 (IGF-1). Pituitary GH is secreted under dual control of GHRH and somatostatin and stimulates release of IGF-1 in liver and elsewhere. IGF-1 has peripheral actions including bone growth and exerts negative feedback to hypothalamus and pituitary.

GH stimulate skeletal & soft tissue growth.

Metabolic action,

- ↑ collagen & protein synthesis
- Promote retention of Ca²⁺, phosphorus & nitrogen, necessary substrates for anabolism
- Oppose the action of insulin

GH release is intermittent-mainly nocturnal, especially during REM sleep

Acute stress, exercise, puberty- ↑ GH release

Hyperglycemia- ↓ GH secretion

Investigations

- ✓ GH level-
 - Not much helpful due to its pulsatile secretion.
 - If undetectable- can exclude acromegaly
 - If detectable- non diagnostic
- ✓ IGF-1 –
 - Used as a screening test for acromegaly.
 - A single plasma level reflects mean GH secretion over the preceding 24 hrs
 - But ,in 25% cases IGF-1 remains normal with ↑GH secretion
- ✓ OGTT-
 - Δtic test.
 - Preparation & procedure-similar to OGTT for DM
 - Take blood samples for GH & glucose at 0, 30, 60, 90, 120, 150 mins
 - Interpretation- Normally GH secretion is inhibited by ↑glucose, so normal subjects will exhibit suppression of GH to undetectable values during the test
 - In acromegaly, there is a failure to suppress GH release
 - False + test- in puberty, pregnancy, hepatic & renal disease, anorexia nervosa & DM
- ✓ Lateral skull X-ray : Double floor appearance
- ✓ MRI scan of pituitary – look for pituitary adenoma
- ✓ Visual field defects
- ✓ Test pituitary functions
- ✓ ECG, Echo- look for complications

Management

↑mortality rate- from HF, CAD, HT related causes & colonic CA.

Thus RX is indicated in all-except in elderly or those with minimal abnormalities

Aim of therapy- achieve a mean GH level <5mU/L

- Surgical Mx-
 - Trans sphenoidal surgery- RX of choice
 - Cure rate- 80% in microadenoma
 - 40% in macroadenoma
 - After 3 months, measure GH,if remains ↑,adjuvant medical / radiotherapy may be needed.
 - Trans frontal surgery-rarely required except for massive macroadenoma
- Radiotherapy -

Normally used after pituitary surgery which fails to normalize GH levels rather than as primary therapy.

Slow biochemical response to radiotherapy- take 10 years or more, thus often combined with with a somatostatin analogue or a dopamine agonist

- Medical Mx-
 - Somatostatin analogue - octreotide & lanreotide

Rx of choice in resistant cases & as a short term Rx while on other modalities

SE-pain at injection site, abdominal cramps, loose stools, ↑ risk of gall Stones, impaired glucose tolerance
 - Dopamine agonists-

Can be given to shrink tumours prior to definitive therapy or to control symptoms and persisting GH secretion

They are probably most effective in mixed growth-hormone and prolactin - producing tumours

Given alone they reduce GH to 'safe' levels in only a minority of cases

But they are useful for mild residual disease or in combination with somatostatin analogues
 - GH antagonists-

Does not lower GH levels or reduce tumour size but, normalize IGF-1 levels in 90% of patients.

Main role is Rx of patients in whom GH and IGF levels cannot be ↓ed to safe levels with somatostatin analogues alone, surgery or radiotherapy.

Is there a tumour?

If there is, how big is it and what *local anatomical effects* is it exerting? Pituitary and hypothalamic space-occupying lesions, hormonally active or not, can cause symptoms by pressure on, or infiltration of:

- the visual pathways, with field defects and visual loss (most common)
- the cavernous sinus, with III, IV and VI cranial nerve lesions
- bony structures and the meninges surrounding the fossa, causing headache
- hypothalamic centres: altered appetite, obesity, thirst, somnolence/wakefulness or precocious puberty
- the ventricles, causing interruption of cerebrospinal fluid (CSF) flow leading to hydrocephalus
- the sphenoid sinus with invasion causing CSF rhinorrhoea.

Arthritis

Age & sex – The DDs change according to these

PC – Joint pain swelling & stiffness

HPC –

- Pain
 - Site
 - Severity
 - Type
 - Aggravating & relieving factors
 - Associated neurological factors (numbness suggestive of nerve pain)

Differential Diagnoses

- Osteoarthritis
- Rheumatoid arthritis
- SLE
- Spondyloarthropathies
- Reactive Arthritis
- Gout
- Pseudo gout
- Trauma

Rheumatoid arthritis

- Common at 30 – 50 years

Articular manifestations -

- Pain, morning stiffness of the joints or at rest (Lasting >1 hour for 6 weeks or more)
- **B/L, symmetrical involvement, polyarthritis, hand joints, feet & cervical spine**
- warm, tender swelling, limitation of movement of large joints
- Swelling & deformities of small joints of hand
- Due to deformities - activities affected

Extra articular manifestation-

- **Nodules , Carpal Tunnel Xn, Tarsal Tunnel Xn** – numbness over the distribution of affected nerves
- Skin rashes, ulcers
- Lung Fibrosis, Pleural effusion – pleuritic pain, DIB, SOB
- Nephrotic xn, amyloidosis – Oedema, frothy urine
- Pan-carditis, LVF - Chest pain, palpitations, SOB, fatigue, orthopnea, PND, ankle edema
- Episcleritis, scleromalacia perforans, Sicca xn - Dry eyes, dry mouth, painful red eyes
- Anaemic symptoms
- Constitutional symptoms - LOA, LOW, fatigue, malaise

Osteoarthritis

- Age over 55years females
- Most of the time asymmetrical involvement
- Pain & stiffness in movement – **DIP joints, knee, wrist, hip**
- Bony swelling, loss of function
- Wasting of muscles

Ankylosing spondylitis

- 18 – 30 years males
- Mostly in young males pain & **stiffness of lower part of the spine**
- Episodic severe pain of the one or both buttocks, low back **pain at rest**, improves with activities (sacro iliac joint inflammation)
- Stiffness worse in the morning & relieved by exercises
- Asymmetrical, peripheral large joints - hips
- Generalized fatigue & nausea
- Iridocyclitis & uveitis – redness of eyes, pain, vision loss, photophobia
- **Anterior chest pain** – costochondritis
- Onycholysis

Reactive arthropathy

- Mostly in males 20 – 40 yrs
- Acute asymmetrical joint involvement of lower limb
- Deformed big toe
- Recent **hx of diarrhea, dysentery**, urethritis in males & cervicitis in females, painless ulcers in glans penis, STI
- Red eyes, painless red plaques & pustules over hands & feet

Enteropathic arthritis

- Associated with **IBD**
- Asymmetrical arthritis – predominantly LL
- Symptoms during flare of IBD

Psoriatic arthritis

- **Skin rash comes first**
- Joint pain, stiffness, swelling – commonly DIPJs, asymmetrical involvement
- Hx of remission
- Skin rash & arthritis may come at the same time & disappear

GOUT

- In middle age males
- Agonizing pain, swelling, redness of **first MTP joint**
- Following too much food, alcohol, dehydration – shell fish, Beer

Pseudo gout

- In elderly females affects knee or wrist
- Similar to gout
- Very painful

Trauma

- Ask for Hx of trauma

After coming to a diagnosis from the history,

- If this is a chronic problem ask about - When was it diagnosed
- What are the initial symptoms
- What are the treatments
- How long was on drugs
- Complications of drugs
- Complications of disease

PMHx - OA -DM, Septic arthritis

Psoriasis, IBD

PSHx – Previous joint surgeries – OA

DHx - Steroids (OA), (diuretics, Aspirin- gout), OCP (delayed RA)

FHx – RA, OA, psoriasis, gout, IBD, ankylosing spondylitis

SHx – Occupation, involve in sports & dancing, where is the home

At home toilets, stair cases, help in home

Examination

General

- Red eyes – Ankylosing spondylitis
- RA – Pallor, red eyes, Vasculitic rash, livido reticularis (micro infarcts around nail), Rheumatoid nodules over bony prominances, pyoderma gangrenous, erythema nodosum, palmar erythema, diffuse thinning of the skin
- OA – Weight, Muscle wasting
- Psoriasis- skin rash, thimble pitting, onycholysis, nail dystrophy
- Reactive arthritis – Red eyes, Keratoderma blenorragica, circinate balanitis in skin

Joint examination

- Look – swelling, rashes , erythema, deformities, contractures, hyper extension, loss of normal range, pain
- Feel – tenderness, warmth, swelling, consistence, joint effusion (**OA**)
- Move – look passive range of movements, instability, pain, crepitus (**OA**)

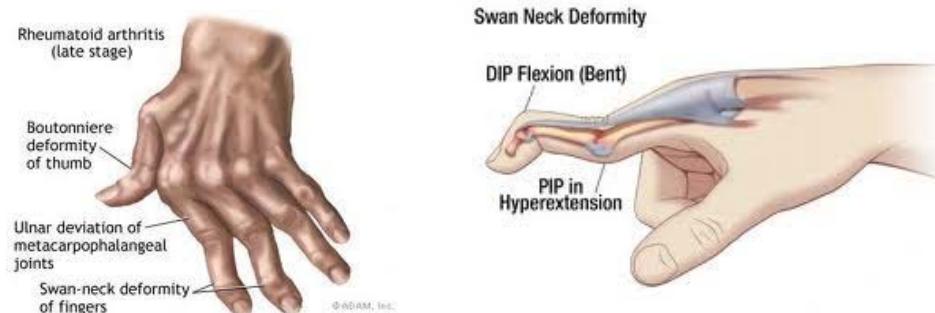
OA –Joint tenderness, Crepitus, limited ROM, joint effusion, bony swelling

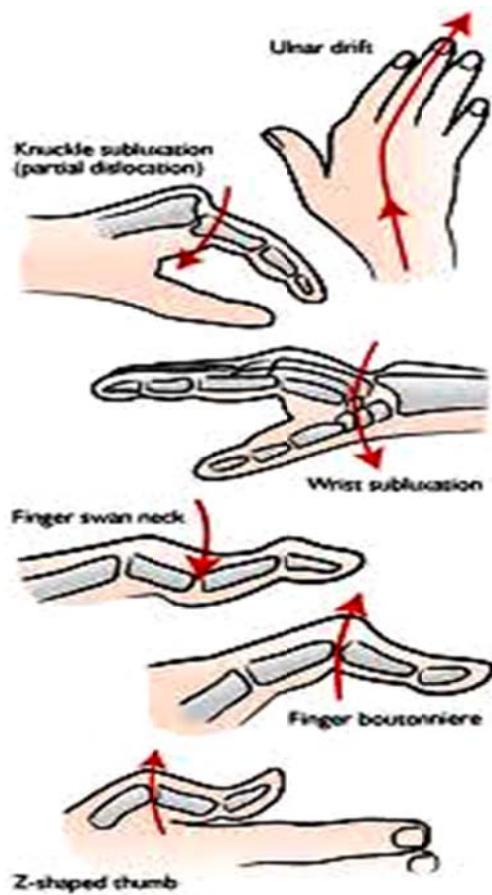
- DIPJ – Heberdons nodules [more often]
- PIPJ – Bourchards nodules [restrict gripping]
- Toes – bunions
- CMC Joints – bony swelling & fixed adduction of thumb cause Squared hand
- Knee – bow legged deformity / varus



RA – Sinovitis [swollen, tender, warm joints]

- CTS [examine sensation over median nerve distribution of palm, muscle wasting]
- PIP Joints – Boutonniere deformity, swan neck deformity, Z thumb
- MCP Joints – Ulnar deviation of the hand
- Shoulders – Painful arc syndrome, upper arm pain at night, later global stiffening
- Elbow – Painful fixed flexion deformity
- Feet – Tender swelling of MTP Joints, broad feet, hammer toe deformity, flat medial arch, and valgus position of ankle, Knee joint Cervical spine – lateral flexed & extended neck





AS – lateral paraspinal muscle wasting, retention of lumbar lordosis during flexion, Schoeber's test for spinal stiffness, fixed flexion deformity of the hip

Reactive arthritis – Knee effusion, sausage toe



Sausage 3rd toe

Respiratory system

↓ Chest expansion with AS

- Pleural effusions- ↓ expansion, stony dullness on percussion, ↓ breath sound, ↓ vocal resonance
- Fibrosing alveolitis - ↓ expansion, mediastinal shift towards lesion, dull on percussion, bronchial breathing, ↓ vocal resonance, coarse crepts

CVS

- PR, BP, shifted apex
- Pericarditis- muffled heart sounds, pericardial rub,
- Murmurs

Abdomen

- Distension, free fluid – nephrotic xn
- Hepatosplenomegaly – Felty's xn

Rheumatoid arthritis

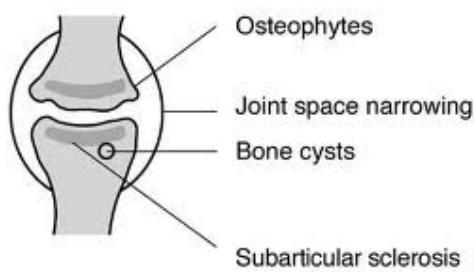
Management

OA

- ESR, CRP, RF, ANA normal
- X-ray changes in advance disease – loss of cartilage, subchondral sclerosis, subchondral cysts, osteophytes



X-ray findings in OA



Primary OA

- Joint space narrowing over the medial side
- Joint spike formation

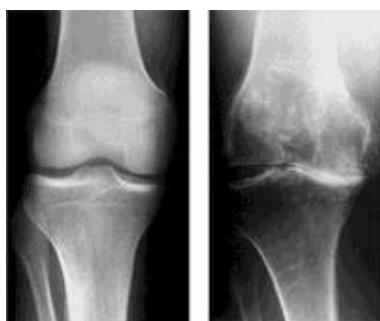
Secondary OA

- Narrowing of both medial & lateral sides
- Joint spike formation
- Osteophyte formation

- Clinical diagnosis
- Patient education – disease, treatment for reduce pain & stiffness, to improve function
- Lifestyle modification – weight control, rest in acute disease, moderate exercise like swimming, walking, local heat before ex on joint & ice packs after, use appliances like walkers, knee bracers, sitting while working, use commode, discourage excessive bending on knees
- Medications – Oral Paracetamol, [NSAIDs only during acute illness]
Corticosteroid intra articular injections for short term improvement
Codeine morphine in severe pain
- Surgery – If not responding to above
Fragment removal, repositioning bone, fusing bones, joint replacement, arthroscopy

RA

- Ix- high ESR, CRP
- FBC for anaemia, thrombocytosis, neutropenia
- RFT – assess nephrotic xn, drug effects
- LFT – ALP, drug effects
- Ferritin level
- Rheumatoid factor +ve or -ve (> 128 titre), ACPA 95% specific (anti citrullinated protein Ab), Anti CCP antibodies (anti citrullinated cyclic peptide) worse prognosis
- X ray – Tissue swelling, juxta articular osteopenia, loss of joint space, peri-articular erosions & subluxations



DIAGNOSTIC CRITERIA

i Box 10.7 Criteria for the diagnosis of rheumatoid arthritis (American College of Rheumatology, 1988 revision)

- Morning stiffness > 1 hour
 - Arthritis of three or more joints
 - Arthritis of hand joints and wrists
 - Symmetrical arthritis
 - Subcutaneous nodules
 - A positive serum rheumatoid factor
 - Typical radiological changes (erosions and/or periarticular osteopenia)
- For 6 weeks or more

Four or more criteria are necessary for diagnosis.

- No cure, symptomatic treatment, prevent further destruction
- Patient education, encourage regular exercise, physiotherapy, occupational therapy
- Pain relief by warm, heat, IR, Paraffin bath

Pharmacology-

- NSAIDs with PPIs or diclofinac sup, dihydrocodeine
- Low dose Prednisolone intra articular injections
- DMARD –
 - Methotrexate –Folic acid antagonist so start with
 - Folic acid, FBC/ LFT monthly.
 - If lung involvement stop & never start again (acute interstitial pneumonitis)
 - If cirrhosis & pancytopenia Stop for a while & restart.
 - Sulphasalazine – Hepatotoxic, skin rashes
 - Hydrochloroquine – Retinal damage may be irreversible refer to eye surgeon, alopecia, rash
 - Leflunomide – Retain in body for 2 years (need to eliminate from the body with cholestyramine, activated charcoal if wish to be pregnant & change to another drug), mouth ulcers, HT, leukopenia
 - Azathioprine – 2nd line drug, especially for extra articular manifestations, marrow suppression & pancytopenia, liver toxicity, contra indicated in breast feeding
 - Penicillamine – 2nd line, limited use due to A/E, proteinuria, thrombocytopenia, aplastic anemia, loss of taste, myasthenia like syndromes
 - Biological agents – Infliximab, etanercept, increase infections, HT, fatigue

AS

- ESR, CRP high
- X ray – syndesmophytes, bamboo spine, fusion of sacroiliac joint, blurring of upper & lower thoraco-lumbar junction
- HLA- B27 +ve
- No cure, pain relief, early diagnosis
- Physiotherapy & morning exercise – maintain spinal mobility, posture, chest expansion.
 - Swimming
- Medication – NSAIDs, opioids to reduce pain, improve sleep,
 - DMARDs – cyclosporin, MTX, SSZ
 - Corticosteroids
 - TNF alpha blockers if severe – etanercept, infliximab
- Surgery – Joint replacement, correct flexed spine

Psoriatic arthritis

- Xray – central erosions, pencil in cup appearance
- Medication –
 - NSAIDs, analgesia
 - Intra articular corticosteroids
 - Sulphasalazine, MTX, cyclosporins, etanercept

Reactive arthritis

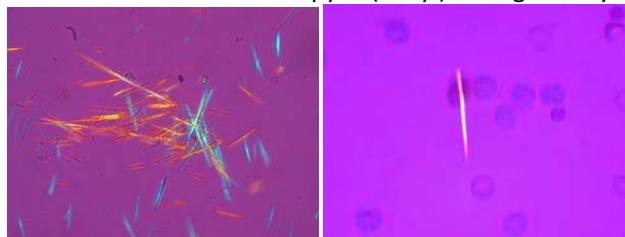
- Urethral, cervical, throat swabs for culture & ABST
- Urine & stool samples culture
- HLA B27 +ve
- Medication – analgesia, steroids, immunosuppressives, antibiotics if organisms present

Enteropathic arthritis

- Xray changes of arthritis
- Treat underlying cause
- NSAIDs
- Intra articular corticosteroids injections
- Sulphasalazine

Gout

- Joint fluid microscopy – (-vely) birefringent crystals under polarized light microscopy



- Serum urate raised
- Joint x ray – Juxta-articular osteopenia
- Medication –
 - NSAIDs [naproxen, diclofenac, indomethazine]
 - Colchicine [cause diarrhea]
 - Probenecid for increase renal excretion
 - Allopurinol [urate reducing agent]
- Reduce alcohol intake, low cholesterol & calorie intake

Pseudo gout

- Joint aspiration reduce pain
- NSAIDs, colchicines
- Due to calcium pyrophosphate deposition in hyaline & fibrocartilage causing acute synovitis resembling GOUT. More common in elderly women. Affects wrists & knee. Very painful attacks.

Discussion

- What is osteoarthritis?
 - Disease of synovial joint with cartilage destruction.
 - Most common arthritis. There is synovial inflammation.
 - Predisposing factors are obesity, hereditary, female gender, hypermobile joints, osteoporosis, trauma
 - Causes of 2ry osteoarthritis are injury, septic arthritis, DM, marfans xn, Alkaptonuria, Haemocromatosis
 - Nodal OA is common among women

- Rheumatoid arthritis
 - Chronic symmetrical polyarthritis
 - Common among women 30 – 50 yrs
 - Inflammation of synovium which destruc the cartilage, Rheumatoid factor +ve in the synovium
 - Articular & extra articular signs
 - Increase risk of MI & CVA
 - The anemia is due to – iron deficiency, chronic disease, folate deficiency, Felty's syndrome' AIHA
 - RF seen in normal population also
 - ACPA [anti citrullinated protein Abs] 95% specific
 - Anti CCP Abs shows worse prognosis
 - What are rheumatoid nodules?
Subcutaneous nodules over bony prominences. Has central areas of fibrinoid necrosis surrounded by macrophages & fibroblasts, lymphocytes, plasma cells. Associated with positive rheumatoid factor. Occur in internal organs
- Ankylosing spondylitis
 - Autoimmune chronic inflammatory arthritis
 - Sero –ve arthritis, express HLA B27 genotype
 - ANCA Abs are associated
 - Common in males of 18 – 30 years. More painful in males
 - Before 18 years large joints are also affected
 - Enthesisitis is there
 - Severe eye pain, blurred vision, photophobia is emergency
 - Failure of exercise & pain relief cause kyphosis, paraspinal muscle wasting
- Reactive arthritis
 - Triggering organisms are *Salmonella*, *Shigella*, *Yersinia*, *Chlamidia trachomatis*
 - Bacterial Ags or bacterial DNA may present in inflamed synovium
- Psoriatic arthritis
 - Equal in both sexes
 - Hydroxychloroquine is CI in psoriasis as it worsen the skin rash

Summary

- PC
- Describe the pc
- Come to appropriate DDs according to age & sex
- Start, duration, progression of illness
- Drugs & A/E
- Complications of the disease
- Ix
- Treatment

Fever with Jaundice

Fever with Jaundice

Acute

Chronic

Hx- short duration

- Fever
- Jaundice
- RHC discomfort
- LOA, N, V

Hx- Fx of CLD – Ankle oedema, ascites

- Haematemesis, malena
 - Other bleeding manifestations
- Fx of HE** – Altered sleep pattern

Aetiology- 1. Viral hepatitis

2. Acoholic hepatitis
3. Leptospirosis
4. Drug induce hepatitis
5. Auto immune hepatitis

- Metabolic** - Hypoglycaemia
- osteomalacia- Bone pain,
- Recurrent fractures
- Proximal myopathy

DD for fever with jaundice

- Viral hepatitis(A,B)
- Leptospirosis
- Malaria
- Drug induced hepatitis
- Alcoholic hepatitis
- Ascending cholangitis

Endocrine – Gynaecomastia

- Impotence
- 2ry loss of body hair

Aetiology- 1. Viral

2. Alcohol
3. Drugs
4. AI diseases
5. NASH
6. Other – Haemachromatosis

Wilson's disease

DD

Pre hepatic

- Malaria (fever, jaundice, splenomegaly, mostly occur in malaria. But as it can occur In hepatitis 1st we have to exclude it)
- Mycoplasma pneumonia

Hepatic

- Viral ; Hepatitis A, B, C, D, E
- Other - CMV, EBV, Dengue
- Bacterial; Leptospirosis
 - Liver abscess- Pyogenic/ amoebic
- Autoimmune hepatitis
- Drug induce hepatitis
- Alcoholic hepatitis

Post hepatic - Cholangitis

History – Diagnostic problem

1. Elaborate more on presenting symptoms
 - Fever – onset, Duration,
 - Associated chills and rigors
 - Type(continuous, remittent, intermittent , every 3rd day fever→ Malaria)
 - response to PCM
 - Jaundice – onset (prior or after the fever), progression, ass. Intermittent pruritus
 - Other ass. Fx- Arthralgia, Myalgia, Headache, N, V, D
2. Ask specific questions to confirm and exclude DD

- **Hepatitis A&E;**

Prodromal symptoms: Fever, Nausea, Vomiting, Malaise, RHC pain
Yellowish discolouration of eyes & body (after about a week from prodromal symptoms)
Contact Hx of jaundice
Dark urine, pale stools
Painful lymphadenopathy
Abdominal discomfort & fullness with transient body rash (vasculitic rash)
Food hygiene, water

- **Hepatitis B&C ; Low grade fever & malaise(same as Hepatitis A)**

- Hx of blood Transfusion
- Needle prick injury
- Drug abuser
- Occupation- health care worker/lab worker
- Sexual promiscuous behaviour

Urticular or maculopapular rash
 Poly arthritis
 GN-haematuria, reduced UOP, periorbital oedema, HT

} Suggest Serum Sickness like immunological Syndrome

- **EBV(IMN)**; sore throat, painful lymphadenopathy, macula popular rash (rash worse with amoxicillin)
- **CMV**
- **Dengue hepatitis** ; Headache, arthralgia myalgia, flushing
Petechiae, bleeding manifestations
RHC pain
- **Leptospirosis** ; high grade fever, arthralgia, myalgia, headache,
Oliguria, haemoglobinuria, red eye
Muddy contact
Travel Hx
Myocarditis Features- syncope, dizziness, chest pain, palpitation
- **Alcoholic hepatitis**; jaundice, high fever, abd pain
alcohol consumption since which age
Amount, type
Dependent or not- Cut down
Anger
Guilt
Eye open
- } 2 out of 4
- **Drug induce hepatitis**; herbal & ayurvedic medication
Anti malarials
Anti TB-Isoniazide, Pyrazinamide, Rifampicin
Anti convulsants- Carbamezapine
Quinalones-Cipro
Anti psychotics
- **Auto immune hepatitis** ; young, female
Fever low grade. may have acne, hirsutism, bruising, striae, ascites
May have migratory poly arthritis, pleurisy, GN)
Hx of other auto immune diseases

Post hepatic – Fx of Cholangitis

Biliary colic
 Intermittent high fever with chills & rigors
 PHx of gall stones, biliary colic(RHC pain)
 OCP, high fat diet, DM, hypercholesterolaemia

Ask for complications

- **Fulminant hepatic failure**
 - Drowsiness, confusion , convulsions
 - **Cholestatic hepatitis**
 - Generalized pruritus, dark urine, pale stools
 - Chronic hepatitis
 - Cirrhosis
 - HCC
 - Carrier state
- } All HV
- } Hep B & C

Examination

O/E

- Looks ill
- Fever
- Jaundice- deep/moderate/mild
- Pale
- Conjunctival injection-lepto
- Parotid swelling, duputryens contractures - alcohol
- Petechiae, purpura, echimosis
- Dengue flushed face, convalescent rash
- Any other rash – EBV
- Tender LN- HAV, EBV
- Choreaathetoid movements, tremors
- Fx of CLD – loss of body hair, spider naevi, gynaecomastia, palmer erythema, leg swelling, leukonychia clubbing, flapping tremors, easy bruising, gum bleeding, pigmentation
- Neck stiffness- lepto meningitis, cola colour urine
- Tattoos ,IV drug abuse (needle marks)

Abdomen

- Distended
- Distended veins (direction of draining)
- Tenderness
- Palpable GB, Murphy's sign
- Hepatomegaly
- Splenomegaly(10% with acute hepatitis)
- Free fluid – shifting dullness
- Genitalia – testicular atrophy

CVS- myocarditis (lepto)

RS – Atypical pneumonia

CNS – HE- confused, ex. Tendon reflexes

Investigations

Acute hepatitis

U ward test-Bile pigment- Fouchette's test
Bile salts - Hess test

UFR - Urobilinogen & Bile

S.bilirubin -↑ (mainly direct)

SGPT, SGOT -↑ SGPT>>>SGOT (liver enzymes raised >1000 in viral hepatitis)

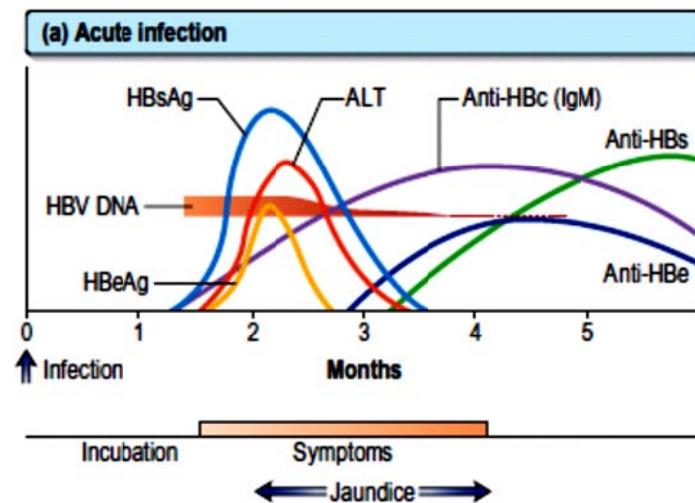
ALP
S.protein
PT

-
NL in uncomplicated hepatitis

(ALP- biliary system NL, S.protein- Albumin very long half life, PT- only reduce in liver cell necrosis, in inflammation cells can still produce clotting factors)

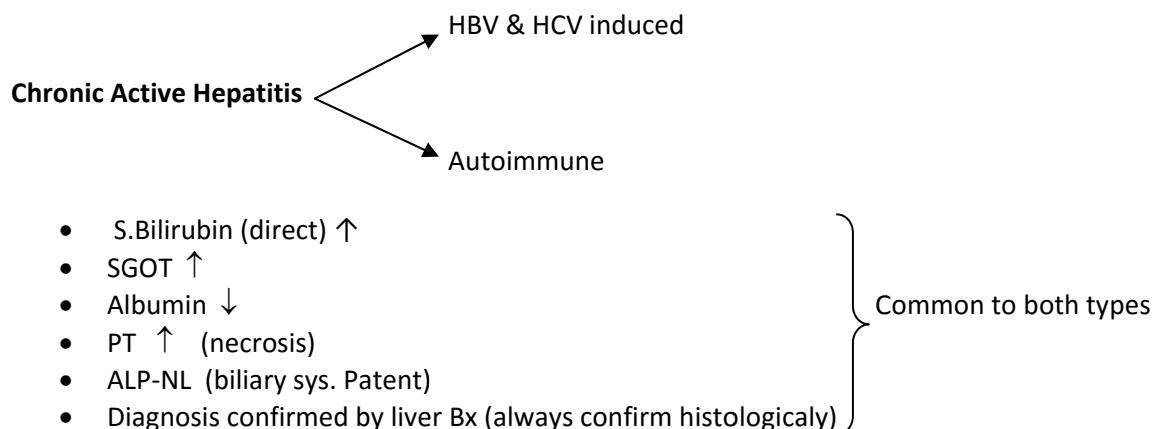
Virological diagnosis-

- HAV in stools, IgM Ab for HAV
- HBs Ag, (from 6 wks – 3 months after an acute infection & then disappears)
- HBe Ag (rises early & usually declines rapidly)
- HBV DNA (continual viral replication)
- Anti HBc IgM (1st anti body to appear & high titres suggest acute and continuing viral replication; only serological indicator of recent HBV infection. b/w HBs Ag disappeared & Anti HBs is not detectable)



Treatment

- Non specific
- Resolve spontaneously
- Rest (duration of icterus)- bed rest not quicken the recovery
- Diet – NL (if choleatasis+ - stop fatty food), plenty of sweets
- Avoid alcohol & hepatotoxic drugs
- Acute HCV, HBV in the immunocompromised- anti viral drugs given
- Prevention
- General- reduce risk behavior
- Vaccines – A,B
- Passive immunisation

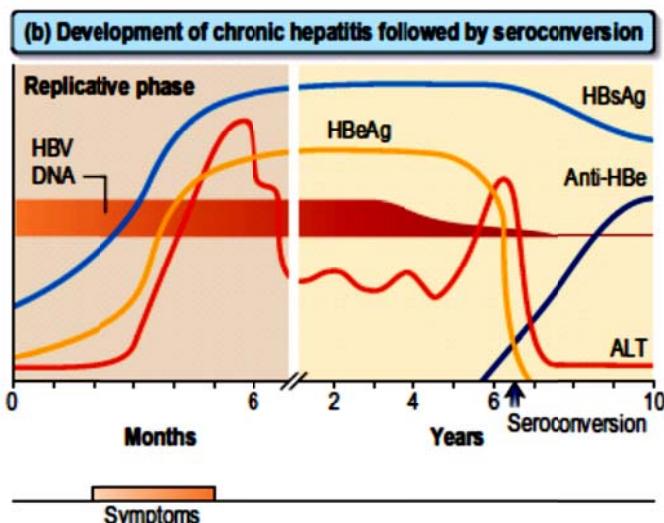


Virological diagnosis

HBs Ag (persists and indicates a chronic infection/ carrier state)

HBe Ag (persists - ↑ severity & infectivity & development of CLD)

When anti HBe develops (seroconversion) the Ag disappears & ↑ ALT



In Autoimmune hepatitis (more than Hep B & C)

- s. IgG ↑
- anti smooth muscle Ab +
- anti-LK microsomal Ab +
- ANA +

Rx for viral Hep- IF alpha, other anti viral drugs

- HBV – IF alpha/ Lamivudine, Adefovir
- HVC – IF alpha + Ribavirin (combination essential)

Rx for autoimmune hep-

Steroids (prednisilone) for at least 2 yrs after LFT's normalize +/- other immune suppressive drugs.

Alcoholic Hep

Ix – Gamma GT ↑
SGOT >>> SGPT
S. Albumin ↓
BP – Megaloblastic anaemia
If extra hepatic biliary obstruction is suspected - ALP ↑

USS Abdomen – to find liver enlargement, parenchymal changes

Dilatation of Extra and intra hepatic biliary tree +GB

FF

FBC & Blood picture – low Hb

Leptospirosis-

IV penicillin 4mu 7-10 days

Pyogenic liver abscess

- These abscesses are uncommon, but may be single or multiple.
- The most common was a portal pyaemia from intrabdominal sepsis (e.g. appendicitis or perforations),
- In the elderly, biliary sepsis is a common cause. Other causes include trauma, bacteraemia and direct extension from, for example, a perinephric abscess.
- The organism found most commonly is E. coli. Streptococcus milleri and anaerobic organisms such as Bacteroides .Other organisms include Enterococcus faecalis, Proteus vulgaris and Staphylococcus aureus.
- Often the infection is mixed.

Clinical features

- Malaise lasting several days or even months.
- Fever, rigors, anorexia, vomiting, weight loss and abdominal pain.
- In these patients a Gram-negative septicaemia with shock can occur.

Examination

- There may be little to find.
- Alternatively, the patient may be toxic, febrile and jaundiced. In such patients, the liver is tender and enlarged and there may be signs of a pleural effusion or a pleural rub in the right lower chest.

Investigations

- Patients who are not acutely ill are often investigated as a 'pyrexia of unknown origin' (PUO) and most investigations will be normal.
 - Often the only clue to the diagnosis is a raised serum alkaline phosphatase.
- Serum bilirubin is raised in 25% of cases.
- **Normochromic normocytic anaemia** may occur, usually accompanied by a polymorphonuclear leucocytosis.
- **Serum alkaline phosphatase and ESR** are often raised.
- **Blood cultures** are positive in only 30% of cases.

Imaging

- Ultrasound -is useful for detecting abscesses.
- chest X-ray -elevation of the right hemidiaphragm with a pleural effusion in the severe case.

Management

- Aspiration of the abscess should be attempted under ultrasound control.
- Drainage of the abscess.
- Antibiotics should initially cover Grampositive, Gram-negative and anaerobic organisms until the causative organism is identified.

Prognosis

- A unilocular abscess in the right lobe has the better prognosis.
- Scattered multiple abscesses have a very high mortality, with only one in five patients surviving.

Amoebic liver abscess

- *E. histolytica* trophozoites invade the colonic epithelium, probably with the aid of their own cytotoxins and proteolytic enzymes.
- The parasites continue to multiply and finally frank ulceration of the mucosa occurs.
- If penetration continues, trophozoites may enter the portal vein, via which they reach the liver and cause intrahepatic abscesses.

Clinical features

- Gradual onset.
- Amoebic
- Liver abscesses often develop in the absence of a recent episode of colitis.
- Tender hepatomegaly, a high swinging fever and profound malaise are characteristic .
- Although early in the course of the disease both symptoms and signs may be minimal
- Right sided pleural effusion
- Jaundice is unusual

Ix

Serological test – Haemagglutination

Amoebic component fixation test

ELISA

Diagnostic aspiration – anchovy sauce

Rx

Metronidazole 800mg tds for 10 days

Aspiration – in pts failing to respond

Multiple or large abscess

Abscess in left lobe

Impending rupture

Advise on discharge of a diagnosed hepatitis B patient

- Discuss the infection with any sexual partners and use a latex condom with every sexual encounter.
- Do not share razors, toothbrushes, or anything that has blood on it.
- Cover open sores and cuts with a bandage.
- Do not donate blood, body organs, other tissues, or sperm.
- Immediate family and household members should be tested for hepatitis B. Anyone who is at risk of hepatitis B infection should be vaccinated.
- Do not share any injection drug equipment (needles, syringes).
- Clean blood spills with a mixture of 1 part household bleach to 9 parts water.
- Hepatitis B cannot be spread by:
 - Hugging or kissing
 - Sharing eating utensils or cups
 - Sneezing or coughing
 - Breastfeeding
- **Liver cancer screening** — Regular screening for liver cancer is also recommended, particularly for older individuals, those with cirrhosis, and patients with a family history of liver cancer. In general, this includes an ultrasound examination of the liver every six months.
- **Diet** — No specific diet has been shown to improve the outcome in people with hepatitis B. The best advice is to eat a normal healthy and balanced diet.
- **Alcohol** — Alcohol should be avoided since it can worsen liver damage. All types of alcoholic beverages can be harmful to the liver. People with hepatitis B can develop liver complications even with small amounts of alcohol.
- **Exercise** — Exercise is good for overall health and is encouraged, but it has no effect on the hepatitis B virus.
- **Prescription and nonprescription drugs** — Many medications are broken down by the liver. Thus, it is always best to check with a healthcare provider or pharmacist before starting a new medication. As a general rule, unless the liver is already scarred, most drugs are safe for people with hepatitis B.
- **Herbal medications — No**

Procedure following accidental prick injury of unknown pt

- Squeeze the blood out at pricked site
 - ↓
- Wash the area thoroughly with soap and water.
 - ↓
- infection control unit
 - ↓
- documentation
 - ↓
- STD clinic
 - ↓
- take blood samples of both exposed person & pt ,rapid test done for HBs Ag

Post-exposure prophylaxis for hepatitis B

Prophylactic treatment to prevent infection after exposure to HBV should be considered in the following situations:

- 1) Perinatal exposure of an infant born to a HBsAg-positive mother.
- 2) Sexual exposure to a HBsAg-positive person.
- 3) Household exposure.
- 4) Inadvertent percutaneous or permucosal exposure to HBsAg positive blood.

1) Perinatal exposure

- For an infant with perinatal exposure to a HbsAg-positive mother,
- a regimen combining **One dose of HBIG at birth and HBV vaccine at 0, 1, 2, and 12 months.**
- Hepatitis B vaccine series started soon after birth (85-95% effective in preventing development of the HBV carrier state)
- Simultaneous administration of HBIG and vaccine should be at two different sites.

2) Sexual partners of person with acute hepatitis B virus infection

- Sexual partners of HbsAg positive person are at increased risk of acquiring HBV infection.
- All susceptible persons whose sexual partners have acute hepatitis B infection should receive
- **A single dose of HBIG and hepatitis B vaccination should be initiated simultaneously.**

3) Household contacts of persons with acute hepatitis B virus infection

- Since infants have close contact with mother or baby care-givers and they have a higher risk of becoming HBV carriers after acute HBV infection,
- **Prophylaxis of an infant less than 12 months of age with HBIG and hepatitis B vaccine is indicated if the mother or primary care-giver has acute HBV infection.**
- **Prophylaxis for other household contacts of persons** with acute HBV infection is recommended
If the index patient becomes an HBV carrier, all household contacts should receive hepatitis B vaccine

4.) Inadvert percutaneous or permucosal exposure to HBs Ag (+)ve blood

Exposed person status	HBs Ag (+)	HBs Ag (-)	HBs Ag status unknown
Unvaccinated	HBIG x 1 Start HBV vaccine (preferably within 24hrs)	Initiate HBV vaccination	Initiate HBV vaccination
Vaccinated responder (with Anti HBs ≥10mIU/ml)	No Rx	No immunization	No immunisation
Vaccinated nonresponder	HBIG x 2 one month apart or HBIG x 1 dose & initiate revaccination	No immunization	If high risk source Rx as if source was HBs Ag (+)
Vaccinated unknown response	Test exposed person for Anti HBs If inadequate HBIG x 1 + HBV vaccination	No immunization	Test exposed person For AntiHBs If no adequate immunization initiate revaccination

Alcoholic hepatitis

- In addition to fatty change there is infiltration by polymorphonuclear leucocytes and hepatocyte necrosis mainly in zone 3.
- Dense cytoplasmic inclusions called Mallory bodies are sometimes seen in hepatocytes and giant mitochondria are also a feature.
- Mallory bodies are suggestive of, but not specific for, alcoholic damage as they can be found in other liver disease, such as Wilson's disease and PBC. If alcohol consumption continues, alcoholic hepatitis may progress to cirrhosis.
- The clinical features vary in degree:
- The patient may be well, with few symptoms, the hepatitis only being apparent on the liver biopsy in addition to fatty change.

Mild to moderate

- ✓ Symptoms of ill-health, occasionally with mild jaundice, may occur.
- ✓ Signs include all the features of chronic liver disease.
- ✓ Liver biochemistry is deranged and the diagnosis is made on liver histology.

Severe case

- ✓ Usually superimposed on alcoholic cirrhosis, the patient is ill, with jaundice and ascites.
- ✓ Abdominal pain is frequently present
- ✓ High fever associated with the liver necrosis.
- ✓ On examination there is deep jaundice, hepatomegaly, sometimes splenomegaly, and ascites with ankle oedema
- ✓ The signs of chronic liver disease are also present.

Investigations show a leucocytosis with markedly deranged liver biochemistry with elevated:

- ✓ serum bilirubin
- ✓ serum AST and ALT
- ✓ serum alkaline phosphatase
- ✓ prothrombin time (PT).
- ✓ A low serum albumin may also be found.

Treatment

- In severe cases the patient requires admission to hospital.
- Nutrition must be maintained with enteral feeding if necessary and vitamin supplementation given.
- Steroid therapy does improve outcome in more severe cases as judged by a discriminant function (DF).

Headache

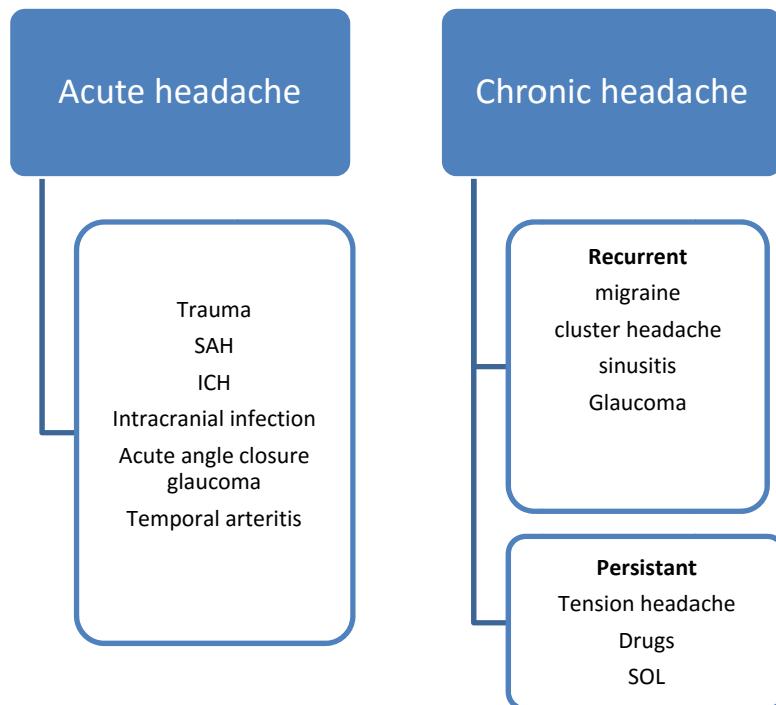
Name

Age

Presenting complaint:

Generalized or unilateral headache –Duration

DD



HPC

- Onset
- Progression
- Site
- Character
- Precipitating factors
- Associated symptoms

Acute onset headache

Subarachnoid haemorrhage

- Abrupt explosive type, severe headache
- Worst headache ever
- In occipital area with neck pain
- Fluctuating level of consciousness → coma
- Meningeal irritation → Neck stiffness
- Photophobia
- Unsteadiness and poor memory
- Family hx of sudden death in young age with Intra-cranial bleed, PCKD
- Past Hx of HT, Coarctation of aorta

ICH

- Severe headache
- Body weakness
- Sensory impairment
- Bladder bowel dysfunction
- Dysarthria
- Hx of HT, hyperlipidaemia, IHD

Meningitis

- High grade fever
- Photophobia
- Vomiting
- Irritability

Acute angle closure glaucoma

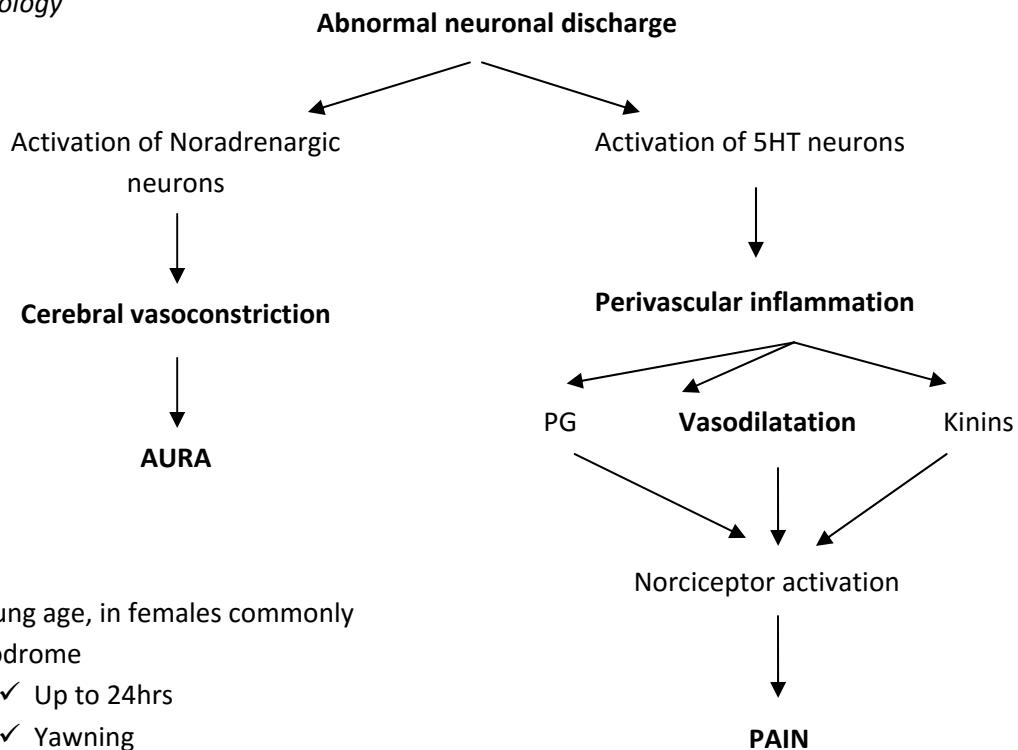
- Middle aged or old people
- Headache-recurrent, orbital or frontal
- Visual impairment (blurring, haloes, discolouration of eyes, clouding of cornea)
- Worse in the dark and with emotions
- Vomiting

Head injury

Chronic or recurrent headache

Migraine

Pathophysiology



- Young age, in females commonly
- Prodrome
 - ✓ Up to 24hrs
 - ✓ Yawning
 - ✓ Hunger
 - ✓ Craving for food
 - ✓ Lethargy and euphoria
- Aura
 - ✓ In classical migraine
 - ✓ 30 min
 - ✓ Visual : zig zag lines, blurring, flashing lights
 - ✓ Paraesthesia (tingling, numbness)
 - ✓ Weakness (hemiplegic migraine)
- Headache
 - ✓ 24- 48 hrs
 - ✓ Severe, unilateral/bilateral, throbbing, pulsatile
 - ✓ Side of the headache can change
 - ✓ Nausea, vomiting, diarrhoea, faintishness, dizziness
 - ✓ Photophobia
 - ✓ Phonophobia
 - ✓ Irritability
- Post-drome
 - ✓ Deep sleep
- Precipitating factors
 - ✓ Hunger ,fatigue, stress, alcohol, menstruation, noise, food (chocolate, cheese), OCP

Cluster headache

- Middle aged men
 - Episodic headache
 - ✓ Almost unilateral, periorbital pain
 - ✓ Very severe
 - ✓ During a particular time at night (alarm clock headache)
 - ✓ Short duration 1/2hr to 3 hr
 - ✓ 1-2 attacks per day
 - ✓ Clusters in 2-8 weeks
 - ✓ Wake up from sleep, agitation, restless, one cheek and nostril become congested
 - Ipsilateral Horner's syndrome
 - Ptosis
 - Lacrimation, conjunctival injection
- } Trigeminal autonomic cephalgia

Tension type headache

- Chronic daily headache
 - ✓ Bilateral occipito-frontal & vertex
 - ✓ Dull, diffuse, band like sensation
 - ✓ Daily headache
 - ✓ Increase In the evening
- Precipitating factors
 - ✓ Worry, noise
 - ✓ Underlying psychological issues

SOL

- Slowly progressive headache
- Features of raised ICP
 - ✓ Headache with laughing , sneezing, coughing ,straining
 - ✓ Headache aggravated by posture
 - ✓ Headache when getting up from sleeping
 - ✓ Altered consciousness
 - ✓ Focal deficits
 - ✓ Seizures

Temporal arteritis

- Old age
- Localized to temporal area
- Touching the temporal area cause pain
- Jaw claudication
- Tongue claudication (pathognomonic of temporal arteritis)

PMHx - CVA, TIA, HT, Convulsions, IHD, Head injury

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Drug Hx - GTN, nifedipine

Family Hx - Brain tumors, CVA, HT

Social Hx

Occupation, marital status, social economic problems
Alcohol abuse

Examination

- Febrile
- GCS
- Conjunctival injections (in glaucoma and cluster headache)
- Petechial rash (meningococcal meningitis)
- Tenderness over the superficial temporal artery with absent pulsation & thickening of the artery
- Neck stiffness , Kernig's sign

CNS

- Higher function
- Motor system (UMN lesion in ICH, SAH, SOL)
- Sensory impairment
- Cranial nerves
 - ✓ II : unilateral visual loss (temporal arteritis)
Visual field defects (SOL)
Fundoscopy
 - Papilloedema In SOL
 - Subhyaloid haemorrhages in SAH

- ✓ III :hazy cornea }
Dilated pupil }
Ptosis
Meosis

Glaucoma

- III CN palsy in SAH – With posterior communicating artery aneurysm
 - Enlarging PCA aneurysm causes painful IIICN palsy

- Transient hemiplegia in migraine

CVS

- PR
- BP (HT)

Abdomen

- Renal masses (polycystic kidney disease)

Management

Ix

- **FBC** : Neutrophil leucocytosis in meningitis , cerebral abscess, systemic infections
- **ESR** : Increased in temporal arteritis - ESR>50 (CRP and ALP are also increased in Temp. Arteritis)

Specific investigations are needed

- Suggestion of SOL
- CNS infection
- Sudden severe headache
- Late onset headache
- Blood culture (meningitis)
- LP (Meningitis)
- CT/MRI (SOL, ICH)
- Temporal artery biopsy (Due to the skip lesions, serial biopsies or long biopsies are taken)

SAH Ix

1. Non contrast CT → If –ve do LP
2. CSF
 - Uniformly blood stained CSF
 - Xanthochromia in spectrophotometry
3. Angiography
 - Conventional contrast angio/DSA
 - CT or MRI angiogram

Treatment

SAH

General care

- ABC
- Strict bed rest (prevent re-bleeding)
- Monitor level of consciousness, RR, PR, BP
- IV access and keep patient well hydrated with IV fluids (2-3 L) to prevent vasospasm
- Maintain sodium, glucose, feeding
- Treat headache with PCM, codeine or tramadol (Pain → ↑BP → Re-bleeding)
- Catheterize to avoid straining (prevent re-bleeding)
- Treat seizures

Specific care

- Nimodipine - vasodilator effect (Blood in SAH → Vascular spasms → Ischaemia → Infarction)
 - ✓ Prevent delayed cerebral ischaemia
 - ✓ Can cause hypoglycaemia
- Neurological evaluation
- Surgery (Aneurysmal clipping/Endovascular treatment – coiling)

Supportive measures (From K&C)

- Control hypertension
- Dexamethasone often given to reduce cerebral oedema

Temporal Arteritis (in old age > 50 yrs) → can give rise to blindness

- ✓ Associated with polymyalgia rheumatica
- ✓ High dose steroids immediately (on suspicion) – 60 to 100mg daily)
- ✓ Refer to neurologist, ophthalmologist

Migraine

- Acute attack treatment

- ✓ Supportive care: analgesics (PCM, NSAIDS, Codeine)
Antiemetics : (Domperidone, metoclopramide)
- ✓ Specific treatment
5HT agonists (Triptans)
Ergotamine

Ergotamine	Sumatriptan	Pizotifen
<ul style="list-style-type: none">• 5HT partial agonist• α adrenoreceptor agonist• cause vasoconstriction• For severe attack• given early in the headache• may precipitate angina	<ul style="list-style-type: none">• 5HT agonist• vasoconstrictor• Oral/SC• Highly effective• Contraindicated in IHD• SE : Malaise, headache, dizziness	<ul style="list-style-type: none">• Antihistamine drug with serotonin antagonist action• Has antimuscarinic SE• Dry mouth, urinary retention, constipation

- Prophylactic treatment

- 5HT Antagonists (Pizotifen, methysergide)
- Beta blockers (propanalol, metaprolol)
- CCB (verapamil, flunarazine)
- Antidepressants (Amitriptylline)
- Antiepileptics (Nodium valproate, gabapentin, topiramate)

❖ Prophylaxis is started if more than two attacks per month or interferes with life

Cluster headache

- Acute attack : High flow O₂

Ergotamine
Sumatriptan

- Prophylaxis: Verapamil

Topiramate
Lithium
Steroids

Tension headache

- ✓ Firm re-assurance - Imaging
- ✓ Avoid long-term analgesics (Consider physical Rx – Massage, Ice packs, relaxation)
- ✓ Give anti-depressants
- ✓ Avoid evident causes – Bright lights

Idiopathic Thrombocytopenic Purpura

History

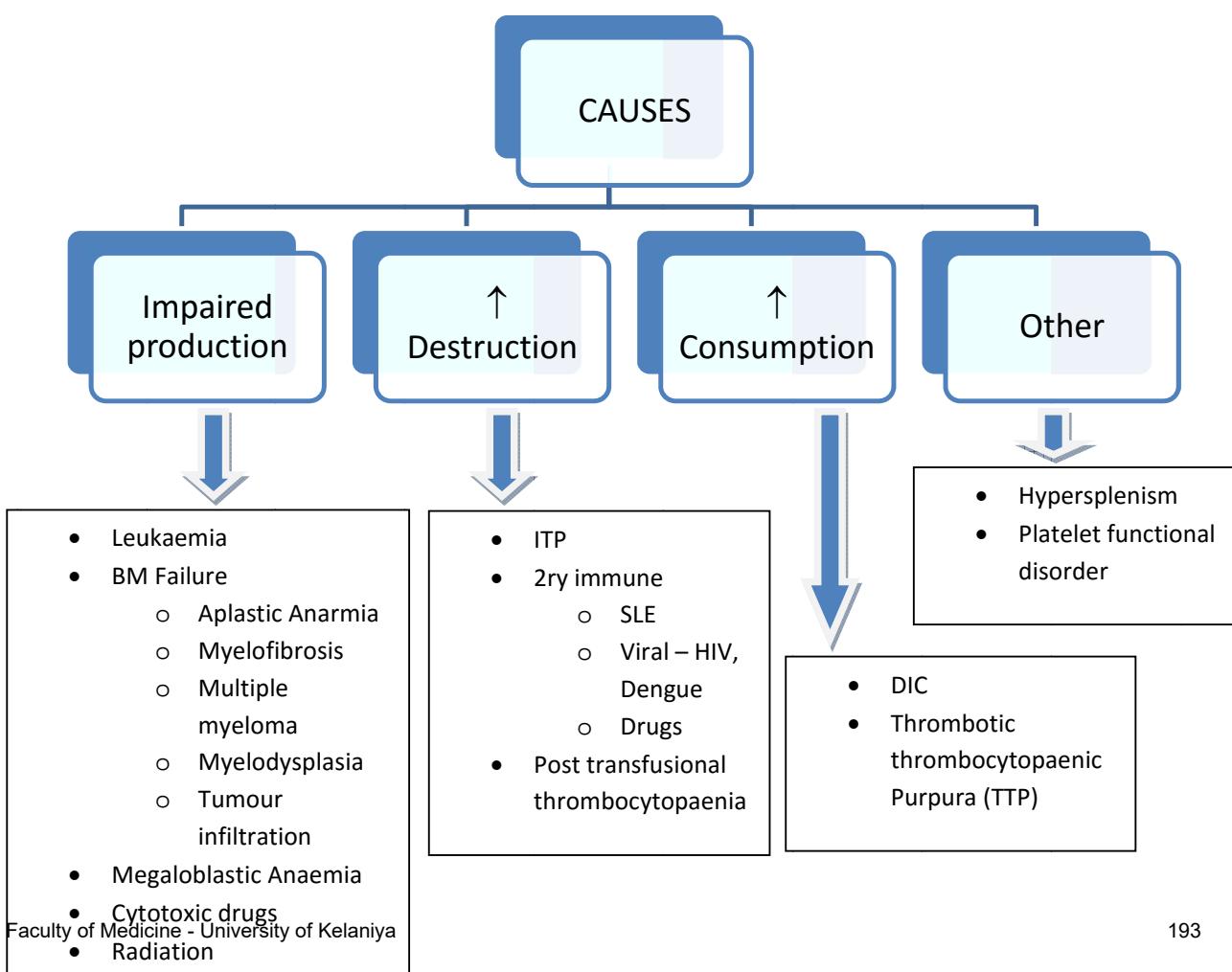
General Information

- Name
- Age
- Sex (Common among females)
- Civil Status
- Occupation

Presenting Complaint – Easy Bruising/Purpura/Epistaxis/Menorrhagia (Major haemorrhage is rare)

History of presenting complaint

- Enumerate the presenting complaint
 - Onset of symptoms
 - Duration
 - Sites involved/Areas of bruising or purpura
 - Progression
 - Other associated features
- Exclude other differential diagnoses



- Exclude other differential diagnoses
 - Dengue/viral fever – Fever, Arthralgia, Myalgia, Retro-orbital pain, Petechiae
 - Leukaemia
 - Fever, LOA, LOW
 - Pancytopenia – Recurrent infections, Features of anaemia, Bleeding tendency
 - Radiation exposure
 - Cytotoxic chemical exposure
 - Aplastic Anaemia
 - Anaemia, Infection, Bleeding
 - Radiation & cytotoxic chemicals
 - Myelofibrosis
 - Fatigue, LOW, Night sweats
 - Pancytopenia features
 - Multiple myeloma
 - Renal involvement – Polyuria, polydipsia
 - Anaemic features
 - Chronic backache
 - Headache
 - Myelodysplasia – Pancytopenia
 - Other malignancy – Paired organs (Breast, Prostate)
 - Megaloblastic anaemia
 - Anaemia features
 - Vitiligo
 - Peripheral neuropathy
 - SLE
 - Young female
 - Low grade fever/malaise
 - Butterfly rash
 - Alopecia
 - Arthritis(Non deforming)
 - Renal/CNS involvement
 - Serositis
 - Haematological – Anaemia, bleeding, infection
 - Drug induced immune thrombocytopenia – Eg : heparin (read hofbrand pg. 281)
 - Recent history of blood transfusion(2-12 days after the blood transfusion) – post transfusional purpura
 - TTP
 - Rare
 - Purpura, fever, haemolytic anaemia
 - Associated renal failure
 - Aetiology : Pregnancy, OCP, SLE, Infections
 - DIC
 - Bleeding, Thrombosis
 - Sepsis, trauma, malignancy(AML), Snake bite, Transfusional reactions
 - Hypersplenism
 - Causes – RA, Lymphoma, portal hypertension(ask features of ch. Liver disease – Jaundice, ascites, Haematemesis)
 - Acquired platelet dysfunction
 - Myeloproliferative disorders
 - Renal & liver disease
 - Paraproteinaemias
 - Drug induced – Aspirin or other anti-platelet drugs

- Establish the diagnosis of ITP
 - More common in children

In Children	In an adults
<ul style="list-style-type: none">• Common in 2-6 years• Present with acute mucocutaneous bleeding• Hx of viral illness – Varicella zoster or measles• Life threatening haemorrhage is rare	<ul style="list-style-type: none">• Less acute than in children• More in females• Associated with SLE, Thyroid diseases, AI haemolytic anaemia, Pts with CLL, Solid tumours and HIV

- Clinical features – Easy bruising, Purpura, Epistaxis, & menorrhagia is common
- Upto now management done in hospital and clinic setting. Ask about the past similar episodes

PMHx – Similar episodes, Liver disease, renal disease

In children – Varicella zoster infection/Measles/recent Varicella-zoster immunisation

In adults – SLE, Thyroid diseases, AI haemolytic anaemia

Hx of haemophilia (episodic joint swelling) – Can present with recent trauma

PSHx – Hx of blood transfusion (HIV, Post transfusional purpura – 2 to 12 days after blood transfusion)

Allergies –

Drugs – Mentioned above

FHx – Mentioned above

Haemophilia, bleeding disorders

SHx – Occupation (contact trauma, Radiation, Gold exposure-Aplastic anaemia)

Monthly income

Dengue endemic area

Sexual promiscuous behavior (HIV)

Nearest hospital

Examination

In ITP, physical examination is normal except for evidence of bleeding. Splenomegaly is rare.

General Examination

- Fever
 - High grade – Dengue
 - Low grade leukaemia
- Pallor – Due to blood loss/pancytopaenia (Leukaemia/Myelofibrosis/Aplastic anaemia)/Megaloblastic anaemia)
- Glossitis (Megaloblastic anaemia – B₁₂ Deficiency)
- Signs of bleeding – Gum bleeding, Petichiae, purpura, epistaxis, bruising
- Butterfly rash, alopecia, oral ulcers – SLE
- Generalised lymphadenopathy – Leukaemia, HIV
- ↑ Capillary re-fill time – Dengue fever
- Bone tenderness – Multiple myeloma, Leukeamia

- Signs of chronic liver disease – Jaundice, Ascites, Leukonychia
- Signs of portal hypertension – Spidernaevi, Palmer erythema
- Features of recurrent infections – Candida (HIV, Pancytopenia)

Abdominal Examination

- Inspection
 - Distension/dilated superficial veins (Liver disease/PHT)
- Palpation
 - Hepatomegaly – Leukaemia
 - Splenomegaly
 - Leukaemia
 - Myelofibrosis (Massive splenomegaly)
 - ITP (rare)
 - Balatable kidneys (Polycystic kidney → Chronic renal failure)
- Percussion
 - Ascites – Dengue
- Auscultation

Respiratory system examination

- Evidence of pleural effusions – Dengue/SLE/RA
- Crepts/Consolidation – Recurrent chest infections (exclude pneumonia)
- Mycoplasma pneumonia – Risk of bleeding tendency

CVS

- Pulse
 - Tachycardia – Dengue
- BP - ↓ & wide pulse pressure in dengue shock syndrome
- Flow murmurs – Anaemia

CNS

- Peripheral neuropathy – Megaloblastic anaemia
- Fundal examination – Retinal haemorrhages
- CNS examination to exclude focal neurological signs (risk of intracranial hemorrhages)

Summary

Problem List

Investigations

- ITP
 - Is a diagnosis of exclusion
 - Only FBC abnormality is thrombocytopenia
 - Normal or ↑ numbers of megakaryocytes found in bone marrow
 - Detection of platelet antibodies is not essential to confirm the diagnosis
- Basic investigations
 - FBC
 - Thrombocytopenia – ITP
 - Pancytopenia – Bone marrow failure (Leukemia, Myelofibrosis, aplastic anaemia, myelodysplasia)
 - Blood picture
 - Leukoerythroblastic BP – Multiple myeloma, Myelofibrosis, Leukemia, 2ndry bone metastasis
 - Megaloblasts – Megaloblastic anaemia
 - Serum creatinine – Renal function
 - ALT/AST – Liver disease
 - PT/INR – Chronic liver disease, DIC, TTP
 - APTT – vWF, Vit k deficiency, Warfarin, Haemophilia
- Other specific investigations to exclude other diagnoses
 - Dengue IgM Antibodies – It's a clinical diagnosis
 - HIV – Antigen (Rapid test)
 - ↑Bleeding time & clotting time – Platelet disorders
 - ↑Fibrin degradation product (FDPs) (Rises after thrombotic event. These are produced by the action of plasmin on deposited fibrin. The most notable subtype of fibrin degradation products is D-dimer.) – To exclude DIC
 - ANA/DsDNA – SLE
 - Bone marrow biopsy
 - Indications for bone marrow biopsy
 - Age >60 Yrs
 - Other abnormal cell lines
 - Lack of response to treatment (before splenectomy)
 - Red flags : Fever, weight loss, bone pain
 - Anti glycoprotein GP11b/11a, GP1a antibodies – Sensitive test to identify specific anti glycoprotein antibodies on the platelet surface
 - Coombs test to exclude autoimmune haemolytic anaemia

Management

Indications for treatment

- Avoid treatment in patients with mild asymptomatic disease
- Do not treat if
 - Platelet > 50,000 and asymptomatic
- Consider treatment if
 - Platelet > 50,000 & mucous membrane bleeding
 - Platelet < 20,000
- Hospitalize if
 - Severe bleeding, regardless of platelet count
 - Platelet < 20,000 & mucous membrane bleeding

Management of chronic ITP / Adult ITP - Less responsive to steroids than childhood ITP

Treatment options

- Corticosteroids
- IVIG
- IV anti-D (component of IVIG)
- Splenectomy
- H. pylori eradication
- Immunosuppressant (2nd line treatment)

} 1st line

1. Steroids (1st line)
 - Prednisolone 1-2mg/kg/day
 - 50-75% response rate
 - In about 3 weeks tail-off if responded
 - Patients who are failed to respond to steroids → Need high doses or splenectomy
 - High dose dexamethasone – 10mg/day/4day/month
 - High dose methyl prednisolone 1g/day for 1-3 days
2. IVIG
 - 1g/kg/2d days, 400mg/day/4 days 1-3 days
 - Responses are only transient (3-4 weeks) with little evidence of lasting effect
 - Useful where a rapid rise in platelet count is needed, especially before a surgery
 - If bone marrow biopsy planned, Steroid and IVIG should be given after bone marrow biopsy. (Nelson)
3. IV anti D (Anti-D binds with D antigen on red cells. Then this complex go to spleen and occupy it. Eventually it reduces sequestration of platelets)
 - 75 microgram/Kg/day
 - Given for Rh +ve patients
4. H. pylori eradication
 - Some data suggest that H.Pylori eradication may lead to remission in mild ITP

Treatment of relapse

- Repeat the initial Rx with longer steroid & taper
- Give IVIG/Anti Rh-D
- Splenectomy in patients with (65% response rate)
 - Continuous significant bleeding (menorrhagia, Epistaxis), despite of 4-6 weeks of treatment
 - If high doses of steroids required to control the disease (>10 mg prednisolone/day for > 6 months)
- Avoid further treatment Rx if platelet > 30,000 & no bleeding.

SPLENECTOMY

- Response is unpredictable
- Younger patients responds better
- Pre-splenectomy Rx
 - IVIG or steroids
 - Platelet transfusion
 - Vaccines
 - H. influenza B
 - Pneumococcus
 - Meningococcus

Refractory ITP

- Defined as platelet <50,000 for 6 months despite glucocorticoids & splenectomy
- No consensus on when or how to treat

Treatment options

- Platelet >10,000-30,000 + No significant bleeding → Withhold treatment
- 1st line therapy – retried, combination therapy
- Accessory splenectomy (removal of residual spleen in the patient who has undergone splenectomy)
- Others : Immunosuppressant/chemotherapy agents (Azathioprin, Danazol, Cyclophosphamide, Vicristine, Anti CD-20 Ab (Rituximab))

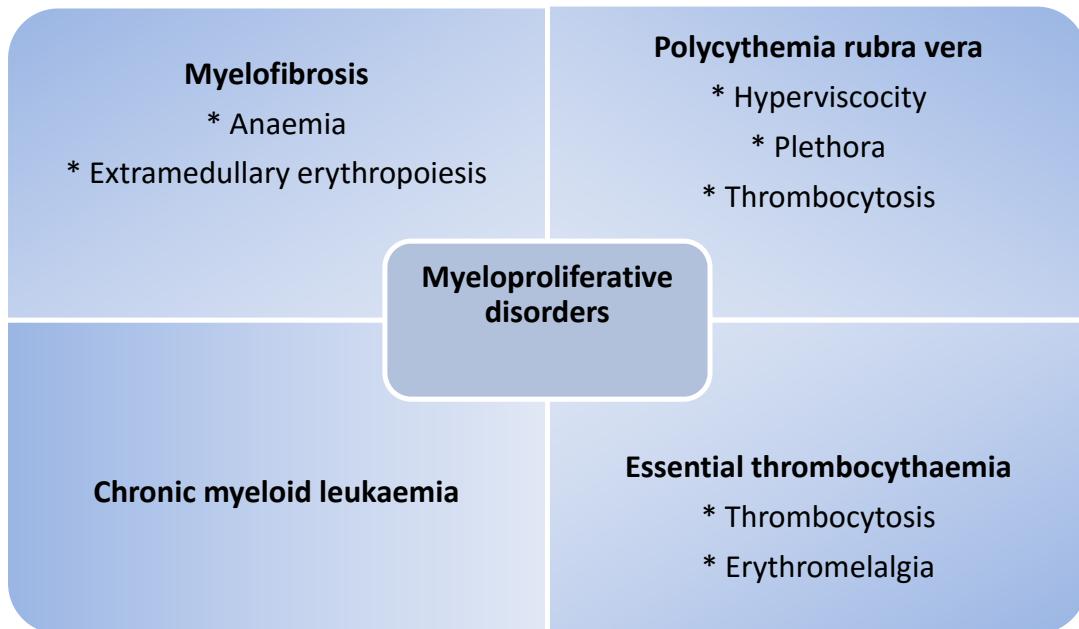
Acute idiopathic thrombocytopenic purpura/Childhood ITP

- Common in children
- Follows vaccines(Eg : Chicken pox)/viral infections (in 75% infectious mononucleosis)
- Most cases spontaneous remission
- Chronic in 5-10% (lasts > 6 months)
- Diagnosis – by excluding others

Management of Acute Idiopathic Thrombocytopenic Purpura

- Remains controversial
- Platelets > 30,000 + No bleeding → No treatment
- Widely accepted to treat for platelet <20,000/L
- Treatment options
 - Steroids (2mg/kg/bw)
 - IVIG
- **Excellent response to steroids**
 - ⊕ Evans Syndrome – Haemolytic anemia + ITP
 - ⊕ Platelet transfusion is not indicated unless life threatening bleed.
 - 1 pack should ↑ platelet count by 12,000.mm³
 - 1 pack/10Kg BW
 - Should transfuse within 5 days of prodution
 - ⊕ Platelet transfusion is contraindicated in TTP & HUS.

Myeloproliferative disorders

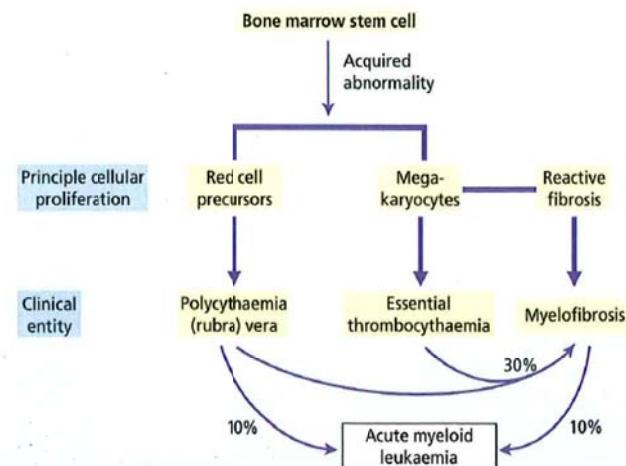


History

- Age – over 60 yrs in PRV
- Sex – common in males (PRV, MF)

PC

- Clinical features of
 - 1) Hypercatabolism
 - 2) Hyperuricaemia
 - 3) Splenomegaly
 - Common to all PRV, MF, ET
- Hypercatabolic features
 - Fatigue
 - LOW
 - Night sweats
 - Pruritus
- Hyperuricaemic features
 - Gout : Arthritis ,nephrolithiasis
 - Aquagenic pruritus : After hot bath
- Features of splenomegaly
 - Left hypochondrial pain
 - Severe pain related to respiration (perisplenitis due to splenic infarcts)
 - Abdominal fullness



Polycythaemia

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Clinical features

- Due to the disease
 - ✓ Hyperviscosity symptoms
 - Headache, dizziness
 - Tiredness, depression, vertigo, tinnitus
 - Visual disturbance
 - Anginal chest pain
 - Hypertension
 - Intermittent claudication, praesthesia, gangrene
 - and a tendency to bleed (due to abnormal platelet function)
 - Peptic ulcer disease
- history of stroke, MI, PVD
- Identify the cause

Exclude secondary polycythaemia

- ✓ Due to appropriate increase in erythropoietin
 - Ask whether the disease was there since birth
 - High altitude living
 - Heavy smoking
 - Congenital heart disease with right to left shunt
 - COPD /chronic lung disease
 - o Recurrent cough
 - o Infective exacerbation
 - o Cor pulmonale
- ✓ Due to inappropriate increase in erythropoietin
 - Bronchial CA
 - o Chronic cough
 - o Haemoptysis
 - o LOA, LOW
 - Hepatocellular CA
 - o Anorexia, LOW
 - o RHC pain
 - o Hep B,C infection
 - Renal cell CA
 - o Painless hematuria
 - o LOA ,Low
 - o Loin pain
 - PCKD
 - o FHx of renal disease, stroke
 - Pheochromocytoma
 - o Episodic sweating, headache, palpitations
 - Cerebellar haemangioblastoma
 - o Cerebellar signs
 - Massive uterine fibroma
 - Drug Hx (erythropoietin given for CRF), steroids, Androgens

Table 8.16 Causes of polycythaemia

Primary	
Polycythaemia vera	
Mutations in erythropoietin receptor	
High-oxygen-affinity haemoglobins	
Secondary	
<i>Due to an appropriate increase in erythropoietin:</i>	<i>Due to an inappropriate increase in erythropoietin:</i>
High altitude	Renal disease–renal cell carcinoma, Wilms' tumour
Lung disease	Hepatocellular carcinoma
Cardiovascular disease (right-to-left shunt)	Adrenal tumours
Heavy smoking	Cerebellar haemangioblastoma
Increased affinity of haemoglobin, e.g. familial polycythaemia	Massive uterine fibroma
Relative:	
Stress or spurious polycythaemia	
Dehydration	
Burns	

- Assess the risk
 - IHD
 - Stroke
 - PVD
- If an already diagnosed patient
 - Onset
 - Symptoms at the onset of the disease
 - Effectiveness of the treatment

Myelofibrosis

- Splenomegaly (due to extramedullary erythropoiesis)
- Hypercatabolism
- Hyperuricaemia
- Anaemia
 - Breathlessness, palpitation, lethargy, weakness
- Thrombocytosis
 - Bleeding, bruising (Functionally abnormal platelets)
- Bone pain
- Attacks of GOUT
- DD are other malignancies infiltrating marrow.

Essential thrombocythaemia

- Haemorrhage (Functionally abnormal platelets)
 - Mucosal bleeding
 - GIT
- Erythromyelgia
 - Burning sensation of hands, that is relieved with aspirin
 - Classical feature suggestive of thrombocytosis
- Exclude before diagnosing ET
 - PRV
 - MF
 - MDS
 - REACTIVE THROMBOCYTOSIS due to:
 - o Chronic infection
 - o Chronic inflammation - CTD
 - o Neoplasm – GIT, GUT, respiratory, post splenectomy
- **All myeloproliferative disorders can be transformed into Acute myeloblastic leukaemia**

Signs of organ infiltration

- Gum hypertrophy
- Skin deposits
- Bone pain (marrow infiltration)
- Lymphadenopathy
- Evidence of pancytopenia
 - Recurrent infection and fever
 - Anaemia
 - Bleeding

Social Hx

- Current quality of life
- Family support
- Availability to medical center in case of emergency (MI , stroke,)

Examination

General

- Face – plethoric , dusky cyanosis in mucous membranes
- Conjunctival suffusion
- Pallor (MF , AML)
- Gout nodules over the big toe
- Venous or arterial ulcers
- Features of CTD (ET)
- Features of COPD , bronchial CA
- Lymphadenopathy (in AML, lymphoma- DD for MF)

Abdomen

- Spleenomegaly
 - MF : massive
 - PRV : moderate
 - ET : moderate later become not palpable
 - AML : mild to moderate
- Hepatomegaly
 - Focal lesions in HCC
- Renal masses
- DRE : hard, irregular prostate (DD for MF)

CVS

- CCF : anaemia in MF, co-pulmonale in COPD)
- PVD : ulcers, gangrene

RS

- COPD
- Bronchial CA

CNS

- Previous or current stroke
- Cerebellar signs

Investigations

- **FBC**
 - Hb raised
 - PCV (most reliable)
 - RBC count
 - Raised or normal WBC
 - Raised or normal platelet

In myelofibrosis

- Anaemia
 - o Due to impaired erythropoiesis
 - o Haemorrhage
 - o Hypersplenism
- WBC count
 - o May be over $100 \times 10^9/L$
 - o And the differential WBC count may be very similar to that seen in chronic myeloid leukaemia (CML)
 - o Later leucopenia may develop
- platelet count
 - o Very high initially
 - o Low in later stages

In AML

- Anemia
- WBC : usually raised
- PLT : low

Blood picture

- MF : Leucoerythroblastic BP with poikilocytes and tear drop cell
- ET : Lot of platelets
- AML : Myeloblasts

Bone marrow aspiration

- PRV : Hypercellularity with trilineage growth (panmyelosis) with prominent erythroid, granulocytic and megakaryocytic proliferation
- ET : Excess, abnormal megakaryocytes
- MF : Unsuccessful aspiration
 - Trephine biopsy
 - Marked fibrosis with hypocellular marrow
 - Elevated clusters of megakaryocytes
 - Abnormal collagen deposition
 - Normoblasts (nucleated RBC)
 - Band forms (N'philis without division)
 - Myelocytes
 - AML:
 - Increased cellularity
 - Reduced erythropoiesis and megakaryocytes
 - Blast cells > 30% in bone marrow

Serum LDH (Reflect the increased but largely ineffective turnover of haemopoietic cells)

- Normal in PRV
- High in MF

High NAP score (Neutrophil alkaline phosphatase score)

- In PRV
- Usually raised MF(can be normal)

USS abdomen

- Massive spleen
- Heptosplenomegaly

CXR

- Hilar LN
- Mediastinal widening

JAK 2 mutation

- PRV
- In about 50% of patients this mutation is present



Box 8.2 Modified from proposed revised WHO criteria for polycythaemia vera (PV)

Major criteria

- Haemoglobin > 18.5 g/dL in men, 16.5 g/dL in women or other evidence of increased red cell volume
- Presence of JAK2 tyrosine kinase V617F or other functionally similar mutation such as JAK2 exon 12 mutation

Minor criteria

- Bone marrow biopsy, showing hypercellularity for age with trilineage growth (panmyelosis) with prominent erythroid, granulocytic and megakaryocytic proliferation
- Serum erythropoietin level below the reference range for normal
- Endogenous erythroid colony (EEC) formation in vitro*

Diagnosis requires the presence of both major criteria and one minor criterion or the presence of the first major criterion together with two minor criteria

*EEC. This is not routinely available but colony formation in the absence of exogenous erythropoietin in vitro is 100% specific and

Management

PRV

- Aim is to maintain blood counts thus preventing the complications particularly thrombosis and haemorrhage.
- Treatment is aimed at keeping the PCV below 0.45 L/L and the platelet count below $400 \times 10^9/L$.
- ✓ There are three types of specific treatment:
 - **Venesection.**
 - Successfully relieve many of the symptoms of PV.
 - Venesection is often used as the sole treatment and other therapy is reserved to control the thrombocytosis.
 - **Chemotherapy.**
 - Continuous or intermittent treatment.
 - Hydroxycarbamide (hydroxyurea)
 - Used frequently
 - Easy to control thrombocytosis and general safe
 - Alkylating agents (busulfan)
 - Increased risk of acute leukaemia.
 - Convenient for elderly people
 - **Low dose aspirin**
 - 100 mg daily with the above
 - Used for patients with recurrent thrombotic episodes
 - **Allopurinol**
 - To restrict uric acid production
 - **H₂ receptor antagonists**
 - Cimetidine for pruritus
 - **Stop smoking**

Treatment of ET

- Cytoreductive therapy with Hydroxyuria, anagrelide or busulfan
- Control the platelet count to less than $400 \times 10^9/L$.
- α -Interferon is also effective; it is administered by subcutaneously.

Treatment of MF

- Palliative care for anaemia and splenomegaly
- Supportive measures
 - Blood, platelet transfusion
 - Analgesia
 - Folic acid
 - Allopurinol
 - Hydroxycarbamide (hydroxyurea) and busulfan are used to reduce metabolic activity and high WBC count and platelet levels.
 - Splenic irradiation
 - Splenectomy

- Spleen becomes very large and painful
- Transfusion requirements are high
- May also result in relief of severe thrombocytopenia

Myelodysplastic syndrome

- Pre malignant condition
- Usually in old age
- Quantitative and qualitative abnormalities in all 3 cell lines
- Characterized by
 - Ineffective erythropoiesis
 - Recurrent infections
 - Bleeding
 - Anaemia
- Examination
 - Pallor
 - Infections
 - Bruising
 - Splenomegaly
- Investigations
 - FBC
 - Anaemia, neutropenia, plt low
 - Bone marrow
 - Bone marrow usually shows increased cellularity despite the pancytopenia. Dyserythropoiesis is present.
 - Granulocyte precursors and megakaryocytes also have abnormal morphology.
 - Ring sideroblasts are present in all types.
 - Multi nucleated normoblasts present.
- Management

< 5% blasts in bone marrow are managed conservatively

 - Anaemia
 - Transfusion
 - Chelation therapy
 - Erythropoietin
 - Thrombocytopenia
 - plt transfusion
 - Neutropenia
 - Granulocyte colony stimulating factor
 - Antimyphocyte globulin(ALG)?????

>5% blast cells

 - ‘Gentle’ chemotherapy (low-dose or single-agent, e.g. azacytidine) may be useful in patients with high WBC counts.
- Prognosis
 - Depends on blasts in BM (> 5 % blasts – poor prognosis)
 - Number of cytopenias at presentation

Pneumonia

Presenting complaint

- ✓ Fever and cough
- ✓ fever and haemoptysis
- ✓ Fever and chest pain

Fever and cough

Differential Diagnosis

- ✓ Pneumonia
- ✓ Atypical pneumonia
- ✓ Tuberculosis
- ✓ Pulmonary embolism
- ✓ Bronchial Ca

History of presenting complaint

Fever duration-Acute /Chronic

- ✓ Acute- Pneumonia, Pulmonary embolism
- ✓ Chronic- TB, Bronchial Ca

Severity of fever

- ✓ High grade fever, may have sweating, rigors-Bacterial pneumonia
- ✓ If low grade fever-TB, Atypical pneumonia (Mycoplasma), Pulmonary Embolism, Bronchial ca

Type of fever-

- ✓ Intermittent fever-TB
- ✓ Continuous fever-Lobar pneumonia
- ✓ Answering to PCM

Symptoms prior to fever-

- ✓ Preceding URTI- Sneezing, Sore throat, Runny nose (Following viral infection)-*Streptococcus pneumoniae, Staphylococcus aureus*
- ✓ Viral infection predispose to bacterial pneumonia by damaging the respiratory epithelium
- ✓ Prominent prodromal features -malaise, Body weakness, Arthralgia, Myalgia- Atypical pneumonia

Cough-

- ✓ Acute-Pneumonia (Productive cough), Pulmonary embolism
- ✓ Chronic (more than 3 weeks)-TB, Bronchial carcinoma

Sputum-

- ✓ Frequency, quantity, appearance of expectorated sputum
- ✓ Blood stained sputum-bronchial Ca, Pneumonia (Rusty sputum in *Streptococcus pneumoniae*, *Klebsiella pneumoniae*-Blood stained sputum), TB, Pulmonary embolism
- ✓ Purulent sputum-Pneumonia, TB

Chest pain-

- ✓ Pleuritic chest pain-pulmonary embolism, Pneumonia
- ✓ Unrelenting pain-more suggestive of bony pain due to metastasis from lung Ca
- ✓ Need to exclude cardiac causes-Chest pain on exertion, Orthopnoea, Paroxysmal Nocturnal Dyspnoea, Palpitations, Oedema

SOB

- ✓ Acute SOB-Pulmonary embolism, Pneumonia, exclude other cardiac respiratory, renal causes

Other symptoms of respiratory system-

- ✓ Associated features- Wheezing, noisy breathing, hoarseness(Laryngitis)

Pneumonia (*Strep. pneumoniae*, *haemophilus influenzae*, *klebsiella*, *Staph aureus*)

- ✓ Fever-Acute onset fever
- ✓ Cough-acute onset, productive
- ✓ Sputum-purulent/Blood stained cause haemoptysis
- ✓ Chest pain(Pleurisy)-Pleuritic type chest pain
- ✓ + or - breathlessness-acute onset

Aetiology

- ✓ Recent hospitalization(Pneumonia by gram -ve)
- ✓ Past chronic lung disease-COPD, chronic bronchitis, Bronchiectasis exacerbated by *H.influenzae*
- ✓ COPD-hx chronic cough, cigarette smoking
- ✓ Bronchiectasis-Purulent foul smelling copious amount of sputum with halitosis

Hx of aspiration-

- ✓ GORD-Regurgitation, acid reflux
- ✓ Period of loss of consciousness in past-Epilepsy
- ✓ Oesophageal obstruction-Dysphagia, past hx Oesophageal Ca, Strictures-any acid ingestions
- ✓ Myasthenia gravis-easy fatigability.
- ✓ Alcohol excess
- ✓ Past hx of abdominal surgery
- ✓ *Klebsiella pneumonia* - Usually occur in elderly people with hx of heart or lung disease, DM, Alcohol excess, Malignancy
- ✓ Sputum purulent, gelatinous or blood stained

Staphylococcus aureus Pneumonia

- ✓ Very ill patient
- ✓ Usually get after proceeding viral infection of influenza illness. CXR-Patchy consolidations, break down to form abscesses. May appear as cysts on x ray. Pneumothorax, Empyema, effusions common.

Tuberculosis

- ✓ Fever-Low grade nocturnal fever long standing
- ✓ Cough-chronic cough>3 weeks
- ✓ Sputum:-Blood stained sputum
- ✓ Loss of appetite, Night sweats, Loss of weight

Aetiology

- ✓ PHx or contact hx of TB

Atypical pneumonia

Aetiology

No response to usual antibiotics (Previous treatment has not answered)

Legionella

- ✓ Previously fit individuals staying in hotels, institutions or hospitals where the shower facilities or cooling system (A/C) have been contaminated with the organism.
- ✓ Sporadic cases where the source of the infection is unknown: most cases involve middle aged and elderly men who are smokers, but it is also seen in children
- ✓ Outbreaks occurring in immunocompromised patients eg:- Corticosteroid therapy
- ✓ Malaise, myalgia, headache, fever with rigors, GIT symptoms :- vomiting, diarrhoea, abdominal pain, haematuria

Complication

- haematuria, Oliguria, reduced urine output(ARF)

Mycoplasma pneumoniae

- ✓ Age-Teens, twenties
- ✓ Address- Boarding institutions
- ✓ Scanty chest signs

Extra pulmonary features

- ✓ Myocarditis, Pericarditis-Fatigue, dyspnoea, chest pain, palpitation
- ✓ Rashes, Erythema multiform
- ✓ Haemolytic anaemia and Thrombocytopaenia→ Lethargy, faintishness
- ✓ Myalgia, Arthralgia
- ✓ Meningo-encephalitis→confusion, headache, weakness of body
- ✓ Other neurological signs
- ✓ Gastrointestinal symptoms Eg:-Vomiting, Diarrhoea

Chlamydia Psittaci

- ✓ Get from infected birds
- ✓ Symptoms:-Malaise, High fever, Muscular pain, Liver and spleen occasionally enlarged.
- ✓ Scanty rose spots may seen on abdomen

Viral

- ✓ Uncommon in adults
- ✓ Viral infection predispose to bacterial infections

Pulmonary embolism

- ✓ Acute onset SOB
- ✓ Low grade fever
- ✓ Chest pain
- ✓ Haemoptysis

Aetiology

- ✓ PHx of DVT/Long term immobility

Bronchial ca

- ✓ Fever-Low grade fever
- ✓ Sputum-Haemoptysis
- ✓ Cough-Chronic cough
- ✓ Anorexia, malaise, weight loss

Aetiology

- ✓ PHx of recurrent pneumonia- Unresolving pneumonia
- ✓ Cigarette smoking

Complications

- ✓ Due to metastases-Jaundice, bone pain, headache
- ✓ Hoarseness of voice
- ✓ Features of anaemia:-Lethargy, faintishness, syncope

Systemic enquiry

GIT-

- ✓ Jaundice (Legionella, Mycoplasma)
- ✓ Epigastric + RHC pain- Atypical(hepatitis) sub phrenic abscess, Amoebic liver abscess, Diaphragmatic pleurisy
- ✓ Associate with dark urine and stools- Mycoplasma (haemolytic anaemia)
- ✓ Diarrhoea-Legionella

Genitourinary- Reduce Urine output-Sepsis- Pre renal ARF/ATN, ARF by legionella, dehydration, Haematuria

CVS-

- ✓ Pericarditis (Commonly with left side pneumonia)- Precordial pain worse on lying down and relieved by sitting forward, Arrhythmias(SVT), Myocarditis-Mycoplasma
- ✓ Postural hypotension-sepsis, cardiogenic shock

Musculo-skeletal system- Polyarthritis-Mycoplasma, Septic arthritis-Sepsis

Nervous system-

- ✓ Non specific headache, photophobia, fits-Meningoencephalitis (Mycoplasma)
- ✓ Confusion, reduced concentration, drowsy-atypical, alcohol withdrawal
- ✓ Focal signs-Slurred speech, weakness (septic emboli--cerebral abscess)

Skin-

- ✓ Non specific rash-Mycoplasma, bleeding in to skin(DIC)

Elderly-Change in mental status

PMHx

HPT, DM, Hypercholesterolemia

Social hx

- ✓ Cigarette smoking- *Streptococcus pneumoniae*, also predispose to bronchogenic Ca
- ✓ Alcohol excess- aspiration pneumonia
- ✓ IV treatment abuse- *Staphylococcus aureus*
- ✓ Bird handlers- Psittacosis, avian influenza
- ✓ Homosexuals, travel hx, sexual hx- HIV (*Pneumocystis carinii*)
- ✓ Animal handlers- *Coxiella burnetii*

Examination

General examination

- ✓ Dyspnoea, Febrile, Ill looking
- ✓ Sputum pot--Purulent(TB/Pneumonia)
- ✓ Pale (Mycoplasma, TB, Bronchial ca)
- ✓ Icteric(Atypical pneumonia)
- ✓ Skin rash
- ✓ Maculopapular erythema multiform→Mycoplasma
- ✓ Echymosis, purpura, bruises, bleeding from puncture site
- ✓ Clubbing-bronchial ca
- ✓ B/L pedal oedema--

Respiratory system

- ✓ Reduced movements on affected side-Pneumonia, Bronchial ca, TB, PE
- ✓ Trachea in mid line
- ✓ Dull on percussion-stony dull if associate with Pleural effusion
- ✓ Increased vocal fremitus (Reduced if Pleural effusion)
- ✓ Reduced air entry in Pleural effusion
- ✓ Coarse crepitations- Pneumonia, bronchial ca, TB

CVS

- ✓ BP- reduce in septic shock, myocarditis
- ✓ Increase JVP, Gallop rhythm->In heart failure
- ✓ Murmur-Infective endocarditis
- ✓ Pericardial rub

Abdominal examination

- ✓ Tender hepatomegaly-Legionella Hepatitis, Liver abscess
- ✓ Massive spleen+Hepatomegaly→Haematological malignancy, Myelofibrosis

CNS

- GCS-Confusion due to atypical pneumonia, sepsis, respiratory failure, severe pneumonia,
- Meningitis
- Cerebral abscess
- Increase intra cranial pressure- Papilloedema
- Focal signs- Meningo encephalitis

Pneumonia	Tuberculosis	Bronchial ca	Pulmonary embolism
Febrile, tachypnoeic, breathless, shallow breathing Bronchial breathing, Increased vocal fremitus, Coarse crepitations,+ or - bronchial breathing	No abnormality Loss of appetite Few crepitations (No clubbing)	Finger clubbing Gynaecomastia Pain in inner aspect of arm and wasting of small muscles of the hand- Pancoast syndrome(Apical tumour locally invading brachial plexus(C8,T1,T2)) Horner's syndrome - Interruption in sympathetic supply to eye--Ptosis, Miosis, Enophthalmos, Ahydrosis. Cervical or axillary lymphadenopathy Superior vena caval obstruction- Mediastinal lymphadenopathy- Headache, Oedema of face, arm and chest, raised JVP, Collateral chest veins Pleural effusion	DVT, JVP, Tender hepatomegaly

Investigations

Pneumonia

- ✓ Full blood count-
- ✓ CXR
- ✓ Klebsiella- CXR upper lobe more commonly affected and the consolidation is often extensive
- ✓ Sputum culture

Atypical pneumonia

- ✓ *Radiological signs are more marked compared to clinical signs*
- ✓ CXR infiltrative changes multi lobar
- ✓ FBC-No leucocytosis
- ✓ Sputum culture-No growth confirmed by serology
- ✓ Legionalle- Lobar and then multilobar shadowing, sometimes with pleural effusion
- ✓ Cavitation is rare
- ✓ Coxiella- Multiple lesions in the CXR
- ✓ Mycoplasma pneumoniae-CXR
 - Usually one lobe
 - but bilateral can be

Tuberculosis

- ✓ Microscopic examination of AFB-sputum
 - Specific, less sensitive can repeat
- ✓ Biopsy-LN biopsy, Trans tracheal aspiration, Broncho alveolar lavage
- ✓ Radiology
 - Non specific but very useful (suspicious x ray should never be treated without sputum examination)
 - Certain features-Strongly suggestive
 - Upper zone-patchy nodular shadow unilateral bilateral
 - Cavitation-Specially>1 calcified shadows
 - Rarely
 - Diffuse small nodular opacities- Miliary TB
 - Normal x ray-Endo bronchial TB
- ✓ New diagnostic techniques Microbiology-PCR
- ✓ Mantoux test is a test for infection in human and not necessarily a disease
- ✓ Tuberculin skin test
 - Positive -10mm swelling (If BCG is not received)
 - 15mm swelling (if BCG is received)
 - Negative-Does not exclude active TB
 - Repeatedly negative-May rule out TB
 - Positive-TB is likely

Bronchial ca

1. CXR/CT thorax

- Rounded shadow, speculated margin, mass at least 1-2cm in size
- Hilar enlargement or superior mediastina widening
- Unilateral pleural effusion
- Elevated hemi diaphragm

2. Fiber-Optic bronchoscopy

- Tissue diagnosis from bronchial epithelium
- biopsy for histology/brush or wash for cytology

3. Transthoracic fine needle aspiration

- Under CT or USS guidance
- Sample for cytology
- Pneumothorax common

4. Mediastinoscopy

- Transthoracic procedure to sample mediastinal lymph node

Pulmonary Embolism

- ECG
- CXR
- D dimer
- V/Q scan
- spiral CT with reconstruction
- Pulmonary angiogram

Management

Pneumonia

General:-

- ✓ Rest
- ✓ Diet increase fluid intake
- ✓ Monitoring
- ✓ Drugs:-For symptomatic management- Paracetamol, NSAIDS, Mucolytics
- ✓ Specific management:- Antibiotics-uncomplicated and mild--B.Penicillin, Ampicillin or Oral amocycillin for 7-10days
- ✓ If allergic-Erythromycin, Clarithromycin
- ✓ If no response-Cefuroxime IV, or Ampicillin + clavulinic acid IV
- ✓ Staphylococcus suspect give-IV Flucloxacillin

Atypical pneumonia

- ✓ Add Erythromycin or Clarithromycin

Bronchial ca treatment

- ✓ Curative or Palliative
- ✓ In bronchial Ca depends on all cell types-
- ✓ Non small cell--Surgery for cure, radiation for palliation
- ✓ Small cell--Chemotherapy for palliation

Pulmonary embolism

Acute management

- ✓ Oxygen
- ✓ IV heparin or LMWH
- ✓ Streptokinase IV in massive embolization
- ✓ surgery

Long term management

- ✓ Warfarin 6 weeks to 6 months
- ✓ Otherwise lifelong treatment
- ✓ IVC filter

Discussion

- ✓ What causes the pneumonias due to opportunistic infections?

1. Cytomegalovirus
2. M.tuberculosis
3. M.avium-intracellulare
4. L.pnuemophila
5. Cryptococcus
6. Pyogenic bacteria
7. Kaposi's sarcoma
8. Lymphoid interstitial pneumonia
9. Non specific interstitial pneumonia

- ✓ Explain why the bronchial breathing sounds are heard over a consolidation?

In a consolidation, the high frequency breath sounds travels through the airways to the chest wall with little loss of sound and thereby the characteristics of tracheal sounds (bronchitis) are faithfully transmitted.

- ✓ What do you understand by whispering pectoriloquy as found in consolidation?

During a whisper, the abducted vocal cords do not oscillate and the low frequency sounds of normal sounds are lost and the high frequency sounds of speech are transmitted across the chest and the widespread speech is then heard

- ✓ How is the diagnosis confirmed? Chest radiograph is often essential for confirmation

- ✓ How the resolution of the consolidation clinically recognized?

Reduction of fever and dyspnea, appearance of coarse crepitations over consolidation and thereafter disappear of other abnormal physical signs and restoration of normal breath sounds

- ✓ What is pneumonia?

Inflammation of lung tissues with accumulation of cells and secretions in alveolar spaces usually following an infection

✓ **How pneumonia is categorized according to aetiology?**

- a. Community acquired pneumonia
- b. Hospital acquired pneumonia
- c. Aspiration pneumonia
- d. Immunocompromised

✓ **What are the causes of community acquired pneumonia**

Bacteria pneumonia-Streptococcus pneumoniae, Klebsiella, Staphylococcus aureus, Haemophilus influenza

Atypical pneumonia- Mycoplasma, Legionella, Chlamydia, Viruses

✓ **What are the pulmonary complications of pneumonia?**

- a. Pleural effusion
- b. Empyema
- c. Lung abscess
- d. Respiratory failure

✓ **Criteria for diagnosis of severe pneumonia?**

CURB 65

C-Confusion

U-BU>7mmol

R-RR>30

B-DBP <60mmhg, SBP <90mmhg

65->65 years

✓ **How will you manage severe pneumonia?**

Oxygen, Nebulisation, Bronchodilators, Chest physiotherapy

Ionotropes- Dobutamine or Vasopressine, Noradrenaline

FFP, Platelets

ICU-IPDV

✓ **In severe pneumonia antibiotics,**

- Broad spectrum antibiotics IV
- 3rd generation Cephalosporin
OR
- Ampicillin + Clavulanic acid
OR
- Quinolone or Clarythromycin
OR
- Penicillin + Gentamycin
OR
- add-->Metronidazole , Erythromycin, Flucloxacillin

Rheumatic Fever

PC – Acute onset Fever (duration), Joint pain (duration), malaise, LOA

HPC –

- Describe fever
- Type, duration, high grade, associated symptoms
- Fleeting (Pass quickly) & flitting (migratory) polyarthritis
- Of large joints (knees, ankles, elbows & wrists)
- Joint pain
- Unintentional movements continues during sleep
- Dropping things
- Mood changes
- Deterioration of hand writing
- Chest pain, shortness of breath(pericarditis, pericardial effusion), palpitations (arrhythmias), orthopnea(LVF)
- Skin rash & nodules
- Recent hx of sore throat or contact hx

PMHx – Previous hx of rheumatic fever

PSHx

DHx

FHx

SHx –

- Education level
- Occupation
- Housing
- Ventilation
- Overcrowding at home

Examination –

- Febrile
- Throat
 - Inflamed
 - Enlarged tonsils
- Cervical lymphadenopathy
- Subcutaneous nodules (painless pea sized hard nodules beneath the skin mainly over bony prominences & non tender. Skin is freely movable over them)
- Skin Rash – erythema marginatum (pink rash with raised edges in trunk or& limbs crescent or ring shape with pale centres)
- Joint examination for arthritis – mainly large joints
- B/L pitting ankle edema (heart failure)

CVS

- Tachycardia
- Displaced apex [cardiomegaly] & parasternal heave (heart failure)
- Thrill(varies according to the murmurs)
- Muffled heart sounds (pericardial effusion)
- Gallop rhythm (heart failure)
- Pericardial rub
- Murmurs
 - MR – high pitched systolic murmur radiates to axilla
 - Mid Diastolic Murmur - **Carey Coomb Murmur** due to swelling of mitral valve leaflets
 - AR – early diastolic murmur

RES

- B/L fine crepts

CNS

- Choriform movements
 - jerky repetitive movements of the limbs & face
 - May be limited to half of the body - Hemichorea
 - Overextension of joints – Dinner fork deformity
 - Supinator sign
 - Hippus pupil
 - Jack in the box tongue
 - Milk maid's grip
 - Hypotonia
- Hippus pupil
 - Also called pupillary athetosis
 - Spasmodic, rhythmic but irregular dilating & contracting pupillary movement
 - Noticeable when pupils tested with light

Discussion

- What is the cause for rheumatic fever?
 - Pharyngeal infection by Group A *streptoccus pyogenous*
- What are the organs affected?
 - Heart, skin, Joints, central nervous system
- Pathogenesis?
 - Autoimmune reaction triggered by cell wall M protein of bacteria & cardiac myosin & laminin.
 - Formation of granulomatous lesion with a central necrotic area in the myocardium – Aschoff nodule
 - Can affect all 3 layers of myocardium
 - Small warty vegetations in endocardium (valves)
 - Pericarditis
 - Inflamed synovial membranes of joints

- How do you diagnose?

Modified Jones criteria

- Major criteria

1. Carditis
2. Polyarthritis
3. Chorea
4. Erythema marginatum
5. Subcutaneous nodules

- Minor criteria

Clinical

1. Fever
2. Arthralgia
3. Previous rheumatic fever

Laboratory

1. Raised CRP, ESR
2. Leukocytosis
3. Prolong PR interval on ECG

- Essential criteria

Evidence of streptococcal infection

1. +ve throat culture of streptococci
2. +ve antistreptolysine O titre >250 units

❖ There should be 2 major criteria, Or 1 major + 2 or more minor

+

Essential Criteria

❖ Exceptions → Chorea And Established Valvular Disease

Does not need to fulfill modified Jones criteria

&

Does not need essential criteria for diagnosis

❖ Rheumatic Recurrence

Patients with established heart disease, or prior rheumatic fever

The presence of 1 major criterion

Or

Fever or arthralgia or high ESR

❖ Suggests recurrence in the presence of evidence of Streptococcal infection

Erythema marginatum



➤

Rheumatic carditis

HEART MURMUR

- Mitral regurgitation - high pitched systolic
 - Murmur at apex radiating to axilla
- Mid diastolic murmur - due to swelling of mitral
 - Valve leaflets - Carey Coomb murmur
- Early diastolic murmur aortic incompetence
- Cardiomegaly
- Pericarditis
- Heart failure

- How do you investigate?
 - FBC - leukocytosis
 - Throat swab culture for streptococci
 - ESR, CRP
 - CXR
 - ECG – prolong PR interval , Echo
 - Anti streptolysin O titre, Anti DNAase B

- How do you manage?
 - Acute disease bed rest
 - Monitor sleeping pulse, temperature chart
 - After improving clinically, bio chemically mobilize the patient
 - Pharmacology
 - No carditis – Aspirin + 2 weeks modified bed rest
 - Minimal carditis – Aspirin + 2 weeks absolute bed rest + 2 weeks modified bed rest
 - Carditis + cardiomegaly – trial of aspirin + steroids + 2 weeks absolute bed rest + 4 weeks modified bed rest
 - Carditis + CCF – steroids + absolute bed rest till symptoms continue + modified bed rest for similar duration
 - Antibiotic – oral penicillin for 10 days
 - Then start on long term antibiotic prophylaxis
 - Anti – rheumatic drugs –
 - ✓ Salsalates - 100mg/kg/ day for 3 – 5 days
75mg /kg for 4 weeks
 - ✓ Steroids –
 - For heart failure or complete heart block
 - Full dosage for 10 days
 - Tail off while adding aspirin
 - Primary prevention
 - ✓ Improve socioeconomic conditions
 - ✓ Streptococcal infection
 - ✓ Early treatment
 - Secondary prevention
 - ✓ Prevent recurrence
 - IM benzathine penicillin 1.2 mu 3 weekly OR
 - Oral penicillin bd
 - No carditis – 5 years or until 21 years
 - Carditis + but no residual lesions – 10 or 21 years
 - Carditis + residual lesions – life long
 - Erythromycin for penicillin allergy pts

- ❖ Treatment of Rheumatic chorea
 - Treatment -bed rest, haloperidol + benzhexol
 - Penicillin prophylaxis

- ❖ Commonly affects mitral (85%) & aortic valves (55%)

Valvular heart diseases

Age, gender, address....

PC

- Exertional chest pain &/or exertional syncope
- Diagnosed patient with a valvular heart disease
- Diagnosed pt complicated with pulmonary HT
- Diagnosed pt complicated with infective endocarditis
- Diagnosed pt complicated with heart failure

DD

- Mitral stenosis
- Mitral regurgitation
- Aortic stenosis
- Aortic regurgitation

HPC

If an undiagnosed pt – Analyze the presenting symptoms

- ✓ Onset
- ✓ Duration
- ✓ Progression of symptoms
- ✓ Associated symptoms

If an already diagnosed pt

- ✓ When and where diagnosed
- ✓ How diagnosed
- ✓ Progression of the disease
- ✓ Interventions done up to now
- ✓ Any routine clinic follow up & compliance to treatment
- ✓ Any complications developed and instances of hospital stay with their management

Complications

Features of pulmonary hypertension (**MS, MR**)

- Severe difficulty in breathing
- Frothy sputum
- Blood tinged productive cough
- Frank haemoptysis(rare)

Features of heart failure

1. Right heart failure (**MS,MR**)
 - Exertional dyspnoea
 - Fatigue
 - Generalized weakness
 - B/L ankle swelling
 - Abdominal distention
2. Left heart failure (**MR, AS, AR**)
 - Orthopnoea
 - Paroxysmal nocturnal dyspnea
 - Recurrent pulmonary infections

Features of atrial fibrillation (MS, MR)

- Palpitations

Features of infective endocarditis

- Fever
- Malaise and lethargy
- Joint pain
- Skin lesions
- Red coloured urine
- Hx of IV drug abuse, indwelling IV catheters, prosthetic heart valves, dental caries

Embolic events (MS)

- Sudden onset blackouts, slurred speech
- Sudden onset limb weakness

Aetiology

- Hx of rheumatic heart disease
- Ischemic heart disease
- Causes for dilated cardiomyopathy
 - Viral myocarditis
 - Alcohol
 - Toxins
- Connective tissue disorders – SLE, Rheumatoid arthritis, ankylosing spondylitis
- Collagen disorders – Marfan's syn. , Ehler Danlos syn.
- Congenital
- Calcification of valves with ageing

PMHx

Rheumatic fever, ischaemic heart disease, connective tissue disorders, collagen disorders

PSHx

Prosthetic valve replacements

DHx

Prophylaxis for infective endocarditis – Benzyl penicillin, diuretics, ACEI

AHx

FHx

Connective tissue disorders, collagen disorders

Valvular heart lesions

SHx

Socio- economic status

Income

Smoking, alcohol

Dietary hx – high fat

Examination

III looking /well looking
Dyspnoeic and propped up
Built
Febrile
Hydration
En gorged neck veins
Pallor
Xanthelesma, corneal arcus
Cyanosis
Malar flush/ mitral facies
Dysmorphic features
Dental caries
High arched palate
Peripheral stigmata of infective endocarditis – clubbing, splinter haemorrhages, janeway lesions, osler's nodes
Palmar erythema
Nicotine stain
Tattoos and evidence of IV drug abuse
Ankle oedema/ sacral oedema

Pulse – rate, rhythm, volume, character.....

- Low volume, thread pulse – in heart failure
- Irregularly irregular pulse – AF
- High volume and collapsing pulse - AR

BP – *low in heart failure*

JVP – elevated in heart failure

Mitral stenosis

Low volume pulse
Sometimes atrial fibrillation present with irregularly irregular pulse
Parasternal heave
Tapping RV impulse
Palpable S1
Apex – Tapping and not shifted
Opening snap +
Loud S1
Rumbling mid diastolic murmur at the apex – Heard from the bell

Mitral regurgitation

Brisk, small volume pulse
Laterally displaced thrusting apex
Palpable S3
Systolic thrill
Soft S1
Wide split in S2

Loud pan systolic murmur at the apex

- It radiates to the axilla
- Best heard at the axilla
- It's louder in expiration

Aortic stenosis

Low volume and slow rising pulse

Low systolic blood pressure

Heaving apex

Systolic trill in the aortic area

Ejection systolic murmur best heard in the aortic area

- It radiates to the carotids
- Is a crescendo decrescendo type murmur

Ejection click

Soft S2 with a **reversed splitting** on expiration

Sometimes S4 +

Aortic regurgitation

Head nodding (De Musset's sign)

Collapsing pulse

Pistol shot femorals (Traube's sign)

Femoral retrograde bruits (Durozier's sign)

Wide pulse pressure

BP in the lower extremity > BP in the upper extremity (Hill's sign)

Visible carotid pulse (Corrigan's sign/ Water hammer pulse)

Nail bed pulsations (Quincke's sign)

Systolic pulsation of uvula (Mueller's sign)

Thrusting apex

Soft high pitched early diastolic murmur at the left sternal edge

- Best heard at end inspiration when pt is seated and leaning forward

Investigations

1. Chest x-ray

A. Mitral stenosis

- small heart with an enlarged left atrium
- Pulmonary venous hypertension
- In late stages – calcified mitral valve
- When severe – signs of pulmonary hypertension and pulmonary oedema

B. Mitral regurgitation

- Left atrial & left ventricular enlargement
- Increase CTR (cardio thoracic ratio)
- Valve calcification

C. Aortic stenosis

- Small heart with a prominent, dilated ascending aorta – due to post stenotic dilatation
- Calcified aortic valve
- CTR increases with heart failure

Duroziez's sign – a to-and-fro murmur heard when the femoral artery is auscultated with pressure applied distally (if found, it is a sign of severe aortic regurgitation)

pistol shot femorals – a sharp bang heard on auscultation over the femoral arteries in time with each heart beat.

Both auscultated using the bell

D. Aortic regurgitation

- Left ventricular enlargement
- Dilatation of the ascending aorta
- Calcified aortic valve – In syphilis

2. ECG

A. Mitral stenosis

- Sinus rhythm with bifid p wave
- Sometimes fibrillatory waves with atrial fibrillation
- With disease progression – right axis deviation with tall R waves in lead V1.

B. Mitral regurgitation

- Bifid p wave
- L. ventricular hypertrophy with tall R waves in the left lateral leads (I & V6)
- Deep S waves in lead V1, V2
- Evidence of L. ventricular hypertrophy with $SV1 + RV5 \text{ or } RV6 = >35\text{mm}$
- AF may be present

C. Aortic stenosis

- Left ventricular hypertrophy and left atrial delay
- Left ventricular strain pattern – due to pressure overload
(depressed ST segments and T wave inversion in leads orientated towards the left ventricle, i.e. leads I, AVL, V5 and V6)
- Usually sinus rhythm, sometimes arrhythmias present

D. Aortic regurgitation

- Left ventricular hypertrophy – tall R waves and deep inverted T waves in left sided chest leads and deep S waves in right sided leads
- Sinus rhythm

3. Echocardiogram

A. Mitral stenosis

- Assess the mitral valve apparatus and the mitral valve area to detect the severity – Helps to determine the choice of treatment
- Assess L. atrial & R. ventricular size and function

B. Mitral regurgitation

- Dilated left atrium and left ventricle
- Evidence of chordal or papillary rupture
- Dynamics of ventricular function

C. Aortic stenosis

- Thickened, calcified and immobile aortic valve cusps
- Left ventricular hypertrophy

D. Aortic regurgitation

- Vigorous cardiac contraction and dilated left ventricle
- Enlarged aortic root
- Diastolic fluttering of the mitral leaflets or septum occurs in severe aortic regurgitation (producing the Austin Flint murmur).

4. Transoesophageal echocardiography (TOE)

A. Mitral stenosis

- Detection of L. atrial thrombus

B. Mitral regurgitation

- Structural valve abnormalities before surgery
- Intraoperatively assess the efficacy of the valve repair

5. Cardiac catheterization

A. Mitral stenosis

- Use in the presence of co-existing cardiac problems (MR ,coronary artery disease)
- Diastolic pressure in the left atrium > Diastolic pressure in the left ventricle
- Gradient of the pressure is proportional to the degree of stenosis

B. Mitral regurgitation

- Prominenet left atrial systolic pressure wave
- Regurgitation occur in to the enlarged left atrium

C. Aortic stenosis

- Detect systolic pressure difference between aorta and left ventricle

D. Aortic regurgitation

- Outline aortic valve abnormalities
- Assess nthe degree of regurgitation

6. Cardiac magnetic resonance (CMR)

A. Mitral stenosis

- Shows mitral valve anatomy accurately

B. Mitral regurgitation

- Shows anatomy better than cardiac catheterization

Management

1) Mitral stenosis

a) Medical Mx

- ✓ Diuretics for heart failure
- ✓ Digitalis/ β blocker/ CCB for rate control/ cardioversion in AF
- ✓ Anticoagulation in AF - Warfarin
- ✓ Prophylaxis for sub-acute infective endocarditis – Benzyl Penicillin

- b) Surgical Mx**
- ✓ Trans septal balloon valvotomy
 - ✓ Closed valvotomy
 - ✓ Open valvotomy
 - ✓ Mitral valve replacement

2) Mitral regurgitation

- a) Medical Mx
 - ✓ Prophylaxis for sub-acute infective endocarditis
 - ✓ ACEI & diuretics – until surgery
 - ✓ Anticoagulants and chemical cardiovertors – AF
- b) Surgical Mx
 - ✓ Mitral valve repair or replacement – Essential

3) Aortic stenosis

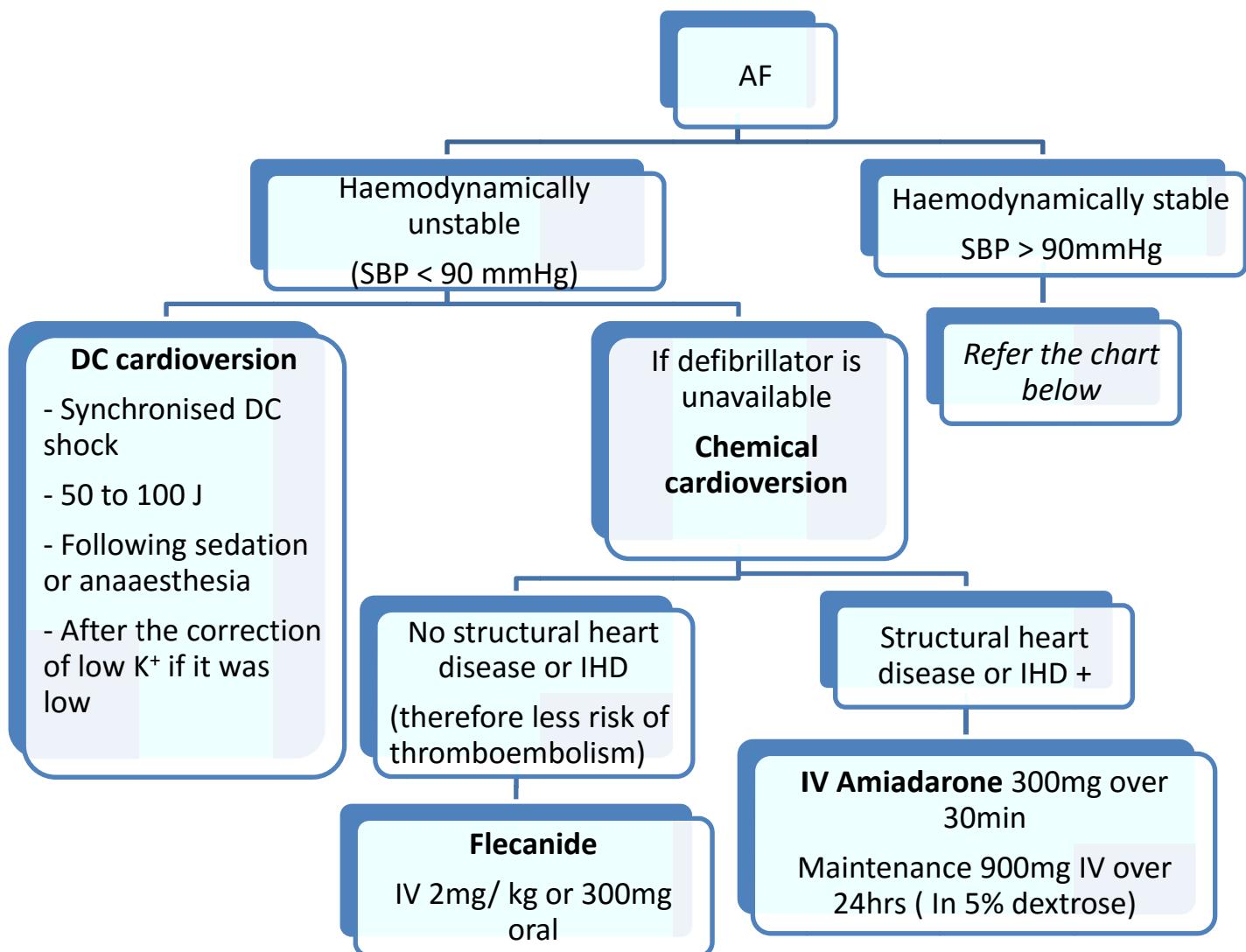
- a) Medical MX
 - ✓ Antibiotic prophylaxis against infective endocarditis
- b) Surgical Mx
 - ✓ Coronary angiography before valvular surgery
 - ✓ Aortic valve replacement
 - ✓ Valvotomy – if critically stenosed in childhood / adolescent
 - ✓ Valvuloplasty (balloon dilatation) – In elderly as an alternative to surgery
 - ✓ Percutaneous valve replacement

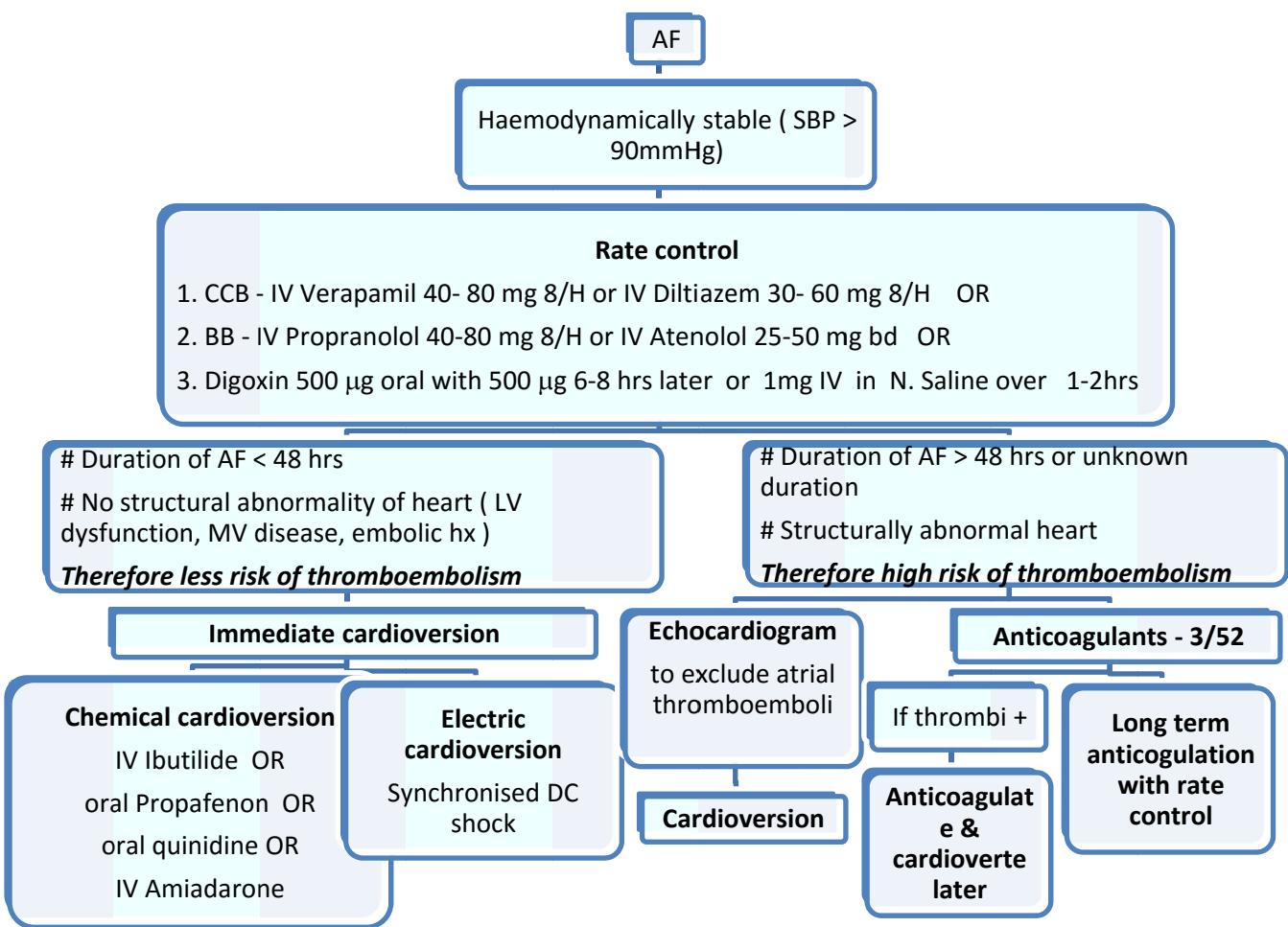
4) Aortic regurgitation

- a) Medical Mx
 - ✓ Specific Rx for underlying cause
 - ✓ Anticoagulants- with mechanical valves
 - ✓ Antibiotic prophylaxis
- b) Surgical Mx
 - ✓ Mechanical prosthesis
 - ✓ Tissue valves – In elderly when anticoagulants are CI

Discussion

Management of AF





Anaemia

Reduction in blood Hb below the reference level for the age and sex; male – 13.5g/dL
Female – 11.5g/dL

MCV – 76-100fL

Hypochromic microcytic	Normochromic Normocytic	Macrocytic	
Iron deficiency	Anaemia of chronic disease	<u>megaloblastic</u>	<u>non megaloblastic</u>
Sideroblastic	Aplastic anaemia	B12	alcohol
Thalassemia	Acute blood loss	Folate	methotrexate
Pb poisoning	Haemolytic anaemia		hypothyroidism
Anaemia of CD	Hypo-thyroidism/adrenalinism/pit.		Liver disease
			↑ reticulocytes

Iron deficiency

Reduced intake – adolescents, pregnant

Reduced absorption – gastrectomy, tea following meals, malabsorption Xn, chronic antacid use (achlorhydria)

Increased utilization – growth spurt, preg. , lactation

Blood loss - GI bleeds – Peptic ulcer disease, oesophageal varices, GI CA, worms – hook worm, Enterobius, whip worm
Excessive anti-coagulation, hereditary haemorrhagic telangiectasia, angiodysplasia of colon

Menstrual blood loss

Sideroblastic anaemia

Congenital/Inherited – x linked recessive (males)

Acquired – INAH, alcohol, phenytoin, MDS, Myeloid leukaemia, Myeloproliferative disorders

Thalassemia – mutated globin chain around haem group

Pb poisoning –

Anaemia

Blue lines of gums (PbS lines near gum margin at sites of teeth infection)

Colic, constipation

Drop – wrist drop + paralysis, musc.atrophy, tremors of extensors + supinators of forearm

Encephalopathy – convulsions, eye/tongue/ finger tremors

Anaemia of CD – infective endocarditis, TB, Osteomyelitis, SLE, RA, PMrheumatica, IBD, malignancy, CRF, multiple myeloma (due to ↓ iron utilization, ↓ body response to erythropoietin, ↓ RC lifespan)

Aplastic anaemia – BM failure

inherited – Dyskeratosis congenita (leuconychia)

Fanconi anaemia – AR, dysmorphic + renal, neuro,skeletal prb

Acquired – infections – EBV, HIV, Parvo, Hep A/B, TB

Rx – Busulfan, Doxorubicin, chemotherapy

Idiosyncratic rx – NSAIDs/Gold/chloramphenicol/carbimazole/phenytoin/ chlorpromazine/
tolbutamide/ methotrexate (transient)

Radiation exposure

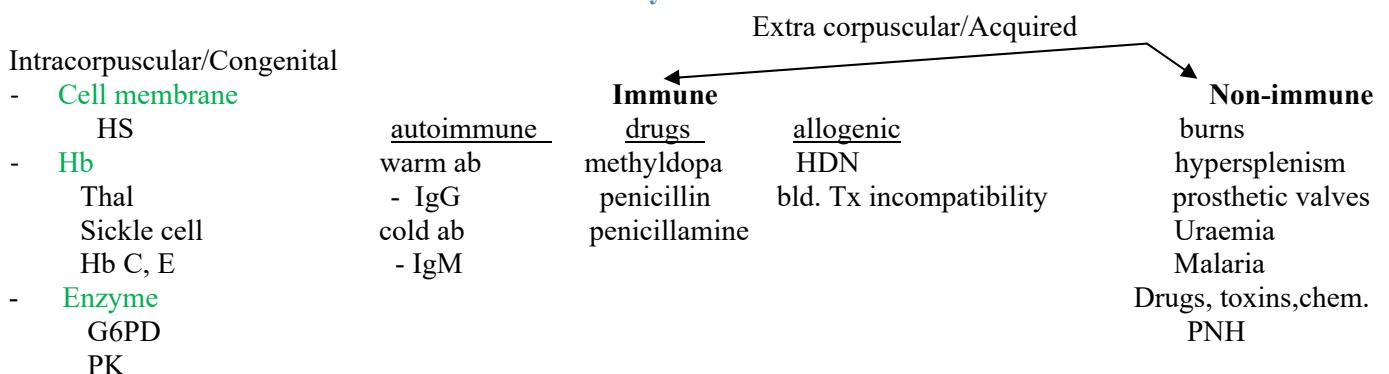
Pregnancy

PNH

Myelodysplasia

Chemical, insecticides

Haemolytic anaemia



Warm Ab – primary, IIry to SLE, lymphoma, HIV

Cold Ab – Mycoplasma pneumonia

BM infiltration – MPD – MF, leukaemia, lymphoma, multiple myeloma

Hx

----- yr old pt. presented with **SOB on exertion, tiredness and faintishness** for -----

DD – anaemia
CCF/ L \heartsuit failure
Subacute bacterial endocarditis
Hypothyroidism
Hypopituitarism

Age – child – thalassemia, congenital HA

Male – GI CA/ PUD/ G6PD/ Sideroblastic anemia

Young female - iron def. / autoimmune HA

Middle aged female – iron def. / pernicious anemia

Elderly – aplastic anemia/ def. anemia

Add. – Kurunegala – thalassemia

HPC

Onset of symp. – Rapid (over days/ 1-2wks) – acute bleeding/ acute leukaemia/ acute haemolysis
Insidious – usually – def./ aplastic anemia

Progression

- Worsening of existing symptoms – exertional angina/ ischemic claudication
- Other anemic features –faintishness/ palpitations/ LOA/ difficulty to concentrate/ headache

Exclude DD –

- CCF – orthopnoea/ PND/ ankle swelling
- SBE – fever, chest pain, palpitations
- Hypothyroidism – cold intolerance, weight gain + ↓ appetite, hair loss
- Hypopituitarism – ↓ skin colour
- Syncope – fainting spells on prolonged standing/ fear/ pain/ exertion (cardiac syncope)

Underlying cause

1) Blood loss

- ACUTE - PPH, recent trauma/ Sx
- CHRONIC
 - ⊕ Haemorrhoids – lump at anus, PR bleeding
 - ⊕ IBD – blood and mucus(mixed with stools) , LOW
 - ⊕ GI CA (oesophageal, stomach, colon) – dysphagia, LOA, LOW, abd. Mass, Altered bowel habits
 - ⊕ PUD/GORD – dyspepsia, haematemesis, chronic NSAID/corticosteroid use
 - ⊕ Hookworm infest – estate workers, children
 - Improper disposal of human excreta, working barefeet, LOA, anti-worm tx
 - ⊕ Menstrual loss - >7days, clots,flooding, >3 pads/day
 - ⊕ Parity, gap between pregnancy
 - ⊕ CLD
 - ⊕ Hx of bleeding disorder – haematuria/haemoptysis/epistaxis/skin bruising

2) Impaired RC production

- Nutrition deficiency
 - Diet** - how often red meat, tea with meals (iron), vegetarian, poor diet (B12), green vegetables (folate)
 - Malabsorption** – chronic diarrhea, steatorrhoea, LOW, poor growth, IBD
 - Past Hx of TB (ileal TB)
 - Intestinal resections – gastrectomy(B12, iron)
 - Losses** – Folate – renal dialysis, chemotherapy, inflammation (high cell turnover)

B12 def. – tingling and numbness of feet>hands, memory disturbance, apathy, visual disturbance, Psychosis

Progressive weakness and ataxia → paraplegia

Gastrectomy, Terminal ilealectomy

Pernicious anaemia – FHx of similar/early graying/ vitiligo(AI)

Blood group A

Homocysteineuria - Subfertility, limb weakness, PVD

Iron def. – pica, dysphagia and sore tongue (Plummer Vinson Xn/Paterson-Brown-Kelly Xn), tinnitus

Celiac disease – reduced iron absorption

Folic acid - tumors (increased cell turnover)

Haemolysis

Pregnancy (increased demand)

Alcohol excess

Drugs: Anticonvulsants,methotrexate

- Anaemia of CD

TB – chronic cough, evening fever, night sweats, back pain

RA – joint pain (B/L symmetrical, small J of hands), NSAID use

IE, osteomyelitis, SLE, CRF, CLD, DM

3) Bone marrow failure

Primary failure

- **Aplastic anemia** – pancytopenia – spontaneous ICH → craniotomy
 - Congenital – fanconi's anaemia (microcephaly, absent thumbs)
 - Acquired
 - Infections – HAV, HBV, **Parvo B19** (skin rash, symmetrical arthralgia, resp. symp)
 - Exposure to radiation, chemotherapy
 - Rx – chloramphenicol, sulphonamide, anti-malarial,anti-thyroid, tolbutamide, phenytoin
 - Sickle cell disease – BM infarcts

- **MDS**

Marrow infiltration

- **Myelofibrosis** – anaemia & thrombocytopenia, abdominal discomfort & early satiety(heptosplenomegaly)
 - Hypercatabolic state – fatigue, pruritus, LOW, LOA (PHx of TB → II^{IV} MF)
- **Leukaemia** – pt. very ill, bone pain (CML – sternal tenderness), back ache (young pt.)
- **Lymphoma** – enlarged LN, fever, night sweats, pruritus, abd discomfort
- **Multiple myeloma/ mets** – back pain, bone pain
 - Hypercalcemia – polyuria, renal colic, constipation
 - ARF

4) ↑ RC breakdown (haemolysis)

Jaundice, dark coloured urine, loin pain, biliary colic

Since childhood + FHx – congenital

INTRAVASCULAR

- **G6PD** – acute haemolysis in a crisis (infection , acute illness , drugs, ‘kuppamenia’)
Eg –antimalarials , Dapsone (anti leprosy),nitrofurantoin, quinolones , aspirin
Past Hx of similar episodes of jaundice and anaemia
- **Malaria** – intermittent fever, travel to malaria endemic area
- **PNH** - haemolysis precipitated by infection , iron therapy , surgery
Dark colour urine voided at night and on waking up
Venous thrombosis – Budd chiari Xn, mesenteric (abdominal pain), cerebral
- **Snake bite, valvular prosthesis**

EXTRAVASCULAR

Family Hx of anaemia with jaundice

Past Hx of splenectomy

- Congenital :
 - **Thalassaemia** – since childhood, frequent blood Tx, splenectomy, pathological # siblings affected, previous HPLC
 - **Sickle cell anaemia**
 - **HS** - Hx of splenectomy, intermittent jaundice, haemolytic crises with infection, gall stones
- Acquired :
 - **AIHA** – Episodic
 - After mycoplasma pneumonia, IMN
 - cyanosis of nose, fingers, ears, toes with exposure to cold (IgM HA)
 - Irry to SLE, lymphoma, CLL (warm Ab)
 - Rx – methyldopa, penicillin, dapsone, sulfasalazine
 - **Hypersplenism** – RA (felty’s Xn)
 - Portal HT

Complications of anaemia

- CCF
- Unstable angina- chest pain at rest ,not relieved by GTN
- Haemolytic anaemia- gall stones - colicky RHC Pain which radiate to the back
 - Acute cholecystitis - above features +high grade fever
 - Chronic cholecystitis - recurrent abd pain , discomfort after meals
 - postprandial discomfort
- Obstructive jaundice: dark urine ,pale stools ,pruritus
- Syncopal attacks - head injury
- Visual disturbances (rapid severe anaemia → retinal haemorrhages)

- Prev. anaemic episodes, bld Tx given, how often – recurrent → thal, MF, acute leukaemia, BM suppression
- Complications of bld. Tx – anaphylaxis
 - Iron overload – pigmentation, abd enlargement, DM, iron chelation done – last when
 - Blood borne infections
- Ix done – BM biopsy, imaging, sputum EX

FHx – AD – Hereditary spherocytosis (each generation affected)

X linked recess – G6PD AR – thal. Investigated for anaemia/bleeding tendency

SHx – neglect/poverty

Occup. – Exposure to toxic chem., human excreta

Alcohol – how much smoking - IBD Freq hosp. – distance, family support

Ex

GE – dysmorphic – bossing of frontal bone, enlarged maxilla – thal
Ill/well

Hypothyroid facies

Acrocyanosis – nose, fingers, ears, toes (IgM HA)

Febrile/not

Pallor – face, conjunctiva

Lemon hue on face – pernicious anaemia

Glossitis – Fe, B12, folate

Angular stomatitis – folate def, Fe def

Mouth ulcers

LN – neck, axilla, groin

Thyroidectomy scar

Nails – Koilonychia, brittle nails – Fe def.

Clubbing – IE, TB

Skin bruises/ ecchymoses – elbows, knees

Vitiligo patches

Cirrhotic feat. – spidernaevi, palmar erythema,

Skin atrophy

Ankle oedema

Leg ulcers – HbS

Urine bag – colour, ↓ UOP – mismatched bld Tx

Features of

- CRF
- CLD
- Hypothyroidism
- Addison's
- Thalassemia
- HA
- deficiency

Abd – distension

Splenectomy scar

Epigastric tenderness

Hepatomegaly – tender/not – CCF

Firm – cirrhosis hard, nodular - hepatoma

Splenomegaly – soft spleen – acute malaria, HA, portal HT, hypersplenism

Splenic rub – leukaemia, malaria

Abd. Mass, para-aortic LN

FF in abd

PR – malaena, prolapsed piles, fissures, mass

Hepatosplenomegaly +

Chronic malaria
Leukaemia, Lymphoma
HS/ thalassemia

No hepatosplenomegaly

Aplastic anaemia
Myeloma

CVS – pulse – tachy, bounding

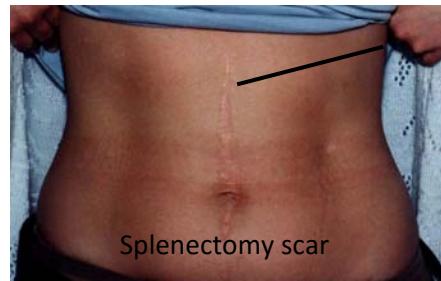
Cardiomegaly – apex shifted

JVP – raised/ not - ♥failure

Systolic flow M – apex

Murmur - IE

↓ BP – Addison's



Splenectomy scar

CNS – symmetrical sensory loss – touch, proprioception – feet, hands

Intact pain, temp

+ babinski sign, absent knee jerk, absent ankle jerk – subacute cord degen.

Fundi – papilloedema, retinal haemorrhages, pallor of optic disc

Respiratory – RR - ↑

TB feat. – apical consolidation

△ sis – anaemia due to ----- complicated with

Discussion

How would you investigate this patient?

Confirm Δ sis – FBC – Hb, RC indices – MCV/ MCH, Hct, RDW, other 2 cell lines

+ Blood picture

Assess severity ECG

Cause ESR – CD
s. creatinine – CRF
LFT

CXR – PA \rightarrow TB, bronchiectasis
USS – Abd – lymphoma

Microcytic hypochromic – s. iron, TIBC, **s. ferritin**

Faecal microscopy – hook worm ova, whip worm
Faecal occult blood (eg: NSAID user – no melaena)
UGIE/ LGIE
Hb electrophoresis
PT/INR - coagulopathy

Macrocytic – s. folate/ RC folate, s.B12

Schilling test
Anti-parietal cell Ab/ anti-IF Ab
Liver function tests
Thyroid function tests

BM Ex – aspiration Bx \rightarrow trephine Bx – aplastic anaemia, marrow infiltration

HA – 1st line \rightarrow reticulocyte count
UCB (indirect bil) ↑
s. LDH ↑
(Urobilinogen ↑)

Find the cause \rightarrow coomb's test – indirect - AIHA
s. Haptoglobin ↓ }
Urine Haemosiderin } IV haemolysis
Cryoglobulin

Investigations in detail

Hb – pregnant female – 11g/dL
Children (1-2yrs) – 10.5g/dL

Hct - male – 40- 54% female – 37- 47%

- Reticulocyte count - ↑ - haemolysis/ corrected deficiency states/ acute blood loss
↓ - iron def., megaloblastosis, anaemia of CD, malignancy (BM fail to produce RC), BM failure
- If retic count >50% \rightarrow High MCV

Platelet decides marrow activity.
Even if RBC & WBCC not that low
 $\downarrow\downarrow$ plt \rightarrow severe pancytopenia

Practical Box 8.1 Techniques for obtaining bone marrow

The technique should be explained to the patient and consent obtained

Aspiration

Site – usually iliac crest
Give local anaesthetic injection
Use special bone marrow needle (e.g. Salah)
Aspirate marrow
Make smear with glass slide
Stain with:
Romanowsky technique
Perl's reaction (acid ferrocyanide) for iron

Trephine

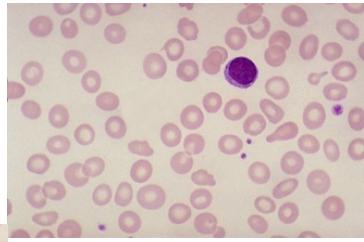
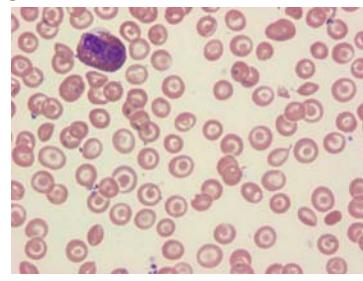
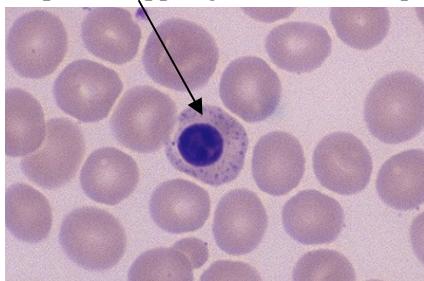
Indications include:
'Dry tap' obtained with aspiration
Better assessment of cellularity, e.g. aplastic anaemia
Better assessment of presence of infiltration or fibrosis

Technique

Site – usually posterior iliac crest
Give local anaesthetic injection
Use special needle (e.g. Jamshidi – longer and wider than for aspiration)
Obtain core of bone
Fix in formalin; decalcify – this takes a few days
Stain with:
Haematoxylin and eosin
Reticulin stain

Microcytic hypochromic

- Blood picture – 1) pencil cells, tear drop cells (variation in shape-poikilocytosis) – iron def
 Variation in size (anisocytosis)
 2) Target cells – thal.
 3) Rouleaux formation – TB, chronic infection
 4) Basophilic stippling – chronic lead poisoning



Iron studies –

Disorder	s. ferritin	TIBC	s. iron	BM iron
Iron deficiency	↓	↑	↓	↓/absent
Thalassemia trait	N / ↑	N	N / ↑	N / ↑
Sideroblastic				
Lead poisoning				
Pyridoxine dependant anaemia				
Anaemia of CD	N / ↑	↓	↓	N / ↑
Iron def. with inflammation	↑	↑	N / ↑	↓

Iron def. also indicated with ↓ in TS (transferring saturation = s. iron/TIBC)

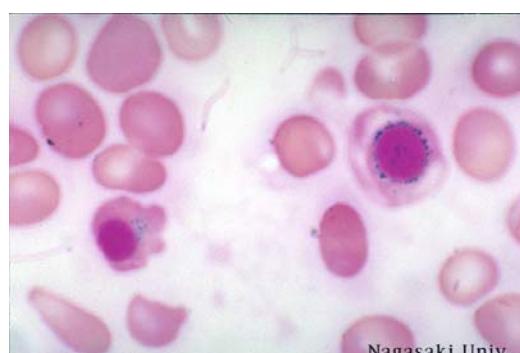
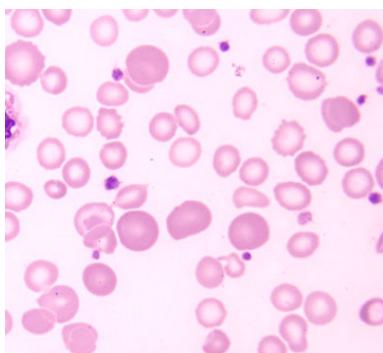
Hb electrophoresis – high performance liquid chromatography – EDTA sample → MRI (also in thalassemia unit)

Sideroblastic anaemia -

Blood picture - Dimorphic blood pic. (microcytic + macrocytic) + damaged RC – also in mixed deficiency (celiac dis.)
 Following Rx with haematinics

BM Bx – ring sideroblasts

Perl stain → prussian blue



Nagasaki Univ.

Anaemia of CD – ESR

CRP

Liver profile

Renal profile

LDH

tumour markers

AI profile



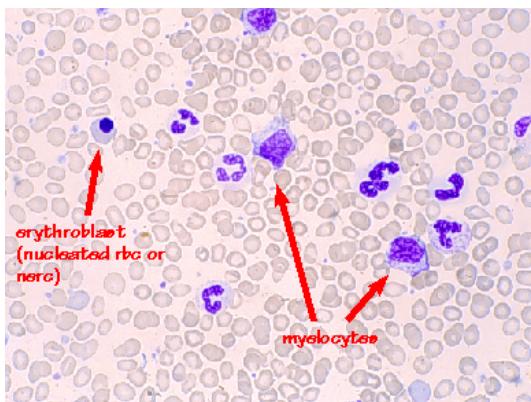
Blood picture - Pancytopenia – Hypersplenism, aplastic anaemia, multiple myeloma, MDS

↑rouleaux formation

Anaemia + blast cells >5% – acute leukaemia

Anaemia + metamyelocytes – CML

Leucoerythroblastic blood picture



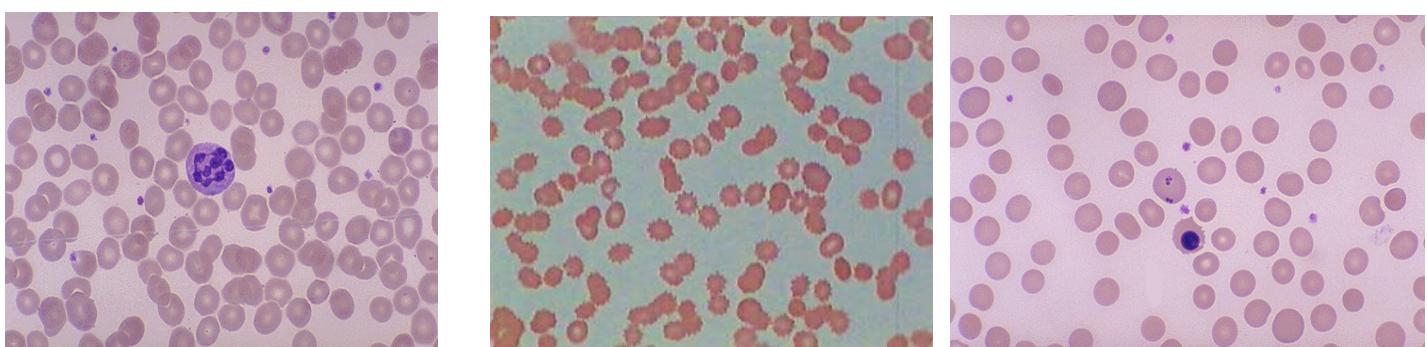
Causes

In cases of marrow infiltration

- MF
- Malignancy :lymphoma
- Amyloidosis
- TB
- Severe sepsis
- Marble bone disease

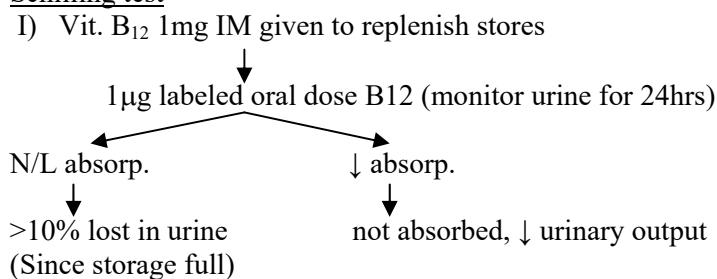
Macrocytic –

- 1) Oval macrocytes, tear drop cells, hypersegmented neutrophils, leuco/thrombocytopenia – megaloblastic anaemia
- 2) Burr cells – renal failure
- 3) Howell jolly bodies, poikilocytosis, nRBC – hyposplenism/post-splenectomy



	s. folate	RC folate	s. B12
Folate def.	↓	↓	N / borderline
B12 def.	N/↑	N/↓	↓

Schilling test

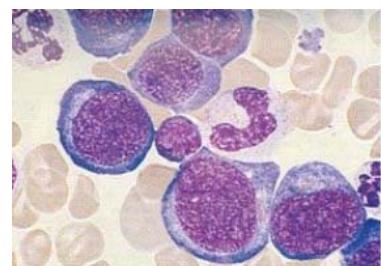


- II) rpt. With IF – if improved output – IF def.
Not improved – IF not cause

- III) Rpt. Aft. Course of broad spectrum AB – improved – blindloop Xn
(-) - not “

BM Bx – hypercellular, megaloblasts, abnormal giant metamyelocytes & band forms

Haematologic - ↑ indirect bilirubin
↑ LDH } marrow cell breakdown



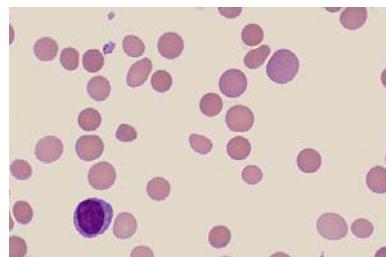
Normocytic normochromic –

1) HS

Blood picture - Cricket ball RC (microspherocytes)

Osmotic fragility - ↑ (early rupture)

Indirect Coomb's - (-)



2) HA

Blood Picture - Reticulocytes (larger + paler), fragmented RC, nucleated RC

Indirect Coomb's - (+)

BM Bx – erythroid hyperplasia

3) G6PD

Blood picture - Basket cells/ bite cells

4) Aplastic anaemia

Blood picture – normocytic/ macrocytic

FBC – leucopenia (↓ granulocytes → if severe lymphocytes also)

Thrombocytopenia

↓ retic count

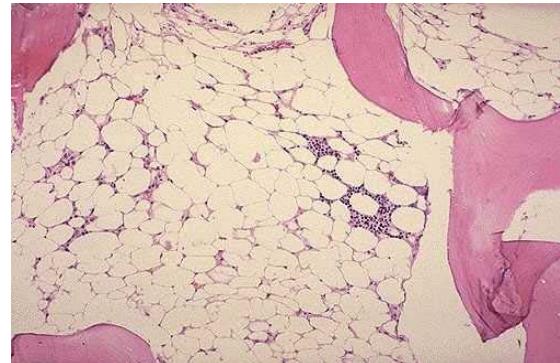
BM Bx – BM aspiration is easy; since marrow soft

hypocellular

More fat cells

Patchy cellular areas – lymphocytes, plasma cells

Megakaryocytes almost absent

**Why is S. ferritin level high in inflammatory disorders?**

S. ferritin give falsely high value if – co-existing infection, inflammatory disorder, during febrile illnesses, acute & chronic liver disease and acute leukaemia

S. Ferritin is an acute phase protein. Therefore ↑ in above

S.Iron falsely high – after blood Tx, while on iron therapy

Low – CRF with/ w/o dialysis

How would you manage this pt.?

1) Relieve acute symptoms (symptomatic)

- Bed rest
- Prop up
- Give O₂

2) Correct low Hb level

- Blood Tx → indicated for those with marrow failure/ need quick correction
- 1 pack → ↑ Hb by 1g/dL
- Target Hb level -
- Max. blood Tx per day
- Indications for blood Tx

3) Correct underlying cause/ palliative Mx

- Iron def. anaemia – i) Haematinics

FeSO₄ 200mg tds for 3 months after the correction of Hb (1 tablet 60mg elemental iron)

Correct therapy will ↑ Hb 1g/dL per week

If intolerant – advise to take with food, change to ferrous gluconate 300mg bd (less Fe)

- ii) Correct underlying blood loss

PUD – H. pylori eradication therapy

Oesophageal varices }
Piles Banding
 sclerotherapy

Space out pregnancies – contraceptive use

Anti-worm treatment – Mabendazole 400mg stat.

- Indications for IV iron – 1) oral intolerance
2) Severe malabsorption
3) IBD

IV preparations

- 1) Iron sorbitol 1.5mg/kg – rpt.d deep IM
- 2) IVI of low molecular wt. iron dextran
Iron sucrose

- B12 – hydroxycobalamin 1000µg IM → repeat to a max. of 5-6mg over 3 weeks

Pernicious anaemia – repeat IM 3 monthly (lifetime supplementation)

Oral Vit B₁₂ 2mg daily – will be absorbed by diffusion w/o IF

- Clinically improve within 48hrs; reticulocytosis seen in 2-3 days
 - Peripheral neuropathy improve in 6-12 months
 - Longstanding spinal cord damage irreversible
- Effects of therapy → hypokalemia, iron deficiency, hyperuricemia (clinical gout unlikely)

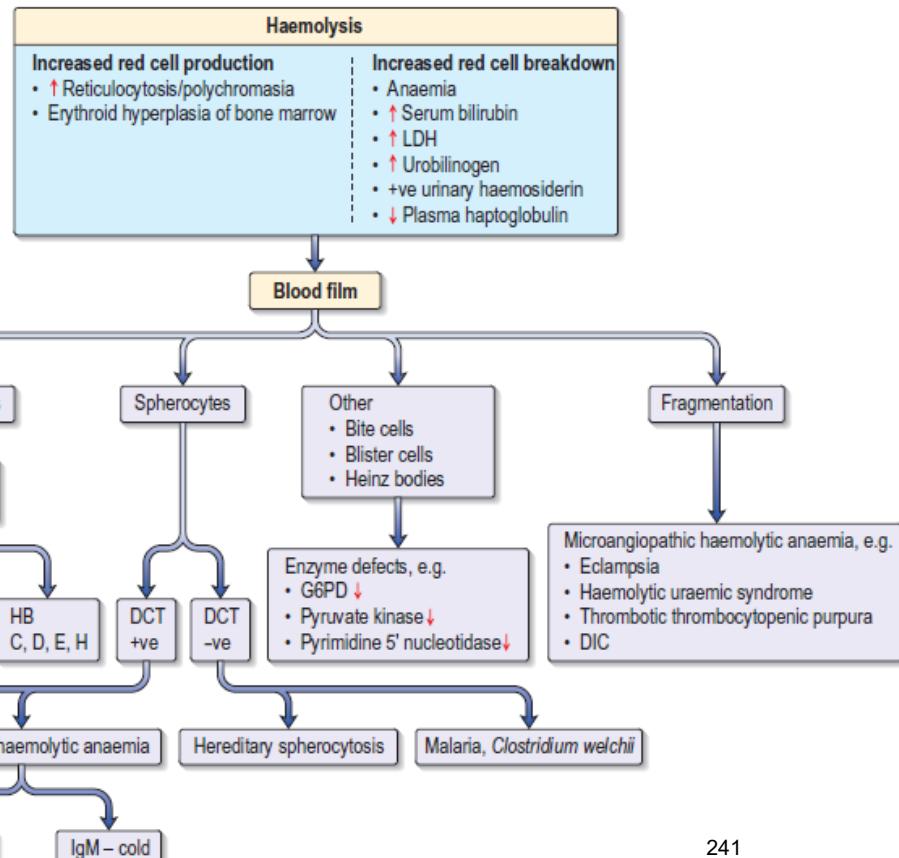
- Folate – o. folic acid 5mg daily for 4 months for stores to replenish

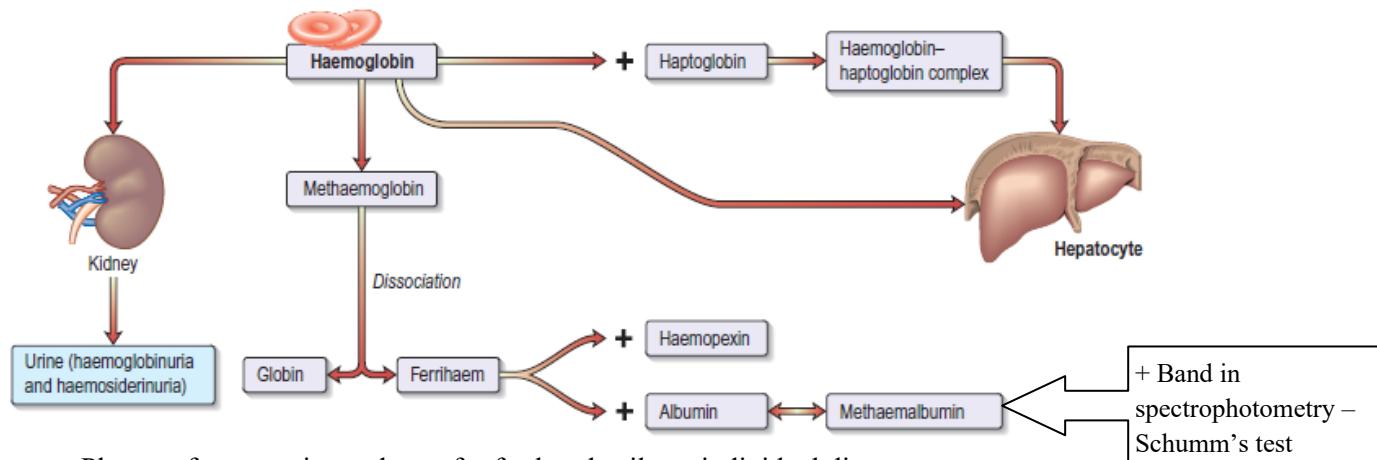
- Anaemia of chronic dis. – treat the cause, recombinant erythropoietin (CRF)

- Sideroblastic anaemia – withdraw causative drugs and alcohol
Some – pyridoxine, folate supplement

- Haemolysis
 - Ix the cause
 - Treat

DCT – direct coomb's





Please refer anaemia paed note for further details on individual diseases

Condition	Mx
HS	Splenectomy Followed by lifelong penicillin prophylaxis Folic acid supplementation
G6PD	Stop offending drug Treat underlying infection Blood Tx during acute haemolysis Splenectomy not helpful
Pyruvate Kinase deficiency	Blood Tx If frequent Tx - splenectomy
Warm AIHA	Prednisolone 1mg/kg daily – remission in 80% Not responding – splenectomy Immunosuppressives – azathioprine and rituximab Blood Tx
Cold AIHA	Treat underlying cause Avoid the cold Some – rituximab (anti CD20) Blood Tx
Paroxysmal nocturnal haemoglobinuria	Leucodepleted blood Tx Longterm anticoagulation – recurrent thrombosis Recombinant humanized monoclonal Ab – Eculizumab (prevent the cleavage of C5 needed to form ‘membrane attack complex’) BM failure – as mentioned

4) Follow up + correct complications

- Iron chelation therapy – desferrioxamine
- Retic count, Hb level

BM failure

- 1) Find cause and correct
- 2) Supportive – give what they lack
Plt. maintain $> 10 \times 10^9$ – below this level risk of spontaneous bleeding
+/- antifibrinolytic therapy (trenexamic acid)

Blood Tx – manage iron overload

Usually with deferasirox (Asunra™)

If febrile and neutropenic – neutrophil < 200 (N/L – 1500)

- Isolate from infective patients (kept among MI pts.)
- Prophylactic broadspectrum AB + oral antifungals
- Granulocyte Tx/ G-CSF

Prognostic factors (2 out of 3)

Neut $< 0.5 \times 10^9$

Retic $< 1\%$

Plt $< 20 \times 10^9$

BM cellularity

- 3) Specific –

Induce remission – freedom from Tx and neutrophil count of $\geq 0.5 \times 10^9$

- Complete (normal counts)/partial
- Agents – 1) Antithymocyte globulin

Expensive ~ 1million

Given in protective isolation, effective in all ages

65% remission

S/E – serum sickness 7days after administration – fever, rash, J.pain

Given with corticosteroids to \downarrow S/E

- 2) cyclosporine +/- ATG

- If 1st course not effective → repeat in 6/12
- Takes around 6/52 to respond
- Most effective in non severe aplastic anaemia

3) Androgens (oxymetholone) – moderate severe AA not responding to immunosupp.

4) Adult pure red cell aplasia – 30% thymoma ass. → thymectomy

Some steroids + cyclosporin

HLA identical BM transplant

- If Sibling available and < 40 yrs, 70-90% successful
- Not recommended over 40 yrs – severe graft vs host disease

Iron deficiency

- Commonest cause
- Only mode of iron loss is via shedding of gut mucosal cells with stored ferritin
- Key regulator of iron absorption – Hepcidin

Sideroblastic anaemia

- Refractory anaemia
- Deformed haem syn. → iron accumulation in mit. Of erythroblasts

Table 8.4 Classification of sideroblastic anaemia

Inherited

X-linked disease – transmitted by females

Acquired

Myelodysplasia

Myeloproliferative disorders

Myeloid leukaemia

Drugs, e.g. isoniazid

Alcohol abuse

Lead toxicity

Other disorders, e.g. rheumatoid arthritis, carcinoma, megaloblastic and haemolytic anaemias

Table 8.2 Factors influencing iron absorption

Haem iron is absorbed better than non-haem iron

Ferrous iron is absorbed better than ferric iron

Gastric acidity helps to keep iron in the ferrous state and soluble in the upper gut

Formation of insoluble complexes with phytate or phosphate decreases iron absorption

Iron absorption is increased with low iron stores and increased erythropoietic activity, e.g. bleeding, haemolysis, high altitude

There is a decreased absorption in iron overload, except in hereditary haemochromatosis, where it is increased

Pernicious anaemia

- AI condition; atrophic gastritis with loss of parietal cell → lack of intrinsic factor and B₁₂
- Common in elderly ♀
- Ass. With other AI disorders (thyroid, vitiligo) and blood group A
- Has a higher incidence of gastric carcinoma – due to achlorhydria

Defect – presence of parietal cell Abs – 90%

Intrinsic factor Ab (specific) – 50% → 2 types

- Blocking Ab – inhibits binding of B₁₂ to IF
- Precipitating Ab – inhibits binding of B₁₂-IF complex to its ileal receptor

Clinical features – anaemia, lemon yellow tinge, glossitis and angular stomatitis

Subacute degeneration of cord – only with v. low s.B₁₂

Symmetrical paresthesia, early loss of vibration and proprioception, progressive weakness, ataxia

Dementia, optic atrophy, delusions and hallucinations

Pathogenesis of megaloblastic anaemia

Inability to methylate deoxyuridine MP



Inability to synthesize DNA



Delayed nuclear maturation in erythroblasts
(megaloblasts)

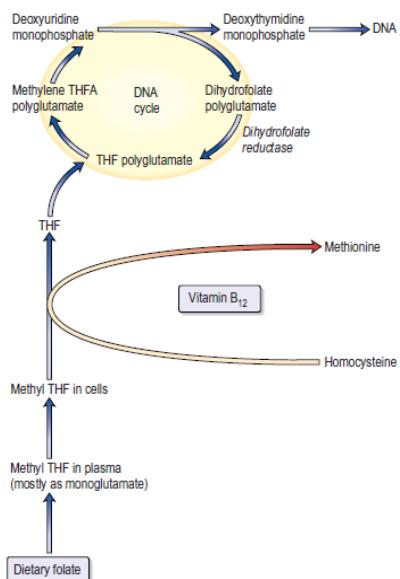


Table 8.6 Causes of folate deficiency

Nutritional (major cause)	Excess utilization
Poor intake	Physiological
Old age	Pregnancy
Poor social conditions	Lactation
Starvation	Prematurity
Alcohol excess (also causes impaired utilization)	Pathological
Poor intake due to anorexia	Haematological disease with excess red cell production, e.g. haemolysis
Gastrointestinal disease, e.g. partial gastrectomy, coeliac disease, Crohn's disease	Malignant disease with increased cell turnover
Cancer	Inflammatory disease
Antifolate drugs	Metabolic disease, e.g. homocystinuria
Anticonvulsants:	Haemodialysis or peritoneal dialysis
Phenytoin	Malabsorption
Primidone	Occurs in small bowel disease, but the effect is minor compared with that of anorexia
Methotrexate	
Pyrimethamine	
Trimethoprim	

Folate deficiency

- Increased loss with cooking
- No body reserves (max 4 months)

What is the defect in HS?

- Deficiency of cell memb. structural proteins → poor support
- → loss of part of the memb. When passing through spleen
- Def. – 1) spectrin - <20%
- 2) ankyrin – 45%
- 3) Band 3 – 20%

Paroxysmal nocturnal haemoglobinuria

- Mutation in a x linked gene PIG-A
- Impaired synthesis of glycosylphosphatidylinositol (GPI)
- Loss of proteins anchored to RC membrane that degrade complements
- Complement mediated haemolysis

Cardinal features

- 1) Haemolysis – precipitated by infec,Sx, Fe therapy
- 2) Hb'uria
- 3) Venous thrombosis – hepatic, mesenteric, cerebral

EPILEPSY

Presenting complaint: Fits

History of presenting complaint

- 1) Is it a seizure/ some thing
- 2) Is it epilepsy/ acute symptomatic seizure (acute encephalopathy state)
- 3) If epilepsy – partial/ secondarily generalized/ generalized
- 4) What triggered it
- 5) 1st episode / recurrence
- 6) Drugs, compliance, S/E
- 7) Ix
- 8) Mx – life style

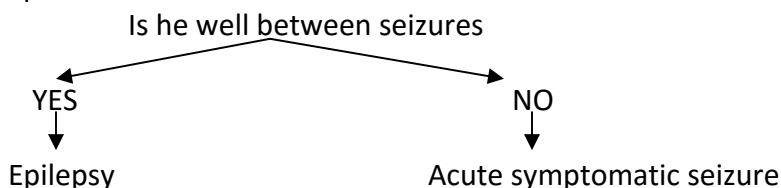
Rx

Description of seizure (according to eye witness)

1. When did the seizure occurred
2. What was she/he doing at the time (sleeping/walking/sitting/standing)
3. Characteristics of the seizure episode
 - Generalized limb jerks
 - Loss of consciousness
 - Frothing from mouth
 - Fallen down/head trauma/burns/fractures
 - Tongue bite (lateral tongue bite)
 - Passage of urine and stools without patient's knowledge
 - Headache/confusion/and amnesia following the episode
4. Duration of the seizure (usually 2-3 mins)
5. Were there recurrent fits if yes, how many
6. Was patient normal in between those fits
7. First aid given at the time of the fit

Differential diagnosis of seizure

1. Exclude other Differential Diagnosis
 - Acute symptomatic seizure



IF NO....

- Encephalitis : Fever with LOC
- Meningitis : Fever, Headache, vomiting, Photophobia
- Cerebral abscess → low grade fever, subacute
 - Hx of bronchiectasis, IE, valvular heart disease, HIV, CSF shunt, splenectomy
- Past History of head trauma, history of previous brain surgeries
- Stroke : Hemiparesis, Difficulty in speaking, PHx of DM, HTN, IHD
- Hypoglycaemia
 - ✓ PHx Of DM
 - ✓ On Oral Hypoglycaemics/ On Insulin
 - ✓ Had meals or not
- Electrolyte abnormalities
 - ✓ Hyponatraemia – Addisons's (Fever, Weight loss, Pigmentation)
 - SIADH (Malignancies, Liver disease)
 - Diuretic therapy
 - ✓ Hypernatraemia – Cushing (Obese, Buffalo hump, Striae)
 - ✓ Increase Urea : Renal failure (Oliguria/polyuria/frothy urine/confusion)
 - ✓ Increase serum creatinine : Renal failure (Oliguria/polyuria/frothy urine)
 - ✓ Hypocalcaemia (Liver failure/ Renal failure)
- Intracranial SOL → chronic headache, early morning headache worsening with LSCS
 - Visual impairments, behavioural changes
 - FHx of brain CA
- SAH : Thunder clap headache, Photophobia
- SDH : Elderly, Chronic alcoholics
- Multiple sclerosis - relapsing and remitting condition

Differentiating pseudo seizures from epilepsy

Features	Epileptic seizures	Pseudo seizures
Onset	Sudden	May be gradual
Consciousness	Rare	Variable
Pelvic thrusting	Unusual	Usual
Asynchronous limb movements	Unusual	Usual
Body rolling	Unusual	Usual
Cyanosis	May occur	Unusual
Tongue biting	Typical lateral	Tip of the tongue
Duration	Seconds/mins	Often prolonged
Gaze aversion	Unusual	Usual
Resistance to passive limb movements or eye opening	Unusual	Usual
Post ictal drowsiness	Usual	Unusual
Induced by suggestion	Does not occur	May occur
Ictal EEG abnormality	May occur	Normal
Environment	Any	Often in front of a crowd

Pseudo-seizures

- Usually females
- With a history of sexual or child abuse
- Emotional situation/In front of an audience

Differentiating syncope from seizures

Features	Epileptic seizure	Vasovagal syncope
Precipitating factors	Sleep deprivation Blinking lights	Prolong standing in hot environment
Posture	Any posture	Only in upright posture
Pallor and sweating	Unusual	Typical
Onset	Sudden	Gradual
Lateral tongue biting	Usual	Unusual
Incontinence	Usual	Unusual
Unconsciousness	Minutes	Seconds
Recovery	Slow	Immediately after lying supine
Post ictal drowsiness	Usual	Unusual

– Gradual onset

- Vasovagal – following prolonged periods of standing, stress
- Cardiogenic - ↑↑ emotion
- Have time to tell someone/ sit / park the car if driving usually
- Syncope – cold clammy peripheries
 - Pale, hypotensive
 - Vasovagal – bradycardia

Epileptic seizure

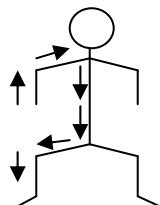
Past episodes

On anti epileptics/Diagnosis cards

- Prodrome - (Idea/insight that they are going to have a seizure) lasts for about hours
 - Unexplainable hunger, irritability, fatigue, euphoria
- Aura
 - ✓ Only on partial seizures
 - ✓ 30min before seizure
 - ✓ Flashing lights/Gustatory sweating/Epigastric sensation going up/Unusual fear/Sounds
 - ✓ Déjà vu(Feeling of already seen) & Jamais vu (Being in a previously lived place) seen in temporal lobe epilepsy(Complex partial)
 - ✓ Light headedness/blurring of vision darkness-(syncope)
 - ✓ Palpitations/breathlessness-(cardiac conditions)

- Ictus

- ✓ Abrupt no time to get support
- ✓ Tonic – Cry, Extensor posturing, Incontinence, Injury, Fall, Drooling of saliva
- ✓ Clonic – 1 to 2 mins limb jerks
- ✓ TLE – Automatism(Oro facial/Lip marking, Motor, Verbal), LOC
- ✓ Partial seizure
 - Jacksonian march/sensory

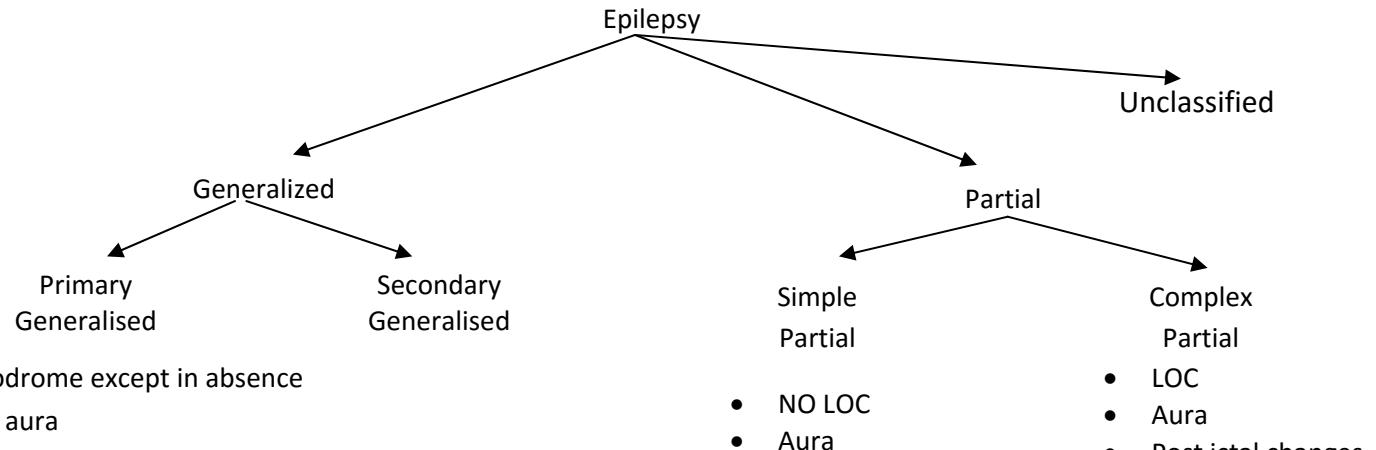


Cross over after spreading to same side
Giving todds paralysis (post ictal)

Flaccidity, faecal/urinary incontinence

- Post ictal changes

- ✓ Can last hours for days
- ✓ Flaccid, Drowsiness, Headache, Body aches, Focal deficits (Todd paralysis)
- ✓ **Beaten up feeling**



- Prodrome except in absence

- No aura

- Types

- ✓ GTCS – No post ictal changes
- ✓ Absence – No post ictal changes
- ✓ Juvenile myoclonic – Post ictal changes

- NO LOC
- Aura

Partial – Aura

Focal onset of jerks

Jacksonian march – Cross over after spreading on one side

Begin on the side opposite epileptic focus

Motor/ somatic sensation - tingling

Partial → No LOC – simple
LOC/ Altered – complex

Generalized → No aura, tonic clonic, LOC
No focal paralysis/neurological deficit

Type → Absence (Petit mal) – Children
No prodrome, aura or post-ictal state
Sudden LOC, cessation of motor activity, stares blankly
No loss of tone/falling
Eye lids twitch, lip smacking, few mus. Jerks of hands

Tonic → With altered LOC
Intensive stiffening

Clonic → Repetitive clonic jerking, often asymmetrical and irregular

Myoclonus → sudden isolated muscle jerks, whole body/group of muscles
Eg:- cause to drop things
Episodes – single/ clusters
Usually following sleep deprivation, alcohol
Onset – sleep deprivation
No aura
Young onset – 15-25yrs

Atonic – sudden loss of tone (generalized/ side) & LOC

Site of origin → **Frontal** - Aura – strange smells, Pilo erection
Conjugate gaze & head deviates away from epileptic focus -**Adversive seizure**
Behavioural change

Temporal – Panic attacks with over-breathing
Auditory – Unformed – hissing, buzzing, ringing (simple partial)
Formed – music (complex)
Visual – formed – animals, houses, and trees
Deja'vu, Jamais'vu
Autonomic - sweating, flushing/pallor, epigastric sensations
Automatism – chewing, wetting lips, lip smacking, picking at clothes
Speech arrest
Sleepy / dreamy state

Parietal – sensory disturbances – tingling sensation in contralat. face/side

Occiput – visual – unformed – flashes of light, scotomas, U/L or B/L blurring
Crude visual shapes

Trigger factors for epilepsy

- Sleep deprivation
- Hunger
- Alcohol Withdrawal

Dependence – C – need to cut down A – annoyed G – guilt E- eye opener

Seizure with withdrawal

Withdrawal symptoms – anxiety, irritability, tremors, confusion, nausea

Sweating, poor sleep

- Fatigue/exercise
- Reflex seizure (Fits only occur in bathing, Rubi cube, Arrhythmic & watching TV)
- Flickering lights
- Any illness/medical procedures
- Menstruation (Cataminal epilepsy)
- Poor drug compliance
- Social stress
- Rx – TCA, MAO (-), Nalidixic acid, Propofol (anaesthetic), amphetamines, phenothiazine
- Emotional stress, hypoglycemia, electrolyte abnormality

Drugs taking

- Drug compliance
- Side effects of the drugs
 - Phenobarbitone (White colour round tablet)
 - ✓ Enhance GABA function
 - ✓ Acathesia
 - ✓ Problems of studying
 - Phenytoin (Like Madatiya seed)
 - ✓ Membrane stabilizer
 - ✓ Potent hepatic inducer (zero order kinetics)
 - ✓ Cognitive impairment
 - ✓ Sedation
 - ✓ Cerebellar ataxia
 - ✓ Gum hypertrophy
 - ✓ Hirsutism
 - ✓ Coarsening of facial features
 - ✓ Anaemia(Megaloblastic) & Osteomalacia (Folate & Vit D are co-factors for phenytoin hydroxylation)
 - Carbamazepine (White colour round tablet divided into 4)
 - ✓ Mechanism is not well understood
 - ✓ Hepatic enzyme inducer
 - ✓ Rashes – Steven Johnson syndrome
 - ✓ Visual disturbances (Blurring, diplopia)
 - ✓ Leukopenia
 - ✓ Drowsiness

- ✓ Megaloblastic anaemia & Osteomalacia
 - ✓ Cognitive impairment (Less than phenytoin)
- Sodium Valproate
 - ✓ Inhibit the GABA transaminase which breaks down GABA
 - ✓ Protein bound
 - ✓ Enzyme inhibitor
 - ✓ Gastrointestinal disturbances (Anorexia)
 - ✓ Thrombocytopenia
 - ✓ Hair loss (Curly hair)
 - ✓ Impaired liver function tests
- Lamotrigine
 - ✓ In GTCS and partial epilepsy not responding to other medications
- Ethosuximide
 - ✓ Absence seizures
- Vigabatrin
 - ✓ Irreversibly inhibit GABA transaminase
 - ✓ For partial, 2ry generalized
 - ✓ Infantile spasms
- Ask whether she is on OCP or pregnant
 - All antiepileptics are teratogenic
 - OCP effect is reduced in all antiepileptics except sodium valproate & lamotrigine)
 - Ask to use barrier method

PMHx

- Previous similar type episodes and hospital admissions
 - Diagnosed when, Ix done
 - Frequency of seizures, initial drug treatments
 - Clinic follow up
- DM, HT, Liver disease, Renal disease
- Encephalitis or meningitis stroke
- Prolong febrile seizures

PSHx

- Intracranial surgeries
- Head injuries
- Congenital heart diseases

Drug Hx

- current drug regime – dose, frequency ,compliance and adverse effects
 - Antihypertensive drugs
 - Antidepressants (TCA)
- } Associated with syncope

Family history

- Faculty of Medicine - University of Kelaniya
- Fits/Epilepsy

Social history

- Occupation Risky – driver/ mason/ coconut plucker/ security officer/ machine operator
Night shifts
Other workers aware of his condition
- Impact on the life style and the family
- Alcohol drug abuse
- Sexual or physical abuse-(non epileptic attacks)
- Danger sites in the house (harth, risky well...ect.)
- Swimming, bathing – unprotected well
- Mode of travel, meals on time, housing – staircases
- Knowledge of the family members regarding the illness

EXAMINATION

Underlying illness – fever, neck stiffness, kernig's test

Head – hydrocephalus, shunt, craniotomy

Pallor

NS - cranial nerve palsy

Fundi – papilloedema

MS – optic atrophy

Focal neurological signs – hemiparesis

CVS – pulse – irregularly irregular (AF)

Murmur – MS, aneurysm

♥ failure

RS – aspiration pneumonia

DISCUSSION

What are the initial investigations?

- EEG – 1) To confirm any seizure activity
2) Any focal origin
3) Exclude encephalopathic state

When performing the procedure artifacts of eye movements should be avoided using eye opening , eye closing and blinking procedure

EEG only supportive not diagnostic

Epileptiform abnormalities may seen in EEG only about 50% of patients and 1% of normal population

This should be performed at least within 4 weeks since the event

Basic – FBC – infection
CBS – hypoglycemia
BU/SE, S.Ca, S. Mg – uraemia, electrolyte abnormality
S. Creatinine
LFT
12 lead ECG (as cardiac arrhythmias can mimic seizure)
Non contrast CT – chronic SDH

Neuroimaging – MRI ; I^o - 1) late onset epilepsy >20yrs
2) Partial seizures
3) Focal neurological deficits
4) Focal EEG changes- Slowing> spikes
5) Poor control despite good drug compliance
6) ↑ ICP

What do you expect? (Focal lesions causing seizures)

- 1) TLE → Hippocampal sclerosis
- 2) SOL
- 3) Scar tissue
- 4) Heterotopia (the displacement of an organ from its normal position)

Neuro psychological assessment should be done those with

- Learning difficulty
- Cognitive dysfunction regarding language and memory

When to start Rx?

AED therapy should be started on the recommendation of a specialist

Therapy should only be initiated once the diagnosis of epilepsy is confirmed

Rx should generally commenced after documented 2nd seizure

Rx consider at 1st seizure if,

- Patient has neurological deficit
- EEG shows unequivocal epileptic activity
- Brain image shows a structural abnormality

AED therapy always commenced with a single drug

What advise will you give?

All drugs once started need to be continued for 2yrs

Abrupt withdrawal can precipitate status epilepticus – do not discontinue for any reason

Eg:- inter-current illness w/o medical advise

Ask to avoid – driving – Heavy vehicles – NEVER

Own car – avoid till fit free for 2-3yrs

Swimming, contact sports, precipitant factors

S/E – esp. Steven Johnson Xn, anaemia, liver toxicity

If 1st mono-therapy fails

If seizure continues despite the maximally tolerated dose of 1st AED

- Review the diagnosis
- Review seizure type/syndrome
- Review dosage and frequency
- Review the compliance

Acceptable combinations of AED treatment

- Carbamazepine + valporate (leads to an enhanced therapeutic efficacy)
- Valporate + ethosuximide (control absent seizures which is not controlled by either drug alone)
- Valporate + clonazepam (used for myoclonic seizures)

Combinations of AED should be avoided

- Carbamazepine + phenytoin (enzyme inducers cause reduction of drug levels of each others)
- Carbamazepine + lamotrigine (enhance each other's side effects)

When to consider Rx withdrawal?

- Withdrawal of AED therapy considered only after seizure free period of at least 3 yrs
- Rx withdrawn over period of 6 months
- If relapse during withdrawal → continue Rx for another 2yrs

Decided on – 1) type of seizure – spontaneously remitting – Absence seizure (Petit mal)
Benign rolandic epilepsy

Non remitting – Juvenile myoclonic epilepsy
Major seizures – easily controllable

- 2) Time of remission – early → better
- 3) Less no. of Rx required for remission
- 4) Associated neurological deficit
- 5) Pt's preference
- 6) Abnormal EEG abnormalities

Increased seizure recurrence following withdrawal of treatment

- Age >16 yrs
- Seizure require > one AED to control
- Recurrence of seizures after starting AED therapy
- Presence of multiple seizure types
- Underlying neurological disorder
- Persistent abnormal EEG
- Longer period of active disease prior to seizure control

Non pharmacological management of epilepsy

- Psychological interventions –relaxation therapy/CBT
- Ketogenic diet with high fat and low CHO
- Vagus nerve stimulation (drug resistant forms)
- Surgery (temporal lobe epilepsy due to mesial temporal lobe sclerosis)

Management of status epilepticus

Epileptic activity persist >30 or more form of continuation seizure or repetitive attacks of seizures without regaining consciousness.

Generally convulsive seizure (tonic clonic)

But non convulsive form (EEG abnormal discharge do not follow convulsion)

Management

Early status epilepsy (1st 30 min)

General

- Secure airway and give oxygen
- Left lateral position
- Suck-out secretions
- Remove objects which can harm the patient
- Asses cardiopulmonary function (pulse, BP, O₂ saturation)
- Establish IV access and take blood for
 - Urgent blood sugar
 - S. electrolytes
 - BU
 - Liver function
 - Calcium and magnesium
 - FBC and clotting profile
- Give 50ml of 50% dextrose with IV thiamin (250mg) if suggestion of alcohol abuse
- Treat acidosis if present
- Consider possibility of non epileptic states

Emergency medication

- Lorazepam IV (0.1mg/kg) bolus -1st choice
- Midazolam IV (0.1-0.3mg/kg) <4mg/min rate
- Diazepam IV (0.2mg/kg usually 10mg) <5mg/min

May be repeated once if seizure recur within 10-15 mins

Start regular AED at this stage

Emergency medication

- Lorazepam iv: 4mg (0.07mg/kg up to 4 mg), rate of injection is not crucial or
- Diazepam iv: 10 mg (0.2mg/kg up to 10mg), rate not exceeding 5mg/min or
- Diazepam rectally: 10 -30 mg or
- Midazolam: buccal: 10 mg, instilled into sublingual area.

If at home, give diazepam rectally (10-30mg), and admit to nearest hospital.

Establish status (next 30-60min)

Request ICU bed and inform anesthetist

Search for metabolic complications like acidosis/electrolyte abnormalities

Emergency medications

- Phenytoin IV infusion 15mg/kg at 50mg/min rate (15-20min) or
- Phenobarbitone IV bolus 10mg/kg in a rate of 100mg/min (5-7 min)

ECG monitoring

Patient managed in ICU

Refractory status epilepticus

Once status continued for 60-90 min with previous therapy

ICU setting is mandatory

General anesthesia and ventilation

Propofol/thiopentone

Pregnancy and epilepsy

- Pregnancy – worsen epilepsy in 1/3rd
 - Major seizures → anoxia + metabolic disorder in fetus
- Anti epileptics → fetal malformations (neural tube defects, microcephaly, growth retardation)
- Plan pregnancy – control the fits → tail off Rx → get preg.
- Folic acid administration to all ♀ with child bearing age
- DOC – carbamazepine
- If gets pregnant while on drugs, continue Rx, meet a doctor immediately
- Continue breastfeeding with anti epileptic Rx
- Advise to watch out for effects in the child

AED therapy for different seizure types

Seizure type	First choice	Second choice	Third choice or Add on therapy
Partial seizures (simple & complex)	Carbamazepine	Valproate, phenytoin	Lamotrigine, topiramate, clobazam
Generalised seizures Second choice depends on the seizure type • Tonic clonic/ clonic • Absence seizures • Myoclonic seizures Unclassified seizures • Under the age of 25 years • Over the age of 25 years	Valproate	Carbamazepine, phenytoin Ethosuximide Clonazepam	Topiramate, lamotrigine, clobazam, phenobarbitone Lamotrigine, clobazam, clonazepam Topiramate, lamotrigine

Haemoptysis

Presenting complaint- Haemoptysis

DD

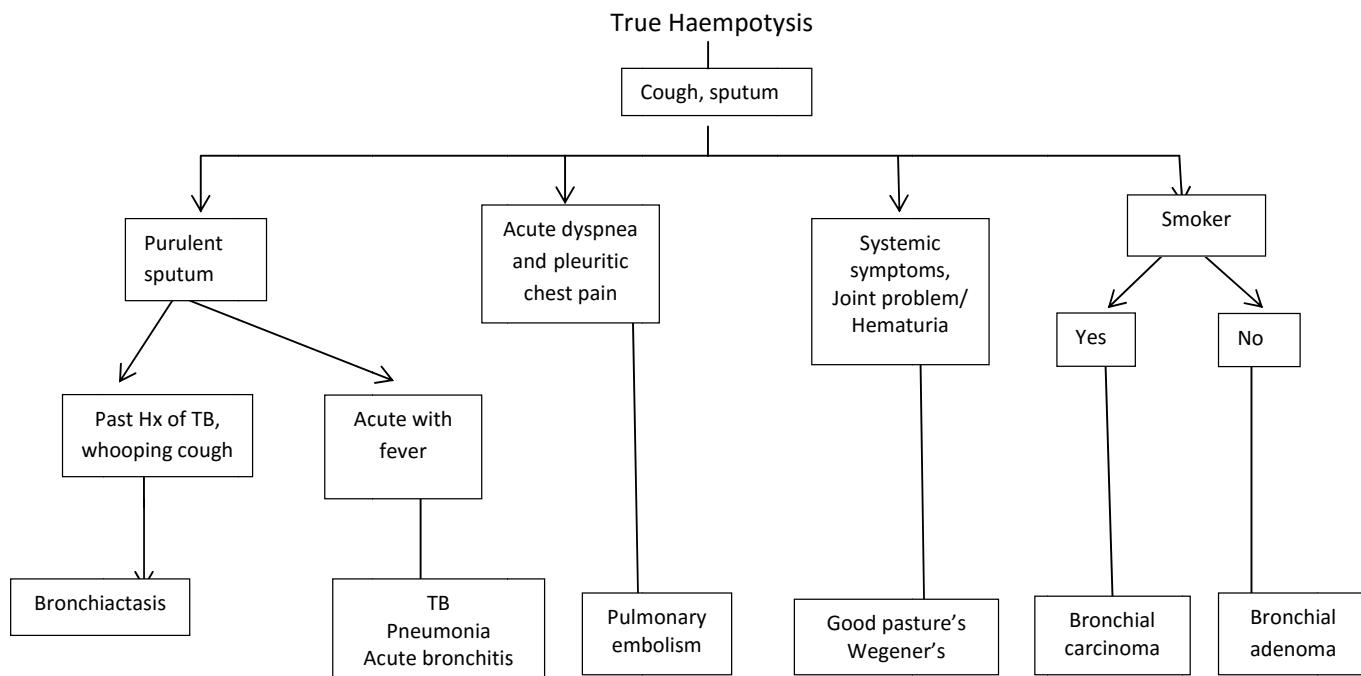
- 1) Bronchiectasis
- 2) Bronchial carcinoma
- 3) TB
- 4) Lung abscess
- 5) Pulmonary embolism

History of presenting complaint-

1) What haemoptysis

- **Nose, mouth, gums- HT, trauma**
- **GI bleed** -gastritis features, Rx for peptic ulcers, haematemesis, Banding (altered color due to gastric acid)
- **Bleeding disorders/vasculitis**- ITP, dengue, Wegener's
-Ass with cough and sputum, bright red in color, froth= True haemoptysis

2) Think DD and ask specific questions-

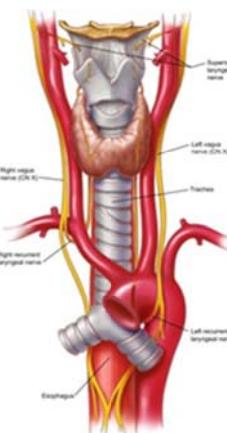


2) Onset
Duration
Progression

Haemoptysis with purulent sputum for several years with LRTI- **Bronchiectasis**
Haemoptysis for week or more- **Lung ca, TB** (in Pneumonia – Rusty sputum)

3) Amount

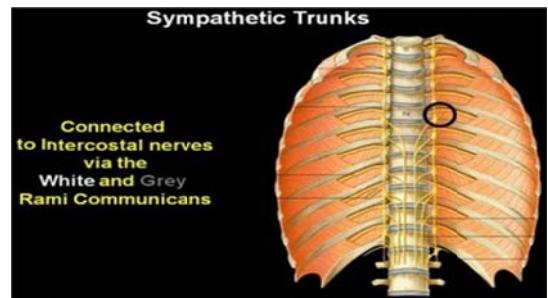
Streaking of clear sputum with blood- **Lung ca**
Mixed with copious purulent sputum-**Bronchiectasis**
Diffuse staining (pink froth) - **Pulmonary oedema**
Massive haemoptysis- **TB, bronchiectasis**
Foul smelling- **Bronchiectasis, lung abscess**



DISEASE	SPECIFIC POINTS IN THE HISTORY
Pulmonary TB	Long standing fever, night sweats, anorexia and malaise Past Hx or contact Hx of TB Features of disseminated TB - Bone, bowel, brain
Bronchial carcinoma	<p>1. smoking</p> <p>2. Associated loss of appetite and loss of weight</p> <p>3. Recurrent LRTI, SOB, past Hx of malignancy</p> <p>4. Features of local spread- Pancoast tumor-small muscle wasting of hands Drooping of eye lid (Horner's Xn) Hoarseness of voice(recurrent laryngeal nerve) Puffiness of the face and prominent veins in the neck (SVC obstruction- Mediastinal lymphadenopathy) Headache, oedema of face, arm and chest, raised JVP Collateral chest veins Pericardium – effusion – chest pain, SOB, abdominal fullness Malignant dysrhythmias - episodic palpitations Progressive dysphagia – oesophageal involvement</p> <p>5. Distant spread-LN-Neck lumps noticed by the patient LIVER-Right hypochondrial pain and discomfort BONE-bone pain, history of # following minor trauma, difficulty in walking BRAIN- Early morning headache + vomiting, adult onset seizures, personality changes</p> <p>6. Paraneoplastic syndromes</p> <p>i. Neurological-seizures, imbalance when walking(cerebellar degeneration) Progressive difficulty in climbing steps (prox. Myopathy) Paresthesia, numbness (peripheral neuropathy) Muscle weakness improving with working (Lambert Eaton myasthenic syndrome)</p> <p>ii. Endocrine –edema, drowsiness, confusion (SIADH) Confusion and constipation (hypercalcemia) Episodes of sweating, hunger & faintishness (Hypoglycemia) Cushing's symptoms (acne, hirsutism, amenorrhea, pigmentation, obesity) – ACTH secreting tumour</p> <p>iii. Haematological – Anaemia and blood Tx Painful migrating pain over LL veins (thrombophlebitis migrans)</p> <p>iv. Carcinoid syndrome (due to serotonin) – flushing of skin, diarrhea, abdominal cramps</p> <p>v. Thyrotoxicosis</p> <p>7. Secondaries from a primary tumor</p> <p>Prostate – hesitancy, poor flow, Haematuria Ovary – post menopausal bleeding, abdominal distension Cervix – post-coital bleeding, discharge, promiscuity Stomach – epigastric pain following meals Bone Breast</p>
bronchiectasis	Copious amount of sputum with halitosis, on and off haemoptysis Symptoms due to general ill health are absent Intermittent night sweats Chest pain Recurrent febrile episodes+/- anorexia, LOW
Lung abscess	Foul smell Swinging fever

Past medical history-

- Post pneumonic, measles, pertussis, Tuberculosis
 - Bronchiectasis
- Mechanical bronchial obstruction
 - TB, Carcinoma, Nodal compression, sarcoidosis



- Recurrent chest infections since childhood-cystic fibrosis(dense/inspissated mucus), kartegener's syndrome, Allergic bronchopulmonary aspergillosis, Gamma globulin deficiency
- HIV (immunocompromised state)-TB, bronchiectasis
 - Past history of breast, kidney, GIT
 - Prostate/cervix/ovarian carcinoma

Drug history

- Anti coagulant therapy

Social history

- Detailed smoking history
- Occupational history
 - Asbestos
 - Chromium
 - Petroleum
 - Coal combustion
- How the disease affects his day today life
- Attitude towards the disease

Examination

General examination

- Febrile, Cachexia, pallor, icterus in the eyes
- Horner's syndrome
- Examine for cervical lymphadenopathy
- Hands for clubbing, hypertrophic pulmonary osteoarthropathy (clubbing + wrist/ankle+periostitis + gynaecomastia)
- Wasting of the small muscles of the hand : pan coast tumor-Apical tumour locally invading brachial plexus (C8, T1, T2)
- kyphoscoliosis
- Ankle oedema

Clubbing

- Bronchial Ca
- Fibrosing alveolitis
- Suppurative lung conditions-
 - Bronchiectasis
 - Empyema
 - Lung abscess

Respiratory system

- Reduced chest expansion –phrenic nerve involvement
- Evidence of pleural effusion-stony dull, fremitus↓ , resonance↓ , air entry↓ – (malignancy, TB)
- Bilateral basal coarse crepts - due to gravitation tendency to accumulate secretions - bronchiectasis
- Lung collapse



Cardiovascular system

Features of aortic stenosis
Apex beat (dextrocardia)

Abdomen

Hepatomegaly
Ascites

CNS-

Cerebellar signs
LL – sensory, power – Peripheral neuropathy
Bone metasasis - LL weakness

Discussion

Can you explain the pathophysiology of hemoptysis in this patient?

Lung has dual blood supply.

–Pulmonary arterial circulation : low pressure, gas exchange.

Pulmonary hypertension in MS, bronchiectasis, pulmonary embolism

–Bronchial arteries : high pressure, supply nutrients to lung parenchyma and major airways.
(inflammation erosion – vasculitis (pulmonary hemorrhages), bronchitis, pneumonia (necrosis of adjacent bronchial vessels), TB (weak vessels due to cavitation)

Malignant invasion- bronchial carcinoma (direct invasion)

rupture of pulmonary artery aneurysm

Bronchiectasis: Abnormal persistent dilatation of the bronchial tree

Mild disease

What are the complications of bronchiectasis?

Pulmonary

1. Lung Abscess
- Pneumonia
- Empyema
2. Chronic Air Flow Obstruction
3. Massive Haemoptysis
4. Respiratory Failure
5. Pulmonary Hypertension
- Cor-pulmonale

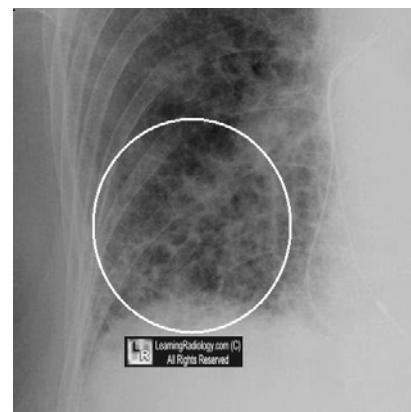
Extrapulmonary

- Septicemia
- Amyloidosis
- Cerebral Abscess

What are the causes for bronchiectasis?

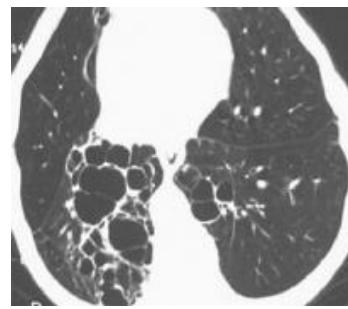
- Allergic bronchopulmonary aspergillosis
- Gamma globulin deficiency
- Immotile cilia syndrome-(kartagener's syndrome)
- Cystic fibrosis- Inspissated mucus(dense mucus)
- Granuloma and fibrosis-Tuberculosis,Sarcoidosis
- Immunological overresponse-
- Immune deficiency-HIV

Common sites-left lower lobe and lingual lobe



What are the possibilities of secondary lung carcinoma?

- 1) Source: breast, kidney, GIT, Prostate, cervix/ovary
- 2) Parenchymal deposits, Asymptomatic
- 3) Lymphangitis carcinomatosa



Investigations

Bronchiectasis

CXR - Cystic changes (characteristic-bunch of grapes and tramline, glove finger shadows app)

Bilateral basal involvement

Evidence of infection- Lobar, patchy

Hyperinflated lungs

Dextrocardia, situs in versus- Kartegener's

FBC / ESR-Underlying infection

Sputum culture-Isolation

ECG-chest pain

Dextrocardia

CT – high resolution --> **confirms the diagnosis**

Lung function tests – severity

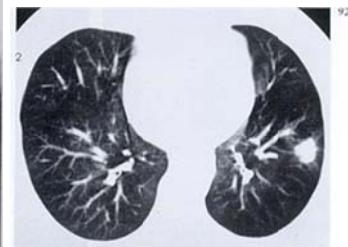
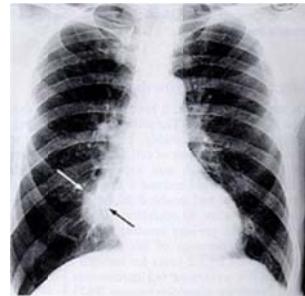
ABG-look for the severity

Ix to look for the causes

sweat sodium

Serum immunoglobulin levels

X ray sinuses etc.



Bronchial carcinoma

What are the investigations you would like to do in this patient?

1. **CXR** - This is the first line investigation-look for a solitary lesion appearing in the chest x ray, pleural effusion, hilar lymphadenopathy
2. **CXR/CT thorax: (usually confirms the disease)**
 - Rounded shadow, spiculated margin, mass at least 1-2 cm in size
 - Widening and loss of sharp angle of carina – Enlarged Mediastinal LN, Vocal cord paresis
3. Sputum – pyogenic culture/ AFB & culture/ cytology
4. CT scan – staging the disease – lung, liver, adrenal gl., brain mets
5. Histological classification of the tumour
 - If peripheral lesion – USS guided FNAC of mass + LN/ direct aspiration
 - Bronchoscopic guided Bx/ bronchial washings + brushings
 - Inoperable Bronchoscopic features – if involving 1st 2cm of main bronchus
6. Haematological – FBC - ↓ Hb – microcytic/ Normocytic
7. Biochemical – RBS - ↓/ N/L
 - s. Ca - ↑
 - Liver function tests
8. Lung function tests – FEV1 > 1L (lobectomy)
FEV1 >1.5L needed for total pneumonectomy

Tuberculosis

CXR

Non specific but very useful (suspicious x ray should never be treated without sputum examination)

Certain features - strongly suggestive

Upper zone - patchy nodular shadow unilateral bilateral

Cavitation - specially >1 calcified shadows

Diffuse small nodular opacities – miliary

Normal x ray - endo bronchial TB

Microscopic examination for AFB – sputum (culture)

Specific, less sensitive, can repeat

Other samples

Biopsy – bronchial – bronchoscope

trans tracheal aspiration

broncho alveolar lavage

New diagnostic techniques

Microbiology –

Polymerase chain reaction (PCR)

Mantoux test is a test for screening

Management

Bronchiactasis

Specific Antibiotics

Oral/IV – may need prolonged treatment

- Mainly Gram +ve
- Later Gram +ve and Gram -ve

Start with

Mild	{	amoxyillin or cephalosporin or erythromycin
Severe	{	IV Quinolone IV Co-amoxiclav IV gentamicin

Prognosis- Effective usage of antibiotics has improved the prognosis.

* Need sputum culture

* Prolonged Rx

1. Bronchodilators
 - Salbutamol
 - Theophyllin
2. Mucolytics
 - Expectorants
3. Analgesics
 - NSAID For Pleurisy
4. Diuretics
 - For Oedema in Cor Pul.
6. O2 Inhalation
 - Respiratory Failure

7. PHYSIOTHERAPY

deep cough

postural drainage. +/- percussion

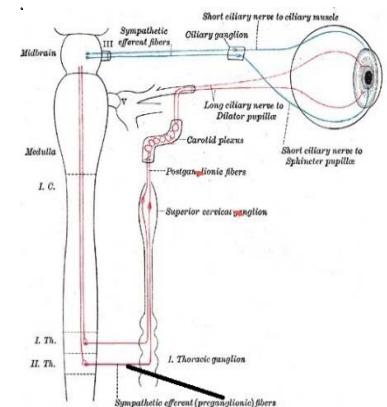
8. SURGERY(for young patient)

bronchiectasis localized to one lobe or segment.

Preparation : CT chest, Lung function test - For evaluation

What's horner's syndrome?

combination of drooping of the eyelid (ptosis) and constriction of the pupil (miosis), sometimes accompanied by decreased sweating of the face on the same side; redness of the conjunctiva of the eye is often also present. It indicates a problem with the sympathetic nervous system.



Pathophysiology of horner's syndrome?

lymph nodes of bronchial carcinoma compress the second order neurons of the sympathetic outflow to the eye. It's a preganglionic lesion.

Management of bronchial carcinoma

The management of bronchial carcinoma depends on the stage of the tumor and histological classification

Bronchial ca

Small cell ca

- Poor prognosis
- Proximal large airways
- Mediastinal involvement
- Early extra-thoracic spread
- Strong association with smoking
- Chemosensitive

Non-small cell

- Adeno carcinoma(40%)
- Peripheral lung masses
 - Metastasize early
- Squamous cell CA(25%)
- Proximal large airways
 - Metastasize late
- Large cell CA (10%)
- Poorly differentiated
 - Early distant mets

Small Cell Lung Cancer SCLC

- The staging of small-cell lung cancer is divided into **limited** and **extensive disease** according to whether or not it is confined to a single anatomical area or radiation field.
- Systemic therapy is the primary therapeutic modality because of the usually disseminated nature of the disease.
- Disseminated disease at presentation (micrometastases)
- Chemotherapy sensitive, doubles survival from 3 to 6 months
- Combination regimens: vincristine, cyclophosphamide, doxorubicin, MTX, etoposide

Non small cell carcinoma

- Surgery can be curative in non-small-cell lung cancer
- Adjuvant chemotherapy with radiotherapy improves response rate and extends median survival in non-small-cell cancer
- Depends on the metastatic spread
- If so palliation only

Non small cell = surgery for cure
radiation for palliation
Small cell = chemotherapy for palliation
Surgery

Neo- adjuvant chemotherapy

- neo-adjuvant chemotherapy may downstage tumours to render them operable and may also improve 5-year survival ,in patients whose tumours are operable at presentation.

Radiotherapy

- Curative – in slow growing small squamous cell CA
- Contraindication – poor lung function
- Complications – radiation pneumonitis (aft. 3months, only part exposed to it)
 - Radiation fibrosis (whole lung in 1year)
 - Not major problems!!

How do you know about the metastatic spread?

clinically

Local invasion: hoarse voice,
SVCO, Pancoast, Horner's,
mediastinal glands, pleural
effusion

Secondary spread:

By investigations

Bronchoscopy-

Vocal cord movement

Tumour close to carina

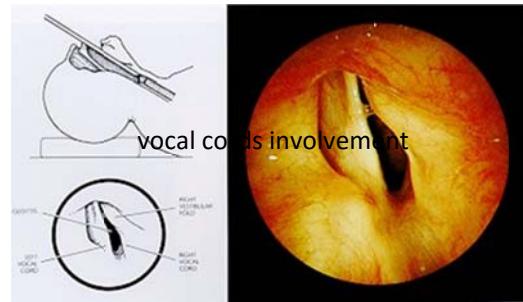
Radionuclide bone scan-

CXR/CT-

Mediastinal adenopathy, pleural effusion

CT brain and abdomen-(liver & adrenals)

Bone pain



When/how to offer palliation?

Palliation of symptoms

Local radiotherapy for bone pain, SVCO, haemoptysis

How to offer palliation?

- Anti pyretics
- Analgesics for pain relief – morphine/ diamorphine SR bds
 - Continuous pump infusion – opiates
- Adequate hydration
- Adequate nutrition, appetite improvement – daily oral prednisolone
- Rectify anaemia
- Look for and treat candidiasis and other oral infections
- Constipation due to opiates – laxatives
- Short course of radiotherapy – palliative
 - To ↓ bone pain, severe cough, haemoptysis
- Counsel Pt. and relatives

Management of Tuberculosis

Kill multiplying bacteria - INAH

Treat persisters (in the macrophages)- rifampicin + pyracinamide

Prevent emergence of drug resistance- ethambutol or streptomycin

1st line-INAH, rifampicin, ethambutol, pyracinamide, streptomycin

2nd line-kanamycin, ofloxacin, ciprofloxacin

Drug and mechanism of action	dose	Side effects
Isoniacid Bacteriocidal and bacteriostatic effect	5mg/kg	Liver toxicity Peripheral neuropathy Mental disturbances Inco-ordination Drug interaction-enzyme inhibitor
Rifampicin Bactericidal effect	10mg/kg	Liver toxicity Orange discolouration of body secretions Skin rashes, thrombocytopenia Oral contraceptive failure
Pyracinamide Kills intracellular persisters	25mg/kg	Liver toxicity
Ethambutol Bacteriostatic effect	15mg/kg	

Emergency

How to manage massive haemoptysis?

- Admit, give high flow O₂(caution in COPD)
- Monitor pulse/UOP/pulse oximetry
- Put pt in recovery position(make sure if pt. lie on side of the affected lung)
- Gain IV access with wide bore cannula, DT and cross match
- Give N/S, if large blood loss give blood ASAP
- Give vit K 5mg IV slowly if pt is on warfarin or liver disease FFP
- If compromised do ABG
- Antibiotics if evidence of infection
- Air way compromised-intubate
- Refer if bronchoscopy available

Urgent CXR- may show evidence of underlying disease (bronchiectasis, malignancy, lung abscess)

FBC, coagulation screen, LFTs, fiberoptic bronchoscopy

CT chest

Thyroid diseases – 1) Hypothyroidism

Age, gender, fertility status, residential area

PC

- Weight gain
- Facial and generalized oedema
- Cold intolerance
- Goiter
- Menstrual disturbances

DD

- Hypothyroidism
- Cushing's syndrome
- Acromegaly
- Chronic renal failure

HPC

Describe the presenting feature

- ✓ Onset
- ✓ Duration

Features associated with the presenting complain

- ✓ Malaise and lethargy
- ✓ Tiredness
- ✓ Forgetfulness
- ✓ Weight gain with reduced appetite
- ✓ Puffy face
- ✓ Change in appearance
- ✓ Deep hoarse voice
- ✓ Dry, brittle hair and hair loss
- ✓ Dry skin
- ✓ Goiter
- ✓ Cold intolerance
- ✓ Constipation
- ✓ Menstrual disturbances – Mainly menorrhagia, oligomenorrhea/ amenorrhoea
- ✓ Reduced libido
- ✓ Subfertility
- ✓ Muscle pain] Difficulty in standing from squatting position
- ✓ Muscle weakness] Difficulty in combing hair
- ✓ Joint pain
- ✓ Depression (mainly) / Psychosis
- ✓ Deafness

Complications

- ✓ Myxoedema coma
 - Hypoglycaemia
 - Hypothermia
 - hypoventilation
 - Hyponatraemia - Convulsions
 - confusion
 - Coma
 - Heart failure

Aetiology

- ✓ Endemic area for goiters
- ✓ Poor iodine consumption
 - Poor intake of fish and dry fish
 - Wrong techniques when using iodized salt
 - Storing iodized salt in a bottle which is exposed to sun light
 - Heating food after adding of iodized salt
 - Storing the bottle of iodized salt closer to the fire place
- ✓ Drugs causing hypothyroidism
 - Antithyroid drugs
 - Carbimazole, Propylthiouracil, Methimazole
 - Lithium
 - Amiodarone
 - Iodides – In cough mixtures & contrast material
 - Interferone
- ✓ Autoimmune
 - Hx of fever with pain and swelling in the thyroid gland
 - PMHx and FHx of autoimmune diseases
 - Type 1 DM
 - Vitiligo
 - Pernicious anaemia
- ✓ Secondary to a viral infection – Post viral thyroiditis (Sub acute thyroiditis)
 - Pain around the thyroid → radiate to jaw and ears
 - Worsen with swallowing & coughing
 - Fever & other systemic features
- ✓ Secondary to pregnancy – Postpartum thyroiditis
 - Occur in postpartum period < 12 months
 - Pain & swelling of thyroid with fever
 - PHx of similar episodes in postpartum period
- ✓ Congenital
 - Features present since birth
 - Short stature
 - Low IQ and poor school performance
- ✓ PHx of thyroid Sx
- ✓ PHx of thyroid irradiation
 - I^{131}
- ✓ Exposure to ionizing radiation – x-ray

Hx in a diagnosed pt

- ✓ When and where diagnosed
- ✓ How diagnosed – Ix findings
- ✓ What Rx has been carried out
- ✓ Follow up of the pt – Compliance to treatment
 - Recent Ix results

Exclusion of DD

❖ Cushing's disease

- Weight gain with puffy face but thin limbs
 - Increased facial and body hair
 - Pink and flushed skin**
 - Thinning of skin**
 - Easy bruising**
 - Proximal muscle pain**
 - Acne
 - Sudden development of DM, HT
 - Pigmented striae
 - Recurrent skin infections and poor wound healing
 - Hx of long term steroid intake
- More discriminatory features



❖ Acromegaly

- Change in appearance
- Increased size of hands and feet**
- Headache or visual disturbances**
- Increased sweating
- Tiredness
- Deep voice
- weight gain
- Proximal muscle pain and weakness
- Amenorrhoea / oligomenorrhoea / galactorrhoea

❖ Chronic renal failure

- malaise, loss of energy
- loss of appetite
- insomnia
- nocturia and polyuria**
- itching**
- nausea, vomiting and diarrhoea
- paraesthesiae due to polyneuropathy
- '**restless legs' syndrome** (overwhelming need to frequently alter position of lower limbs)
- bone pain
- paraesthesiae and tetany
- amenorrhoea in women; erectile dysfunction in men.

PMHx

Hyperthyroidism

Psychiatry disease – BAD (Lithium)

Cardiac arrhythmia (Amiodarone)

Ischaemic heart disease and angina (as thyroxine worsen these)

PSHx

Thyroid surgeries

DHx

Antithyroid drugs - Carbimazole, Methimazole, Propylthiouracil

Lithium

Amiodarone

Interferone

Iodides

Steroids (Cushing's disease)

SE of Thyroxine – Angina, arrhythmias, MI

FHx

Autoimmune diseases

Thyroid diseases

SHx

Occupation

Effect on daily activities

Attitude towards the disease

Examination

Signs of Hypothyroidism

- Overweight / obese
- Loss of lateral 1/3rd of eyebrows
- Loss of hair and dry, brittle hair
- Peri orbital oedema
- Facial puffiness
- Pallor
- Hoarse, deep voice
- Goiter
 - Enlarged & tender – subacute thyroiditis
- Coarse, dry, thin skin
- Cold peripheries
- Sinus bradycardia
- Mental slowness
- Slow relaxing tendon reflexes
- Poverty of movements
- Signs of carpal tunnel syn
- Sensory neural deafness

Signs of Acromegaly

- **Prognathism (Prominent chin)**
- **Inter dental separation**
- **Large tongue**
- **Spade like hand and feet**
- **Hirsutism**
- Signs of carpal tunnel syn
- Visual field defects
- Hypertension

Signs of Cushing's syndrome

- Overweight/ Obese
- **Moon face**
- **Hirsutism**
- Acne
- **Buffalo hump**
- Purpuric rash
- **Truncal obesity**
- **Pigmented abdominal striae**
- Thin wasted limbs
- Skin ulcers
- Signs of carpal tunnel syn

Signs of CRF

- **Periorbital oedema**
- **Generalized oedema**
- **Half half nails**
- **Evidence of pruritus**
- **Pigmented skin**
- Bruising
- Peripheral neuropathy
- Hypertension

Goitre + hypothyroidism → 1. Hashimoto's thyroiditis
2. Endemic goiter with iodine deficiency

Hypothyroidism + w/o goiter → 1. Atrophic (autoimmune) hypothyroidism
2. Post-surgical hypothyroidism
3. Hypothyroidism secondary to drugs

Investigations

3rd generation TSH – **high (mcq- Ix of choice)**

- [Ix of choice because of ; - high sensitivity
- quick results in early disease state
- relatively cheap.]

Free T4 (thyroxine) levels - **Low**

FBC – **low Hb**

- Normocytic normochromic (as low thyroxine levels reduce the stimulation of erythropoietin)
- Microcytic hypochromic – If associated menorrhagia
- Macrocytic hyperchromic – If associated pernicious anaemia

Creatine kinase – **High (due to proximal myopathy)**

AST (SGOT) – **High (due to associated liver and/ or muscle involvement)** AST = aspartate transferase

Serum cholesterol – **High (As thyroxine is responsible in reducing plasma cholesterol levels)**

Serum electrolytes

- Serum sodium – **Low (due to increased ADH secretion)**

Thyroid autoantibodies - **High TPO (thyroid peroxidase) Ab titres**
High TSH receptor IgG antibodies (TRAb)

Management

Thyroxine (T₄)replacement for life long

- Start with 100 µg daily (if an elderly – 50 µg, In the presence of IHD – 25 µg)
- Check TSH after 6/52 → Increase by 25- 50 µg
- Re check TSH in 6-8/52
- Increase dose till TSH is normal
- **Monitor with THS levels**
- Maintenance dose = 100- 150 µg
- Clinical improvement with Thyroxine – Occur in 2/52
- Full resolution of symptoms – take 6/12

Discussion

1. Exceptions for lifelong Thyroxine Rx

- Post-partum thyroiditis
- Post viral thyroiditis
- Hypothyroidism 2nd to drugs (Thyroxine is required only as long as the other drug is needed)

2. Advice given to a pt on Throxine

- ✓ Take early in the morning with an empty stomach – *As the rate of absorption reduces with food*
- ✓ Store in a cool dry place w/o any exposure to sun
- ✓ Lifelong treatment with good compliance is necessary
- ✓ Monitor with TSH levels

3. Pharmacology of Thyroxine

T_4 - Oral only

T_3 - IV only

>99% of thyroxine is protein bound

AE

- ✓ Angina
 - ✓ Cardiac arrhythmia
 - ✓ Myocardial infarction
 - ✓ Hyperthyroidism
- } Do an ECG before starting thyroxine

4. What are the conditions in which a different maintenance dose is required

➤ A high maintenance dose

- in pregnancy
- when co-administered with drugs like phenytoin, ferrous sulphate, rifampicin

As the thyroid binding globulin levels increase

5. What are the common aetiologies and their presentations

a) Atrophic (autoimmune) hypothyroidism

- **Most common cause world wide**
- More in females of 40 – 50 yrs
- Incidence increase with ageing
- An organ specific autoimmune disease
- Associated with other autoimmune disorders
- Associated with anti-thyroid autoantibodies leading to lymphoid infiltration of the gland and eventual atrophy and fibrosis.

b) Hashimoto's thyroiditis

- More in late middle aged females (40- 50 yrs)
- High titres of autoantibodies are present – TPO Ab
- produces atrophic changes with regeneration, leading to goitre formation.
- Can be hypothyroid or Euthyroid
- May go through a toxic phase (Hashi toxicity) initially

c) Endemic goitre

- Due to dietary iodine deficiency
- Common in mountainous areas
- Replacement of iodized salt reduces the incidence
- Can be Euthyroid or Hypothyroid & most with endemic goitre are Euthyroid

d) Sub-acute (de quervain's) thyroiditis

- Virus induced (Coxakie, mumps)
- More in 20 – 40 yr females
- Is a transient inflammation of the thyroid

e) Postpartum thyroiditis

- Hx of postpartum period (<12 months)

6. What is sub clinical hypothyroidism

TSH = high

FT4 = Low normal

FBS = Low normal

- Pt must be monitored
- Progression to overt thyroid failure is high in the presence of antithyroid peroxidase Ab or TSH > 10mU/L

7. Myxoedema coma

Severe hypothyroidism with confusion and coma

Is a medical emergency

Rare

Occur in elderly

Precipitating factors

- ✓ Infections
- ✓ MI
- ✓ Stroke
- ✓ Trauma
- ✓ Non-compliance with medication

Clinical features

- ✓ Hypothermia
- ✓ Severe cardiac failure
- ✓ Hypoventilation
- ✓ Hypoglycaemia
- ✓ Hyponatraemia
- ✓ Bradycardia
- ✓ Seizures
- ✓ Coma
- ✓ Hyporeflexia

Mortality rate is high (50%)

Management of Myxoedema coma

- oxygen (by ventilation if necessary)
- monitoring of cardiac output and blood pressures regularly
- Rewarming
- Hydrocortisone 100mg IV 8/H
- 5% dextrose infusion to prevent hypoglycaemia
- Treated in the ICU – **IV T₃ (Triiodothyronine) 5 - 20 µg Slow IV**
- If suspicious of any infection – IV Cefuroxime 1.5g 8/H

2) Hyperthyroidism

Age, gender, fertility status

PC – LOW, Tremor, palpitations

HPC

Describe the PC –Onset, duration.....

LOW despite increased appetite

Irritability & restlessness

Tremor

Breathlessness

Palpitations

Features of heart failure – exertional dyspnoea

Heat intolerance

Excessive sweating

Thirst

Vomiting

Diarrhea

Itching

Oligomenorrhoea

Loss of libido

Gynaecomastia

Muscle stiffness

Proximal muscle weakness – Difficulty in combing hair & standing from squatting position

Goiter

Changes in eyes and nails – **Only in Grave's disease**

Tall stature (in children)

Complications

➤ Thyroid crisis / thyroid storm

- Fever
- Extreme restlessness
- Hx of stress, infection, surgery in an unprepared patient or radioiodine therapy.

DD

- **Hyperthyroidism**
- **Phaeochromocytoma**
- **Anxiety disorder**
- **Malabsorption syn**
- **Tuberculosis**
- **Malignancy**

Aetiology

- Autoimmune – Grave's disease
 - Changes in eyes
 - Nail changes
 - PMHx or FHx of autoimmune diseases
 - Type 1 DM
 - Vitiligo
 - Pernicious anaemia
 - Myasthenia gravis
- 2^{ry} to viral infections – De quervain's thyroiditis
- 2^{ry} to pregnancy – Postpartum thyroiditis
- Toxic multinodular goiter (Plummer disease)
 - More cardiovascular features (palpitations, breathlessness, features of heart failure)
 - In a > 60 yr old pt
- 2^{ry} to radiation
- 2^{ry} to drugs
 - Amiodarone
 - thyroxine

Hx in a diagnosed pt

- ✓ When and where diagnosed
 - ✓ How diagnosed – Ix findings
 - ✓ What Rx has been carried out
 - ✓ Follow up of the pt – Compliance to treatment
- Recent Ix results

Exclusion of other DD

❖ Phaeochromocytoma

- Episodic headache
- Episodic sweating
- Panic attacks
- Tremor
- Palpitations
- Weight loss
- Diarrhea / constipation

❖ Anxiety disorder

- Tremor
- Palpitations
- Excessive sweating
- Presence of these symptoms in relation to an anticipatory event

❖ Malabsorption syn.

- Diarrhoea
- Steatorrhoea – pale, greasy, foul smelling & floating stools
- Features of anaemia – SOB on exertion, palpitations, dizziness, faintishness
- Features of nutritional deficiencies – Gum bleeding, bleeding into skin, night blindness, dry & friable hair

❖ **Tuberculosis**

- LOA
- LOW
- Nocturnal cough
- Nocturnal fever and sweating
- Haemoptysis

❖ **Malignancy**

- LOA
- LOW
- Nocturnal fever and sweating

PMHx

Cardiac arrhythmias (Amiodarone)

Hypothyroidism (Thyroxine)

Hyperthyroidism (relapses and remissions)

Bronchial asthma, Congestive cardiac failure, occlusive arterial disease

(As β blockers are used for symptomatic control)

PSHx

Thyroidectomy

DHx

Amiodarone

Thyroxine

AE of antithyroid drugs

- Agranulocytosis within last 3/12
 - Sore throat and fever
- Skin rashes
- Gum bleeding or bleeding into skin

AE radioiodine – I¹³¹

- Hypothyroidism
- Metallic taste
- Excessive salivation
- Excessive secretions
- Diarrhea
- Productive cough
- Chicken pox like rash
- Worsening of eye signs
- Thyroid storm

FHx

Thyroid disease

Autoimmune diseases

SHx

Occupation
Effect on daily activities
Attitude towards the disease
Awareness of the disease

Examination

Weight loss

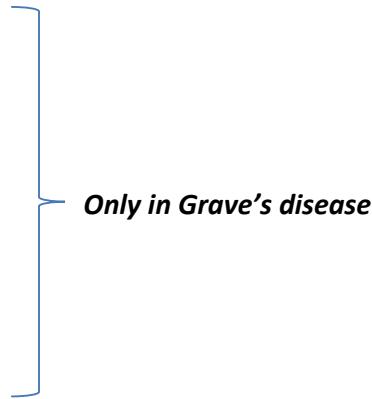
Hyperkinesis

- Irritability
- Psychosis

Exophthalmos

Lid lag & 'stare'

Lid retraction
Proptosis
Conjunctival oedema
Chemosis
diplopia
Ophthalmoplegia
Periorbital oedema
Papilloedema
Loss of vision (by optic atrophy)



Goitre (bruit)

Fine tremor

Palmar erythema
Graves' dermopathy (*Only in Grave's disease*)
Onycholysis
Thyroid acropatchy (*Only in Grave's disease*)

Warm vasodilated peripheries

Tachycardia

High volume pulse – Collapsing pulse

Systolic hypertension

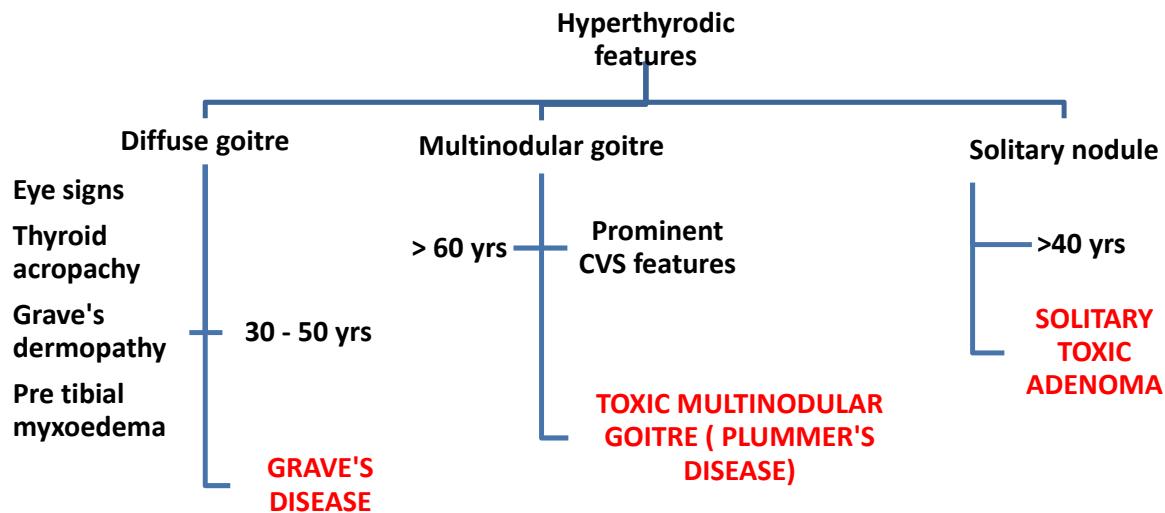
Atrial fibrillation – Irregularly irregular pulse

Signs of cardiac failure

Proximal muscle painy

Proximal muscle wasting

Pretibial myxedema (*Only in Grave's disease*)



Signs of Phaeochromocytoma

- Fever
- Pallor or flushing
- Tachycardia
- Arrhythmias
- Intermittent or constant hypertension
- Postural hypotension
- Signs of hypertensive damage – retina, heart

Signs of malabsorption syn

- Cachectic
- Dehydrated
- Pallor, glossitis, angular stomatitis, koilonychia
- Brittle nails
- Dry hair
- Gum bleeding
- Ecchymotic patches, purpura, petechiae

Tuberculosis

- LOW
- Haemoptysis
- SuprACLAVICULAR lymph nodes
- Absence of BCG scar
- Positive mantoux
- Signs of a apical consolidation

Investigations

3rd generation TSH – Low

Free T₄ – Increased

Free T₃ – Done only if Free T₄ is normal with a low TSH.

} Requested on Radioimmuno assay form

TPO (Thyroid peroxidase enzyme) and anti-thyroglobulin Abs – Present in Grave's disease

FNAC or thyroid scan – To exclude malignancy

USS of neck – For the nodularity of thyroid

Whether a solid or cystic

Management

1. Anti-thyroid drugs
 - ❖ Thionamides
 - Carbimazole
 - Methimazole
 - Propylthiouracil
 - ❖ Iodide
 - Lugol's iodine
 - Potassium iodide
2. Radioactive iodine – I¹³¹
3. blockers – For symptomatic treatment only
4. Monitoring with – T₃ and T₄ levels

A. Mx of Grave's disease

1st episode- Anti thyroid drugs – **Main stay of treatment**

If recurrent – Radioiodine

Surgery

Mx of Grave's ophthalmopathy

- Thyrotoxicity should be treated. (however, avoid hypothyroidism)
- Stop smoking
- Methylcellulose or hydromellose eye drops
- Systemic steroids – to reduce the inflammation
- Surgery – lid surgery, Surgical decompression of the orbit, corrective eye muscle surgery
- Irradiation of the orbits

B. Mx of MNG with thyrotoxicosis / Plummer syn

Radioiodine

Surgery

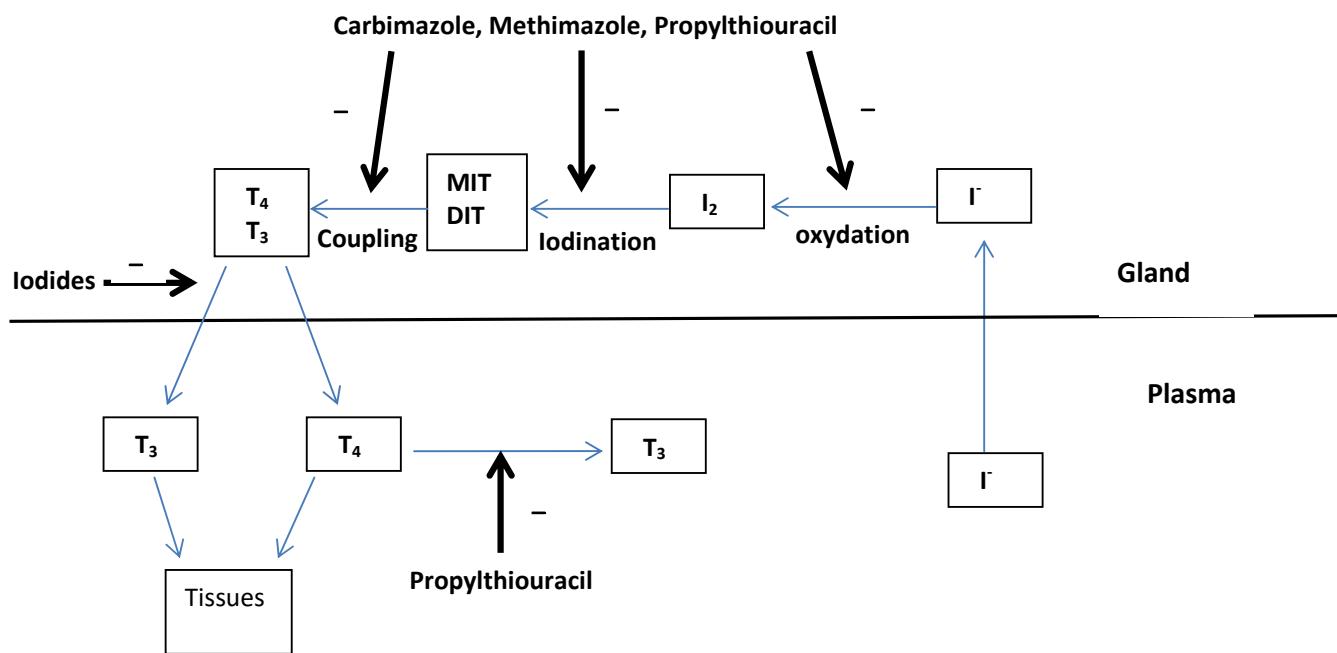
C. Mx of Solitary toxic adenoma

Surgery – Hemi thyroidectomy

Radioiodine

Discussion

1. Anti-thyroid drugs



Carbimazole

- ✓ Different administration methods are available

A. Gradual dose titration - Start with a high dose and reduce the dose later

- 20-40 mg daily for 4-6 wks
- Review in clinic with freeT4 levels and adjust the dose
- Then review in 2-3 months and adjust the dose
- Reduce to 5mg daily over 6 – 24 months
- Stop carbimazole when Euthyroid on 5mg

B. Block and replace regime

- Start with a full dose of Carbimazole - 40mg daily (to suppress the thyroid completely)
- In addition replace thyroid activity with 100 µg of levothyroxine daily once euthyroidism has been achieved.
- Continued for 18 months

- Advantage – Avoidance of over & under treatment
To use the immunosuppressive action of Carbimazole better
- CI – Pregnancy (as Carbimazole crosses the placenta faster than thyroxine)
- ✓ Has anti-thyroid and immunosuppressive effects
- ✓ Uses
 - In Grave's disease
 - Prior to radioiodine therapy or surgery – *To prevent thyroid crisis/storm*
- ✓ AE
 - Major
 - Agranulocytosis (Rare- **Less common than in Propylthiouracil**)
 - Cholestatic hepatitis
 - Minor – **More common**
 - Headache
 - Anorexia
 - Nausea
 - Skin rashes and urticarial
 - Arthralgia
 - Fever
- ✓ Advice given to pt
 - To stop the drug and go to a Dr. immediately if a fever or sore throat occur
 - Importance of regular monitoring of fT₄ levels
 - Advice on planning pregnancies (Carbimazole crosses the placenta thus is cautious in pregnancy)

Propylthiouracil

- ✓ Similar to Carbimazole in action
- ✓ AE are similar to that of carbimazole
But, cause more agranulocytosis & less minor SE than Carbimazole)
- ✓ Is the preferred drug in pregnancy & breast feeding (Due to less placental crossing & no teratogenicity)
- ✓ Used in the treatment of thyroid storm

Radioiodine - I¹³¹

- Given orally – as a single dose
- Cause the destruction of functioning thyroid cells
- Therefore anti thyroid drugs and β blockers should be given prior to I¹³¹
- Take 3/12 for the effect – therefore antithyroid drugs have to be continued in the 1st 3/12
- AE
 - Hypothyroidism
 - Iodism – Metallic taste, excessive salivation, excessive secretions, diarrhea, productive cough, chicken pox like rash
 - Induction or worsening of ophthalmopathy
 - Radiation thyroiditis

- Teratogenicity – Avoid pregnancy till 12 months
- Subfertility
- Risk of thyroid CA and leukemia
- Clinical indications
 - Toxic MNG
 - Relapse of Grave's disease
 - Hot thyroid nodule causing hyperthyroidism
 - As an adjunct to surgery in metastatic thyroid disease
- CI
 - Pregnancy and breast feeding
 - Children
- Advice given to a pt on radioiodine
 - Avoid going to public places in the 1st few days
 - Avoid meeting pregnant females

Iodides

- ✓ Inhibits the release of stored Thyroxine and reduce the vascularity of the gland
- ✓ Has a transient effect lasting for 10 – 14 days
- ✓ Indications
 - Thyroid crisis
 - Prior to surgery
- ✓ AE – Iodism

β blockers

- Does not interfere in :
 - The correction of thyroid hormone levels
 - Disease process
 - Basal metabolic rate
- Only cause a symptomatic control
(Reason for increased adrenogenic activity in thyrotoxicosis - As high thyroxine levels have increased the hypersensitivity of tissues to catecholamines)
- CI – Bronchial asthma, Congestive cardiac failure, occlusive arterial disease

2. What is thyroid crisis ?

- A medical emergency
- A sudden rise in thyroid hormone levels occur
- Rare
- Mortality up to 10%
- Is a rapid deterioration of hyperthyroidism with associated:
 - Hyperpyrexia
 - Extreme restlessness
 - Severe tachycardia
 - Palpitations
 - Arrhythmias – specially AF

- High output cardiac failure
 - Anxiety
 - Fits
 - Coma
 - Sweating
 - Diarrhoea
- Precipitating factors
 - Infection
 - Stress
 - Radioiodine therapy w/o making the pt euthyroid
 - Surgery w/o making the pt euthyroid
 - [extra point – Reason for not doing Sx in hypothyroid pts w/o doing sx – risk of delayed recovery from anaesthesia)
- Mx
 - IV Propranolol
 - Oral propylthiouracil or oral Carbimazole
 - Oral Lugol's iodine (5% iodine + 10% KI in aqueous solution)
 - IV hydrocortisone 200mg stat
 - Supportive measures
 - Temperature control
 - Hydrate with IV N.saline infusion
 - Correct hypoglycaemia
 - Monitor the cardiac rhythm
 - If AF – Give digoxin
 - Treat infections with antibiotics

3. What is Sick thyroid syndrome (Non thyroidal illness)

- Biochemical findings
 - TSH – Normal
 - fT₄ – Normal
 - fT₃ - Low
- Occur in acute stress & following surgeries
- In tissues T₄ is converted to active T₃ and reverse T₃ (rT₃). Reverse T₃ is an inactive form.
- Following stress reverse T₃ production increases leading to a reduction in the formation of active T₃.
- Thus free T₃ levels reduce.

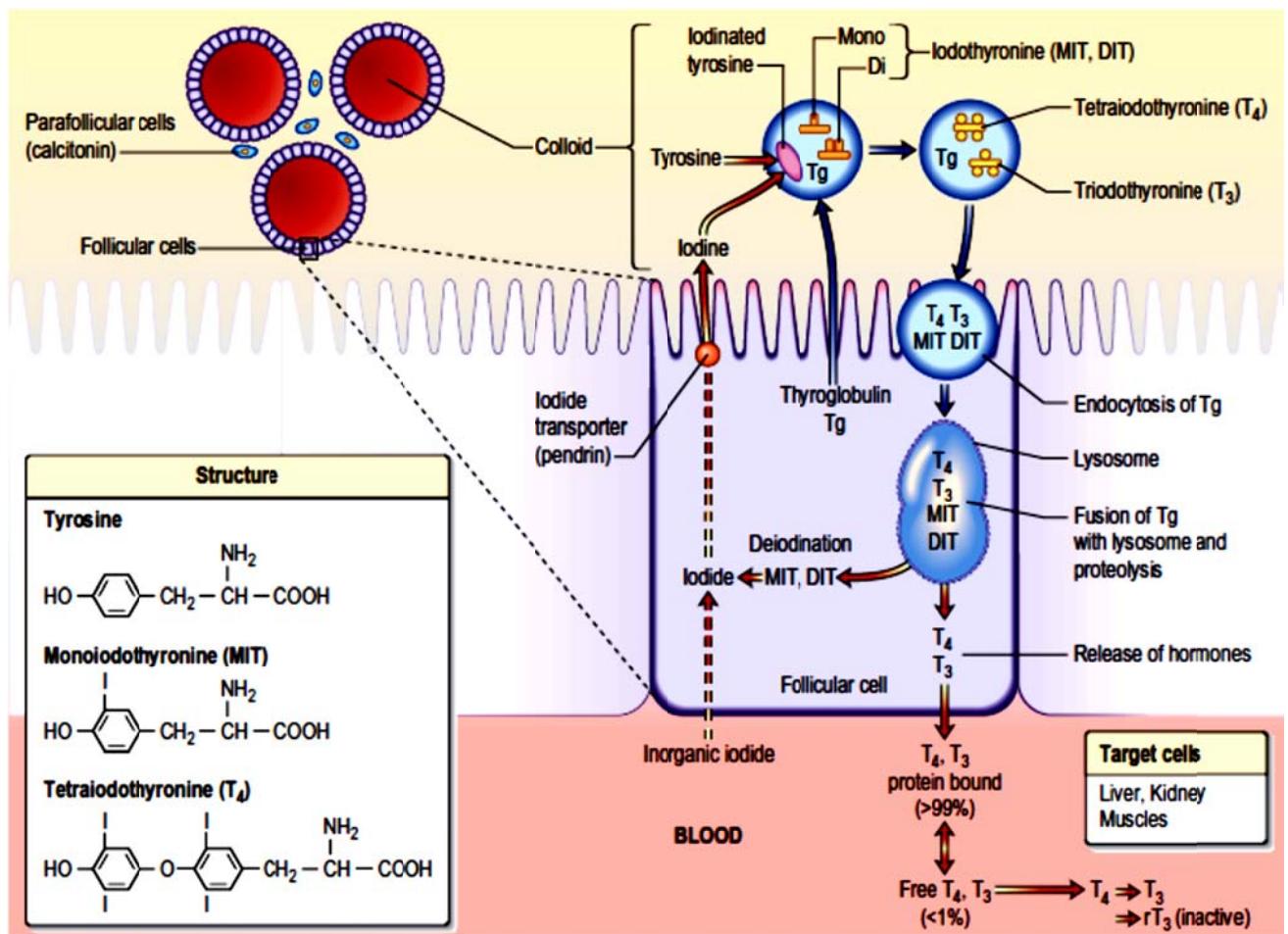


Fig. 18.14 Synthesis and metabolism of the thyroid hormones.

Infective endocarditis

P/C

Can present with

- Fever - PUO
- Cardiac involvement
- Consequences due to embolic phenomenon
- Fx due to immune complex
- Can present with mixed picture

H/P/C

Whether the pt is having

- IE or not – exclude other possible infections
- Is it complicated with
- Cardiac involvement
- Embolization
- immune reaction
- risk factors
- what happened up to now – Hx of series of cultures, ECHO

DD for fever

- Simple bact. infection
- viral fever
- dengue fever
- PUO - classical- >3wks / not diagnosed after 1 wk in the wd

Constitutional complaints

Fever and chills (most common) symptoms;

Anorexia, weight loss, malaise, headache, myalgias, night sweats, shortness of breath, cough or joint pains

Clinical features may due to

1. Infection
2. Cardiac lesion
3. Embolization
4. Immune complexes : skin, eye, renal

Focus of infection

- Resp – sore throat, cough, pluritic type chest pain
- GI – diarrhoea, vomiting, abd pain
- Urinary – dysuria, urgency, frequency
- CNS – headache, vomiting, photophobia
- Dengue fever – retro orbital pain , arthralgia, myalgia, RHC pain, chest pain (myocarditis)

Primary cardiac disease (due to valvular insufficiency)

- CCF - SOB on exertion, orthopnoea, PND, chest pain
- Conduction defects – palpitation
- Acute valvular dysfunction
- Intra cardiac abscess formation, septal rupture

Embolic phenomenon

- Cardiac- MI- chest pain, palpitation, faintishness
- Vascular – PVD – intermittent claudication
- Brain – cerebral abscess,- seizures, focal deficits, altered consciousness
 Stroke - hemiparesis
- Spine – osteomyelitis- back pain
- Lungs – pulmonary abscess, pulmonary Infarction – cough, DIB,
(Tricuspid valve endocarditis)

Immunological

- Vasculitis – rash
- GN – oedema, haematuria

Risk

Presence of organism in the blood stream – bacteremia

Source of organism;

- Poor dental hygiene
- Iv drug use
- Soft tissue infection
- Iatrogenic
- Dental Surgery
- Iv cannulation
- Cardiac surgery – valve replacement
- Abortions
- UTI , urinary catheterization
- Cystoscopy, endoscopy

Abnormal cardiac endothelium (facilitating the adherence & growth of organism)

- Congenital Valvular lesions –
 - Jet lesions (VSD) less common in low pressure systems (Tetralogy of Fallots > bicuspid aortic valve> coarctation of aorta > VSD)
 - Secundum ASD very rare
 - Surgical correction does not exclude from risk in major CHD
- Acquired Valvular lesions
 - Rheumatic heart disease
 - AS / AR / MR predisposes commonly
 - Rare in MS
 - Mitral valve prolapse
 - Commoner in young females (~ 20%)
 - Common in ballet dancers (~59%; lean body)
 - MVP predisposes primarily when there is associated regurgitation with a systolic murmur
 - 10 – 100 fold increase in risk compared to general population
 - Important in children and age >50yr
 - Degenerative valve disease
 - 25% in > 40 yrs
 - 50% in > 60 yrs
 - Senile aortic stenosis
 - Mitral regurgitation

PMHx – History of valvular heart disease, DM, immunocompromise, Rheumatic fever

PSHx – Any procedures

DHx – Antibiotic Rx, steroids, cytotoxic drugs (immunocompromise)

FHx

SHx- IV drug use

O/E

General Ex

- Pallor
- Vasculitis rash – 50%
- Clubbing -10%
- Splinter h'age – 10%
- Janway lesions – 5%
- Oslers nodes -15%
- Roth spots – 5%
- AGN – oedema, ↓UOP

CVS

- CCF -↓ BP, ↓Pulse volume, features of shock, gallop rhythm
- Conduction defects – irregular pulse
- Changing murmur- 90% new

Abdomen

Firm splenomegaly

CNS

- Stroke- focal neurological signs, long tract signs, sensory impairment, cerebellar signs

RS

- Pulmonary infarction/ abscess - ↓AE, chest pain, SOB, Fx of pulm. HT

High clinical suspicion

- New valve lesion – Regurgitant murmur
- Embolic events of unknown origin
- Sepsis of unknown origin
- Haematuria, GN, suspected renal infarction
- Prosthetic valve
- High disposition for IE (drug abuse)
- newly developed ventricular arrhythmias or conduction disturbances
- First CCF
- cutaneous (Osler, Janeway) or ophthalmic (Roth spots) manifestations
- Peripheral abscess (renal/splenic/spine) of unknown cause
- Predisposition to recent bacteraemia (diagnostic/ therapeutic)

Diagnosis

Modified Duke criteria

Major

1. A positive blood culture for IE

- Typical organism in 2 separate culture/
or
- Persistently +ve blood culture
- Blood cultures obtain >12hrs apart
- All 3 or 3/4 or more separate blood cultures, with 1st & last cultures obtained at least 1hr apart

2. Evidence of endocardial involvement

- Echo findings
- Presence of oscillating intra-cardiac mass
- Abscess
- Newly identified partial dehiscence of prosthetic valve
- New valvular regurgitation

Minor

1. Fever $\geq 38^{\circ}\text{C}$
2. Predisposition to IE; cardiac cause / iv drug use
3. Vascular phenomenon; major arterial emboli, mycotic aneurysms, septic pulm. Infarcts
Conjunctival H'ages, ICH, janeway lesions
4. Immunological phenomenon ; Roth spots, oslers nodes, GN, rheumatoid factor
5. Microbiological evidence (not meeting above)
6. Echo-cardiography (not meeting above)

2 major criteria or 1 major criterion + 3 minor criteria or by 5 minor criteria

Investigations

Purpose of Ix

- Confirm the diagnosis of IE
- Identify the causative organism to ensure appropriate therapy
- Monitor the pt, response to Rx

Blood cultures; (+ve >90%)

- At least 3 blood cultures within 1st 24 hrs
- From 3 separate sites
- With aseptic precautions
- Taken during fever spikes

Never draw only 1 set of blood cultures; 1 is worse than none. Two sets of blood cultures have greater than 90% sensitivity when bacteraemia is present

For diagnosing sub-acute IE, draw 3-5 sets of blood cultures over 24 hours. This helps detect 92-98% of cases in patients who have not recently received antibiotics. In the case of acute IE, 3 sets may be drawn over 30 minutes (with separate venous punctures) to help document a continuous bacteraemia.

When blood culture results fail to show an infectious agent after blood is drawn 48 hours after antibiotic therapy has been stopped, the second set of blood for cultures must be drawn approximately 7 days later. If these later culture results remain negative, the diagnosis of IE must be reconsidered. In general, blood for culture should not be drawn through intravenous (IV) lines unless this is part of an approach for diagnosing line infection

Echo

- Transthoracic – visualizing vegetations
- Transthoracic – higher sensitivity & specificity for abscess formation
Visualizing prosthetic valves

-ve echo doesn't exclude endocarditis

However echocardiography is indicated for all pts suspecting IE

Basic investigations

- FBC – Normocytic normochromic anaemia, PMN leucocytosis
- BU/SE – renal dysfunction (complication of sepsis)
- ESR /CRP- ↑(non specific inflammatory markers)
- UFR – protein urea, microscopic haematuria
- LFT - ↑ALP
- Ig - ↑
- Complements – total & C3 ↓
- ECG – show evidence of MI(emboli), conduction defects,
- New AV block suggestive of abscess formation
- Suspected IE pt →ECG on presentation & Rpt regularly
- CXR – evidence of → heart failure
Multiple pulm. Emboli & / abscess (right sided IE)

The major goals of therapy for infective endocarditis (IE)

1. To eradicate the infectious agent from the thrombus
2. Address the complications of valvular infection.
3. Manage intracardiac and extracardiac consequences of IE

General measures

- Treatment of congestive heart failure
- Oxygen
- Hemodialysis (may be required in patients with renal failure)
- Empirical antibiotic therapy tailored to the patient's history and circumstances may be administered
- No special diets are recommended for patients with endocarditis; however, if the patient has congestive heart failure, administer a sodium-restricted diet.
- Activity limitations are determined by the severity of the illness, complications (eg, stroke), and the presence of significant congestive heart failure.

- Mild congestive heart failure resulting from valvular insufficiency or myocarditis may be managed with standard medical therapy

Antibiotics remain the mainstay of treatment for IE.

Soon as possible to minimize valvular damage

Three to 5 sets of blood cultures are obtained within 60-90 minutes,

Followed by the infusion of the appropriate antibiotic regimen

The **initial antibiotic choice is empiric in nature, determined by clinical history and physical examination findings**

Adjust according to culture results.

- ❖ Except pt who have recently received antibiotics

↓

Delay starting AB therapy for 48-72 hrs to await culture results

↓

Prevents further AB confounding the picture

This delay is only possible in haemodynamically stable pts

Eradicating bacteria from the fibrin-platelet thrombus is extremely difficult because

- (1) The high concentration of organisms present within the vegetation (ie, 10-100 billion bacteria per gram of tissue)
- (2) Their position deep within the thrombus
- (3) Their location in both a reduced metabolic and reproductive state
- (4) The interference of fibrin and white cells with antibiotic action

↓

For all of these reasons

↓

bactericidal antibiotics are considered **necessary for cure** of valvular infection.

IV administration is preferred because more reliable therapeutic levels are achieved with this route.

- Benzyl penicillin 2.4g (4mu) IV 4 hrly
- Gentamicin 80 mg IV 12 hrly
- If suspect acute IE add Flucoxacillin 2g IV 6 hrly
- Gentamycin may be stopped after 2 wks if response is good
- Continue penicillin for further 2wks period
- If penicillin allergy use → Ceftriaxone 2g bd(4 weeks)/Vancomycin 1g IV 12hrly instead
- **IV therapy must continue for at least 2-4 wks**

❖ Cont. Rx longer in prosthetic valve disease

Clinical endocarditis, culture results awaited No suspicion of staph	Penicillin 1.2g 4 hrly Gentamycin 80 mg 12 hrly
Suspect staphylococci endocarditis <ul style="list-style-type: none"> • IV drug use • Recent intra vascular device • Cardiac Sx • Acute infection 	Vancomycin 1g 12 hrly Genatamycin 80 – 120 mg 8 hrly
Streptococcal endocarditis	Benzyl penicillin 2.4g (4mu) 4 hrly Gentamicine 80 mg 12 hrly
Enterococccal endocarditis	Ampicillin/ amoxicillin 2g 4 hrly Gentamycin 80mg 12 hrly
Staphylococcal endocarditis	Vancomycin 1g IV 12hrly or Flucoxacillin 2g IV 6 hrly or Vancomycin 1g 12 hrly + Genatamycin 80 – 120 mg 8 hrly

- Reassess the pt for signs of cardiac failure, new embolic phenomenon & AV block, treat accordingly.
- Adjust AB once sensitivities are known
- Monitor gentamycin & vancomycin levels
- SE : ototoxicity, nephrotoxicity – by both
- Consult microbiologist if service are available
- Consult a cardiothoracic surgeon if severe valve destruction or ongoing embolic phenomenon

Persistent fever

- Should respond within 48 hrs of appropriate AB therapy.
- Evidence by
 - o Resolution of fever
 - o ↓CRP
 - o Relief of systemic symptoms

If not

- Perivalvular extent of infection & possible abscess formation
- Drug reaction (fever will resolve after drug withdrawal)
- Nosocomial infection (venous access site)
- Pulm. Embolism(R side IE)
- Samples for culture should be taken from all possible sites
- **Changing AB dosage or regimen – avoided unless +ve cultures or drug reaction suspected**

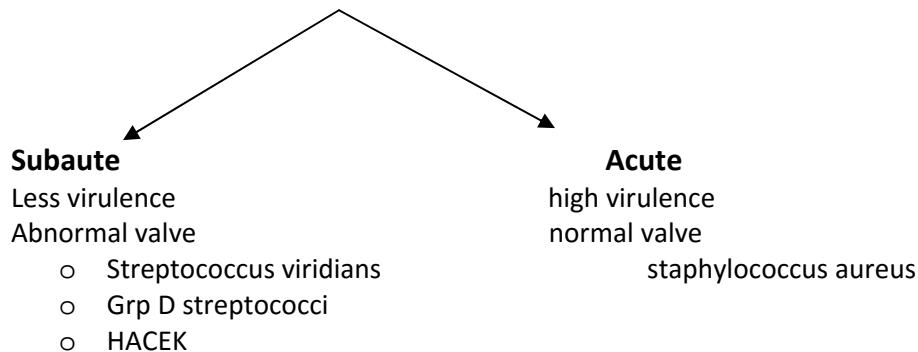
Surgery

- Extensive damage to valve
- Prosthetic valve endocarditis
- Persistent infection despite therapy
- Large vegetations
- Serious embolization
- Myocardial abscess
- Fungal endocarditis
- Progressive cardiac failure

Antibiotic prophylaxis

People with valvular lesions who are at moderate to high risk of developing IE are recommended to receive AB therapy before undergoing procedures likely to result bacteremia.

- Dental Rx
- Endoscopy
- Surgical instrumentation



The clinical course of endocarditis

Endocarditis occurs as an **acute** and a **more insidious 'subacute'** form.

The subacute form may abruptly develop acute life-threatening complications such as valve disruption or emboli.

Subacute endocarditis

- This should be suspected when a patient known to have congenital or valvular heart disease develops a persistent fever, complains of unusual tiredness, night sweats or weight loss, or develops new signs of valve dysfunction or heart failure.
- Less often, it presents as an embolic stroke or peripheral arterial embolism.
- Other features include
 - ✓ Purpura and petechial haemorrhages (the skin and mucous membranes)
 - ✓ Splinter haemorrhages (under the fingernails or toe nails).
 - ✓ Osler's nodes (painful tender swellings at the fingertips)
 - ✓ Digital clubbing (late sign).
 - ✓ The spleen is frequently palpable
 - ✓ Coxiella infections the spleen and the liver may be considerably enlarged.
 - ✓ Microscopic haematuria
- The finding of any of these features in a patient with persistent fever or malaise is an indication for re-examination to detect unrecognized heart disease.

Acute Endocarditis

- Presents as a *severe febrile illness* with *prominent and changing heart murmurs* and *petechiae*.
- Clinical *stigmata of chronic endocarditis are usually absent*.
- Embolic events are common
- Cardiac or renal failure may develop rapidly.
- Abscesses may be detected on echocardiography.
- Partially treated acute endocarditis behaves like subacute endocarditis.

Four categories of IE

- Native valve endocarditis
- Prosthetic valve endocarditis
- IE in intravenous drug misusers
- Nosocomial IE

Key issues in pathogenesis in IE

- Predisposing host factors
- Characteristics of micro-organisms
- Role of transient bacteremia
- Ability of immune system to eradicate micro-organisms once they are located on endocardium



Characters of micro-organism

- Greatest ability to adhere and colonize damaged valves (*S. aureus*, *Strept. Spp*, > 80% IE ; greatest ability to adhere)
- Direct invasion of endothelial cells (*coxiella*, *chlamydia spp*, *Staph aureus*)

Aetiology: culture + ve endocarditis

- *Streptococcus viridans* (~50% of cases)
 - ❖ Oropharyngeal flora
- *Enterococcus faecalis*
 - ❖ Genito-urinary infections, pelvic surgery
- *Staphylococcus aureus*
 - ❖ IV catheters, parenteral feeding, abscesses
- *Staph. Epidermidis*

Aetiology: culture - ve endocarditis

- *Coxiella burnetii*
- *Chlamydia spp.*
- *Histoplasma, Candida*
 - ❖ IV drug users, alcoholics

B/L LL oedema + Frothy urine (nephrotic Xn)

Hx

PC – oedema – duration – if less than 1 week – **acute**

B/L LL swelling only -DD	U/L chronic LL swelling – DD
<ul style="list-style-type: none">1) CCF2) NS/CRF3) CLD4) Malabsorption/malnutrition5) Myxoedema6) Fluid overload	<ul style="list-style-type: none">1) Lymphoedema2) Venous<ul style="list-style-type: none">- Varicose V.- Obstruction to VR → PregnancyPelvic tumourIVC obstructionPost phlebitis3) Congenital malformations (AV fistula)4) Paralysis5) Dependency

HPC – **oedema**

Site of onset & spread – Periorbital → generalized (renal)

Generalized from the start, pedal

Ascitis → generalized (liver)

Site it is more prominent – Facial, peri-orbital - renal

Abdominal (liver)

Pedal - cardiac body

Time when marked – Peri-orbital swelling marked in the morning (renal)

Ankle oedema worse in the evening – dependant oedema (cardiac)

Associated symptoms – urinary/ abdominal/ in pedal oedema exclude joint pain and swelling

What is the cause for oedema?

- 1) Cardiac(RHF) – exertional SOB, orthopnoea, PND, RHC pain, valvular ♡ disease, IHD
- 2) Liver (decompensated cirrhosis) – haematemesis, melaena, jaundice, abd. Distension, inverted sleep pattern
- 3) Anaemia
- 4) Myxoedema – features of hypothyroidism – wt gain despite low appetite, cold intolerance, lethargy, ♀- menorrhagia, oligomenorrhoea
- 5) Malnutrition/malabsorption – weight loss despite normal appetite, chronic diarrhoea, nutritional deficiency, steatorrhoea
(Malnutrition severe enough to cause oedema is rare in SL. Above symptoms except chronic diarrhoea and Hx of poor diet)
- 6) Renal – frothy urine on normal micturition, polyuria/oliguria, painless haematuria, HTN (headache, blurring of vision)

Which renal cause?

AGN – Oliguria, haematuria, mild oedema, HTN, uremic features – N, V, pruritus, LOA

NS – UOP – normal/↓, significant oedema, previously diagnosed, UFR found to have proteinuria of 3+

CRF – Polyuria, N,V, pruritus, LOA, irretactable hiccups, cramps, back ache, Bone pain, pigmentation, HT

NS – Aetiology – Metabolic – DM, Amyloidosis – pure proteinuria

If diabetic – duration – usually 15-25 years after diagnosis

other microvascular complications – retinopathy, neuropathy

CT disorders – SLE – alopecia, oral ulcers, malar rash, photosensitive rash

RA – B/L symmetrical small J arthritis with DIPJ sparing

Due to gold use

Thyroiditis – painful swelling of thyroid gland following URTI

Sjogren's syndrome – Dry burning eyes, difficulty chewing, dysphagia

Nasal crusting

Infections – poststreptococcal GN – Hx of sore throat/cellulitis, OM 1-3weeks back

Children, common – nephritic picture

HBV, HCV, HIV – Risky sexual behavior – hetero/homo

Blood Tx over past 6/12

Needle prick injuries

EBV, CMV, fungal & spirochaetal infections

Leprosy – numbness, rash

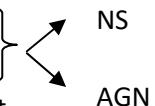
Syphilis

Malaria – Intermittent fever, travel to endemic area/India

Endocarditis – Fever with chest pain, palpitations

Hx of rheumatic/congenital heart disease

Schistosomiasis – Travel to south America, Africa, far-east



Drug and toxins – Gold, NSAIDs, penicillamine, captopril, probenecid (bile sequestrant), Hg

Malignancy – MM – Pancytopenia, back ache, bone pain

Lymphoma – low grade fever (PUO), night sweats, LOA, LOW, Neck lumps

CA of lung – chronic cough, haemoptysis

CA of colon – altered bowel habits, bleeding PR

CA of stomach – severe LOA, epigastric pain after meals, early satiety

CA of breast – breast lumps

Hereditary – congenital NS – FHx of NS

Cryoglobulinaemic disease - ♀ - 40's and 50's

Purpura, arthralgia, leg ulcers, raynaud's phenomenon,

polyneuropathy, hepatic involvement

HSP – children, rash over buttocks and extensor aspect of LL, Hx of URTI, abdominal colic, joint pain – small & large J.s

Idiopathic

- Complications –
- 1) Hypercholesterolemia – acute MI, CVA, PVD, Renal A thrombosis
 - 2) Infections – cellulitis, chest infections, spontaneous bacterial peritonitis
 - 3) Pleural/ pericardial effusions
 - 4) Venous thromboembolism – DVT – swollen, tender LL following immobility
 - U/L worsening of swelling/asymmetrical swelling
 - Renal V. thrombosis – loin pain, flank pain, gross haematuria
 - Pulmonary embolism – sudden severe breathlessness, haemoptysis
 - Mesenteric vein thrombosis – severe abdominal pain
 - Portal v./ cerebral/ sagittal V.
 - 5) Hypovolemia → ARF – oliguria

NS Hx – if already diagnosed – onset, when, diagnosed where

Renal Bx done/not, similar episodes, frequent relapsing/not – how many episodes/year
 Drugs the pt. is on, response to steroids – steroid sensitive/ resistant
 S/E of drugs – steroids

PMHx – atopy (\uparrow incidence of minimal change disease)

PSHx – kidney transplant (cause for membranous GN)

FHx – Renal disease, kidney transplant/CKD, atopy

SHx – Effect on family, schooling

Ex

GE – Generalized oedema

Dyspnoeic - CCF

Pallor – CRF

Stigmata of CLD – Jaundice, loss of body hair, spider naevi, palmar erythema, leuconychia

Stigmata of CRF – Pruritus, pigmentation, half-half nails, dialysis AV fistula

CT disease features – alopecia, oral ulcers, skin rashes, swollen tender joints

IE – clubbing, splinter haemorrhages, janeway lesions, Osler's nodes

Steroid therapy– moon face, hirsutism, purple striae, orange on sticks app.

CVS – CCF – \uparrow JVP, cardiomegaly, TR murmur, tender hepatomegaly

BP - \uparrow - AGN, NS with bad prognosis (HT, haematuria)

Tachycardia, \downarrow BP, Muffled ❤ sounds – pericardial effusions

JVP not raised and no pulmonary oedema - NS

RS – Pleural effusions

Abd – Tenderness

CLD – splenomegaly, FF

IE – just palpable spleen

Lymphoma – hepatosplenomegaly, para-aortic LN

NS – higher functions – uraemic encephalopathy – GCS, exaggerated reflexes, peripheral neuropathy

Diagnosis – frequent relapsing/ in remission steroid sensitive/resistant NS due to (possible aetiology)
 complicated with -----

Discussion

How would you investigate this pt?

1) Confirm the diagnosis

- Urine protein ward test – 2/3rd of tube with fresh urine + acidify with 1% acetic acid + heat → dense Coagulum - Proteinuria ≥ 3+

No turbidity – 0
Turbidity +, but can read the letters - +
Turbidity, cannot read but can see as black - ++
Cannot see through - +++
Precipitate - +++++

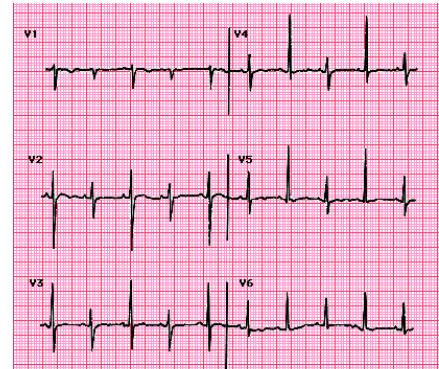
- 24hr urinary protein - >3.5g/day/1.73m² (not done immediately)
Or urine protein: creatinine > 200mg/mmol or >3mg/mg
- S. albumin - <30g/L
- Lipid profile - ↑ LDL, ↑ TG in 50%, N/L HDL

2) Assess renal function

- S. creatinine
- BU & SE

3) Basic Ix – exclude complications and other causes

- FBC - sepsis
- LFT - CLD
- ECG – Pericardial effusion – low voltage QRS complexes
Electrical alternans
- CXR – Features of CCF
Irradiating causes – bronchial CA, lymphoma – widened mediastinum
- USS – KUB – kidney size enlarged – amyloidosis
Size small – CRF
Loss of cortico-medullary demarcation, loss of echogenicity – renal parenchymal disease
- ABD – CLD



Electrical alternans Sinus tachycardia with electrical alternans which is characterized by beat-to-beat alternation in the QRS appearance (best seen in leads V2 to V4). These findings are strongly suggestive of pericardial effusion, usually with tamponade. The alternating ECG pattern is related to back-and-forth swinging motion of the heart in the pericardial fluid. Courtesy of Ary Goldberger, MD.

4) Find the cause (secondary Ix)

- UFR – Appearance : turbid
Protein - >300mg/day
Cells – Red cells
Pus cells – UTI
Casts – Hyaline casts – minimal change disease
RC casts
- FBS – DM
- ESR >100 suggest inflammatory/infective cause
↓
- ANA – SLE (confirmed by anti-ds DNA)
- ANCA (anti neutrophil cytoplasmic Ab) – vasculitis

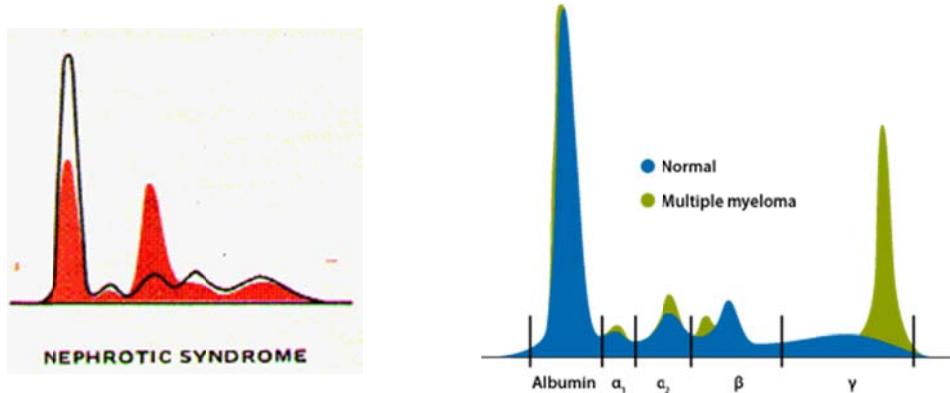
NS with bland urine sediment (pure proteinuria)

- pure nephrotic

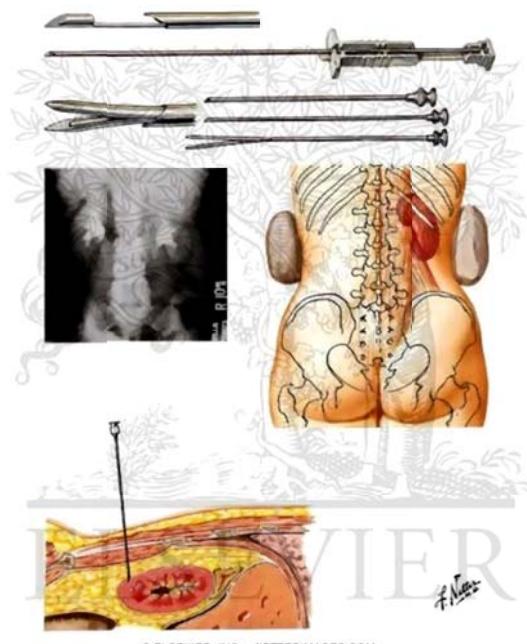
NS with active urine sediment (RC, RC casts)

- nephrotic-nephritic mixed

- Blood picture
- Hepatitis screen – HBs Ag
HCV IgM Ab
HIV Ab
- ASOT – if suspecting post-streptococcal GN
- Blood culture, 2d- echo → IE
- Serum protein electrophoresis to differentiate from multiple myeloma



- Complement levels – C3,C4 ↓
- S. cryoglobulin ↑
- **Renal Bx –**
 - I° - doubts about presence of minimal change NS
Suspecting other GN
 - Not I° - In children, since most MCD
Long standing DM – insulin dependant, with retinopathy/neuropathy
Drug induced – Drug stopped first



Practical Box 11.1
Transcutaneous renal biopsy

Before biopsy

1. A coagulation screen is performed. It must be normal.
2. The serum is grouped and saved for crossmatching.
3. The patient is given a full explanation of what is involved and consent obtained.

During biopsy

1. The patient lies prone with a hard pillow under the abdomen.
2. The kidney is localized by ultrasound.
3. Local anaesthetic is injected along the biopsy track.
4. The patient holds a breath when the biopsy is performed.

After biopsy

1. A pressure dressing is applied to the biopsy site and the patient rests in bed for 24 hours.
2. The fluid intake is maximized to prevent clot colic.
3. The pulse and blood pressure are checked regularly.
4. The patient is advised to avoid heavy lifting or gardening for 2 weeks.

Table 11.2 Complications of transcutaneous renal biopsy

Macroscopic haematuria - about 20%

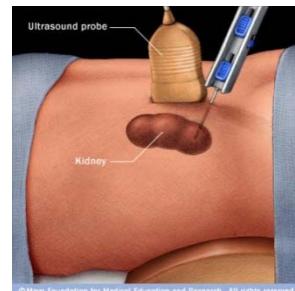
Pain in the flank, sometimes referred to shoulder tip

Perirenal haematoma

Arteriovenous aneurysm formation - about 20%, almost always of no clinical significance
Profuse haematuria demanding blood transfusion - 1-3% Profuse haematuria demanding occlusion of bleeding

vessel at angiography or nephrectomy - approximately 1 in 400

Introduction of infection The mortality rate is about 0.1 %



NS definition

- 1) Gross proteinuria ($>3.5\text{g}/1.73\text{m}^2/\text{day}$)
- 2) Hypoalbuminemia $<30\text{g/L}$
- 3) Oedema
- 4) +/- hypercholesterolemia

Pathology

Proteinuria – 1) Structural damage to the glomerular basement membrane $\rightarrow \uparrow$ in size & no. of pores
2) \downarrow of fixed (-) charge in glomerular capillary wall – less repulsion of proteins

Hypoalbuminemia – 1) Urinary protein loss

- 2) \uparrow Catabolism of reabsorbed albumin in the proximal tubules
- 3) High dietary protein intake $\rightarrow \uparrow$ albuminuria

Oedema – Marked Na retention + hypoalbuminemia

Activation of the renin angiotensin system due to increased Na load to the DCT

Hyperlipidemia - ↑ in LDL, VLDL & IDL; normal HDL

- 1) Low plasma albumin → ↑ lipoprotein synthesis
- 2) Reduced clearance of chylomicrons, VLDL

Classification of causes

I NS with bland urinary sediments (no RC)

Primary – Minimal change disease

Membranous

FSGS

Congenital

Secondary – Diabetic

Amyloidosis

II NS with active sediment (RC and RC casts)

Primary – MCGN (mesangiocapillary)

MPGN (mesangiproliferative)

Secondary – SLE

Cryoglobulinemic disease

HSP

II Depending on histology

Non proliferative – EM – Minimal change GN

Membranous GN

Proliferative – LM – Mesangial proliferative GN

Mesangio-capillary GN

	Minimal change disease	Membranous GN	FSGS	Mesangio-capillary GN
LM	Normal glomerulus	Uniformly thickened GBM Diffuse and global glomerulosclerosis	Focal and segmental sclerosis	Hypercellular Capillary BM Splitting/tram line
EM	Fusion of the foot processes of podocytes	Loss of foot processes Irregular subepithelial deposits Electron deposits	Diffuse effacement of foot processes Hyaline deposits	Subendothelial immune deposits
IF	No deposits	Diffuse granular deposits (C3, IgG)	C3, IgM deposits	Granular deposits – C3, IgG
	20-25% adult NS		Classical – benign Collapsing – severe 50% ESRF in 10yrs	3 types

How would you manage this pt.?

- 1) Symptomatic treatment – to control oedema
 - Thiazide diuretic
 - Dietary Na & H₂O restriction depending on OP – approx. 3g salt/day

If unresponsive and after excluding hypovolemia

 - Frusemide 40-120mg daily + spironolactone (25mg tds, 50mg tds) – may require IV
Gut mucosal oedema → malabsorption
 - Monitor s. creatinine & BU/SE – EOD
 - Monitor postural BP (can be hypovolemic), IP/OP chart, daily body weight
 - Albumin infusion – if oliguria + uraemia w/o severe glomerular damage Eg:- MCD
- 2) Reduce proteinuria
 - ACEI/ Angiotensin II receptor blockers – lower glomerular capillary filtration pressure
 - Monitor BP and renal function
 - Normal protein intake (high protein diet → ↑ loss)
- 3) Specific therapy
 - MCD – High dose steroids (60mg/m²/day → 4 weeks followed by 40mg/m²/day EOD x 4 wks)
Adults require longer course – daily steroid x 12 weeks → EOD 12 weeks
+/- cyclophosphamide/ ciclosporin
 - Adults (FSGS, membranous) → Poor response to steroids
2nd line – Cyclophosphamide
Cyclosporine - ↓/stop proteinuria
Azathioprine
Chlorambucil
Mycophenolate mofetil
Anti-B lymphocyte therapy → ↓ autoabs
Anti-CD20 Abs (Rituximab)
- 4) Mx of complications
 - Venous thromboembolism
 - Due to loss of anticoagulants (anti thrombin) in urine + ↑ hepatic synthesis of fibrinogen and hypovolemia
 - Long term prophylactic anticoagulation - enoxaparin
 - Avoid prolonged bed rest
 - Sepsis
 - Due to loss of Igs in urine
 - Early detection & aggressive treatment -AB
 - Pneumococcal vaccination
 - Hyperlipidemia
 - Statins +/- fibrates

Case definitions

Relapse	<ul style="list-style-type: none">• While on remission• Urinary prot. excretion $> 3.5\text{g/day}/1.73\text{m}^2$ or $\geq 2+$ for 3 consec. days• Recurrence of proteinuria at any level with hypoalbuminemia $<3\text{g/d}$
frequent relapses	<ul style="list-style-type: none">• ≥ 2 in the first 6/12 after diagnosis• 4 relapses in any 12 month period
steroid sensitive	<ul style="list-style-type: none">• Remission achieved by steroids alone
steroid dependant	<p>2 consecutive relapses while on steroids OR Relapse within 14days of cessation of therapy</p>
steroid resistant	<p>Failure to achieve remission after 28days of prednisolone at $60\text{mg/m}^2/\text{day}$</p>

Drug	Facts	S/E
Cyclophosphamide	- can induce remission in SRNS and long lasting remission in SDNS	Leucopenia – FBC weekly Haemorrhagic cystitis - hydrate Infertility in males
Cyclosporine	Need to do renal Bx prior to starting as it can change the architecture of the glomerulus	Hirsutism Gum hypertrophy Renal failure – monitor renal functions & drug level
Chlorambucil	Alkylating agent	Reversible pancytopenia
Azathioprine	Inhibits purine synthesis	Hypersensitivity Marrow suppression Liver toxicity
Mycophenolate mofetil	Reversible inhibitor in purine synthesis (esp guanine syn) → impair T and B cell proliferation	High blood glucose Hypercholesterolemia

Pyrexia of Unknown origin

PC

- (PUO), Fever a temperature higher than 38.3 C (100.9 F) lasting more than three weeks; and a failure to reach a diagnosis despite one week of inpatient investigation.

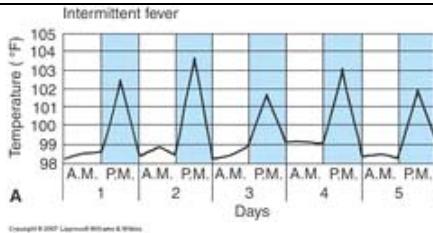
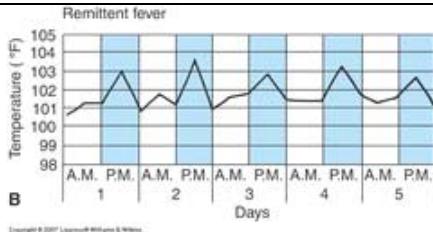
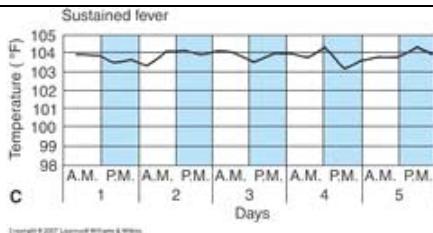
History of presenting complaint

Describe fever

1. Onset of fever, Describe any specific proceeding events
2. Describe the progression of fever
3. Type of fever(Fever pattern)→best can do with a graphical representation of fever
4. State the temperature at the height of fever, Duration of a fever spike and then the duration of fever free period.
5. Describe the symptoms associated with high fever spike→Associated with Chills and Rigors
6. Describe how the patient is between episodes
7. Respond to PCM/any relieving factors

Differential Diagnoses

- Infective causes
 - Bacterial(5)
 1. Infective endocarditis
 2. Pyogenic abscess→Liver, Pelvic , subphrenic
 3. Tuberculosis
 4. Typhoid
 5. Leptospirosis
 - Viral(4)
 1. Glandular fever (EBV)
 2. CMV infection
 3. Viral influenza
 4. HIV
 - Fungal infections
 - Protozoal – Malaria, Lyme disease, Brucellosis
- Collagen vascular disease(5)
 - RA
 - SLE
 - Wegener's granulomatosis
 - Giant cell arteritis
 - Adult still's disease
- Malignancies(4)
 - Lymphoma
 - Leukeamia
 - Renal cell CA
 - Hepatocellular ca
- Metabolic – Hyperthyroidism(1)
- Miscellaneous(6)
 - Drug fever, Sarcoidosis, Granulomatous hepatitis(TB,Sarcoidosis), Factitious fever, Familial Mediterranean fever, IBD

Fever pattern	Description	Clinical Eg:-
Intermittent	<p>Intermittent fever</p>  <p>A</p> <p>High spiking fever which reaches baseline</p>	<p>Pyogenic infections</p> <p>TB</p> <p>Lymphoma</p> <p>systemic onset JIA</p>
Remittent	<p>Remittent fever</p>  <p>B</p> <p>Fluctuating fever, does not reach baseline</p>	<p>Viral infections - CMV</p> <p>IE</p> <p>Lymphoma</p> <p>Amoebiasis</p> <p>Kawasaki</p>
Continuous	<p>Sustained fever</p>  <p>C</p> <p>Little or no fluctuation (fluctuates within 1°C)</p>	<p>Typhus</p> <p>Typhoid (slow stepwise and high plateau)</p> <p>Lobar pneumonia</p> <p>UTI</p> <p>Brucellosis</p>

Relapsing	<p>Relapsing fever Febrile episodes separated by 1 days w/o fever</p>	<p>Malaria Lymphoma</p> <p>Saddle back fever Dengue Leptospirosis Borrelia</p>
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History of presenting complaint

Disease	History
Infective Endocarditis	<p>Clinical features due to infection, Septicaemia--> Fever(intermittent), Rigors, fatigue, Malaise, sweats(night), weight loss, LOA, Arthralgia, Myalgia</p> <p>Clinical features due to cardiac effects→ <i>Cardiac failure→</i> Exosomal dyspnoea, Orthopnoea, Paroxysmal nocturnal Dyspnoea, Lethargy, RHC discomfort, Pain, ascites, ankle oedema</p> <p><i>Conduction defects→ arrhythmias(palpitation, faintishness)</i></p> <p><i>Immunological phenomena - Proteinuria, haematuria, increase BP, Oedema Vasculitis-Skin patches, gangrene</i></p> <p>Aetiology</p> <ul style="list-style-type: none"> ✓ Hx of congenital heart disease(Increase risk of IE) ✓ What was the abnormality (Tetralogy of fallots>Bicuspid aortic valve>Coarctation of aorta>VSD) Secundum ASD very rare cause IE(It is a low pressure system) ✓ If yes→previous surgical correction (But surgical correction does not exclude from risk in major CHD) ✓ Prophylaxis antibiotic taken correctly prevent IE. ✓ Rhuematic fever hx previously(AS/AR/MR predispose s commonly)rare in MS ✓ Prophylactic antibiotic taken correctly following RF ✓ Early medical intervention ✓ Hx of Valvotomy, plasty, when it was done(prosthetic valves high IE incidence) ✓ Whether patient is on anticoagulation ✓ Is he an IV drug abuser, heroin user (high incidence of IE) ✓ whether he has a pace maker ✓ Central venous catheterization recently(as a complication IE) ✓ Dental problems, any recent surgical interventions ✓ Hx of DM (Immunocompromised state) ✓ Long term catheterization poor care ✓ What has done so far in the ward.. ✓ In ward taken blood culture, echo antibiotic by now

	<p>Complications</p> <ul style="list-style-type: none"> ✓ Cerebral abscess-Seizure, Loss of consciousness, headache (Sinister feature) ✓ Focal neurological signs-limb weakness ✓ Paresthesia ✓ Renal abscess-Loin pain, discomfort ✓ Cerebral infarction-Acute onset weakness of limbs, difficult to talk ✓ Bowel infarction-Abdominal pain following meal ✓ Renal infarction-haematuria ✓ Glomerular nephritis
Pyogenic abscess	<ul style="list-style-type: none"> • Fever with chills Rigors • Depending on the site :- <ul style="list-style-type: none"> Liver→Right side plueritic chest pain, abdominal pain Lung→plueritic type chest pain
Glandular fever(IMN/EBV)	<ul style="list-style-type: none"> • Sore-throat, fever, Malaise, Generalized lymphadenopathy, palatal petechiae (reduce platelet), Right side abdominal pain(Hepatitis), yellowish discolouration of eyes, rash-Macular body rash • Rash worsen on taking Ampicillin, Amoxicillin • Peripheral neuropathy-peripheral numbness
Tuberculosis	<ul style="list-style-type: none"> • Fever-Low grade nocturnal fever long standing • Cough-chronic cough>3 weeks • Sputum:-Blood stained sputum • Loss of appetite, Night sweats, Loss of weight • PHx or contact hx of TB
Typhoid	<ul style="list-style-type: none"> • During 1st week of fever→Malaise, headache, Anorexia, Abdominal pain, Non productive cough, Constipation, High fever can cause cloudiness • During 2nd week→Diarrhoea, step ladder fever(Organisms are in localize lesions), Alteration of consciousness • In Minority of patients→rash over body <p>Aetiology</p> <ul style="list-style-type: none"> • Contaminated food→food from outside • When making food wash hands, prior to consumption of food wash hands, toileting, Travel hx-India <p>Complications</p> <ul style="list-style-type: none"> • 2-3 week of onset of illness • Intestinal perforaton→abdominal pain • Intestinal haemorrhage→Melaena, PR bleeding • Myocarditis→chest pain, faintishness due to arrhythmias • Osteomyelitis→bone pain • Meningitis→Photophobia, rash
Weil's disease-Leptospirosis	<ul style="list-style-type: none"> • Caused by Leptospira interrogans • Spread by contact with infected rat urine eg:-in slums or while swimming, marshy lands • Abrupt onset of fever, Myalgia, cough, chest pain + or - haemoptysis- then recovery or jaundice, meningitis, uveitis, renal failure • Cola colour urine-Haemoglobinuria
Viral Influenza	<p>Spread by droplets</p> <p>Fever ,Headache, malaise, myalgia, prostration-Lethargy, nausea, vomiting, Conjunctivitis/eye pain(also photophobia)</p>

HIV	<ul style="list-style-type: none"> • Night sweats • Diarrhoea • Weight loss • Minor opportunistic infection-eg:-Oral candidiasis, Oral hairy leukoplakia, Herpes zoster, Recurrent herpes simplex seborrhoeic dermatitis, Tinea infection, AIDS in stage in HIV infection
Fungal	Candidiasis→Immunocompromised state-DM, chronic illness, on steroids long term, Itchy skin rash, recurrent infections
Protozoal (Malaria)	<ul style="list-style-type: none"> • Non specific flu like prodrome :-Headache, Malaise, Myalgia, Anorexia followed by fever and chills -/+ faints • Classic periodic fever (Peaking every third day) and rigors are unusual initially • Travel to Anuradhapura <p>Complications of Malaria</p> <ul style="list-style-type: none"> • Confusion • Coma • Seizures • Extensor posturing • Teeth grinding • Anaemia
SLE	Rash, Photosensitivity, seizures, Oral ulcers, Joint pain
Rheumatoid arthritis	<ul style="list-style-type: none"> • Pain, morning stiffness of the joints or at rest • B/L, symmetrical involvement, polyarthritis ,hand joints ,feet & cervical spine Wrist, elbow, shoulder, knee, ankle –warm, tender swelling , limitation of movement Swelling & deformities of small joints of hand Due to deformities- activities affected • Extra articular manifestation- Lung Fibrosis, Pleural effusion – pleuritic pain, DIB, SOB Nephrotic xn, amyloidosis – Oedema, frothy urine Pancarditis, LVF- chest pain, palpitations, SOB, fatigue, orthopnea, PND, ankle edema, Episcleritis, scleromalacia perforans, Sicca xn - Dry eyes, dry mouth, painful red eyes Anemia– chronic disease, drugs
Temporal arteritis	<ul style="list-style-type: none"> • Headache, • temporal artery and scalp tenderness, (eg:- on combing hair) • Jaw claudication • Amarosis fugax or sudden blindness in one eye
Lymphoma	<ul style="list-style-type: none"> • Pruritus • Significant weight loss • Night sweats • Lymphadenopathy • Anorexia, fatigue • Cough breathlessness
Leukaemia	<ul style="list-style-type: none"> • Anaemia symptoms • Infection lung functions • Bleeding manifestations • Lymphadenopathy • Abdominal discomfort • Bone pain
Renal cell CA	Haematuria, LOA, LOW
Hepatocellular	LOW, LOA, yellowish discolouration of eyes, abdominal pain

CA	
Thyroid	<ul style="list-style-type: none"> • Increase appetite despite that reduction in body weight • Oligomenorrhoea, amenorrhoea, undue sweat, Heat intolerance, diarrhoea, Neck lump-thyroxine treatment
IBD	<p>Alteration of bowel habits</p> <ul style="list-style-type: none"> • Diarrhoea blood and mucus • Anterior uveitis • Joint involvement

SHX

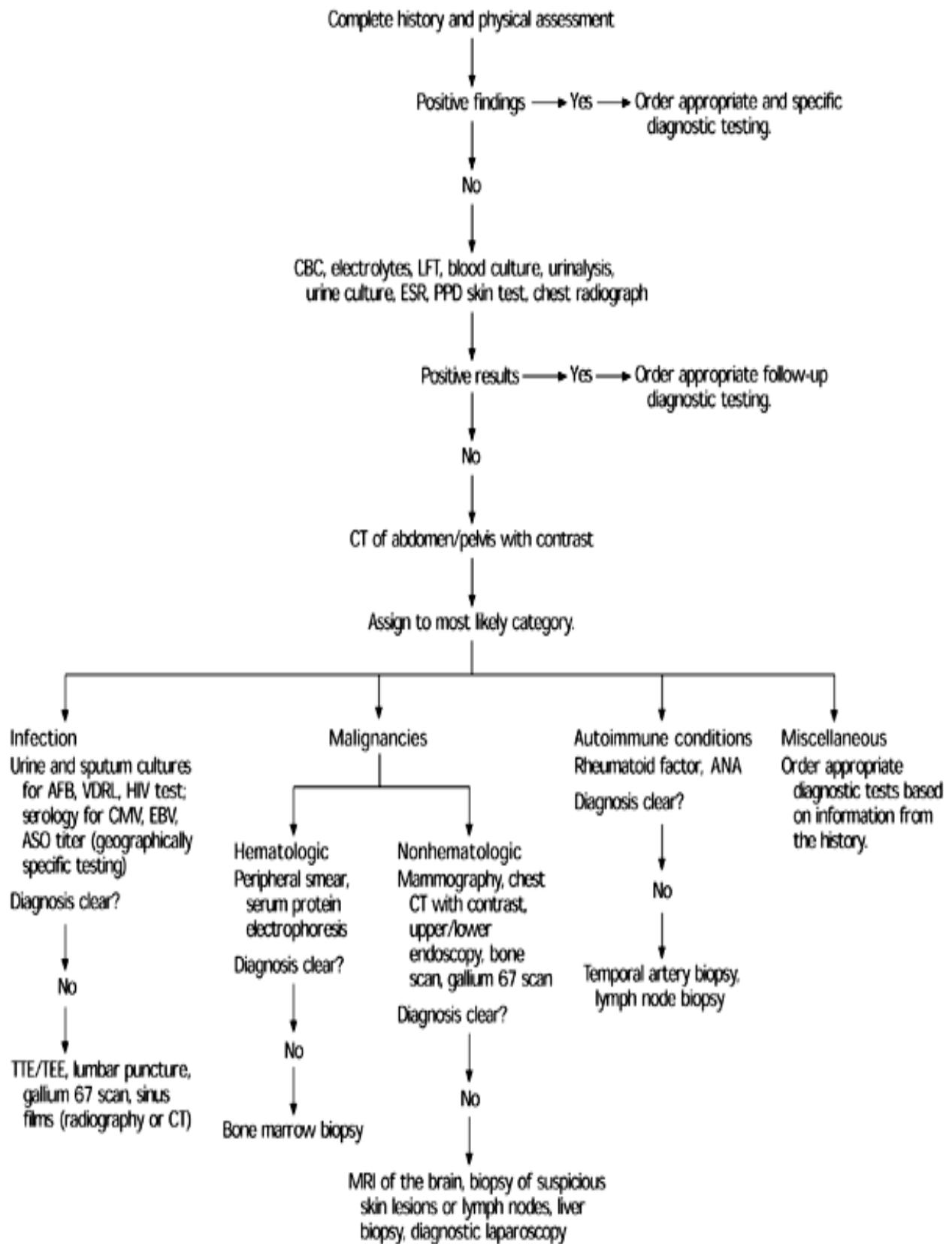
- Family support
- Long term hospital stay how affect to his job and family problem
- Income (lot of investigations)
- TB-Stigmata

Disease	Examination findings
Ex of Infective endocarditis	<ul style="list-style-type: none"> • Fever • Hands- Clubbing • Sphincter haemorrhages on finger and toe nails • Osler's nodes-Painful pulp infarcts in fingers and toes • Jane-way lesions - Painless palmar or plantar macules • Abdominal examination - Firm splenomegaly • CVS examination - A new murmur or change in the nature of a pre existing murmur • Fundus examination-Roth spots(Boat shaped retinal haemorrhages with pale center)
Ex of glandular fever	<ul style="list-style-type: none"> • Pale, Jaundice(Haemolysis), Lymphadenopathy, palatal petechiae, Oral leukoplakia • Abdominal examination - Splenomegaly, tender liver(Hepatitis) • Hepato-splenomegaly • CNS ex - peripheral neuropathy-sensory motor impairment in peripheries • Meningitis - Neck stiffness, alteration in the consciousness
Examinations Typhoid	<ul style="list-style-type: none"> • Febrile • In minority of patients in 2nd week→Relative bradycardia, splenomegaly, Rose spots(skin rash-Erythematous macular popular rash appear over chest and abdomen in 2-3 week of illness)
Ex of Leptospirosis	<ul style="list-style-type: none"> • Fever • Conjunctival injection no suppuration • RHC pain(Hepatitis)
Ex of fungal disease	<ul style="list-style-type: none"> • Oral thrush • Vaginal whitish secretions
Ex of malaria	<ul style="list-style-type: none"> • Febrile • Anaemia • Jaundice • Hepatosplenomegaly-spleen??? • No rash or lymphadenopathy

Ex SLE	<ul style="list-style-type: none"> • Malar rash • Alopecia • Pallor, Anaemia, Red eye, Febrile • Discoid rash • Mouth ulcers • Lymphadenopathy • Arthritis:-Tenderness, swelling, effusion
Ex temporal lobe arteritis	<ul style="list-style-type: none"> • Non pulsatile tender temporal artery

Investigations

1. What are the first line investigations of PUO?
 - ✓ Full blood count→Including differential white cell counts and blood film
 - ✓ Erythrocyte sedimentation rate(ESR)
 - ✓ Serum urea and electrolytes, Liver biochemistry and blood glucose
 - ✓ Blood cultures→several sets from different sites at different times
 - ✓ Microscopy and culture of urine, sputum and faeces
 - ✓ Baseline serum for virology
 - ✓ Chest X ray
 - ✓ Serum rheumatoid factor and antinuclear antibody
2. What are the 2nd line investigations of PUO
 - ✓ Abdominal imaging with ultrasound, CT or MRI to detect occult abscess and malignancy
 - ✓ Echocardiography for infective endocarditis
 - ✓ Biopsy of liver and bone marrow, Temporal artery biopsy should be considered in elderly
 - ✓ Determination of HIV status
 - ✓ Radionuclide scanning



Infective endocarditis	<ul style="list-style-type: none"> • FBC-Neutrophil leukocytosis, Thrombocytopenia • High ESR/CRP • UFR-RBC, Protein, casts • LFT-High alkaline phosphatase, abnormal LFT High IGs, low C3 compliment(Not indicated routinely) • ECG-MI /conduction defects • CXR-for complications cardiomegaly
Glandular fever investigations	<p>a. Blood film →Lymphocytosis, Atypical lymphocytosis(Large irregular nuclei)</p> <p>b. Heterophil antibody test (Monospot, Paul bunnell) Usually heterophil antibodies develop in 90% of patients by week 3 disappearing after 3 months False +ve of test can be in→Hepatitis, Lymphoma, Leukaemia, SLE</p>
Tuberculosis Investigations	<p>Microscopic examination of AFB-sputum specific, less sensitive can repeat</p> <p><u>Other samples</u> Biopsy-LN biopsy, Trans tracheal aspiration, Broncho-alveolar lavage</p> <p><u>Radiology</u> Non specific but very useful (suspicious x ray should never be treated without sputum examination) Certain features-Strongly suggestive Upper zone-patchy nodular shadow unilateral bilateral Cavitation-Specially>1 calcified shadows Rarely Diffuse small nodular opacities-miliary Normal x ray-Endo bronchial TB</p> <p>New diagnostic techniques Microbiology-PCR Mantoux test is a test for infection in human and not necessarily a disease</p> <p><u>Tuberculin skin test</u> Positive -10mm swelling (If BCG is not received) 15mm swelling (if BCG is received) Negative – Doesn't exclude active TB Repeatedly negative - May rule out TB Negative-Positive - TB is likely</p>
Ix Leptospirosis	<ul style="list-style-type: none"> • Blood cultures +ve only upto day 4 of illness.
Ix viral fever	<ul style="list-style-type: none"> • Viral WBC counts(leukocytosis lymphocytic)
Ix of SLE	<p>To confirm diagnosis –</p> <ul style="list-style-type: none"> • ESR -raised • CRP – normal unless superimposed infection • FBC and blood picture – pancytopenia, HA(fragmented rbc) • ANA – (+) in 95% (also in pregnancy, RA, malaria, pneumonia) • Anti ds-DNA – specific for SLE, (+) ve in 50% • RF – (+)ve in 25%, require a titre>128 to be (+)

Ix Rhuematoid arthritis	<p>Ix- high ESR, CRP. FBC for anaemia, thrombocytosis, neutropenia RFT – assess nephrotic xn, drug effects LFT – high CRP, ALP drug effects Ferritin level Rheumatoid factor +ve(>128 titre) or -ve , ACPA(anti citrullinated protein antibodies) - 95% specific, Anti CCP(Anti citrullinated cyclic peptide) - antibodies worse prognosis X ray – tissue swelling, juxta articular osteopenia, loss of joint space, erosions & subluxations</p> <p><u>DIAGNOSTIC CRITERIA</u></p> <p>At least 4 of</p> <ul style="list-style-type: none"> • Morning stiffness for > 1 hour at least 6 weeks • Arthritis of > 3 joints for at least 6 weeks • Arthritis of hand joints for at least 6 weeks • Symmetrical arthritis • Rheumatoid nodules • Rheumatoid factor • Joint erosions
IX for temporal arteritis	<p>High platelets Alkaline phosphatase high Haemoglobin reduce Get a serial biopsy(skip lesions present, Get temporal artery biopsy within 3-4 days</p>

Management

Infective endocarditis	<p>Bacterial antibiotics start - Intravenous, Higher doses, 4-6 weeks, manage complications and do surgery if indicated Streptococcus viridians - Penicillin(4weeks) + gentamycin(2 weeks) or Ceftriaxone(4 weeks) Most patients respond within 48 hrs of treatment started if didn't respond by then its due to some other problem:-</p> <ol style="list-style-type: none"> Perivalvular extension and abscess formation Drug reaction Nosocomial infection Pulmonary embolism(2ry right sided endocarditis) <p>Indication for surgery Refractory cardiac failure caused by valvular dysfunction Persistent sepsis by a surgically removable focus/Myocardial abscess/Prostheses Persistent life threatening embolization Large vegetations by fungi</p>
Glandular fever	<p>Prednisolone per oral for severe symptoms or complications as thrombocytopenia Never give Ampicillin or Amoxicillin for sore-throats. Often causes severe rash in these with acute EBV infection</p>

Pulmonary TB	<ul style="list-style-type: none"> • 6 months treatment • 1st 2 months - Rifampicin, INAH, Ethambutol, Pyrazinamide • Next 4 months-Rifampicin, INAH <p>Longer regimens</p> <ul style="list-style-type: none"> • Bone TB-9 months regime • TB meningitis-1 Year regime
Pyogenic abscess	Antibiotics, Physiotherapy→positional drainage
Typhoid treatment	<ul style="list-style-type: none"> • Ciprofloxacin DOC • Chronic carriers→Ampicillin
Treatment Leptospirosis	<ul style="list-style-type: none"> • IV penicillin or Amoxicillin • Prophylaxis :- Doxycycline 200mg/week may have a role-eg:-for water sports in dangerous places
Viral fever Influenza treatment	<ul style="list-style-type: none"> • Bed rest • Antivirals-Oseltamivir(Tamiflu) eg:-75mg/12hrly per oral for 5 days is an alternative (if >13 years old) <p>SE of Tamiflu-Dyspepsia, Headache, Insomnia, Dizziness, Conjunctivitis, Epistaxis, rash, rarely hepatitis, Stevens-Jhonson</p> <p><u>Prevention</u></p> <p>Trivalent vaccine:-from inactivated viruses, Reserving split(fragmented virus) for those <13 years.</p> <p>It is prepared from current serotypes and takes <2 weeks to work.</p>
Fungal treatment	Antifungals - Ketoconazole topical
Management Rhuematoid arthritis	<p>No cure, symptomatic treatment, prevent further destruction</p> <p>Patient education, encourage regular exercise, physiotherapy, occupational therapy</p> <p>Pain relief by warm, heat, IR, Paraffin bath</p> <p>Pharmacology- NSAIDs with PPIs or diclofinac sup, dihydrocodeine</p> <p>Low dose Prednisolone intra articular injections</p> <p>DMARD – Methotrexate – with folic acid, FBC/ LFT monthly. If lung involvement stop& never start again. If cirrhosis & pancytopenia Stop for some time & restart.</p> <p>Sulphasalazine – hepatotoxic, skin rashes</p> <p>Hydrochloroquine – retinal damage may be irreversible refer to eye surgeon</p> <p>Leflunomide – retain in body for 2 years, leucopenia</p> <p>Azathioprine – 2nd line drug, marrow suppression & pancytopenia, liver toxicity,</p> <p>Penicillamine – 2nd line, limited use due to A/E, proteinuria, thrombocytopenia</p>
Treatment-temporal arteritis	prednisolone-40-60mg per oral

Discussion

Exclusion of Differential Diagnosis

1. Classic,
2. Nosocomial,
3. Immune deficient,
4. Human immunodeficiency virus-related.

Classification of Fever of Unknown Origin (FUO)

Category of FUO	Definition	Common etiologies
Classic	Temperature $>38.3^{\circ}\text{C}$ (100.9°F) Duration of >3 weeks Evaluation of at least 3 outpatient visits or 3 days in hospital	Infection, malignancy, collagen vascular disease
Nosocomial	Temperature $>38.3^{\circ}\text{C}$ Patient hospitalized ≥ 24 hours but no fever or incubating on admission Evaluation of at least 3 days	Clostridium difficile enterocolitis, drug-induced, pulmonary embolism, septic thrombophlebitis, sinusitis
Immune deficient (neutropenic)	Temperature $>38.3^{\circ}\text{C}$ Neutrophil count ≤ 500 per mm^3 Evaluation of at least 3 days	Opportunistic bacterial infections, aspergillosis, candidiasis, herpes virus
HIV-associated	Temperature $>38.3^{\circ}\text{C}$ Duration of >4 weeks for outpatients, >3 days for inpatients HIV infection confirmed	Cytomegalovirus, Mycobacterium avium-intracellulare complex, Pneumocystis carinii pneumonia, drug-induced, Kaposi's sarcoma, lymphoma

Classification of PUO

Infections→Tuberculosis(especially extra-pulmonary), Abdominal abscess, Pelvic abscess, Dental abscess, Endocarditis, Osteomyelitis, Sinusitis, Cytomegalovirus, Epstein-Barr virus, Human immunodeficiency virus, Lyme disease, Prostatitis, Sinusitis

Malignancy→Chronic leukaemia, Lymphoma, Metastatic cancers, Renal cell carcinoma, Colon carcinoma, Hepatoma, Myelodysplastic syndromes, Pancreatic carcinoma, Sarcomas

Autoimmune→Adult Still's disease, Polymyalgia rheumatica, Temporal arteritis, Rheumatoid arthritis, Rheumatoid fever, Inflammatory bowel disease, Reiter's syndrome, Systemic lupus erythematosus, Vasculitis

Miscellaneous→Drug induced fever, Complications of cirrhosis, Factitious fever, Hepatitis (Alcoholic, granulomatous or lupoid), DVT, sarcoidosis

Discussion Infective endocarditis

What is the commonest organism cause Infective endocarditis?

- ✓ Streptococcus viridans

Other organisms causing Infective endocarditis

- ✓ HACEK organisms
- ✓ H-Haemophilus
- ✓ A-Actinobacillus
- ✓ C-Cardiobacterium
- ✓ E-Eikenella
- ✓ K-Kingella
- ✓ Coxiella burnetii, Chlamydia
- ✓ Fungi-Candida, Aspergillus, Histoplasmosis

Other causes of IE-SLE, Malignancy

How do you diagnose Duke criteria for Infective endocarditis

Major criteria

1. Positive blood culture
 - Typical organism in 2 separate cultures or
 - Persistently +ve blood cultures, eg 3 > 12h apart (or majority if ≥ 4)
2. Endocardium involved
 - Positive echocardiogram (Vegetation, abscess, dehiscence of prosthetic valve) or
 - New valvular regurgitation (Change in murmur not sufficient)

Minor criteria

1. Predisposition (Cardiac lesion, IV drug abuse)
2. Fever $> 38C$
3. Vascular/Immunological signs
4. Positive blood culture that do not meet major criteria
5. Positive echocardiogram that does not meet major criteria

How to diagnose:-definite Infective endocarditis: 2 major + 1 minor or all 5 minor criteria (If no major criterion is met)

How will you manage Infective endocarditis?

Principles of management

1. Start treatment on suspicion
2. Bactericidal antibiotics
3. Intravenous
4. Higher doses
5. Higher doses
6. Longer periods
7. Manage complications
8. Surgery when indicated

Antibiotics

- ✓ start with depend on the suspected organism
- ✓ change when culture/ABST is available
- ✓ eg:-*Streptococcus viridans*
- ✓ -Penicillin(4 wks)+ Gentamycin(2 wks) or
- ✓ -Ceftriaxone(4wks)
- ✓ Indication for surgery
- ✓ -Refractory cardiac failure caused by valvular dysfunction
- ✓ -Persistent sepsis by a surgically removable focus/Myocardial abscess/Prosthesis
- ✓ -persistent life threatening embolization
- ✓ -Large vegetations by fungi

IMN

- **What are the other diseases which develop heterophil antibodies in blood film?**

Hepatitis, lymphoma, leukaemia, SLE

- **What is the ideal time to do Paul bunnel test?**

Usually heterophil antibodies develop in 90% of patients by week 3, disappearing after 3 months

Thalassemia

Presenting complaint:-

- Diagnosed patient with Thalassemia
- Jaundice with Abdominal distension(splenomegaly)
- Anemia

In medicine cases most of the time a diagnosed patient, or presenting with anemia with thalassemia trait.

Already diagnosed

Demographic data:- Age, Area

This time presentation

Why came for this time blood transfusion?

- Hemoglobin count < 9g/dl

Already Diagnosed

- When it was diagnosed
- Where it was diagnosed by whom
- What were then symptoms
- What were the investigations done, results→Initial Hb count, whether maternal and paternal HPLC (High performance liquid chromatography-EDTA bottle) done
- What was the treatment given→Any blood transfusions, Hb following blood transfusions
- Whether extended matching done/not
- Any blood transfusion reactions occurred
- Last serum ferritin level
- Iron chelation therapy started? When? At which blood transfusion?
- Serum ferritin level at which blood transfusion started
- Progression of the disease
- How frequently regular checking of Hb
- How frequently blood transfusions done
- Amount of blood given at a time
- Following blood transfusions how often child was admitted for re transfusion what were the symptoms, In between transfusion child normal
- Father and mother karyotype, consanguineous marriage
- His siblings affected by this, FHx

How the clinical evaluation done

Clinical evaluation of,

- Echo
- Hearing
- Eyes
- TSH, FSH, LH

Complications of blood transfusions

- Any symptoms of iron overload- Blackish spots over abdomen and limbs
- Polyuria, Polydipsia, nocturia which suggestive of renal involvement
- SOB on exertion or loss of appetite suggestive of cardiomyopathies
- Liver haemosiderosis- Jaundice, abdominal pain
- Hypoparathyroidism- bone pain, joint pain, lethargy, Dry skin, brittle hair
- Vaccination given for hepatitis B
- Any transfusion related infections, any transfusion related reactions

Features of inadequate blood transfusions

- Heart failure- Palpitations, oedema, dyspnoea
- Growth retardation
- Facial changes- Flat nasal bridge, Bossed skull and prominent frontal and parietal bones, enlarged maxilla
- Leg ulcers
- Abdominal distension- Organomegaly
- Infections- anaemic child more prone to get infections

Iron overload

- As a result of regular blood transfusion (500 ml of blood gives 200 mg of iron)
- Increased intestinal absorption of iron

Iron chelation

- Iron chelation started age
- How it was started- Initial investigations (S.ferritin, which transfusion number started iron chelation)
- what is the type of iron chelation using, dose, frequency, any side effects developed, any change in medication, dose, regular monitoring for side effects done
- Any difficulties with that, Cost of it
- How it is done at home

SE of iron overload

- organomegaly, cirrhosis, hepatic fibrosis
- skin pigmentation
- cardiomegaly, CCF & arrhythmias
- diabetes mellitus
- pituitary failure
 - Hypothyroidism
 - growth failure
 - delayed puberty
 - hypoparathyroidism

PMHx : Malaria, Hepatitis, PHx of recurrent infections, DM, HPT, IHD

PSHx- Splenectomy done, any intention to do future splenectomy,
Vaccination of pneumococcal, meningococcal, Hep B, Hib

FHx

- Parental screening for thalasaemia
- Screening of siblings
- Consanguinity
- FHx of repeated blood transfusions
- FHx-parents consanguineous
- Mother and father area
- Any children affected by the same disease

Social hx

- Mother, father jobs
- Family support
- Awareness about the illness of father and mother or patient
- Who is staying with the child during hospital stay, what will happen to other child
- Effect on family, expenses due to the disease, parental education, compliance to therapy, care about the child
- Family problems- Jobs/other children
- School performance
- How far to hospital from home

Dietary hx

- Avoid meat/green leaves (avoid iron containing food)
- Taking a plain tea after a meal
- Other nutritional support

Examination

General examination

- Growth, stunted
- Facies:-Frontal bossing, depressed nasal bridge, Maxillary prominence
- Pubertal assessment(Tanner's)
- Dyspnea
- Febrile
- Pale (Due to haemolysis)
- Icterus(Due to haemolysis)
- Pigmentation(Due to iron overload as a result of repeated blood transfusions)
- Features of hypothyroidism-Dry skin, loss of lateral eye brows, oedematous,obese,
- Sacral or ankle oedema→Heart failure due to anaemia, Iron overload cardiomyopathies
- Broad thick hands

- Features of Liver disease
- Leg ulcers, ankle swelling

Abdominal examination

- Scars:-liver biopsy, splenectomy, Pump given (Iron chelation pump-<2yrs), Puncture sites of iron chelation over abdomen
- Hyperpigmented patches over abdomen, abdomen distended
- Splenomegaly, can be hepatomegaly
- Can be free fluid

CVS examination

PR-tachycardia, arrhythmia
BP
Apex-RV heave/cardiomegaly
S3,
Flow murmur (Anaemia)

RS examination

Usually NAD
IF HF→B/L crepitations
Evidence of infections

CNS examination

Vision, hearing

Musculoskeletal

Bone pain/Joint pain

Problem list

1. Medical problem
 - a. Acute
 - b. Chronic
2. Social problem
3. Psychological problem
4. Economical problem

Skeletal deformities in thalassaemia

- skull bossing
- scaphocephaly
- prominent maxilla
- flat nasal bridge
- malocclusion of teeth
- pigmentation of the skin
- bone tenderness and fractures
- deformities in legs similar to rickets

} Typical Thal facies

Investigations

- ❖ FBC→
 - Haemoglobin reduce in thalassaemia
 - Red cell indices
 - If haemoglobin <5g/dl (FBC exclude pancytopenia)
- ❖ Increase retic count
- ❖ LFT→Jaundice hepatitis increase liver enzymes
- ❖ HPLC-Diagnostic
- ❖ Blood picture
 - Hypochromic microcytic anaemia
 - Normoblasts/target cells and basophilic stippling
- ❖ Haemoglobin electrophoresis
 - Absence/almost complete absence of HbA the almost all the circulating haemoglobin being Hb F
 - Hb A2 % → reduce/slightly increase
 - Thal beta major→Hb F high
 - Thal minor→Hb A2 high
- ❖ Assessment of iron status
 - Serum ferritin→keep between (1000-1500 µgrams per liter)

Follow up

1. S. ferritin every 6/12 Iron/TIBC
2. Weight/Height
3. Urine sugar→once a month
4. Liver, spleen size→3/12
5. Echo, TSH/T4→once a year
6. Eyes→slit lamp→once a year
7. Hearing at least once
8. Annual x ray-Bone growth

Other investigations

LFT/ECG/Endocrine

Skull X-ray→Hair on end appearance, widened diploid spaces

Monthly

- Liver & spleen size
- Hb
- S. Creatinine (If taking Asunra™)

3 monthly

- FBC
- Height
- S. ferritin

6 monthly

- SGPT/SGOT
- TSH
- S. Ca⁺², PO₄⁻³, ALP
- FBS

Annually

- ENT & Eye referral
- 2D Echo

Management

1. Blood Transfusion
 - Expected Hb drop → 1g /week
 - Maintain haemoglobin >9.5g/dl
 - Usually every 3-5 weeks
 - Blood should be <7days old
 - Ideally → Leucocyte depletion RBC
 - Most → washed RBC
 - To reduce febrile reactions

Calculation of blood volume

Blood volume → $\{(12.5 - \text{Current haemoglobin}) \times 4 \times \text{weight}\} + 20\text{ml}/\text{weight}$

If exceed more than 20ml/kg do as >1 blood transfusions

Transfusion related problems

1. Infection- Hep B,C, HIV, malaria, CMV, syphilis
2. Reactions
 - Haemolytic reactions
 - Febrile reactions (due to WBC in blood. To prevent this leukodepleted washed red cells given. This should be given within 6 hours from preparation)
3. Iron overload
 - Screening for iron overload → child >2 yrs
 - After 10th transfusion
 - Gold standard for screening is liver biopsy and measure iron level
4. Iron chelation
 - Usually after >10th transfusion
 - Serum ferritin >1000 micrograms/L

Desferrioxamine

- Subcutaneous/IV
- Dilute in 7-10 ml and the starting dose is 20ml/kg
- Infusion over 8-12 hours → at least 5 nights per week with Vitamin C
- Excrete iron in urine and stools.
- Reduction of hepatic iron overload, Hepatic fibrosis, endocrine and cardiac dysfunction
- Complications → Hypersensitivity, Ototoxicity, Ocular toxicity, growth retardation, bone pain, Yersinia enterocolitis
- Monitor serum ferritin → adjust the dose

Deferiprone

- Children less than 6 years → not recommended
- Only available in oral preparation
- Use as combine therapy with Desferrioxamine (not indicated for monotherapy)
- Reduce serum ferritin
- But does not reduce hepatic iron content
- SE → GI disturbances, Red brown urine discolouration, Neutropaenia, agranulocytosis, Zn deficiency (weekly check neutrophil count)

Deferasirox (Asunra™)

- Equally effective as Desferrioxamine
- 20-40mg /kg/day
- 400mg tablet, oral tablet
- Use with vitamin C
- Early morning empty stomach. Until ½ hour don't eat or drink anything. Take with fruit juice.
- Need to check renal function tests
- Side effects
 - Abdominal pain, nausea, vomiting, diarrhoea, skin rashes and increases in serum creatinine, liver transaminases
- If S.Ferritin is > 3000 → restart Desferrioxamine

Anaphylactic reaction → Need to know to mx

Stop blood transfusion

IV hydrocortisone

IV chlorpheniramine

Iron chelation

Usually iron chelation start after 10 blood transfusions. Ideally serum ferritin > 1000mg/dl

SE of iron chelation

Monitor SE of Desferrioxamine → Visual disturbances, hearing problems, infection site reactions, asthma, GI problems, Arthralgia, Myalgia

Types of iron chelation

1. Desferrioxamine-Subcutaneous
2. Deferiprone-Combine with Desferrioxamine, this drug also oral
3. Deferasirox- Oral Asunra™

Diet advice

- Reduce use of vitmin C
- Reduce iron containing food
- Avoid Nivithi, meet, Liver
- Take tea after meals(tannins in tea prevent absorption of iron)

Counselling of parents

- ❖ Other drugs→Folic acid supplements 5mg/dl, Endocrine therapy
- ❖ Other non pharmacological→Parental proper education regarding disease, Marriage councelling, Immunization

Splenectomy (wait till 5 years of age to do splenectomy)

- ❖ ↑ Transfusion requirement (>200ml/Kg/Year)

$$\text{Calculation} = \frac{\text{Last year transfusion volume}}{\text{Mid year weight}}$$

- ❖ Hypersplenism
- ❖ Very large spleen (risk of rupture)

Bone marrow transplantation-The definitive cure

HLA matched sibling

- Only curative procedure
- Problems-GVHD, Immuno-supresive therapy

Discussion

1. How many haemoglobin molecules present in a RBC?

Approximately 300 millions

2. What causes beta thalassaemia major?

*Genetic - point mutations(Beta thal)>>gene deletions(alpha thal)

3. What do you know about Thalassaemia minor(trait)?

Usually more severe than alpha thalassaemia

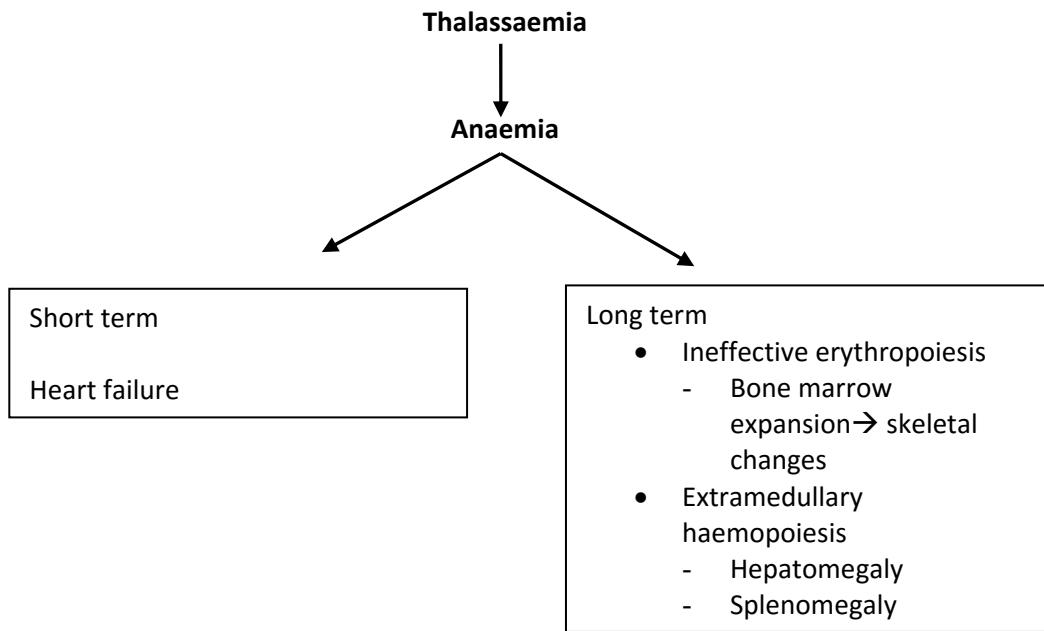
4. Thalassaemia intermediate?

Thalassaemia of moderate severity (Hb- 7-10g/dl)

Do not need regular transfusions

❖ What is the pathophysiology in Beta thalassaemia?

- Reduce beta chain synthesis
- Accumulation of alpha chains occur
- Excess α chains precipitates in red cell precursors,
- Makes the cell prone to early removal/lysisMost cell lysis happens in bone marrow ineffective erythropoiesis



❖ **How bone marrow expansion occur?**

Ineffective erythropoiesis cause anaemia, leads to Hypoxia, this stimulates secretion of Erythropoietin, Cause bone marrow expansion

❖ **What is the clinical presentation of Beta thalassaemia trait?**

β-thalassemia trait (carrier)

- Essentially asymptomatic, often detected incidentally
- Hb ranges from 8.5g/dl to 12g/dl
- MCV, MCH, MCHC reduced
- Hypochromic microcytic red cells
- HbA₂ raised (>3.3%)

❖ **Diagnosis of Beta thalassaemia Major?**

- Clinical features
- FBC- Hypochromic microcytic anaemia
- Hb electrophoresis- very high HbF levels (>90%)
- HPLC- (chromatography)
- Family studies (screen both parents)

❖ **What is Thalassemia intermedia?**

- Patients who have “intermediate severe” disease compared to trait and major
- Very variable presentation
- different causes BUT in Sri Lanka the most important cause is **Haemoglobin E-β thalassaemia**
- **30% patients with “severe thalassaemia” have Hb E- b thalassaemia**

❖ **Haemoglobin E-beta thalassemia?**

- Very variable clinical presentation
- Age of presentation from 8months to 55 years!!
- No single transfusion policy
- More work necessary
- Chelation still necessary

❖ **How thalassaemia minor and Iron deficiency red cell indices differ?**

	RDW	RBC	MCHC
Thal trait	normal(Small cells)	reduce	reduce
Iron def anaemia	Increase	reduce	reduce

❖ **Alpha thalassaeama minor present as?**

Anaemia, Microcytic hypochromic

❖ **Alpha thal major? Hydrops fetalis**

❖ HbH→(beta 4)

❖ Hb barts→(gamma 4)

❖ **What is the chromosome involved in alpha gene?** Chromosome 16

	Acute Diffuse Prol. G.N	RPGN (Crescentic G.N)	Minimal Change Disease	Focal segmental Glomerulosclerosis	Membranous glomerulopathy	Membranoproliferative GN	IgA Nephropathy	Mesangioproliferative GN	Focal Proliferative GN	Alport Syndrome
Clinical presentation	Acute Nephritic Syn.	* Acute Nephritic syn. * Severe glomerular injury * Rapid & progressive loss of renal function	Nephrotic syn.	Nephrotic syn.	Nephrotic syn.	Nephrotic + Nephritic	Nephrotic Syn.	Nephrotic + Nephritic	Nephrotic syn.	Nephritic syn. * Accompanies by - Nerve deafness - Various eye disorders
Pathogenesis	Endo. Ag - SLE Exo. Ag - Post strep GN	T-1: Anti GBM IgG Ab (goodpasture syn) T-2: Immune complex (post strep GN, SLE, HSP) T-3 : No Ab or Complexes (Systemic vasculitis)	No immune deposits	* Podocyte damage (Cytokine induced) * Sclerosis - Entrapment of plasma proteins - Increased EC matrix deposition	* Chronic Ag-Ab complex * No inflammatory cells * Uniform presence of compliments * Damage by the formation of Membrane attack complexes	T-1: Immune complex Classical & alternative pathways T-2: Alternative pathway T-3: Final common pathway	IgA deposition in mesangial region due to immune response ---> Immune complexes ---> Activation of complements	1. IgM Nephropathy IgM & complement deposits 2. C1q nephropathy C1q deposits(l like IgM)	Focal necrosis & Fibrin deposition Should be differentiate from FSGS	X linked(common)/AR/AD
Macroscopy	* Symmetrically enlarged kidneys * Cut surface : pale renal cortex due to oedema	* Kidney - Enlarged due to oedema - Smooth subcapsular surface - Petechial haemorrhage on surface - Cut surface bulges out & pale			* Kidneys - Initially large - cut surface : pale & smooth subcapsular surface - Later normal/small kidneys					
LM	* Glomeruli - Diffusely enlarged - Globally hypercellular (infiltration & proliferation) - swollen cells * Capillaries - Bloodless - Fibrin deposition in capillary lumina & mesangium * Tubules - RBC casts - Protein casts * Interstitium - Oedema ---> Fibrosis - Focal inflammatory cell infiltrate	* Glomeruli - CRESENT FORMATION * Capillaries - Narrowing of capillary lumen - Intimal thickening * Tubules - Red cell casts - Tubular atrophy * Interstitium - Oedema ---> Fibrosis - Focal inflammatory cell infiltrate	* Glomeruli - No abnormality * Tubules - Vacuolated epithelial cells	* Glomeruli - Focal & segmental sclerosis - Increased in matrix * Capillaries - Hyaline thickening of afferent arterioles * Tubules - Atrophy * Interstitium - Fibrosis	* Glomeruli - Uniformly thickened GBM (Diffuse & Global)	* Glomeruli - Large & hypercellular (Mesangial proliferation, Leucocyte infiltration & Parietal epithelial crescents) - Lobular appearance (Mesangial proliferation) - Thickened GBM - "double contour"/ "Tram-track appearance of BM - Inclusion of cell processes into GBM	* Glomeruli - May normal - May show mesangial widening - Mesangial proliferation - Focal proliferative changes			No LM Changes
EM	BM - Subepithelial dome shaped deposits "Humps"	Rupture in GBM	* Uniform & diffuse obliteration of foot processes	* Diffuse obliteration of foot processes * Focal detachment of epithelial cells & denudation of GBM * Fine granular electron dense deposits in sclerotic areas	Loss of foot processes	T-1: Subendothelial electron dense deposits T-2: GBM - On lamina densa irregular ribbon like dense deposits(Dense deposit disease)	Electron dense deposits in the mesangium(IgA)			* Early - Diffuse GBM thickening * Later - Glomerular sclerosis - Vascular sclerosis - Tubular atrophy - Tubular fibrosis GBM - Irregular foci of thickening alternating with thinning
IF	Granular deposits IgG & C3 in BM	* Linear deposits in Goodpasture syn. * Granular deposits in Post streptococcal GN	No immune deposits	IgM & C3 deposition on sclerotic areas & mesangium	Irregular subepithelial deposits (IgG & C3)	C3 & IgG granular deposits in capillary BM	Mesangial deposits of IgA			
Prognosis	Glomeruli return to normal with recovery		Podocyte changes are completely reversible							

	Diabetes Mellitus	Benign Hypertension	Malignant Hypertension	SLE	Amyloidosis	Multiple Myeloma	Acute Pyelonephritis	Chronic Pyelonephritis
Pathogenesis	* Hyperglycaemia * Glycation end products damage Glomerular filtration membrane * Hyperfiltration --> diabetic glomerulopathy	* Benign nephrosclerosis ↓ Ischaemia of the organ	* Malignant nephrosclerosis ↓ Patchy ischaemic atrophy of Paranchyma	* Circulating autimmune antibody deposition on GBM causing immune reaction			* Ascending infection (Gram -ve bacilli) - Incompetent VU valves - Haematogenous spread(IE,TB)	* Chronic UT obstruction ---> Recurrent UTI * VU reflux & intrarenal reflux --> recurrent infections(starts in childhood)
Macroscopy	* Granular contracted kidneys * Subcapsular scarring	* Fine even granular surface * symetrically contracted kidneys * cortex thinned	* Pinpoint haemorrhages(flee bitten kidney)		* Normal/enlarged * Cut surface - waxy & pale		* one kidney or both * Kidneys enlarged with bulging out surface * Abscesses on the cortex & surface * Eatensive wedge shaped areas of suppuration in cortex * Papillae daining the abscesses show yellowish streaks * Pelvic & mucosae are congested	* Unilateral or bilateral course granular contracted kidneys * Large scars in upper & lower poles * Dilatation of pelvi-calyceal system * Distortion of calyceal system
Microscopy	* Glomeruli - Thickening capillary BM - Increase mesangial matrix - Difuse mesangial sclerosis - Nodular glomerulosclerosis (Kimmelstiel Wilson lesions) - Exudative lesions (accompanies nodular GS) localized accumulations of eosinophilic matrix in differerbt parts of glomeruli - Glomerular hyalinization(CRF)	* Glomeruli - Periglomerular fibrosis - Sclerosis * Tubules - Tubular atrophy	* Glomeruli - Thrombosed capillaries - Necrosis - Collapse of GBM * Vessels - Arterioles : Hyaline arteriolosclerosis - Arteries : Fibroelastic hyperplasia	* Vascular - Arteriolosclerosis - Necrotizing vasculitis * Tubules - Periglomerular fibrosis - Total sclerosis * Vessels - Arterioles : Hyaline arteriolosclerosis - Arteries : Fibroelastic hyperplasia	* Glomeruli - BM thickening - Mesangial widening - Narrowing of capillaries - Later confluent masses of amyloid * Tubules - Amyloid deposition in wall - Later tubular atrophy * Vessels - Hyperplastic arteriolitis(onion skin appearance) - Fibrinoid necrosis ---> arterioles * Interstitium - Fibrosis	1. Myeloma cast nephropathy - DCT & CD light chain casts - DCT is Surrounded by foreign body giant cell - Epithelial cells necrosis & atrophy 2. Light chain deposition - Amyloid deposition in wall - Later tubular atrophy * Vessels - Amyloid deposition in the walls of small arteries ---> Narrowing & ischaemia	* Affected areas destruction of normal renal structure * PMN fill tubules & CD(granular casts) * Interstitial infiltration by polymorphs-----> Abscess * Tubules - Thickening of tubular BM 3. Amyloid deposition - AL amyloid (light chain derived) - In interstitium, tubular BM, Vessel wall - Occassionally glomeruli	* Interstitium - Fibrosis - Inflammatory cell infiltration(L'cytes, plasma cells, E'phils) * Tubules - Dilated - Epithelial atrophy - Lumen contains pinkish glassy material (Thyrodization) - PMN in tubules(Granularcasts) * Vessels - Intimal thickening * Glomeruli - Periglomerular fibrosis
Clinical Features	* Micrualbuminuria * Proteinuria * Nephrotic Syndrome * CRF			* Haematuria * Proteinuria * Hypertension * Nephrotic syn. * Nephritic syn.	* Proreinuria * Haematuria	* Proteinuria * Renal failure	* loin tenderness * Fever + chills * Vomiting * Abdominal guarding	

CHRONIC KIDNEY DISEASE

GENERAL INFORMATION

- ✓ Name, age
- ✓ Gender (AD-PCKD rate of deterioration is rapid in male)
- ✓ Residence – CKD of Unknown origin

P/C

- ✓ Can be a diagnosed patient with CKD
- ✓ Or coming in first time with symptoms

H/P/C

Early stages → asymptomatic

Usually become symptomatic when S.urea >40 mmol/l

- Initially vague symptoms – malaise, lethargy, LOA, insomnia
- Itching
- Nausea, vomiting, diarrhoea
- Nocturia, **polyuria** – poor concentration ability
- Paraesthesiae due to polyneuropathy
- ‘restless legs’ syndrome (overwhelming need to frequently alter position of lower limbs)
- Bone pain and tetany due to metabolic bone disease
- Paraesthesiae and tetany due to hypocalcaemia
- Symptoms due to salt and water retention – peripheral or pulmonary oedema
- Symptoms due to anaemia
- Amenorrhoea in women; erectile dysfunction in men
- In more advanced uremia (serum urea >50–60 mmol/L), these symptoms become more severe, and CNS symptoms are common:
Mental slowing, clouding of consciousness, and seizures myoclonic twitching.
Terminal-oliguria

Presenting feature	Causes for it	Symptoms
Polyuria	Diabetes mellitus	Polydypsia LOW Lack of energy Visual blurring Pruritus vulvae/balanitus Skin infections
	Hypercalcaemia	Renal colics Haematuria Abdominal pain Bone pain
	Diabetes insipidus	Increased thirst, Polyuria

Oedema	Cardiac failure	Predominantly leg oedema Worse towards the end of the day Peri orbital & abdominal-minimal Associated cardiac symptoms; Dyspnoea Orthopnoea PND Past Hx of IHD,HT
	Liver failure	Dependant oedema with predominant ascitis Associated liver symptoms Jaundice Bleeding manifestations Loss of body hair Inverted sleep pattern Hx of alcohol abuse, HBV/HCV
	Malnutrition & malabsorption	Dependent oedema of legs & abdomen Diarrhoea, steatorrhoea LOW Features of protein energy malnutrition Features of nutritional deficiency Vit. A deficiency - Night blindness, keratosis Vit. K deficiency – Bleeding tendency Vit. D deficiency – Osteomalacia
Recent onset intractable HT		
Anaemia		

Aetiology	Features
Congenital and inherited disease <ul style="list-style-type: none"> Polycystic kidney disease (adult and infantile forms) 	Acute loin pain and/or haematuria Abdominal discomfort Subarachnoid haemorrhage associated with Berry aneurysm rupture - FHx Young hypertension - FMHx, PMHx
Glomerular disease <ul style="list-style-type: none"> 1ry glomerulonephritis 2ry GN : DM, SLE 	Haematuria Hypertension Oliguria Skin rashes, arthralgia
Tubulo-interstitial disease <ul style="list-style-type: none"> TM, Myeloma, Nephritis 	
Vascular disease <ul style="list-style-type: none"> Hypertension 	Evidence of vasculitis
Reflux nephropathy	Recurrent UTI(childhood and adult life) Fever with chills and rigors Frequent hospital admissions
Urinary tract obstruction	Loin to groin pain Haematuria BOO symptoms

Known patient with CKD;

When did the diagnosis made, where, aetiology (DM, HT)

Investigations up to now and results, -,

- Serum creatinine level – last value
- USS - what they have said
- Renal biopsy

Plan for dialysis, renal transplant

Follow-up

Medications given - response

Dialysis - Done or not, which type, frequency, relief of symptoms after dialysis

Already transplanted - when, live or cadaveric, improvement of symptoms, medications, follow up

Complications

system	Features
General	Malaise, lethargy, insomnia
GIT	LOA, nausea, vomiting, diarrhea Reflux oesophagitis – belching, burping, heart burns Peptic ulceration Acute pancreatitis Constipation (specially in patients with continuous ambulatory peritoneal dialysis)
CVS	Uremic pericarditis (chest pain with respiration, relieving on leaning forward) Cardiac failure - dyspnoea, orthopnoea, PND Myocardial infarction HT ; headache, blurring of vision PVD - intermittent claudication
Anaemia	Lethargy, breathlessness, palpitation
RES	Pulmonary oedema (DIB, pinky frothy sputum)
GU	Nocturia, polyuria, oliguria in latter
CNS	Severe uraemia ; confusion, reduced higher functions, coma, fits and muscle twitching Peripheral neuropathy -parastheasias
Musculo skeletal	Muscle weakness, bone pain, tetany
skin	skin pigmentation, Pruritus, Dry skin
Endocrine	Amenorrhea, erectile dysfunction, infertility, hyperparathyroidism

PMHx ; DM, HT, SLE

DM-

- Duration
- Follow-up
- Control,
- Complications(retinopathy, neuropathy)
- Any relative with renal transplant- high risk

Hypertension

- Brief history
- Control
- Follow-up
- Drug ingestion, including non-steroidal anti-inflammatory agents, analgesic and other medications(ayurvedic)- **Drug history**

PSHx ; renal tract and parathyroid

Dietary history; Better to have 24 hr dietary recall

- ✓ Compare the current diet and standard diet
- ✓ Any discrepancy
- ✓ Salt restriction
- ✓ No added salt
- ✓ Restrict food with high salt; marmite, salty snacks, soup cubes, jadi
- ✓ Small amount of chicken without skin and fish
- ✓ 2 eggs/wk without the yolk
- ✓ Non fat milk
- ✓ Sugar control
- ✓ Desirable amount of vegetable & fruits
- ✓ Reduce K containing foods if has hyperkalemia (banana, tomato, spinach, king coconut)

Family Hx - Renal disease

SHx

- ✓ Knowledge about disease
- ✓ Compliance for Rx and followup
- ✓ Affordability to dialysis
- ✓ Any plans for transplantation
- ✓ Other social issues
- ✓ Income

Examination

General;

- ✓ Short stature-childhood
- ✓ Fever
- ✓ **pallor** (due to anaemia)
- ✓ eyes; **cataracts**
- ✓ fundi; HT retinopathy, DM retinopathy
- ✓ signs of fluid overload (facial puffiness)
- ✓ Skin : Dry , scratch marks, increased photosensitive pigmentation (pseudo –porphyria)
 - Epistaxis, Bruising- due to platelet dysfunction
 - cutaneous vasculitic lesions → in systemic vasculitides
- ✓ Nails: brown discoloration of the nails, half-half nails
- ✓ scars over subclavian vein, jugular vein (haemodialysis), femoral vein
- ✓ A-V fistula-radio-cephalic and brachio-cephalic
- ✓ Gout (swollen, tender big toe)
- ✓ evidence of peripheral vascular disease

- ✓ evidence of spina bifida or other causes of neurogenic bladder.(to find the cause)
- ✓ Assess hydration (dehydration)
- ✓ Nutritional deficiency features

CVS

- ✓ Pulse-rate(arrhythmias-pericarditis), volume
- ✓ BP for HT(both lying and standing)
- ✓ JVP-CCF
- ✓ Apex-cardiomegaly
 - Flow murmurs(AR,MR,PR)
 - MVP in ADPCKD
- ✓ Pericardial rub

Respiratory

- ✓ Pleural effusions
- ✓ Pulmonary oedema in LVF
- ✓ TB-apical flattening & fibrosis, LN

Abdominal

- ✓ Surgical scars (nephrolithotomy, RT)
- ✓ Femoral scar(RAS- catheters inserted over femoral)
- ✓ Pain in Right hypochondrium (cysts)
- ✓ Renal angle tenderness
- ✓ Masses-renal (large, irregular+/- hepatomegally - ADCKD)
- ✓ Ascites
- ✓ Renal bruits
- ✓ Paralytic ileus, peritonitis, hydrocele – PD
- ✓ DRE & VE – **Must perform**

To find-out obstruction of urinary tract

CNS

- ✓ Higher functions(speech-disabilities, interlectual abilities-uraemia,dylasis)
- ✓ Cranial nerves
- ✓ Motor system
 - Flapping tremors (uraemic)
 - Restless leg (uraemia)
 - Slow relaxing jerks (hypothyroidism)
- ✓ Sensory impairment due to peripheral neuropathy

Investigations

Purpose	Investigation	
To confirm uraemia/CKD	BU	
	S.creatinine (for estimation of GFR)	Compare with previous
	SE	may↑(drugs)/↓(CKD)
	24 hr urine for creatinine clearance	Better than estimated GFR
	USS abdomen	B/L contracted except in hydronephrosis, PCKD, amyloidosis
	Urine osmolality	Low with good fluid intake
Determine the underlying cause	GFR	Gold standard with insulin clearance(difffic) With creatinine clearance or calculate
	Urine ward test for protein and reducing substance	Heavy proteinuria-glome; disease Glycosuria-common with CKD
	FBS/Hb A _{1c} (haematology)	DM
	ESR	MM and vasculitis
	UFR	RBC, pus cells(infection), RBC casts(GN) WBC, granular casts-sterile pyuria-renal TB, papillary necro. Protenturia Eosinophilia-allergic TI nephritis
	Urine culture & ABST	
	Urine biochemistry	
	24h urine protein	
	Electrophoresis, immunofixation	Detect light chain(MM)
	Early morning urine for AFB	TB
Assess complication	Serum biochemistry-pro; electroporesis	MM
	Immunology-ANA,Ds DNA,ASOT	
	HIV status/ hep B/C status	
	Radiology-USS abdo/X ray KUB	Hydronephrosis/hydroureter
	Investigations for TB	
	Transcutaneous USS guided renal Bx	RPGN Unexplained RF with normal size kidney)must)
	FBC/BP	
	Lipid profile	
	CXR	Cardiac size, effusions
	ECG	
	ECHO	
	Xray KUB/IVU	Stones, nephrocalcinosis
	ABG	
	LFT/CT/MRI?angiogram	

Bone profile	
S. calcium/ionized)	Low
S. phosphste	High
ALP	High
PTH	High
X ray	Hyperparathyroidism features
DEXA	Osteoporosis
Determine the progression	S. creatinine & clearance BU/SE, FBC

Investigations

Urinalysis

- **Haematuria** may indicate **glomerulonephritis**, but other sources must be excluded.
- **Proteinuria**, if heavy, is strongly suggestive of **glomerular disease**. UTI also cause proteinuria.
- **Glycosuria** with normal blood glucose is common in CKD.
- Urine culture, including early-morning urine samples for TB.

Urine microscopy

- WBC → active bacterial urinary infection (rare cause for renal failure)
- sterile pyuria → papillary necrosis or renal TB
- Eosinophiluria → allergic tubule interstitial nephritis or cholesterol embolization.
- Granular casts are formed from abnormal cells within the lumen → active renal disease.
- Red-cell casts → glomerulonephritis.
- Red cells in the urine may be from anywhere between the glomerulus and the urethral meatus

Urine biochemistry

- 24-hour creatinine clearance → severity of renal disease.
- Measurements of urinary electrolytes are unhelpful in chronic kidney disease.
- Urine osmolality is a measure of concentrating ability.
- A low urine osmolality is normal in the presence of a high fluid intake but indicates renal disease when the kidney should be concentrating urine, such as in hypovolaemia or hypotension.
- Urine electrophoresis and immunofixation is necessary for the detection of light chains, which can be present without a detectable serum paraprotein (MM)

Serum biochemistry

- Urea and creatinine with calculation of eGFR.
- Electrophoresis and immunofixation for myeloma.
- Elevations of creatine kinase and a disproportionate elevation in serum creatinine and potassium compared to urea suggest rhabdomyolysis.

Haematology

- Eosinophilia → vasculitis, allergic tubulointerstitial nephritis, or cholesterol embolism.
- Markedly raised viscosity or ESR → myeloma or vasculitis.
- Fragmented red cells and/or thrombocytopenia suggest intravascular haemolysis due to accelerated hypertension, HUS or TTP
- Tests for sickle cell disease should be performed when relevant.

Immunology

- Complement components may be low in active renal disease due to SLE, mesangiocapillary glomerulonephritis, post-streptococcal glomerulonephritis, and cryoglobulinaemia.
- Autoantibody screening is useful in detection of SLE, scleroderma, Wegener's granulomatosis and microscopic polyangiitis and Goodpasture's syndrome.
- Cryoglobulins in unexplained glomerular disease, particularly mesangiocapillary glomerulonephritis.
- Antibodies to streptococcal antigens (antistreptolysin O titre (ASOT), anti-DNAase B) if post-streptococcal glomerulonephritis is possible.
- Antibodies to hepatitis B and C may point to polyarteritis or membranous nephropathy (hepatitis B) or to cryoglobulinaemic renal disease (hepatitis C).
- Antibodies to HIV raise the possibility of HIV-associated renal disease.

Radiological investigation

- **Every patient should undergo ultrasonography** (for renal size and to exclude hydronephrosis), **and plain abdominal radiography and**
- **CT** (without contrast) to exclude low-density renal stones or nephrocalcinosis, which may be missed on ultrasound.
- CT → retroperitoneal fibrosis and some other causes of urinary obstruction, also cortical scarring.
- MRI. Magnetic resonance angiography in reno-vascular disease.
- For gadolinium used as contrast in renal failure,
- Intravenous urography is seldom necessary in advanced renal disease.

Renal biopsy

- This should be performed in every patient with unexplained renal failure and normal-sized kidneys, unless there are strong contraindications. If rapidly progressive glomerulonephritis is possible, this investigation must be performed within 24 hours of presentation if at all possible.

What are the causes of CKD?

Table 11.19 Causes of chronic kidney disease

Congenital and inherited disease
Polycystic kidney disease (adult and infantile forms)
Medullary cystic disease
Tuberous sclerosis
Oxalosis
Cystinosis
Congenital obstructive uropathy
Glomerular disease
<i>Primary glomerulonephritides</i> including focal glomerulosclerosis
<i>Secondary glomerular disease</i> (systemic lupus, polyangiitis, Wegener's granulomatosis, amyloidosis, diabetic glomerulosclerosis, accelerated hypertension, haemolytic uraemic syndrome, thrombotic thrombocytopenic purpura, systemic sclerosis, sickle cell disease)
Vascular disease
Hypertensive nephrosclerosis (common in black Africans)
Reno-vascular disease
Small and medium-sized vessel vasculitis
Tubulointerstitial disease
Tubulointerstitial nephritis – idiopathic, due to drugs (especially nephrotoxic analgesics), immunologically mediated
Reflux nephropathy
Tuberculosis
Schistosomiasis
Nephrocalcinosis
Multiple myeloma (myeloma kidney)
Balkan nephropathy
Renal papillary necrosis (diabetes, sickle cell disease and trait, analgesic nephropathy)
Chinese herb nephropathy
Urinary tract obstruction
Calculus disease
Prostatic disease
Pelvic tumours
Retroperitoneal fibrosis
Schistosomiasis

Complications of CKD

system	Features
Anaemia	Breathlessness, lethargy, palpitation-find out the cause
Renal osteodystrophy	Hyperparathyroid bone disease (increased osteoclastic activity, cyst formation, bone marrow fibrosis→ostitis fibrosa cystica) Osteomalacia Osteoporosis Osteosclerosis Adynamic bone disease (bone formation and resorption are depressed)

Cardiovascular	<p>Greatly increased risk of CVD –</p> <ul style="list-style-type: none"> ✓ MI, CCF, sudden cardiac death, stroke ✓ Coronary artery calcification <p>Hypertension</p> <p>Cardiac hypertrophy</p> <ul style="list-style-type: none"> ✓ due to HPT, anaemia & obesity ✓ Systolic & diastolic cardiac dysfunction <p>Vascular calcification in all vessels – ↑ atherosclerosis risk Hyperparathyroidism contributes</p> <p>Pericarditis –</p> <ul style="list-style-type: none"> ✓ due to Uraemia – severe uraemia or under-dialysis ✓ Dialysis – intercurrent illness <p>Hypercholesterolaemia –</p> <ul style="list-style-type: none"> Increase CVD risk Treated with statins
Skin	<p>Pruritus is common</p> <p>Due to –retention of nitrogenous waste products</p> <ul style="list-style-type: none"> hypercalcaemia hyperphosphataemia ↑ CaXPO₄ product hyperparathyroidism iron deficiency <p>Dry skin</p> <p>Eczema (sp near AV fistula)</p> <p>Pseudo-porphiria</p>
GIT	<p>Reflux oesophagitis</p> <p>Peptic ulceration</p> <p>Acute pancreatitis</p> <p>Constipation (sp in CAPD)</p>
Endocrine	<p>Hyperprolactinaemia → galactorrhoea</p> <p>↑ LH</p> <p>↓ Testosterone → impotence</p> <p>Absence of normal cyclical changes in female sex hormones → oligo/amenorrhoea</p> <p>GH abnormalities</p> <p>Thyroid hormone abnormalities</p>
Nervous system	<p>Severe uraemia → depressed cerebral function, convulsions, tremors, myoclonus</p> <p>Dialysis disequilibrium – due to cerebral swelling</p> <p>Dialysis dementia – due to aluminium</p> <p>Carpal tunnel syndrome – due to amyloidosis</p> <p>'Restless legs' syndrome - in uraemia</p> <p>Polyneuropathy</p>

Treatment

1. Treat underlying cause where ever possible

- Control HT
- Good control of DM
- Obstructive uropathy-relieve

2. Renoprotection

- CKD due to any cause, once established, will progress to ESRD
- Rate of progression varies –
- Depends on - underlying disease
 - hypertension
 - proteinuria

Goals of treatment

- BP < 120/80
- Proteinuria < 0.3 g/24 hours

Box 11.6 Renoprotection

Goals of treatment

BP <120/80
Proteinuria <0.3 g/24 hours

Treatment

- Patients with chronic kidney disease and proteinuria
>1 g/24 hours:
- ACE inhibitor increasing to maximum dose
 - Add angiotensin receptor antagonist if goals are not achieved*
 - Add diuretic to prevent hyperkalaemia and help to control BP
 - Add calcium-channel blocker (verapamil or diltiazem) if goals not achieved

Additional measures

- Statins to lower cholesterol to <4.5 mmol/L
- Stop smoking (threefold higher rate of deterioration in CKD)
- Treat diabetes (HbA1c <7%)
- Normal protein diet (0.8–1 g/kg bodyweight)

*In type 2 diabetes start with angiotensin receptor antagonist

3. Correction of complications

Anaemia

- ✓ Investigate & correct treatable causes
 - gut blood loss
- ✓ **Haematinics** – iron, B12, folate
- ✓ **Synthetic Erythropoetin therapy** –

Using recombinant human erythropoietin (epoetinalfaor- β , or the longer-acting darbopoetin- α or polyethylene glycol-bound epoetin- β).

Given sc(alpha) or iv 3 times a week

Blood pressure, haemoglobin concentration and reticulocyte count are measured every 2 weeks and the dose adjusted to maintain a target haemoglobin of 11–12 g/dL

Failure to respond to 300 U/kg weekly, or a fall in haemoglobin after a satisfactory response, may be due to iron deficiency, bleeding, malignancy, infection, inflammation or formation of anti-EPO neutralizing antibodies

The demand for iron by the bone marrow is enormous when erythropoietin is commenced. Patients on EPO therapy are regularly monitored for iron status and considered iron deficient if plasma ferritin is < 100 µg/L, hypochromic RBCs > 10%, transferring saturation < 20%

The disadvantages

Expensive and causes a rise in blood pressure in up to 30% (particularly in the first 6 months)

Peripheral resistance rises in all patients, owing to loss of hypoxic vasodilatation and to increased blood viscosity.

Rarely encephalopathy with fits, transient cortical blindness and hypertension

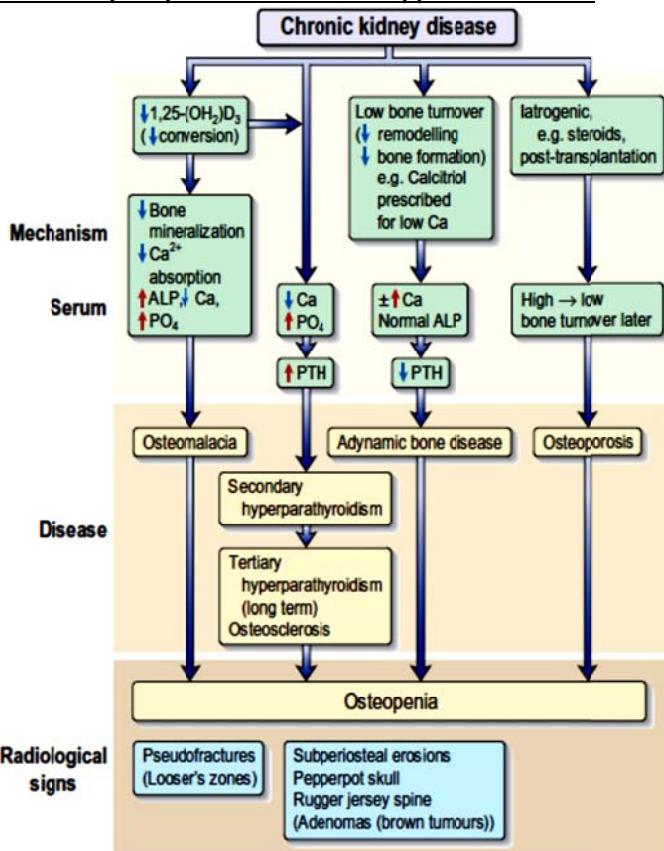
Correcting anaemia improves quality of life, exercise tolerance, sexual & cognitive functions & LVH

Avoid blood transfusions – sensitization to HLA Ag is a barrier to kidney transplantation

Causes of anaemia

- ✓ erythropoietin deficiency (the most significant)
- ✓ bone marrow toxins retained in renal failure
- ✓ bone marrow fibrosis secondary to hyperparathyroidism
- ✓ haematinic deficiency – iron, vitamin B12, folate
- ✓ increased red cell destruction
- ✓ abnormal red cell membranes causing increased osmotic fragility
- ✓ increased blood loss – occult gastrointestinal bleeding, blood sampling, blood loss during haemodialysis or because of platelet dysfunction
- ✓ ACE inhibitors (may cause anaemia in CKD, probably by interfering with the control of endogenous erythropoietin release).
- ✓ Red cell survival is reduced in renal failure. Increased red cell destruction may occur during haemodialysis owing to mechanical, oxidant and thermal damage

Calcium and phosphate control and suppression of PTH



- ✓ Treat ↓ calcium & ↑ phosphate
- ✓ Check PTH regularly
- ✓ Restrict dietary phosphate
- ✓ Oral **calcium carbonateacetate** reduces gut absorption of phos:(contraindicated where there is hypercalcaemia or hypercalciuria)
- ✓ Aluminium containing gut phosphate binders – short term only
(but absorption of aluminium poses the risk of aluminiumbone disease and development of cognitive impairment. They are now rarely used)
- ✓ **Sevelamer** – gut phosphate binder
Reduces the calcium load and attenuates vascular calcification and also lowers cholesterol levels by 10%
Lanthanum carbonate is a new non-calcium, non-aluminium phosphate binder that is effective and has a good safety profile
- ✓ **Calcitriol**
- ✓ Vitamin D analogues – **alfacalcidol**
- ✓ **Calcimimetics**
(vitamin D may worsen hyperphosphataemia)

Hyperkalaemia –

- ✓ restrict dietary potassium
- ✓ stop potassium-retaining drugs
- ✓ emergency management
 - ion-exchange resins
 - dialysis

Management of hyperkaleamia

- Investigations
 - U & E : S. K⁺ > 6.5 mmol/L needs urgent treatment
 - Blood glucose : low in Addison's disease
 - ABG : Look for metabolic acidosis
 - CPK : Raised in rhabdomyolysis
 - ECG : changes in ↑ K⁺
 - Tall tented "T" waves
 - Small P waves
 - Prolong PR interval
 - Widening of QRS complexes 'sine waves'
- Management
 - Gain IV access
 - Monitor cardiac rhythm
 - Give **10% calcium gluconate 10ml IV over 10 minutes** (preferably while monitoring cardiac rhythm) Repeat until ECG normalizes in 10-20 mins durations.
 - Give **Salbutamol 5mg via nebulizer**
 - Give **10 units of soluble insulin together with 50 ml of 50% dextrose IV over 15 mins.** (After 2 hrs → check K⁺ → repeat till K⁺ comes upto 6)
 - Consider **8.4% NaHCO₃ 50ml IV** in severe acidosis with ARF
 - Start oral chelating agents Eg : Calcium resonium(Cal bind) 15g tds
 - Repeat Serum K⁺, if still high repeat insulin & dextrose
 - Treat underlying cause Eg: stop offending drugs (Spironolactone, ACEI, ARB)
 - Haemodialysis may be necessary in ARF
 - Advice not to eat fruits which contains more K⁺ (Grapes, Banana, King coconut, Green leaves)

Acidosis -

- ✓ sodium bicarbonate supplements
- ✓ calcium carbonate
- ✓ dialysis

Drug usage

- ✓ Avoid nephrotoxic drugs –
 - tetracycline, NSAIDs
- ✓ Caution when using drugs excreted by kidneys –
 - check levels – Gentamicin
- ✓ Potassium-sparing agents, such as spironolactone and amiloride, pose particular dangers, as do artificial salt substitutes, all of which contain potassium.
- ✓ Refer BNF if in doubt, *sp in advanced disease*

Male erectile dysfunction

- ✓ Testosterone deficiency should be corrected
- ✓ oral phosphodiesterase inhibitors, e.g. sildenafil, tadalafil and vardenafil, are effective in end-stage renal failure and are the first line of therapy (Cl –nitrates usage)

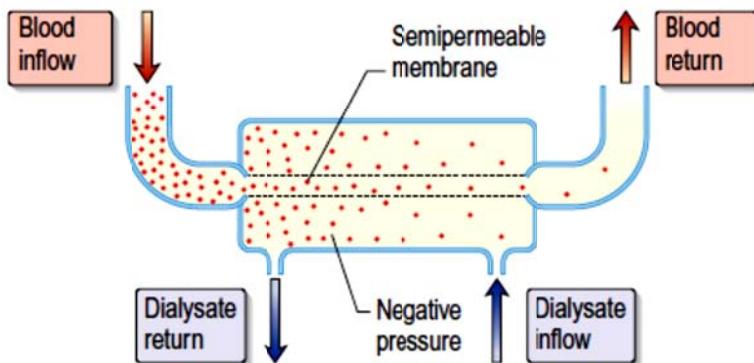
RENAL REPLACEMENT THERAPY

- to mimic the excretory functions of the normal kidney, including excretion of nitrogenous wastes
- maintenance of normal electrolyte concentrations, and maintenance of a normal ECF

Haemodialysis

Basic principles

- blood from the patient is pumped through an array of semipermeable membranes (the dialyser) which bring the blood into close contact with dialysate, flowing countercurrent to the blood.
- The plasma biochemistry changes towards that of the dialysate owing to diffusion of molecules down their concentration gradients



- The dialysis machine comprises a series of blood pumps, with pressure monitors and bubble detectors and a proportionating unit, also with pressure monitors and blood leak detectors.
- Blood flow during dialysis is usually 200–300 mL per minute and the dialysate flow usually 500 mL per minute.
- The efficiency of dialysis in achieving biochemical change depends on blood and dialysate flow and the surface area of the dialysis membrane.
- Dialysate is prepared by a proportionating unit, which mixes specially purified water with concentrate, resulting in fluid with

Sodium	130–145
Potassium	0.0–4.0
Calcium	1.0–1.6
Magnesium	0.25–0.85
Chloride	99–108
Bicarbonate	35–40
Glucose	0–10

- Bicarbonate has replaced acetate which contributed to hypotension.
- Highly permeable synthetic membranes allow more rapid haemodialysis than cellulose-based membranes (highflux haemodialysis).

Access for haemodialysis

- Adequate dialysis requires a blood flow of at least 200 mL per minute.
- The most reliable long-term way of achieving this is surgical construction of an **arteriovenous fistula** using the radial or brachial artery and the cephalic vein.
- This results in distension of the vein and thickening ('arterialization') of its wall,
- so that after 6–8 weeks large-bore needles may be inserted to take blood to and from the dialysis machine.
- In patients with poor-quality veins or arterial disease (e.g. diabetes mellitus) arteriovenous polytetrafluoroethylene (PTFE) grafts are used for access.

- However, these grafts have a very high incidence of thrombosis and 2-year graft patency is only 50–60%.
- Dipyridamole or fish oils improve graft patency but warfarin, aspirin and clopidogrel do not and are associated with a high incidence of complications.
- If dialysis is needed immediately, a large-bore doublelumen cannula may be inserted into a central vein – usually the subclavian, jugular or femoral.
- Semipermanent duallumenous catheters can also be used, usually inserted via a skin tunnel to lessen the risk of infection.
- Nevertheless, local and systemic sepsis is high, with increased morbidity and mortality.
- Stenosis of the subclavian vein is also common, and the jugular route is preferred.

Dialysis prescription

Dry weight

- patient is neither fluid overloaded nor depleted.
- Patients are weighed at the start of each dialysis session and the transmembrane pressure adjusted to achieve fluid removal equal to the amount by which they exceed their dry weight.

The dialysate buffer

- The dialysate buffer is usually acetate or bicarbonate.
- The sodium and calcium concentrations of the dialysate buffer are carefully monitored.
- A high dialysate sodium causes thirst and hypertension.
- A high dialysate calcium causes hypercalcaemia,
- whilst a low-calcium dialysate combined with poor compliance of medication with oral calcium carbonate and vitamin D may result in hyperparathyroidism

Frequency and duration

- adjusted to achieve adequate removal of uraemic metabolites and to avoid excessive fluid overload between dialysis sessions.
- An adult of average size usually receives 4–5 hours' treatment three times a week.
- Twice-weekly dialysis is adequate only if the patient has considerable residual renal function.
- Adequate/optimal dialysis should be adjusted to individual patients' needs.
- All patients are anticoagulated (usually with heparin) during treatment as contact with foreign surfaces activates the clotting cascade

Complications

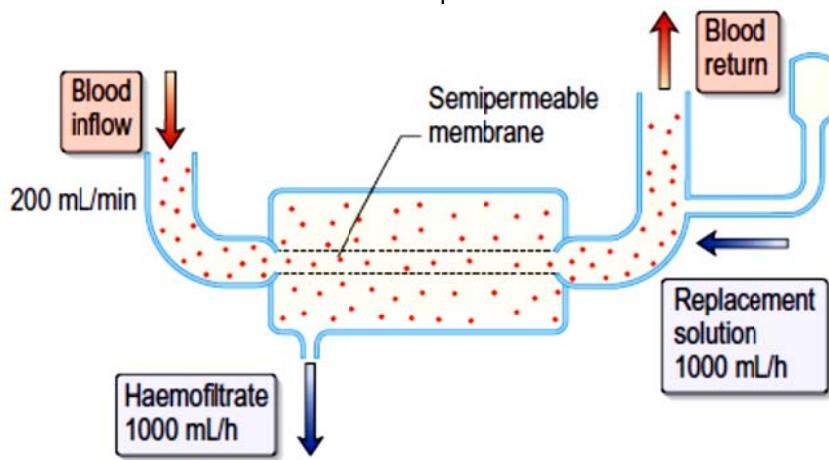
- **Hypotension** during dialysis is the major complication(excessive removal of ECF, inadequate 'refilling' of the blood compartment from the interstitial compartment during fluid removal, abnormalities
- **venous tone, autonomic neuropathy, acetate intolerance** (acetate acts as a vasodilator) and left ventricular hypertrophy.)
- Very rarely patients may develop **anaphylactic reactions to ethylene oxide**, which is used to sterilize most dialysers.
- Patients receiving ACE inhibitors are at risk of **anaphylaxis if polyacrylonitrile dialysers** are used.
Other rare, complications include the
- **Hardwater syndrome** (caused by failure to soften water resulting in a high calcium concentration prior to mixing with dialysate concentrate),
- haemolytic reactions and air embolism.

Adequacy of dialysis

- Symptoms of underdialysis are non-specific and include insomnia, itching, fatigue despite adequate correction of anaemia, restless legs and a peripheral sensory neuropathy.
- Adequacy of dialysis may be assessed by computerized calculation of urea kinetics, requiring measurement of the residual renal urea clearance, the rate of rise of urea concentration between dialysis sessions, and the reduction in urea concentration during dialysis.
- Haemodialysis is the most efficient way of achieving rapid biochemical improvement, for instance in the treatment of acute kidney injury or severe hyperkalaemia.
- This advantage is offset by disadvantages such as haemodynamic instability, especially in acutely ill patients with multi organ disease, and over-rapid correction of uraemia can lead to 'dialysis disequilibrium'.
- This is characterized by nausea and vomiting, restlessness, headache, hypertension, myoclonic jerking, and in severe instances seizures and coma owing to rapid changes in plasma osmolality leading to cerebral oedema.

Haemofiltration

This involves removal of plasma water and its dissolved constituents (e.g. K⁺, Na⁺, urea, phosphate) by convective flow across a high-flux semipermeable membrane, and replacing it with a solution of the desired biochemical composition

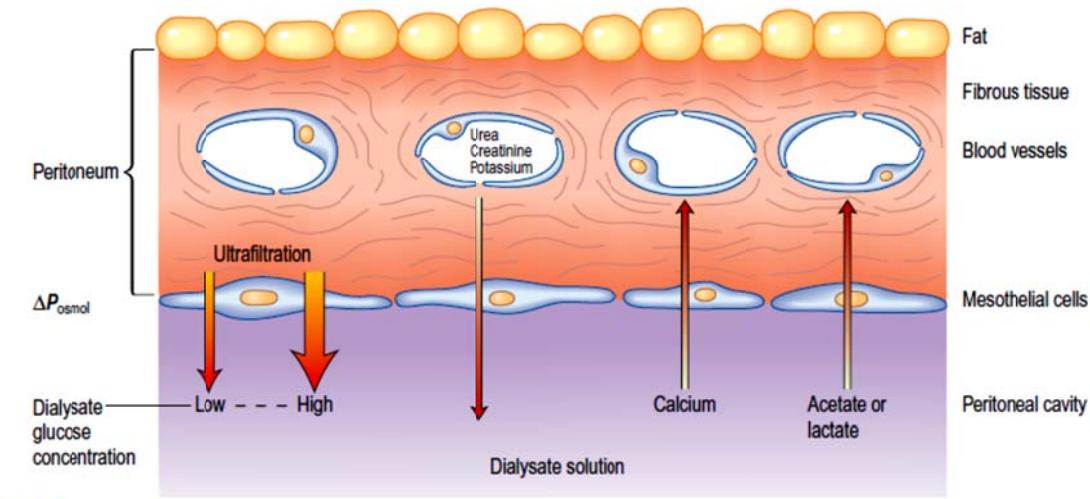


Lactate is used as buffer in the replacement solution because rapid infusion of acetate causes vasodilatation, and bicarbonate may cause precipitation of calcium carbonate.

Haemofiltration can be used for both acute and chronic renal failure and is used in mainland Europe for CKD patients with haemodynamic instability. High volumes need to be exchanged in order to achieve adequate small molecule removal

Peritoneal dialysis

Peritoneal membrane as a semipermeable membrane, avoiding the need for extracorporeal circulation of blood. Very simple, low-technology treatment compared to haemodialysis.



A tube is placed into the peritoneal cavity through the anterior abdominal wall. Dialysate is run into the peritoneal cavity, usually under gravity.

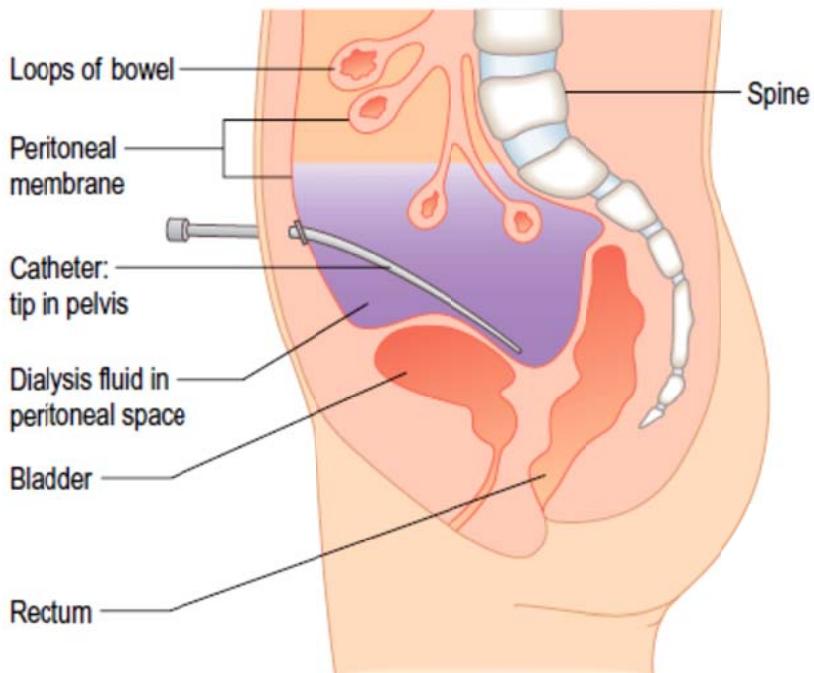
Urea, creatinine, phosphate and other uraemic toxins pass into the dialysate down their concentration gradients.

Water (with solutes) is attracted into the peritoneal cavity by osmosis, depending on the osmolarity of the dialysate. This is determined by the glucose or polymer (icodextrin) content of the dialysate.

Sodium	130–134
Potassium	0
Calcium	1.0–1.75
Magnesium	0.25–0.75
Chloride	95–104
Lactate	35–40
Glucose	77–236
Total osmolality	356–511 mOsm/kg

The fluid is changed regularly to repeat the process.

Chronic peritoneal dialysis requires insertion of a soft catheter, with its tip in the pelvis, exiting the peritoneal cavity in the midline and lying in a skin tunnel with an exit site in the lateral abdominal wall



This form of dialysis can be adapted in several ways.

Continuous ambulatory peritoneal dialysis (CAPD).

Dialysate is present within the peritoneal cavity continuously, except when dialysate is being exchanged.

Dialysate exchanges are performed three to five times a day, using a sterile no-touch technique to connect 1.5–3 L bags of dialysate to the peritoneal catheter; each exchange takes 20–40 minutes. This is the technique most often used for maintenance peritoneal dialysis in patients with end-stage renal failure.

Complications

- *Peritonitis*
- Bacterial peritonitis is the most common s.

Clinical presentations include abdominal pain (guarding and rebound tenderness are unusual), and a cloudy peritoneal effluent, without which the diagnosis cannot be made.

Microscopy reveals a neutrophil count above 100 cells per mL.

Nausea, vomiting, fever and paralytic ileus may be seen if peritonitis is severe. The incidence of Empirical antibiotic treatment is started, with a spectrum which covers both Gram-negative and Gram-positive organisms.

Antibiotics may be given by the oral, intravenous or intraperitoneal route; most centres rely on intraperitoneal antibiotics.

Common causative organisms

	Approximate percentage of cases
<i>Staphylococcus epidermidis</i>	40–50
<i>Escherichia coli</i> , <i>Pseudomonas</i> and other Gram-negative organisms	25
<i>Staphylococcus aureus</i>	15
<i>Mycobacterium tuberculosis</i>	2
<i>Candida</i> and other fungal species	2

*In approximately 20%, no bacteria are found

Infection around the catheter site

It should be treated aggressively (with systemic and/or local antibiotics) to prevent spread of the infection into the subcutaneous tunnel and the peritoneum.

The most common causative organisms are staphylococci, including MRSA.

Other complications

- CAPD is often associated with constipation,
- Dialysate may leak through a diaphragmatic defect into the thoracic cavity, causing a massive pleural 'effusion'.
- Dialysate may also leak into the scrotum down a patent processus vaginalis.
- Sclerosing peritonitis is a potentially fatal complication of CAPD.

Contraindications

- ✓ Unwillingness
- ✓ Previous peritonitis
- ✓ Presense of stoma
- ✓ Active intra abdominal sepsis
- ✓ Abdominal hernia
- ✓ Visual impairment
- ✓ Sever arthritis

Complications of all long-term dialysis

- Cardiovascular disease and sepsis are the leading causes of death in long-term dialysis patients
- *Dialysis amyloidosis*

Transplantation

Successful renal transplantation offers the potential for almost complete rehabilitation in end-stage renal failure.

Factors affecting success

- ABO (blood group) compatibility between donor and recipient is required
- *Matching donor and recipient for HLA type*
- *Adequate immunosuppressive treatment*

Immunosuppression for transplantation

- Corticosteroids
- Azathioprine.
- Mycophenolate mofetil
- Ciclosporin (CSA)
- Tacrolimus
- Sirolimus
- Antibodies

Complications

- *Acute tubular necrosis (ATN)*
- *Technical failures*
- *Acute rejection (AR)*
- *Infections*
- *Post-transplantation lymphoproliferative Disorders*
- *Chronic allograft nephropathy (CAN)*
- *Malignancy*
- *Cardiovascular disease*
- *Post-transplant osteoporosis*
- *Recurrent disease*

FEVER WITH CONFUSION

GENERAL INFORMETIONS

P/C; Fever and altered behavior

D/D;

1. Encephalitis/meningo-encephalitis
2. Cerebral malaria
3. Septicaemia
4. Cerebral abscess
5. Encephalopathy

HPC;

Onset, progression and duration of symptoms

Fever

- High grade or low grade
- Type(intermittent, remittent & continuous)
- Associated features(chills and rigors)
- Response to treatment

Behavior change;

- Explain features
- How patient feels and how others felt

Cause	Features
Encephalitis	Fever, Altered consciousness, disorientation, behavioral changes, seizures, focal deficits, headache, drowsy
Meningo-encephalitis	Above+ meningeal irritation, photophobia, vomiting
Septicaemia	Pyrexia and rigors, Nausea, vomiting, Rash and meningism, Bleeding due to coagulopathy, focus
Cerebral abscess	Low grade fever, mild meningeal irritation, sub-acute onset, act as SOL(focal deficits, seizures, increased ICP(headache, vomiting)
Cerebral malaria	Travelled to malarial endemic(trinco, anuradapura, polonnaruwa, mahiyanganaya) areas or countries (last few months), fever (but always not a feature of it), convulsions roughly 3/24h,no meningeal irritation

PMHx; DM, malignancies, immunocompromised states, ENT infections

PSHx; any skull surgery, trauma

Drug Hx; any immunosuppressive drugs

FMHx;

SHx

Examination

General

- Ill looking ,febrile ,LN, throat
- Skin rash
- Auroscopy, mastoid tenderness, sinuses tenderness
- Any infective focus
- Evidence of cranial surgeries
- Back for congenital meningeal defect

CVS, RS

Abdominal examination-to find out a source

Full CNS examination

- GCS
- Higher functions
- Motor system
- Sensory system
- Cerebellar functions
- Cranial nerves
- Funduscopy –papilloedema (BP, Pulse)-cerebral oedema
- Neck stiffness
- Kernig's sign

MENINGITIS

- Bacterial meningitis is fatal unless treated
- Mode of transmission
 1. By direct extension from the ears, nasopharynx, cranial injury or congenital meningeal defect.
 2. bloodstream spread
- Immunocompromised patients (e.g. HIV, cytotoxic drug therapy) are at risk of infection by unusual organisms
- Non-infective causes
 - ✓ Malignant cells
 - ✓ Intrathecal drugs
 - ✓ Blood following subarachnoid haemorrhage

- classification of meningitis
 - Acute pyogenic- bacterial
 - Aseptic- viral
 - Chronic-TB, Spirochaetal, Cryptococcal

acute bacterial meningitis	chronic infection (e.g. TB),
<ul style="list-style-type: none"> Pia-arachnoid is congested with polymorphs Layer of pus forms May organize to form adhesions, causing <ul style="list-style-type: none"> cranial nerve palsies hydrocephalus 	<p>Brain is covered in a viscous grey-green exudate with numerous meningeal tubercles</p> <p>Adhesions are invariable.</p> <p>Cerebral oedema occurs in any bacterial meningitis.</p>

In viral meningitis lymphocyte predominate CSF reaction without pus formation, polymorphs or adhesions;

little or no cerebral oedema unless encephalitis develops

Table 21.41 Infective causes of meningitis in the UK

Bacteria

*Neisseria meningitidis**

*Streptococcus pneumoniae**

Staphylococcus aureus

Streptococcus Group B

Listeria monocytogenes

Gram-negative bacilli, e.g. *E. coli*

Mycobacterium tuberculosis

Treponema pallidum

Viruses

Enteroviruses:

ECHO

Coxsackie

Poliomyelitis

Mumps

Herpes simplex

HIV

Epstein-Barr virus

Fungi

Cryptococcus neoformans

Candida albicans

Coccidioides immitis, *Histoplasma capsulatum*, *Blastomyces dermatitidis* (USA)

Table 21.42 Clinical clues in meningitis

Clinical feature	Possible cause
Petechial rash	Meningococcal infection
Skull fracture	
Ear disease	
Congenital CNS lesion	
Immunocompromised patients	HIV opportunistic infection
Rash or pleuritic pain	Enterovirus infection
International travel	Malaria Poliomyelitis Leptospirosis
Occupational: (work in drains, canals, polluted water, recreational swimming)	
Clinical: myalgia, conjunctivitis, jaundice	

*These organisms account for 70% of acute bacterial meningitis outside the neonatal period. A wide variety of infective agents are responsible for the remaining 30% of cases. *Haemophilus influenzae* b (Hib) has been eliminated as a cause in many countries by immunization. Malaria often presents with cerebral symptoms and a fever.

The meningitic syndrome

- This is a simple triad: **headache, neck stiffness and fever**.
- Photophobia and vomiting are often present.
- In acute bacterial infection there is usually intense **malaise, fever, rigors, severe headache, photophobia and vomiting**, developing within hours or minutes
- The patient is **irritable** and often prefers to lie still.

- **Neck stiffness and positive Kernig's sign** usually appear within hours
- In uncomplicated meningitis, consciousness remains intact, although anyone with high fever may be delirious.
- **Progressive drowsiness, lateralizing signs and cranial nerve lesions** indicate complications such as venous sinus thrombosis severe cerebral oedema, hydrocephalus, or an alternative diagnosis such as cerebral abscess or encephalitis
- Papilloedema may develop

<i>Acute bacterial meningitis</i>	<i>Viral meningitis</i>
Onset is typically sudden, with rigors and high fever	This is almost always a benign, self-limiting condition lasting 4–10 days. Headache may follow for some months. There are no serious sequelae, unless an encephalitis is present

Complications of meningitis

local	Systemic
increased ICP Abscess CN palsies-6,8 Fits Hydrocephalus Subdural empyema Venous thrombosis Artrritis-infarcts	Septicaemia DIC SIADH Adrenal crisis endocarditis

Chronic meningitis

- ✓ **Tuberculous meningitis (TBM) and cryptococcal meningitis**
- ✓ Commence typically with vague headache, lassitude, anorexia and vomiting.
- ✓ Acute meningitis can occur but is unusual.
- ✓ Meningitic signs **often take some weeks to develop**.
- ✓ **Drowsiness, focal signs** (e.g. diplopia, papilloedema, hemiparesis) and **seizures** are common.
- ✓ **Syphilis, sarcoidosis and Behçet's** also cause chronic meningitis.
- ✓ In some cases of chronic meningitis an organism is never identified.

Behçet's disease (BEH-chets), sometimes called **Behçet's syndrome, Morbus Behçet, or Silk Road disease**, is a rare immune-mediated systemic vasculitis that often presents with mucous membrane ulceration and ocular involvements.

Malignant meningitis

- ✓ Malignant cells can cause a subacute or chronic noninfective meningitic process.
- ✓ A meningitic syndrome, cranial nerve lesions, paraparesis and root lesions are seen, often in confusing and fluctuating patterns.
- ✓ The CSF cell count is raised, with high protein and low glucose.
- ✓ Treatment with intrathecal cytotoxic agents is rarely helpful.

ENCEPHALITIS

Means inflammation of brain parenchyma, usually viral

Acute viral encephalitis

- **Herpes simplex**
- ECHO
- Coxsackie
- Mumps and Epstein–Barr viruses.
- Adenovirus
- Varicella zoster
- Influenza
- Measles and other viral encephalitides are less common.

Clinical features

- Many encephalitides are mild; recovery occurs.
- In the minority, serious illness develops with high fever, headache, mood change and drowsiness over hours or days.
- Focal signs, seizures and coma ensue.
- Death, or brain injury follows; herpes simplex (HSV-1) accounts for many of these

Differential diagnosis

This includes:

- ✓ Bacterial meningitis with cerebral oedema
- ✓ Cerebral venous thrombosis
- ✓ Brain abscess
- ✓ Endocarditis
- ✓ Acute disseminated encephalomyelitis
- ✓ Cerebral malaria
- ✓ Septicaemia, vasculitis
- ✓ Toxic confusional states.

Acute disseminated encephalomyelitis (ADEM)

- ADEM follows many viral infections (e.g. measles, varicella zoster, mumps and rubella) and rarely immunization against rabies, influenza or pertussis.
- The syndrome is often similar to acute viral encephalitis, with additional focal brainstem and/or spinal cord lesions due to demyelination
- Viral particles are not present in the lesions, which are well seen on T2 weighted MRI.
- Prognosis is variable.
- Mild cases recover completely.
- When there is coma, mortality remains approximately 25%.
- Survivors often have permanent brain damage.
- Treatment is supportive, with steroids and anticonvulsants.

Cerebral abscess

- Local spread-contiguous suppurative foci (OM, sinusitis, mastoiditis, dental sepsis)
- Haematogenous spread-
- Penetrating head injury, neurosurgery- staph
- 20% no apparent cause
- Common organisms
 - Staph(aureus, coagulase -ve, MRSA)
 - Strep(pneumonia, viridans)
 - Anaerobes
 - G -VE
 - Pseudomonas
- Polymicrobial infection common

Presentation

- As a SOL(focal deficit, seizures, increased ICP, altered consciousness)
- Subacute onset
- Fever-low grade
- Meningeal irritation-mild

Cerebral malaria

- Is the commonest manifestation of severe malaria
- Syndrome defined by an un-arousable coma, not attributable to other cause, with any level of *P.falciparum* parasitemia
- 2% of *p.falciparum* infections progress to Cerebral malaria (5-40% will die)
- Usually seen children <2 yrs
- Patients with *p.falciparum* infections who show any impairment of consciousness and other signs of cerebral dysfunction should treated as cerebral malaria(utmost urgently)
- Symptoms and signs may develop after several days in adult but may be as short as 2 days after the onset of fever in children
- Ideally diagnosis of severe or complicated malaria (CM specially) should be confirmed by finding asexual forms of *p.falciparum* in the blood but if exposure to PF is a possibility a therapeutic trial of an effective anti malarial should be carried out as smear negative CM is well known
- Adults who recover from cerebral malaria usually have no permanent neurological deficits
- But they may occur in children especially if the malaria has been further complicated by hypoglycemia

Investigations

Disease	investigations	results
Meningitis	Blood culture Lumbar puncture FBC,ESR,CRP Blood glucose BU/SE CXR	
Encephalitis	Lumbar puncture EEG Radiology (CT, MRI)	Generalized slow waves
Cerebral abscess	Neuroimaging (CCT, MRI) EEG, Microbiology(blood culture, aspirate from abscess)	
Cerebral malaria	Thick and thin blood film for malarial parasites Rapid test for Ag detection	

Table 21.43 Typical CSF changes in viral, pyogenic and TB meningitis

	Normal	Viral	Pyogenic	Tuberculosis
Appearance	Crystal clear	Clear/turbid	Turbid/purulent	Turbid/viscous
Mononuclear cells	<5/mm ³	10-100/mm ³	<50/mm ³	100-300/mm ³
Polymorph cells	Nil	Nil*	200-300/mm ³	0-200/mm ³
Protein	0.2-0.4 g/L	0.4-0.8 g/L	0.5-2.0 g/L	0.5-3.0 g/L
Glucose	½ blood glucose	> ½ blood glucose	< ½ blood glucose	< ½ blood glucose

*Some CSF polymorphs may be seen in the early stages of viral meningitis and encephalitis.

Management

Meningitis

After taking blood for culture and ABST

Start antibiotics empirically IV

- ✓ Ceftriaxone/cefotaxime+/- vancomycin
- ✓ Penicillin+ chloramphenicol
- ✓ Add ampicillin –old age immunocompromised, suspecting listeria

IV dexamethazone

- ✓ 0.15mg/kg 6h for 4D
- ✓ Given before or with the first dose of AB

Cerebral abscess

Start empirical antibiotics

Continue for 6-8 weeks

- ✓ Cephalosporin or penicillin/chloramphenicol
- ✓ + Metronidazole
- ✓ +/- Vancomycin

Surgery

Supportive care-fits

IV dexamethasone

Treat primary focus

Cerebral malaria

Specific

IV quinine; 20mg kg loading dose

Followed by 10mg/kg over 4h in dextrose solution tds(for 7 days, give IV until cannot take orally)

Primaquine-45mg single dose

Co-aetum(age and weight) for 3 days

Supportive

Management of unconscious patient

Avoid dehydration

Manage ARF

Avoid hypoglycaemia

Viral encephalitis

IV acyclovir for 14-21 days

Fever and lymphadenopathy

localised	Generalised
<p><u>Local infection-</u></p> <p>B-pharyngitis, dental abscess, otitis media, actinomycetes</p> <p>V-rubella</p> <p>Cat scratch fever</p> <p>Lymph granuloma venerum-inguinal LN</p> <p><u>Lymphoma-</u></p> <p>Hodgkin's lymphoma</p> <p>Non-Hodgkin's lymphoma</p> <p><u>Secondary carcinoma-</u></p> <p>Thyroid, lung, breast, stomach, nasoparyngeal carcinoma</p>	<p><u>Infection-</u></p> <p>B-2nd syphilis, TB, brucellosis, salmonella, endocarditis</p> <p>V-IMN, measles, rubella, HIV</p> <p>F- histoplasmosis</p> <p><u>Non infectious-</u></p> <p>Rheumatoid arthritis, sarcoidosis, SLE</p> <p><u>Malignant-</u></p> <p>Leukemia -CLL,ALL</p> <p>Hodgkin's lymphoma</p> <p>Non-Hodgkin's lymphoma</p> <p>rarely secondary malignancies</p> <p>drugs-phenytoin, carbamazepine</p> <p>other-hyperthyroidism</p>

Presentation-Fever with lymphadenopathy

Age at presentation-hodgkin's -young adults

Non hodgkin's-55-75 years

ALL- (children)-3-7 years

CLL (elderly) -65-70years

IMN,TB- any age

HIV,syphillis-mainly sexually active period

History of presenting complaint

Fever- high grade-infection

Low grade-malignancy

Lymphadenopathy-

onset, duration, progression in size, sites, pain,
persist more than 4 weeks-significant

Any other symptom – ‘B’ symptoms

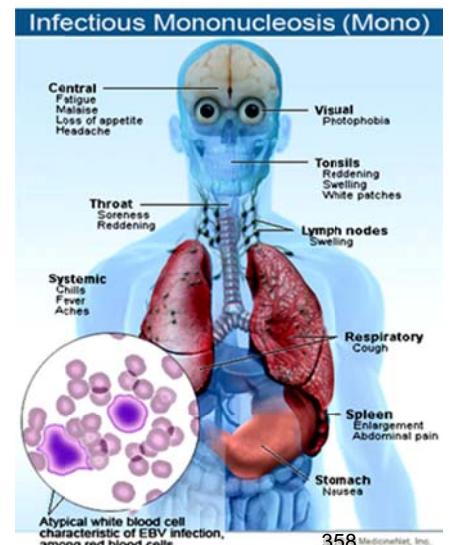
B symptoms

Fever

Night sweats

LOW, LOA

Pruritus



1) First exclude infective causes

IMN- prodromal symptoms-fatigue,prolonged malaise,sore throat,dry cough,stiff neck

Morbilliform rash,severe headache,photophobia,conjunctivitis

TB - contact Hx, chronic cough >3 weeks, low grade fever, night sweats, LOA, LOW
Dull ache in the chest(unresolving pneumonia,PE,lung collapse)
extra-pulmonary TB,Painless cervical LN ◊ abscess and discharging sinus



secondary syphilis-6-8weeks after chancre

Constitutional symp – mild fever, malaise, headache
Later – generalized LN
Rash on trunk, limb-palms, soles
Warty plaques (Condylomata lata) on vulva/perianal region
Mucosal lesions – genitalia, mouth, pharynx

Immunocompromised state –

DM, long term steroid use

HIV- Recurrent infections, persistent generalized LN
Unexplained diarrhea, LOW, skin changes, CNS infections, opportunistic infections

2) Then look for other CT disorders

SLE – rashes, gum bleeds, alopecia, joint pain, photophobia

RA - Joint pain (B/L, symmetrical, small joints of hands), morning stiffness, dry painful eyes- episcleritis

3) primary malignancy– Malaise, fever, night sweats, lumps, LOW, LOA, pruritus

(CLL, HL, NHL) BM suppression – anaemia, infection, spontaneous bruising

HL – alcohol induced LN pain

Mediastinal LN enlargement ◊ bronchus/ SVC obstruction, pleural effusion - cough, breathlessness

Symptoms due to involvement of; lung, bone, liver

NHL – asymmetrical LN involvement

Features of Haemolytic anaemia

Oro-pharyngeal involvement – sore throat, noisy breathing

Extra-nodal manifestations – gut – acute abd symp., brain, testis, lung, thyroid, skin

CLL – usually asymptomatic, AIHA, herpes zoster, ITP

PMHx – dental caries, malignancy, cat scratches, local trauma, epilepsy, TB, syphilis/VDRL done, RA

DHx – phenytoin, carbamazepine

FHx - leukaemia

EXAMINATION

GE – Cachexia – lymphoma

Pallor – primary malignancy conjunctivitis, Jaundice - IMN

Mouth – tonsillar enlargement – IMN, NHL

Neoplastic tumours and ulcers

Palatal petechiae & pharyngitis - IMN

Dilated neck veins, venous engorgement of face – SVC obstruction (mediastinal LN)

Linear scratches – lymphoma, cat scratch disease
 Bruising,rashes,SLE

Infection – reactive hyperplasia	<0.5cm, discrete, mobile B/L, non tender No ass. Inflamm.
LN infection	Larger,matted , warm,red,tender
TB	Non tender, matted, attached to skin, sinuses
Malignancy	>2cm, non tender, hard, discrete/matted, fixed to skin/underlying tissue
Lymphoma	Asymmetrical, Non tender, firm, rubbery, matted
ALL, CLL	symmetrical

LN – Site

Tender/ non tender
 Firm/hard, rubbery-rock hard-primary malignancy
 Tender,rubbery-infection
 Discrete/ matted
 Mobility –immobile,matted-metastatic carcinoma
 Freely mobile-infection,collagen vascular disease,lymphoma
 Size – cervical >1cm
 Inguinal >2cm

Check cervical, axillary, epitrochlear and inguinal LN

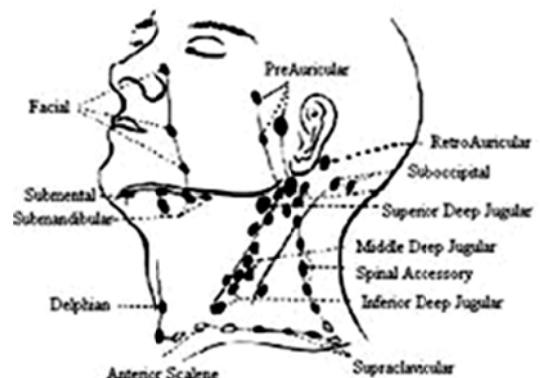
HL – mainly cervical, discrete/matted NHL – superficial/ peripheral

IMN – post. Cervical nodes , discrete

Septic focus at LN draining sites

LN Drainage areas

Upper cervical -	Chest, breast, UL, ENT
Lower cervical & supraclavicular	Thyroid, chest, abdomen, testis
Axillary-	Chest, breast, UL
Inguinal -	LL, external genitalia



ABDOMEN

- condylomata lata – lry syphilis
- Testicular enlargement – leukaemia(ALL)
- Hepatomegaly
- Splenomegaly – IMN, lymphoma, CLL, acute leukaemia

RESPIRATORY

- pleural effusion – HL

CNS

- cranial n. palsies – TB, lIrry syphilis
- Focal neurological signs , meningism
- Peripheral neuropathy

} IMN

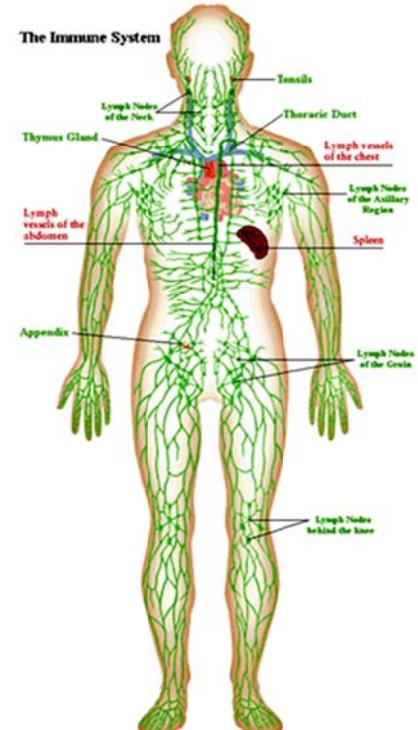
DISCUSSION

How do you classify generalised and regional lymphadenopathy?

- Localised- enlarged lymph nodes in one region
- Regional- enlarged lymph nodes in 2 or more contiguous regions
- Generalised-enlarged lymph nodes in 2 or more non-contiguous regions

What are the causes for regional lymphadenopathy?

- Cervical
 - Infection – bacterial pharyngitis, dental abscess, OM, IMN, CMV, toxoplasmosis, hepatitis
 - Malignancy – NHL, HL, squamous cell CA of head & neck
- Supraclavicular-
 - highly suspicious of a malignancy(left subclavian nodes)
 - Virchow's node – **thoracic/ abdominal neoplasm**, bronchogenic,breast carcinoma
- Axillary –
 - Infection – staph, strep infection of UL skin, cat scratch fever,
 - Malignancy – HL, NHL, CA of breast,metastatic melanoma
- Epitrochlear – (rare in healthy)
 - Lymphoma, CLL, IMN
 - HIV, sarcoidosis,CT disease
 - UL infections,HIV,2ry syphilis
- Inguinal – rare in healthy(>2cm significant)
 - Malignancy – external genitalia (skin), anal canal, lower third of the vagina and lower extremities,lymphoma,leukemia
 - Cellulitis, syphilis, chancroid, genital herpes, lymphogranuloma venereum



Causes for generalized lymphadenopathy?

- Infections – TORCH, TB, secondary syphilis, brucellosis, HIV
- CT disease – RA, SLE
- Neoplasm – lymphomas, CLL, ALL
- Drugs – phenytoin,carbamazepin

Lymphatic drainage in the body

Causes for splenomegaly with lymphadenopathy?

- Infectious mononucleosis
- Some haematological malignancies
- Lymphoma
- Tuberculosis
- HIV
- Collagen vascular disease.

How would you investigate this patient?

1. FBC – Hb ↓
2. Plt ↓
3. WBC ↑ - infection, leukaemia

Causes for anaemia in lymphoma – 1) BM infiltration
2) Hypersplenism
3) AIHA

- HL – initially ↑Neu, ↑ eosinophils
- NHL -↓ Neu
- HIV – progressive ↓ lymphocytes
- CLL - ↑lymphocytes
- IMN - “

Blood picture – leucoerythroblastic BP – lymphoma
Smudged cells - CLL
Atypical lymphocytes - IMN

ESR - - tumour, infection

LFT – malignant infiltration of liver

Clotting profile – bleeding disorder, IMN

Serology – viral titres – EBV, HIV

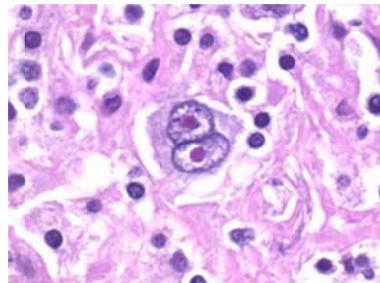
CXR – B/L hilar glands – sarcoidosis

TB

Secondary deposits

Mantoux test

Swabs – local infection



Specific Ix

Ab screen – SLE, RA

Toxoplasmosis (IgM)

Blood culture – septicaemia

VDRL – syphilis

CT – nodal distribution, staging of HL

LN – FNAC – malignancy vs benign, cannot use to diagnose

Bx – Excisional Bx – tissue diagnosis - Hodgkin's disease, secondary deposits

Avoid inguinal LN unless only node – reactive enlargement due to leg ulcers

HL – Reed Sternberg cells (+)

s. LDH – lymphoma (prognostic indicator)

Monospot test, Paul Bunnell test - IMN

BM Bx – in pancytopenia; BM aspiration & trephine Bx – for staging

ACUTE LEUKEMIA

Diagnosis

Hx, Ex

FBC -↓ / ↑/ → WBC, pancytopenia

Blood picture – abnormal blast cells

BM Ex – hypercellular marrow

Leukaemic blast cells >20% of total number of cells

Immunological studies – differentiate between AML, ALL

Chromosome analysis – assess prognosis

How do you manage a patient with leukemia?

General Mx

- 1) Counseling & psychological support
- 2) Analgesics for pain relief
- 3) Establish good fluid and electrolyte balance
- 4) Nutritional support
- 5) Control of infections – broad spectrum AB
Prophylaxis for pneumocystis carinii – co-trimoxazole
- 6) Antiemetics for nausea and vomiting (metochlopramide, phenothiazine)
- 7) Anaemia – RC concentrate Tx thrombocytopenia – Plt. Tx
- 8) Manage tumour lysis Xn (\uparrow urate) – Allopurinol, IV fluids
- 9) Manage coagulopathy if present – Vit K and FFP
- 10) Optimize before transfer to specialized unit

Specific Mx

- Chemotherapy given in 3 phases
 - Remission induction (4-6 weeks)
 - Kill most tumour cells
 - Prednisolone, Vincristine
 - 98% \rightarrow 4 weeks \rightarrow if poor response another 2 weeks
 - After treatment \rightarrow 5% blast cells in BM Bx, normal peripheral blood film
 - Intensification / consolidation
 - High dose multi drug chemotherapy \rightarrow \downarrow tumour burden to very low levels
 - Rx – cyclophosphamide, daunorubicin, cytosine
 - \uparrow Complications – tumour lysis Xn
 - Temporary withholding of drugs until WBC $>$ 5000; if not WBC $<$ 2000 \rightarrow DEATH
 - If low Hb \rightarrow Tx, AB, anti-fungals
 - Maintenance
 - ♀ & adults – 2yrs young ♂ - 3yrs (to reduce testicles)
 - O. mercaptopurine – daily
 - O. methotrexate – weekly
 - IV vincristine
 - Prednisolone for 5days monthly/ 3 monthly
 - High risk of varicella and measles \rightarrow prophylactic Igs on exposure
 - Cranial prophylaxis for CNS disease
 - IV/ intrathecal methotrexate
 - Cranial irradiation \rightarrow avoided
- 2) Treatment of relapses
 - 3) BM transplant
 - HLA matched, ideally monozygotic twin/ other sibling \rightarrow deposit harvested BM cells
 - Before irradiation \rightarrow sperms conserved – sperm bank
 - Complications – graft rejection/ failure

Allogenic stem cell transplantation – take peripheral blood of Pt. \rightarrow filter stem cells and transfer

CHRONIC LEUKEMIA

CLL

Diagnosis

- 1) FBC – Lymphocytosis
- 2) Warm AIHA
- 3) Special stains and immunological studies – diagnosis, prognosis

How do you manage?

Symptomatic treatment

Special treatment reserved for;

- 1) Evidence of BM failure
- 2) Progressive systemic therapy
- 3) AIHA

Treated initially with chlorambucil

LYMPHOMAS

Clinical - LN	Mainly cervical Start from single peripheral LN region and contiguous spread	Unpredictable and haphazard spread
	Mediastinal involvement	Oropharyngeal LN
Extra-nodal spread	Rare	Common
Leukaemic phase	Rare	Common
Constitutional symp.	Common	Rare
Ix – FBC	Initially leucocytosis	↓ WBC
BU/SE		Check renal impairment Ureteric obstruction → intra-abd LN
LN Bx	Reed Sternberg cells	No RS cells
Mx	Early stage - radiotherapy	Multi drug chemotherapy
	Advanced disease – chemotherapy +/- radiotherapy	

Staging of HL

Stage I – one LN group only

Stage II - 2 LN groups on 1 side of the diaphragm

Stage III – both sides of diaphragm + spleen

Stage IV – disseminated (bone, liver, other)

A – asymptomatic

B – symptomatic

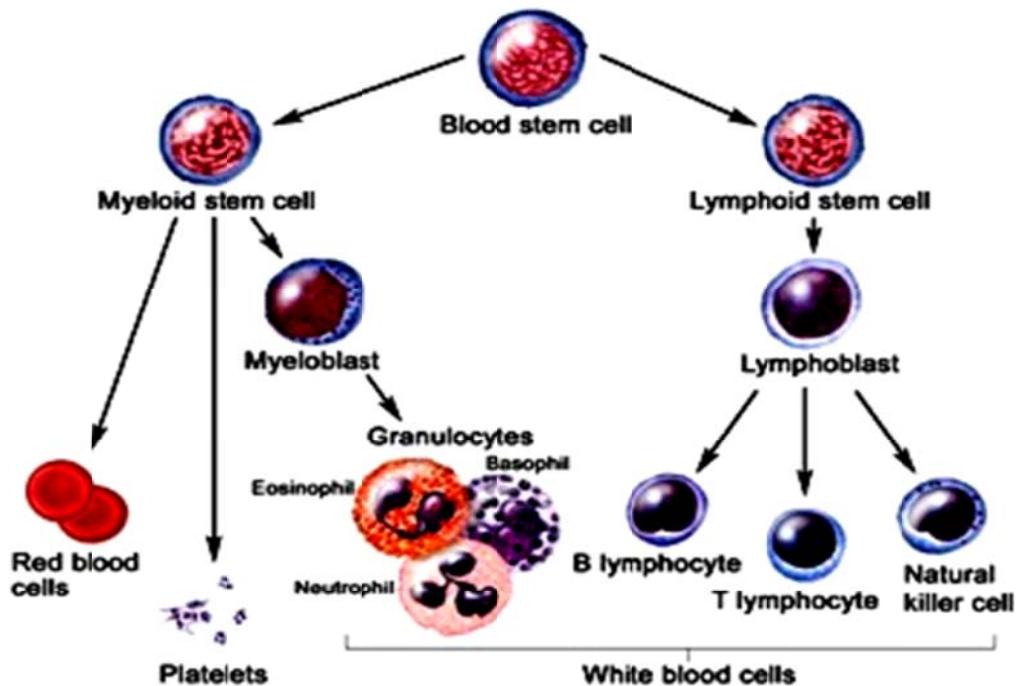
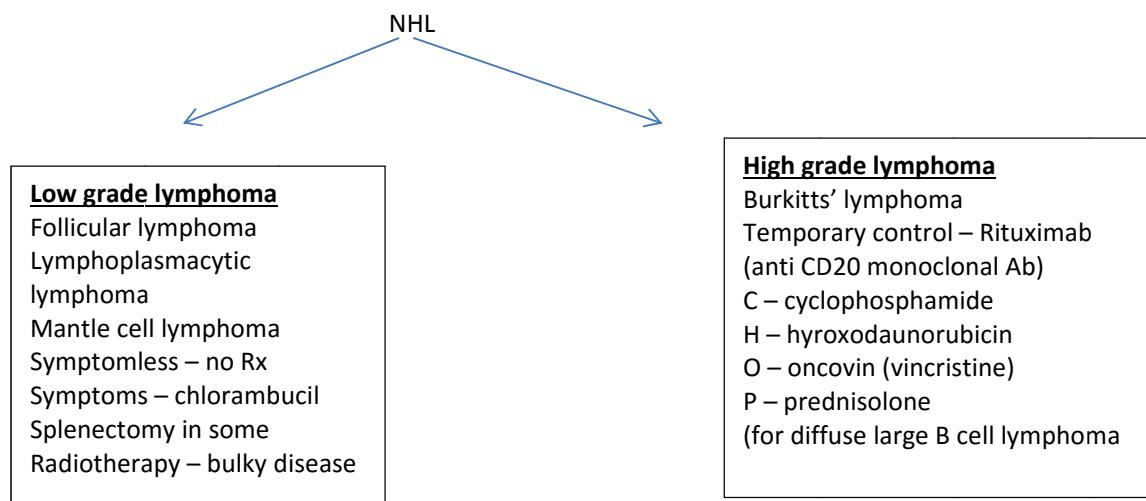
Mx depends on stage, sites, bulk of LN masses, (+) of B symp.

Chemotherapy followed by radiotherapy for large mediastinal masses. Why?

Radiotherapy → ↑Breast CA

↓Cardiac function

30% relapse



Acute Breathlessness – Asthma

PC – intermittent dyspnoea

Wheezing

Cough (often nocturnal)

DD – asthma

COPD exacerbation – persistent SOB, chronic productive cough, scanty mucoid sticky sputum

Cardiac failure (Pulmonary oedema) → MI

Broncho pneumonia

ARDS, Renal failure

Large air way obstruction (foreign body)

HPC - Describe current symptoms/(if known pt with asthma-when dx, how presented, hospital admissions, how severe past episodes were,(acute severe exacerbation, life threatening, ventilation, ICU admission) treatments given, how often exacerbations occurring, drug compliance, inhaler technique)

SOB – onset, progression since onset, duration, worse in the night and early morning ,at rest or on exertion, exercise tolerance, and in daily tasks.

Chest pain-nature, radiation, precipitants, reliving factors, associations(MI/angina)

Wheezing – polyphonic (musical sound)

Cough – duration, dry/productive, haemoptysis

sputum – amount, colour – white, yellow, green

Preceding URTI

Precipitants- (Triggering factor)

Asthma/COPD

- Exposure to high dust
- Travel to cold, dry area
- Defaulted treatment
- LRTI-Fever, pleuritic type chest pain
- URTI – sore throat, rhinorrhoea, excessive sneezing
- Any sudden psychological stress
- Contact Hx of common cold
- Contact Hx of cigarette smoking
- Occupational exposure
- Taking β blockers (Atenolol), NSAIDs, aspirin
- Menstruation, pregnancy

MI/angina-anxiety/ excretion/ life style

Diurnal variation -in symptoms or peak flow (worse in evenings, early morning),

Worse after exercise – quantify the exercise tolerance

Disturbed sleep-nights per weeks, day time symptoms

Other atopic disease-eczema(long standing itchy skin rashes), hay fever, allergy, allergic rhinitis(runny nose, sneezing frequently)

Associated -acid reflux-BA

(LOA, LOW, fever-TB ?)

Improvement after bronchodilator therapy

Previous episodes (for all 3 DD)

When was the previous episode?

How severe – O₂ given, nebulized, ICU admission

Duration of hospital stay

Inhaler use – dose, frequency, technique, clinic

Inhaler –steroid or bronchodilator, compliance to treatment, drug side effects, storage of drugs and buffer stock

Complications

Asthma – pneumothorax – sudden onset SOB (within seconds/ minutes)

Pulmonary hypertension

Bronchiolitis

Irreversible airway obstruction

COPD – pulmonary hypertension

Respiratory failure

Bronchiectasis – seizures – brain abscess,

PMH- childhood asthma, allergic rhinitis, eczema, co-morbidities associate with COPD - IHD, HT, DM, heart failure, cancer, osteoporosis, depression

Allergic Hx-more prone to get allergies

Drug Hx-β blockers- Atenalol - bronchoconstriction

NSAID's-ibuprofen, aspirin-reduce broncho dilator PGE2 synthesis

Histamine releasers-broncho constriction by acting on H1 receptors

Family Hx-asthma

Atopic conditions like allergic rhinitis and eczema

COPD-α1 anti-trypsin deficiency

SHx – Smoking (COPD, BA) – number of cigarette smoke for how many yrs,

Pack years=smoking 1pack/day ,for 1yr

1pack yr= 20×1 ×1yr

If not smoker passive smoking – father, husband

Ventilation, distance between houses, windows number and size ,how many people sleep in the room, windows opened or closed at night

Close to main road-dust

Occupation – textile worker, mill, farmer, symptoms remit at weekends or holidays

Pneumonitis- asbestos, silicon

Use of firewood, kerosene, chimney, pets

How often changing linen, sweep house, mobbing

Places where release lot of smoke around the house

Pillow cover cotton, sleep in bed or floor

Effect on ADL (Days per week off work or school), understanding about the disease & predisposing factors

Family support – knowledge, what to do during an exacerbation

Financial problem, monthly spent for medications, income

Examination-

GE – Dysphonic, use of accessory mus., chest recession, flaring of alae , propped up, audible wheezes

Cyanosed – life threatening asthma, COPD

Plethora - COPD

O₂ given – check the rate, IV line

Effects of long term steroids – hirsutism, moon shape face, oral candidiasis, hoarse voice

Can speak a sentence in one breath

Febrile

RR-tachypnoea

Hand – Clubbing – bronchiectasis
 Nicotine stain,
 Palmer erythema, flapping tremors - hypercapnia
 Eczematous rashes
 Sputum cup

COPD – pursed lips, face- flushed, thin/ obese
 Bronchiectasis – pt. ill, halitosis, febrile, emaciated

RS – **Inspection** – Hyper inflated chest/ barrel chest
 Chest movements – poor

} COPD

Palpation – Trachea – Deviated – pneumothorax (evidence of complications)
 Chest movements Vocal fremitus - ↑

Percussion – Resonance ↑ , absent/↓ heart and liver dullness – COPD

Auscultation – Vesicular breathing, prolonged expiration

B/L expiratory rhonchi (polyphonic) – high pitched whistling sounds

COPD -

CVS – PR - ↑ - acute asthma, septicemia

Pulsus paradoxus -

Evidence of complications – pulmonary HT – JVP ↑, parasternal heave, loud 2nd ♡ sound

CNS – focal neurological signs – cerebral abscess (bronchiectasis)

Grading severity – acute episode

Mild	Moderate	Severe
Normal activity	Disturbed	Severely disturbed
No audible wheeze	Present	Marked
Accessory mus. Not used	used	Marked
Chest indrawing (-)	(+)	Marked
RR <40/min	RR – 40-50/min	RR ≥ 25/min
HR < 100/min	100-120/min	>120/min
Talks in sentences	Talks in phrases	Talks in words

Life threatening asthma-silent chest, cyanosis, bradycardia, exhaustion, PEF<33%of predicted, confusion, feeble respiratory effort

Figure 2. Levels of Asthma Control			
Characteristic	Controlled (All of the following)	Partly Controlled (Any measure present in any week)	Uncontrolled
Daytime symptoms	None (twice or less/week)	More than twice/week	Three or more features of partly controlled asthma present in any week
Limitations of activities	None	Any	
Nocturnal symptoms/ awakening	None	Any	
Need for reliever/rescue treatment	None (twice or less/week)	More than twice/week	
Lung function (PEF or FEV ₁) [‡]	Normal	< 80% predicted or personal best (if known)	
Exacerbations	None	One or more/year*	

* Any exacerbation should prompt review of maintenance treatment to ensure that it is adequate.

† By definition, an exacerbation in any week makes that an uncontrolled asthma week.

‡ Lung function testing is not reliable for children 5 years and younger.

Figure 7. Questions for Monitoring Asthma Care

IS THE ASTHMA MANAGEMENT PLAN MEETING EXPECTED GOALS?

Ask the patient:

*Has your asthma awakened you at night?
Have you needed more reliever medications than usual?
Have you needed any urgent medical care?
Has your peak flow been below your personal best?
Are you participating in your usual physical activities?*

Action to consider:

Adjust medications and management plan as needed (step up or step down). But first, compliance should be assessed.

IS THE PATIENT USING INHALERS, SPACER, OR PEAK FLOW METERS CORRECTLY?

Ask the patient:

Please show me how you take your medicine.

Action to consider:

Demonstrate correct technique.
Have patient demonstrate back.

IS THE PATIENT TAKING THE MEDICATIONS AND AVOIDING RISK FACTORS ACCORDING TO THE ASTHMA MANAGEMENT PLAN?

Ask the patient, for example:

So that we may plan therapy, please tell me how often you actually take the medicine.

Action to consider:

Adjust plan to be more practical.
Problem solve with the patient to overcome barriers to following the plan.

What problems have you had following the management plan or taking your medication?

During the last month, have you ever stopped taking your medicine because you were feeling better?

DOES THE PATIENT HAVE ANY CONCERNs?

Ask the patient:

What concerns might you have about your asthma, medicines, or management plan?

Action to consider:

Provide additional education to relieve concerns and discussion to overcome barriers.

Diagnosis - Pt. with (severity grade) asthma presenting with acute (severity) episode triggered by -----
Discussion

Definition of asthma

Chronic relapsing inflammatory disorder characterized by hyper responsive airways leading to episodic reversible bronchial constriction

Airway obstruction caused by; 1) bronchial constriction

- 2) Chronic inflammation → mucus plugs
- 3) Wall oedema

How would you manage a pt. admitted to casualty wd. with an acute exacerbation of asthma

- Admit pt and give a bed
- Assess the severity of the episode

Acute severe asthma	Life threatening asthma
Inability to complete a single sentence in one breath	Exhausted, confused, comatosed
RR ≥ 25/min	Poor respiratory effort
HR >120/min	Bradycardia & hypotension
-	Cyanosis, silent chest
PEFR – 50-33% best/ predicted	PEFR <33% of expected/predicted

- Connect to pulse oximeter – measure O₂ saturation
- Prop up the pt.
- Administer high flow O₂ via facemask
- IV line – if dehydrated – hydrate
- Take blood - FBC
- Give O₂ driven nebulization with salbutamol 5mg every 15 -30min
- Add Ipratropium bromide 500µg nebulized every 6 hours
- Monitor the response
- Give hydrocortisone 200mg IV every 4hly for 24hrs/ oral prednisolone 30mg daily
- If pt. not responding to the initial treatment;
- Aminophylline IV bolus dose 250mg over 20min and continue with an infusion. Omit the bolus if pt. on oral theophylline
- Exclude pneumothorax – CXR
- IV salbutamol
- IV magnesium sulphate
- IV AB only if RTI present
- At this point perform an ABG and try to obtain ICU care for the Pt.
- If PCO₂>7kPa → require ventilation

What are the principles of asthma Mx

- Patient education and lifestyle modification
- Basic facts about asthma
- Importance of drug compliance, action of drugs
- How to use the various devices and their care
- Monitoring response by use of a symptom diary
- Environmental modifications of asthma
- How to recognize an acute exacerbation of asthma and when to seek treatment
- Modifications in the household
- Remove pets
- Improve ventilation, keep windows open
- Arrange cooking outside – if using firewood
- Frequent change of bed linen, mopping and dust removal
- Advise males to stop smoking at home

Asthma pharmacotherapy 2 aspects;**1) Long term Mx 2) Mx of exacerbations of asthma****Goals of pharmacotherapy**

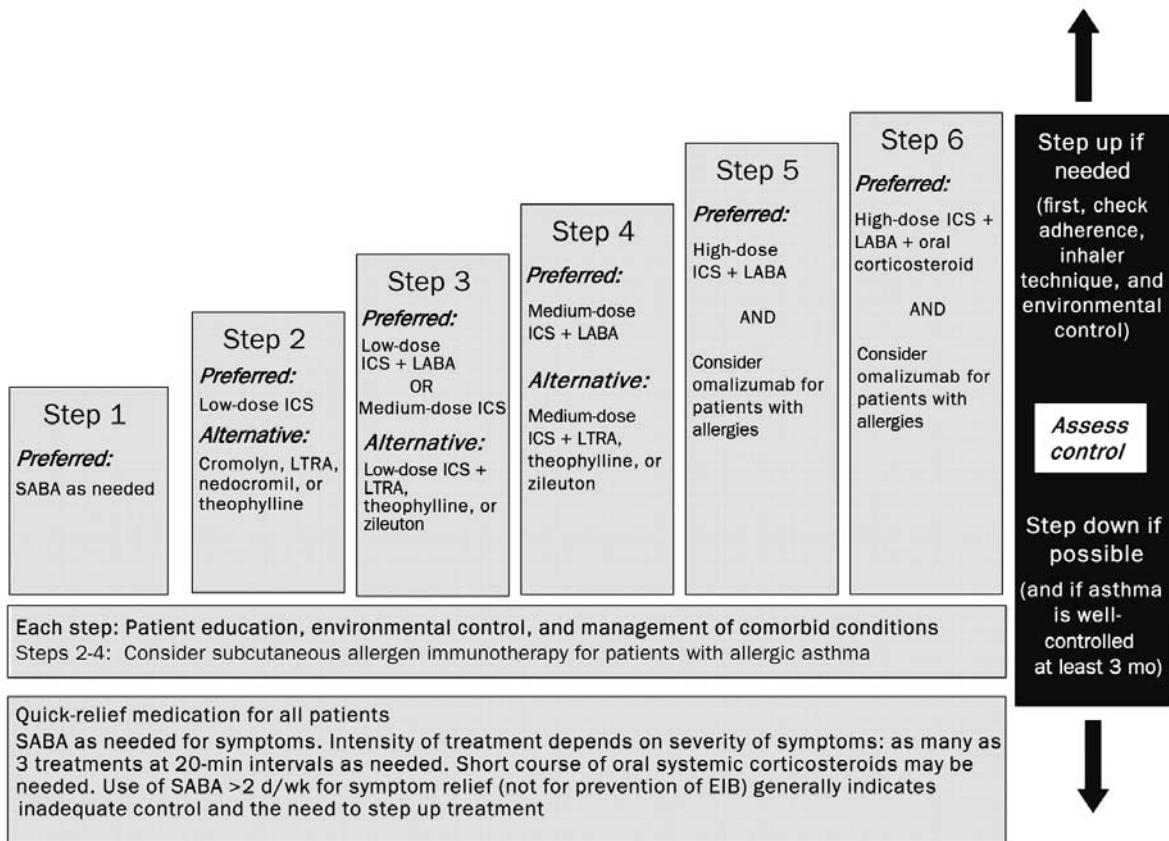
- Minimal /no chronic symptoms during day and night
- Minimal /no exacerbations
- No limitations on activity
- Minimal adverse effects of Rx

Step wise approach to long term management of asthma

Level of severity	Daily controller medication	Other treatment options
Intermittent	none	1)Short acting β_2 agonists as needed
Mild persistent	Low dose inhaled corticosteroid	1) 2) SR (slow release)– theophylline/ Cromone/ leukotriene modifier
Moderate persistent	Low to medium dose corticosteroid + long acting inhaled β_2 agonist - inhaled	1) 2) medium dose inhaled corticosteroid + SR – theophylline / MDIC + long acting o. β_2 agonist/ MDIC + Leukotriene modifier/ High dose inhaled corticosteroid
Severe persistent	HDIC + long acting inhaled β_2 agonist + SR – theophylline or Long acting o. β_2 agonist or o. glucocorticosteroid	1)
In addition to regular daily controller therapy SABA as needed to relieve symp. 3-4times/day		

2 categories of Rx 1) preventer medication

2) Reliever medication



- Indications for reliever medication in BA
 - Chronic persistent asthma
 - After an episode of life threatening asthma
 - Recent ↑ in severity /frequency of acute exacerbations
 - Nocturnal asthma which disturbs the child from sleep
 - Frequent episodic asthma which interferes with normal life
 - Severe exercise induced asthma
 - Inaccessibility of medical care
- Regular assessment and follow up – what to assess
 - Signs & symptoms of asthma
 - Pulmonary function
 - Quality of life and functional status
 - Acute exacerbations during this period
 - Adequacy of Mx – pharmacotherapy – consider step up/ step down every 3 months
 - Environmental modifications
 - Assess for S/E of Rx – esp. steroids
 - Assess wt. and height
 - Measure BP
- Encourage exercise
- Adequate dietary Ca supplementation
- Ophthalmological assessment

MECHANISMS FOR ASTHMA DRUG THERAPY

- Preventing mediator formation
- Preventing mediator release
- Preventing mediators reaching targets
- Physiological antagonism of mediators

DRUGS

Relievers

- SALBUTAMOL
- Terbutaline
- Salmeterol
- IPATROPIUM
- THEOPHYLLINE

RELIEVERS-Drugs that reverse acute bronchoconstriction:

β_2 agonists

Methylxanthines

Anti-muscarinics

Anti-leukotriene agents)

Preventers

GLUCOCORTICOIDS

Beclomethasone

Budesonide

Fluticasone

Na cromoglycate

PREVENTERS

Do not cause acute bronchodilatation:

no use for acute treatment

'Anti-inflammatory action'

reduce bronchial hyper-reactivity

reduce entry of inflammatory cells

inhibit release of mediators from cells

reduce formation of mucosal oedema by mediators

INHALER TECHNIQUE

- Sitting or standing position ,not lying down
- Shake canister
- Seal with lips
- Exhale to FRC(functional residual capacity)
 - end of tidal breathing, not RV
- Simultaneously activate inhaler and inhale to TLC
- Hold breathe for 10 seconds, exhale
- Maximally 15% reaches bronchial tree
- SPACER DEVICES

MANAGEMENT OF OUTPATIENT ASTHMA

Principles of Management

Educate patients on deteriorating control

Aim to gain control of symptoms rapidly

Use *short courses* of oral steroids as required

Monitor compliance & inhaler technique

Once well controlled, reduce doses progressively until symptoms rea

Asthma drugs

Chericof- chlopheniramine,
dextromethophan hydrobromide

Ascoril-salbutamol , bromhexine
hydrochloride

Expectorant- salbutamol , bromhexine
hydrochloride

Phensedyl-chlopheniramine , codane
phosphate

Piriton- chlorpheniramine

Hydryllin- aminophyllin

Tusq-x- terbutaline,bromhexine
hydrochloride

Actifed -triprolidine
hydrochloride,pseudoephedrine
hydrochloride

Ventolin-salbutamol sulphate

Seretide-fluticasone
propionate+salmetarol

Asthalin-salbutamol sulphate

Seroflo-salmetarol +fluticasone

Foracort-formoterol
fumarate+budesonide

Beclamethasone cclosion-
beclamethasone dipropionate

COMPLICATIONS

- Pneumothorax
- Allergic bronchopulmonary aspergillosis and bronchiectasis
- Chronicity: irreversible airway obstruction
- Cor Pulmonale



Practical Box 14.4 Inhaled therapy

Patients should be taught how to use inhalers and their technique checked regularly.

Use of a metered-dose inhaler

1. The canister is shaken.
2. The patient exhales to functional residual capacity (not residual volume), i.e. normal expiration.
3. The aerosol nozzle is placed to the open mouth.
4. The patient simultaneously inhales rapidly and activates the aerosol.
5. Inhalation is completed.
6. The breath is held for 10 seconds if possible. Even with good technique only 15% of the contents is inhaled and 85% is deposited on the wall of the pharynx and ultimately swallowed.

NB Chlorofluorocarbon (CFC) propellants have been/are being replaced by hydrofluoralkane (HFA) propellants. The new aerosols may feel and taste different and patients need reassurance of their efficacy.

Spacers

These are plastic conical spheres inserted between the patient's mouth and the inhaler. They are designed to reduce particle velocity so that less drug is deposited in the mouth. Spacers also diminish the need for coordination between aerosol activation and inhalation. They are useful in children and in the elderly and they reduce the risk of candidiasis.

Chronic Obstructive Pulmonary Disease (COPD)

Chronic bronchitis + Emphysema

Chronic bronchitis: cough with sputum on most days for at least 3 months of the year for more than 2 consecutive years

Emphysema: dilatation and destruction of lung tissue distal to the terminal bronchiole

Emphysema

- centri-acinar -more common, less severe
- pan-acinar – less common, more severe

Aetiology-

Cigarette smoking most important cause

Infection Link uncertain, but accelerates damage

α_1 -antitrypsin deficiency (AD)-

MM, MZ, ZZ homozygotes develop severe SOB, basal emphysema (esp smokers) and liver disease

History-

Cough with sputum

Dyspnoea

Wheeze

Cigarette smoking

20 cigs/day for 1 year = 1 pack-year

E.g. 15 cigs/day for 15 yrs = $15/20 \times 15 = 11.2$

Examination-

Tachypnoea

Prolonged expiration with pursed lips

Hyperinflated chest

Poor expansion

Loss of cardiac and liver dullness

Wheeze

Clinical patterns-

Pink puffer:

- Thin & frail
- Severe SOB
- Heart failure rare
- Near normal gases
- Severe obstruction
- CXR emphysema
- Better prognosis

Blue bloater:

- Obese & plethoric
- Mild SOB
- Heart failure
- Respiratory failure
- Good RFT's
- CXR no emphysema
- Poor prognosis

Grade severity of COPD-

Measured FEV1 as a % of predicted FEV1

Mild 60 – 80%

Moderate 40 – 59%

Severe <40%

Use post-bronchodilator result

Investigations-

- To confirm diagnosis
Largely a clinical diagnosis
- To grade severity
For treatment
For prognosis

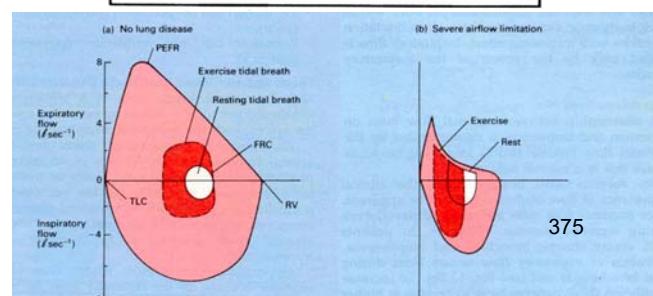
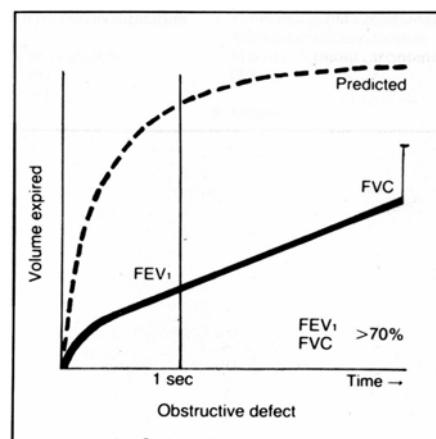
Chest Xray

Lung function test-

Spirometry- obstructive defect

Flow volume loop

Gas trapping – increased FRC and TLC



Measured by helium dilution

Reduced diffusion capacity

Measured by CO diffusion

Assesses access to pulmonary capillary circulation

Management-

Non pharmacological

Stopping cigarette smoking single most important intervention

- nicotine replacement helps
- monitor CO levels
- Regular exercise, pulmonary rehabilitation programmes
- Treat obesity and poor nutrition
- Influenza vaccination

Pharmacological

Treatment is symptomatic & unsatisfactory:

Mild disease: with symptoms, trial of inhaled β agonist or anticholinergic agent; if ineffective stop

Moderate disease: single inhaled bronchodilator

Severe disease: combination of inhaled bronchodilators, oral sustained-release theophyllines

Place of inhaled corticosteroids under investigation

Pulmonary infection is a complication, in pulmonary infection

Diagnosis:

Increase in SOB, sputum volume or development of purulent sputum

Differential diagnosis:

Pneumonia, PTX, LVF, PE, Ca bronchus

Place of management:

Usually in the community

Oxygen therapy

Do not use FIO₂ > 28% or nasal canulae > 2 l/min

Nebulised bronchodilators

Driven by air, continue O₂ inhaled

Antibiotics

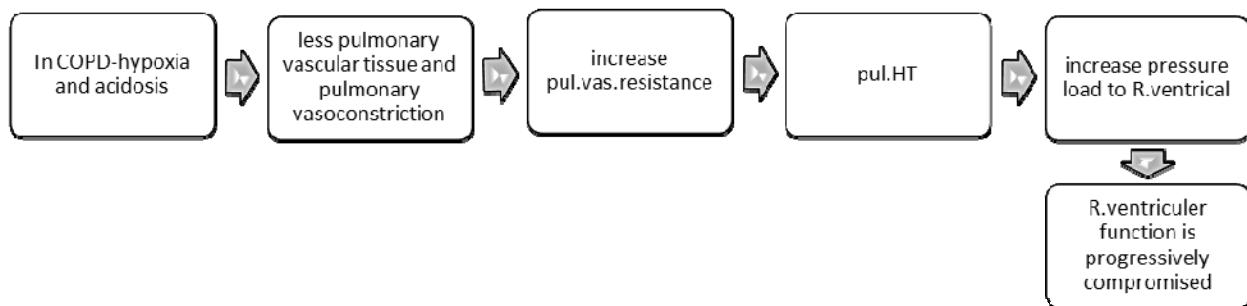
H. influenzae, S. pneumoniae, M. catarrhalis

Amoxycillin, cephalosporin, tetracycline

Acute	Subacute	Chronic
Foreign body	Asthma	and chronic
Pneumothorax (p735, fig 1)	Parenchymal disease	parenchymal diseases
Acute asthma	eg alveolitis	Non-respiratory causes
Pulmonary embolus	effusion	eg cardiac failure
Acute pulmonary oedema	pneumonia	anaemia

Cor-pulmonale

Cor-pulmonale is enlargement of the right ventricle because of increase in after-load that is due to diseases of the thorax, lung and pulmonary circulation; the presence of right ventricular failure is not necessary for the diagnosis of cor-pulmonale.



Clinical features-

- Chest pain, exertion dyspnoea, syncope
- Fatigue - The symptoms of pulmonary heart disease depend on the stage of the disorder. In the early stages, one may have no symptoms but as pulmonary heart disease progresses, most individuals will develop the symptoms like:
- Shortness of breath which occurs on exertion but when severe can occur at rest
- Wheezing
- Chronic wet cough
- Swelling of the abdomen with fluid (ascites)
- Swelling of the ankles and feet (pedal edema)
- Enlargement or prominent neck and facial veins
- Bluish discoloration of face

Examination-

- Dysphonic, tachycardia
- Cyanosis
- Puffy face
- Chest deformity
- Clubbing
- Abdominal Distension-hepatomegaly
- Oedema of feet
- Pulse normal/AF
- JVP elevated –prominent ‘a’ and ‘v’ waves
- BP normal to low-SEVERITY BY HYPOTENSION
- Apex usually normal
- Right ventricular impulse –left parasternal heave
- Heart sound-soft/loud P2
- Murmurs-pan systolic blowing murmur with TR - Early diastolic graham steel murmur

Investigations

- Chest X-ray may show right ventricular enlargement and right atrial dilatation. The pulmonary artery is usually prominent and the enlarged proximal pulmonary arteries taper rapidly. Peripheral lung fields are oligaemic.
- ECG demonstrates right ventricular hypertrophy (right axis deviation, possibly a dominant R wave in lead V1, and inverted T waves in right precordial leads) and a right atrial abnormality (tall peaked P waves in lead II)

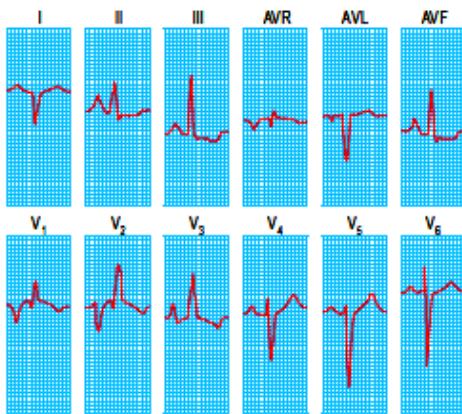


Fig. 13.100 Pulmonary hypertension shown by a 12-lead ECG. There is right axis deviation ($+120^\circ$), right ventricular hypertrophy (dominant secondary R wave [R'] in V_1) and a combination of left and right atrial conduction abnormalities.

■ Echocardiography will usually demonstrate right ventricular dilatation and/or hypertrophy. It is often possible to measure the peak pulmonary artery pressure indirectly with Doppler echocardiography. The echocardiogram may also reveal the cause of pulmonary hypertension, such as an intra-cardiac shunt. Other investigations may also be required to evaluate the cause of pulmonary hypertension and to look for treatable conditions, such as left-to-right shunts, mitral stenosis or left atrial tumours. With direct measurement of pulmonary artery pressure and pulmonary wedge pressure, cardiac catheterization is necessary in some patients with severe pulmonary hypertension of unknown cause. Pulmonary angiography may be indicated if multiple pulmonary emboli are suspected, but it is dangerous. If no other cause is found, then a diagnosis of primary pulmonary hypertension is made

Rx-

- Treat for underline cause-COPD ,pulmonary infection
- Treat respiratory failure-
- In acute situation 24% O₂ if PaO₂<8kpa
- Monitor ABG
- In COPD patient –long term O₂ therapy increase survival
- Treat for cardiac failure-
- Diuretics-furosemide
- Monitor U&E and give amiloride or k+ supplements if necessary
- Alternative-spironolactone
- Consider venesection if haemotocrit is >55%
- (heart lung transplantation)

Discussion-

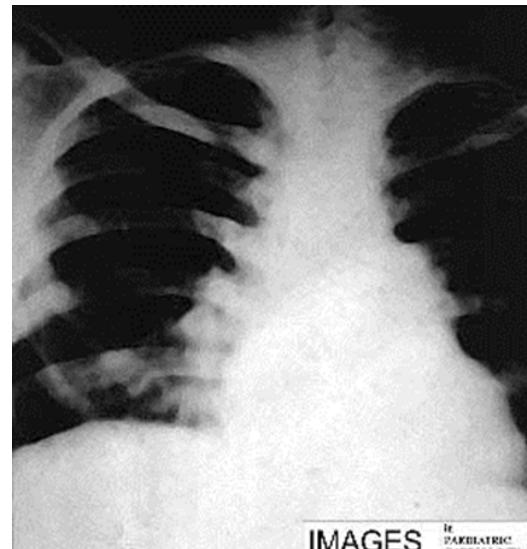
- Pulmonary HT- Pulmonary hypertension is defined as an mPAP of greater than 25 mmHg at rest or of greater than 30 mmHg during exercise

Causes of cor-pulmonale

1. Lung disease
 - Asthma-severe, chronic
 - COPD
 - Bronchiectasis
 - Pulmonary fibrosis
 - Lung resection
2. Pulmonary vascular diseases
 - Pulmonary emboli
 - Pulmonary vasculitis
 - 1ry pulmonary HT
 - ARDS
 - Sickle cell disease
 - Parasite infestation
3. Thoracic cage abnormalities
 - Kyphosis
 - Scoliosis
 - Thoracoplasty
4. Neuromuscular disorders
 - MG
 - Poliomyelitis
 - Motor-neurone disease
5. Hypoventilation
 - Sleep apnoea
 - Enlarged adenoids in children
 - Cerebrovascular diseases



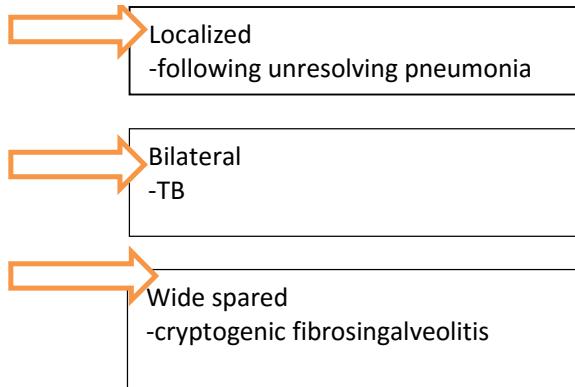
Pulmonary artery hypertension Chest radiograph in PA view showing enlarged pulmonary arteries (arrows) due to pulmonary hypertension induced by anomalous pulmonary venous drainage. Courtesy of Sven Paulin, MD, Beth Israel Hospital, Boston.



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CARDIOLOGY

Pulmonary fibrosis.

❖ Affect the peripheral gas exchanging areas of the lung and are characterized by a restrictive ventilatory defect.



Symptoms

- Exertional dyspnoea
- Chest pain (occasionally)
- Cough (non productive)
- wheezing

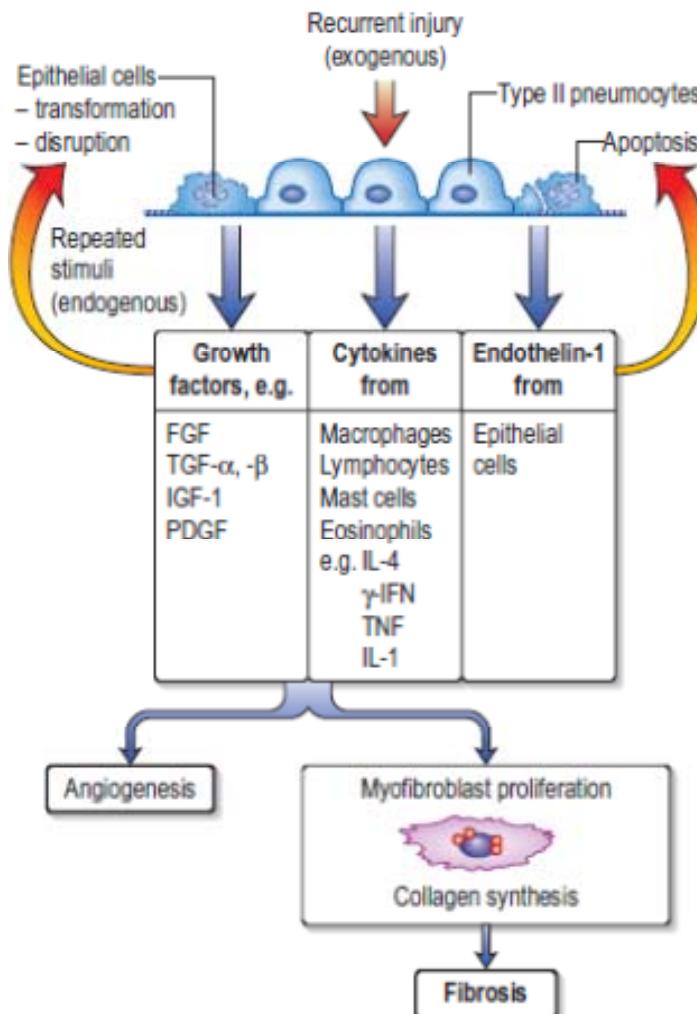


Fig. 14.41 Pathogenesis of pulmonary fibrosis.

Classification according to cause-

- 1) Inherited substances
 - Inorganic
- Silicosis
- Asbestosis
- Beryliosis
- Coal
 - Organic
- Hypersensitivity pneumonitis (extrinsic allergic pneumonitis)
- 2) Drug induced
 - Antibiotics
 - Chemotherapeutic drugs
 - Anti-arrhythmic agents
 - paraquat
- 3) Connective tissue disorders
 - Systemic sclerosis
 - Polymyositis
 - Dermatomyositis
 - SLE
 - RA
- 4) Infection
 - Atypical pneumonia-CMV
 - Pneumocystis pneumonia (PCP)
 - Milliary TB
 - Idiopathic
 - Sarcoidosis
 - Idiopathic pulmonary fibrosis
 - Hamman rich Xn
- 5) Malignancy
 - Lymphangitis carcinomatosis
- Hereditary disorders
 - Cystic fibrosis
 - Neurofibromatosis
 - Tuberous sclerosis
 - Alveolar microlithiasis
 - Bronchiectasis(dyskinetic cilia Xn)
- 6) Miscellaneous diseases
 - Eosinophilic granulomata
 - Lymphangiomyomatosis
 - Pulmonary alveolar proteinosis
 - Eosinophilic lung disorders

.Hx-

- Dyspnea, cough , wheeze- sarcoidosis
- Malaise, wt↓, arthralgia
- Hemoptysis-vacuities/lung CA as complication/TB
- Chest pain-sarcoidosis leads to pneumothorax, granulomatous and vasculitic inflammation
- PMhx -medical disorders –respiratory, IE(penicillin), TB , MI, arrhythmias, asthma, COPD, RA, CAO, Hospital admission due to dyspnea
- Occupational exposure-e.g. asbestos, silica, animal proteins
- details of respiratory protection-masks/type of mask
- Hobbies and pastimes-e.g keeping birds especially pigeons & budgerigars
- Travel history-Parasitic disease can cause pulmonary eosinophilia
- Immunodeficiency states e.g. HIV and opportunistic infection/malignancy

Complications-

- Type 1 respiratory failure
- Increase risk of lung CA

Drug induced-

Idiosyncratic-

- Phenytoin, penicillin, nitrofurantoin

Dose related-

- Bleomycin, interleukin-2, amiodarone, busulfan, methotrexate

- Allergy
- Drug-anti arrhythmic, penicillin,...radiation tx

- FHx-lung /collagen vascular disease-IPF
- SHx -smoking

Examination-

- Dyspnea
- Hypoxemia
- **Cyanosis**
- **Clubbing** in-IPF ,asbestosis ,cystic fibrosis, bronchiectasis ,lung CA,
(Almost never seen in- emphysema, sarcoidosis)
- Crackels-in IPF, but rare in sarcoidosis, EG, fine bilateral end-inspiratory in CFA
- Signs of pulmonary hypertension and cor-pulmonale rash: connective tissue disease
- Uveitis/iritis: sarcoid
- Raynaud's: systemic sclerosis
- Erythema nodosm
- Sjogrens face/scleroderma facies
- Neurofibroma, caf-au lai spots
- Pericarditis : SLE
- Arthritis:
- Haematuria
- Oral candida: HIV disease

erythema nodosm-sarcoidosis



Sjogren's syndrome--SLE ,RA, Scleroderma



sarcoid iritis



- neurofibromatosis-

Neurofibroma, café au lai spots



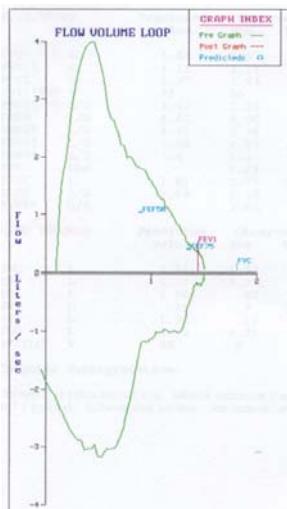
Scleroderma facies



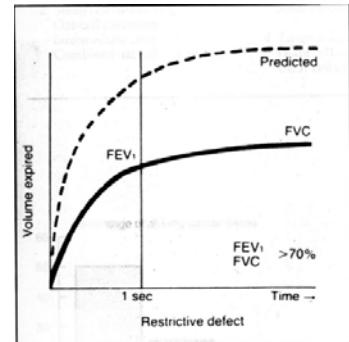
oral candida



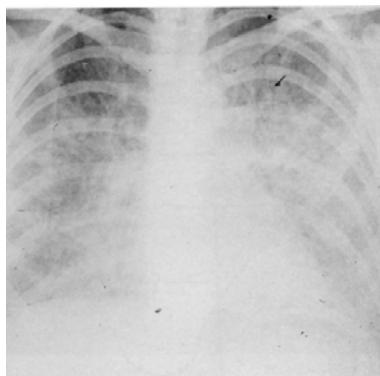
Spirometer-restrictive pattern



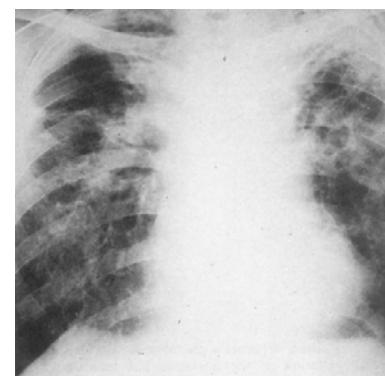
		Predicted Value	Observed Pre	%Pred
FVC	L	1.81	1.5	82
FEV.5	L	1.11	1.11	100
FEV1	L	1.37	1.44	105
FEV1/FVC %		75	96	128
PEFR 25-75 L/S		1.42	2.38	167
PEFR L/S		4.62	4.00	86
PEFR 25 L/S		4.31	1.74	40
PEFR 50 L/S		1.05	2.85	271
PEFR 75 L/S		.4	1.4	350
FET Sec			1.29	
FIFC L		1.81	1.77	97
PIFR L/S		3.08	3.18	103
FIF50 L/S			3.03	



CXR- Extrinsic allergic alveolitis



Acute stage



chronic stage

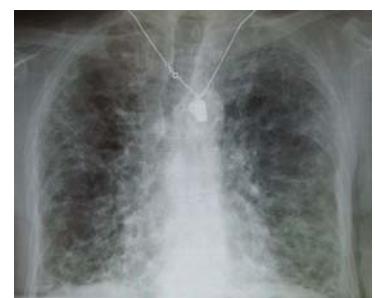
Ix-

- FBC & eosinophil count, urine sediment, U&E's, LFT's, ANF, RF
- ANA, anti-GBM, SACE, Ca2+, serum precipitins
- Chest x-ray -Usually abnormal but non-specific, occasionally diagnostic (in context) e.g. sarcoid and pulmonary eosinophilia. Typical findings-Small lung volumes, In CFA, bilateral lower zone peripheral interstitial shadows honey comb lungs in widespread fibrosis
- Chest CT
- ABG-paO₂↓,paCO₂↑
- Pulmonary function tests-restrictive pattern,FVC-Reduce,FEV1/FVC-supper normal, all lung volumes-TLC,FRC,RV-are reduced, pressure volume curve of lung is displaced downwards and flattened.
- Bronchoscopy with trans bronchial lung biopsy
- Surgical lung biopsy
- Tests for connective tissue diseases such as rheumatoid arthritis, lupus, or scleroderma

Treatment-

- Treat underlying disease
- remove precipitating cause: drugs, dusts
- optimize treatment of systemic disease
- Anti-inflammatory and immunosuppressive regimens
- usually involve corticosteroids: daily oral doses of prednisolone or pulsed methylprednisolone
- additionally methotrexate, cyclophosphamide, cyclosporin can be added
- Sarcoidosis very responsive to prednisolone
- Fibrosing alveolitis very unresponsive
- Lung transplantation last

Fibrosing alviolitis



Fever with splenomegaly

❖ Infective-

Bacterial	Viral	Parasite
<ul style="list-style-type: none"> • Typhoid • TB • SABE(sub acute bacti endocarditis) • Splenic abscess • typhus 	<ul style="list-style-type: none"> • IMN-EBV • Leptospirosis • Acute hepatitis • HIV • CMV 	<ul style="list-style-type: none"> • malaria

❖ Connective tissue disorders- SLE

❖ Neoplastic-

- leukemia-CML
- Lymphoma

❖ Other-RA

HISTORY - Fever-

- Duration- long- TB, SLE, RA
Short-IMN, lepto, acute hepatitis
- Severity-low grade-TB, HIV, acute hepatitis
High grade-typhoid, malaria
- Type-continues-
 - Intermittent
 - Remittent
- Other associated symptoms
- Response to PCM

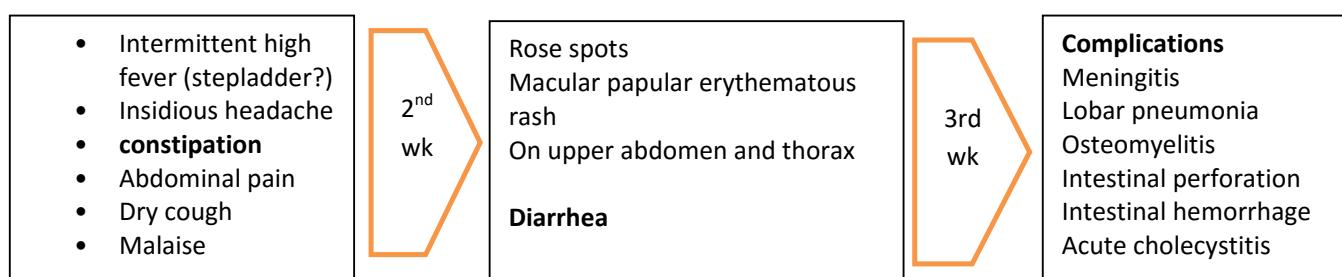
Typus-(archetypal rickettsial disease)

Sudden onset fever, severe frontal headache, vomiting, photo phobia, confusion, jaundice
Hx of foreign travel, insect bite

Typhoid-

(salmonella typhi, s.paratyphi –A,B,C)

Onset is insidious and non specific



After clinical recover -5-10% become convalescent carriers

-1-4% become chronic carriers-associate with gall stones

4th wk

Gradual improvement

TB-

- **LOW, LOA, evening pyrexia, night sweating, cough**
- Past hx of TB, **contact hx of TB**

SABE-sub acute bacterial endocarditis-(stepto pneum/staph aureus)

- Fever, rigors, fatigue, malaise, sweats, weight loss, night sweat ,anemia,-due to septicemia
 - Cardiac failure (SOB, PND, orthopnea, ankle oedema)
 - Acute valvular defects
 - Intra-cardiac abscess formation
 - Vasculitis
 - Glomerulonephritis
 - Embolization-TIA/stroke
 - **Hx of RF/rheumatic heart disease, congenital heart disease, prostatic valves, dental procedure, IV drug abuse**
- } Due to effects on heart
} Due to complication

Splenic abscess-

- Hx of IE, lung abscess, immuno compromise

IMN-(EBV)

- In adolescent and young adults
- Fever, headache, malaise, sore throat
- Mild hepatitis
- Rare complications-
 - Myocarditis
 - Meningitis
 - Encephalitis
 - Mesenteric adenitis
 - Splenic rupture

Leptospirosis (splenomegaly is uncommon)

- Severe head ache, malaise, sudden onset fever, chills, anorexia, myalgia, sub conjunctival hemorrhage, oliguria, haematuria, jaundice, haemoptysis, sore throat, cough, chest pain, rash, confusion, meningism
- Hx of contact with rats, mud, swimming in river
- In severe disease-
 - Hepatic failure
 - Renal failure-
 - Nephritis, acute tubular necrosis
 - Haemolytic anemia
 - Cardiac failure/myocarditis/pericarditis
 - Pulmonary haemorrhage
 - Haemoptysis+/-ARDS
 - DIC

Acute hepatitis-

- Mild fever, LOA, RHC pain, jaundice, dark urine, pale stool
- Hx of blood transfusion, IV drug abuse, sexual contact, contact hx of hep A

HIV-

- Low grade fever, LOW, LOA
- Recurrent infections
- Hx of unprotected sex, contaminated blood/blood products, IV drug abuse

Malaria-(*p.falciparum/vivax/ovale/malaria*)

- Fever-peak in every 3rd day
- headache, malaise, myalgia, anorexia, chills, faints, rigors
- cerebral malaria (*p.falciparum*)-confusion, coma, fits
- focal signs are unusual
- travel to malaria endemic areas (around 2 months back)
- complications-
 - Cerebral malaria
 - **Severe anemia** –Hb<5g/dl
 - Hyperpyrexia
 - Hypoglycemia
 - **Pulmonary oedema- SOB, PND, orthopnoea**
 - Fluid, electrolyte, acid disturbance
 - **Renal failure - oliguria**
 - Hepatic dysfunction
 - Circulatory collapse
 - Massive intra vascular haemolysis - black water fever
 - DIC

SLE-

- Young female
- Arthritis, oral ulcers, alopecia, malar rash, discoid rash, photosensitivity
- Fever associate with marked malaise and tiredness
- Symptoms of cardiac, renal ,cerebral involvement

RA-

- 25-50yr female>male
- Polyarticular symmetrical joint involvement sparing DIP joints
- Morning stiffness lasting >1hr
- Associated oedema, effusion, warmth, tender to palpate
- Joint stiffness
- Can have non –articular manifestation

Leukemia-**CML-**

- Anemia-SOB on exertion, excessive tiredness, weakness
- Recurrent infections
- Bleeding ,bruising
- Bone pain

CLL-

- Splenomegaly appears in late stage

MF-

- Disease present insidiously
- Older people
- Anemia, lethargy, weakness, LOA, LOW, night sweating, bleeding, bone pain, gout

Lymphoma-

Hodgkin lymphoma

- Generalized lymphadenopathy
- Wt loss, fatigue, malaise
- Fever with night sweats
- Pruritus, anorexia



NHL

- Anemia
- Lymphadenopathy
- Repeated infections
- Fever, sweats, anorexia, wt loss

Examination-

- Febrile
- Dyspnoea/not
- Ill looking-Malaria well looking-
- Built-TB,HIV
- Alopecia-SLE
- Pallor-malaria
- Icterus-malaria/lepto/hep
- Conjunctival suffusion-lepto
- Roth spots in fundi
- Eschar site (place of insect bite – typhus)
- Dental caries-IE
- Oral ulcers-SLE
- Palatal petechia -IMN
- Bleeding from gums
- LN-generalized-HIV
-Localized- IMN
- Skin rashes-maculopapular(roth spots)-typhoid
-Trancient maculer rash-IMN
-Vasculitic rash-SLE, RA, IE
-Malar rash/discoid rash-SLE
- Bruises
- Subcutaneous nodules-RA
- Clubbing
- Splinter hemorrhages
- Janeway lesions
- Oslers nodules
- Joint deformities, tender, warmth, swollen joints-RA

} IE

Abdomen-

- Abdominal tenderness
- Hepatomegaly-typoid,malaria,IMN,leukrmia,MF,lepto,hepatitis,SLE
- Splenomegaly-

Mild (<5cm)

- Acute malaria
- Tphoid
- Miliar TB
- CTD?

Moderate (5-10cm)

- Hepatitis
- Splenic abcess

Massive (>10cm)

- CML
- MF
- Chronic malaria

Small liver +large spleen

- CML
- Chronic malaria
- MF

Large liver +small spleen

- Typhoid
- hepatitis

CVS-

- Changing murmur-IE
- Signs of carditis

RS-

- Signs of infection
- pulmonary fibrosis-RA
- Pulmonary oedema-malaria

CNS-

- Higher functions-
 - ALL- meningeal Xn
 - SLE
 - malaria
- Spinal cord compression-RA, spinal TB
- Signs of TIA/stroke-IE

Investigations-

USS abdomen-splenomegaly/hepatomegaly

FBC-HB%-n/n anemia-HL, NHL, ALL, CLL, SLE

heamoltic -NHL,SLE,malaria

- ↑WBC- infection
- ↓Neu- lymphoma
- ↑Neu- IE
- ↑WCC, ↑Lym, ↓neu- ALL
- ↑WCC- CLL
- ↓WCC- Typhoid
- Atypical lym-IMN
- Leucopenia/lymphopenia-SLE

- Plt-
 - IMN
 - Lymphoma,leukemia
 - If get hypersplenism –pancytopenia
- Blood picture-evidence of haemolysis
 - Malaria parasite
 - Malignancy-CML,ALL
- ESR- ↑ RA, SLE, malignancy, infection-IE
- ↑CRP- Acute infection/test to confirm dx
- Sputum analysis/mantoux-TB
- culture -
 - blood
 - stool
 - urine
 - CSF
 - BM aspirate
- Ag test for S.typhi/paratyphi
- Compliment fixation test-lepto
- Monospot test
- EBV IgM Ag
- ELISA/immunofluorescence-typus
- Thin and thick blood smear-(prepare from capillary blood/leishman's, giemsa stain)
- Rapid diagnosis test-Ag/parasitic lactate dehydrogenase
- Microscopic agglutination test(MAT)-leptospirosis
- ($\times 4$ rise of IgM Ab)
- Hep A-IgM Ab
- Hep B-surface Ag(sAg)
- Rheumatic factor-RA
- ANA/anti Ds DNA-SLE
- LN biopsy-lymphoma
- BM aspiration/trephine biopsy-leukemia, MF

Management-

❖ **Typhoid**-antibiotics-

- chloramphenicol, cotrimoxole, amoxicillin
- Rx of choice-ciprofloxacin 500mg bd
- If resist –azithromycin

❖ **IMN**-supportive care/no need specific Rx

❖ **Malaria-Tx**

1. Acute attack-to eliminate blood schizonts(*p.vivax/uncomplicated p.falciparum*)
- Chloroquine oral-10mg/kg single dose D1,10mg/kg single dose D2,5mg/kg single dose D3
In children according to BW &age

2. Radical cure-eliminate liver hypnozoites
 - Primaquine 7.5mg bd ×15days
 - Children-0.3mg/kg /day×15 days
 - p.falciparum-sulphadoxine 500mg+pysrimethamine25mg ,3tablet single dose for adults
 - quinine 10mg/kg oral 8hr for 7days
 - mefloquine/halofantrine
 - uncomplicated but resistant forms- Chloroquine oral-10mg/kg single dose D1,10mg/kg single dose D2,5mg/kg single dose D3
3. prevention of transmission-eliminate gameteocytes
primaquine 45mg single dose at the end of acute attack treatment.
4. Chemoprophylaxis-destruction of merozoites emerging from liver cells
 - Indications-
 - non immune visitors to endemic areas
 - Pregnant women living in endemic area
 - In areas with low resistant to treatment-

Chloroquine 5mg /kg once a wk-start 1wk before and continue for 4wk after returning

 - In areas with moderate resistant-

Chloroquine 5mg/kg once a wk +proguanil 200mg daily-start 1wk before and continue 4 wk after return

 - Areas with high resistant-

Chloroquine +mefloquine 250mg daily-start 2 ½ wk before and continue for 4wk after

❖ **Leptospirosis-**

Benzyl penicillin 1.2g (2mu) IV or IM 6hrly
or doxycycline 200 mg PO stat then 100mg PO 12 hrly or erythromycin 500mg PO 12 hrly

splenomegaly

Acute splenomegaly

Tender-

- malaria-infarction
- sub capsular hematoma
- infection-typoid
- infarction-sickle cell anemia ,embolism

Anemia + bleeding-

- acute leukemia
- auto immune hemolytic anemia

Fever –

- malaria
- typhoid
- SABE
- TB

LN enlargement-

- IMN
- SLE
- Lymphoma
- Sarcoidosis

LN+ fever +skin rash-

- IMN
- SLE

Chronic splenomegaly-

- S+ arthritis -felty's xn
- S+LN enlarge-CLL, lymphoma
- S+ plethora- polycythemia
- S+ wt loss-leukemia, thal ,MFD
- S+ jaundice- hemolytic anemia
- S+ non tender hepatomegaly- cirrhosis, hemolytic anemia, Fe def anemia
- S+ ascites- portal HT, cirrhosis, hepatoma
- S+ chronic lung disease –cor-pulmonale

Hepato- splenomegaly-

HS+ anemia-

- hemolytic anemia
- Malaria
- Leukemia
- Lymphoma
- Fe def anemia

HS+ jaundice-

- Hemolytic anemia
- Typhoid
- Leptospirosis
- Cirrhosis
- CHF??
- Drug induced

HS+LN-

- CLL
- Leukemia

HS+ bone pain-

- CML
- Lymphoma
- Leukemia
- Haemolytic anemia
- Meloma

HS+ joint pain-

- SLE

HS+ gynaecomastia-

- Cirrhosis

HS+ bleeding/ purpura-

- Severe anemia?
- Leukemia
- TTP

HS+ fever-

- IMN
- Malaria typhoid
- leukemia