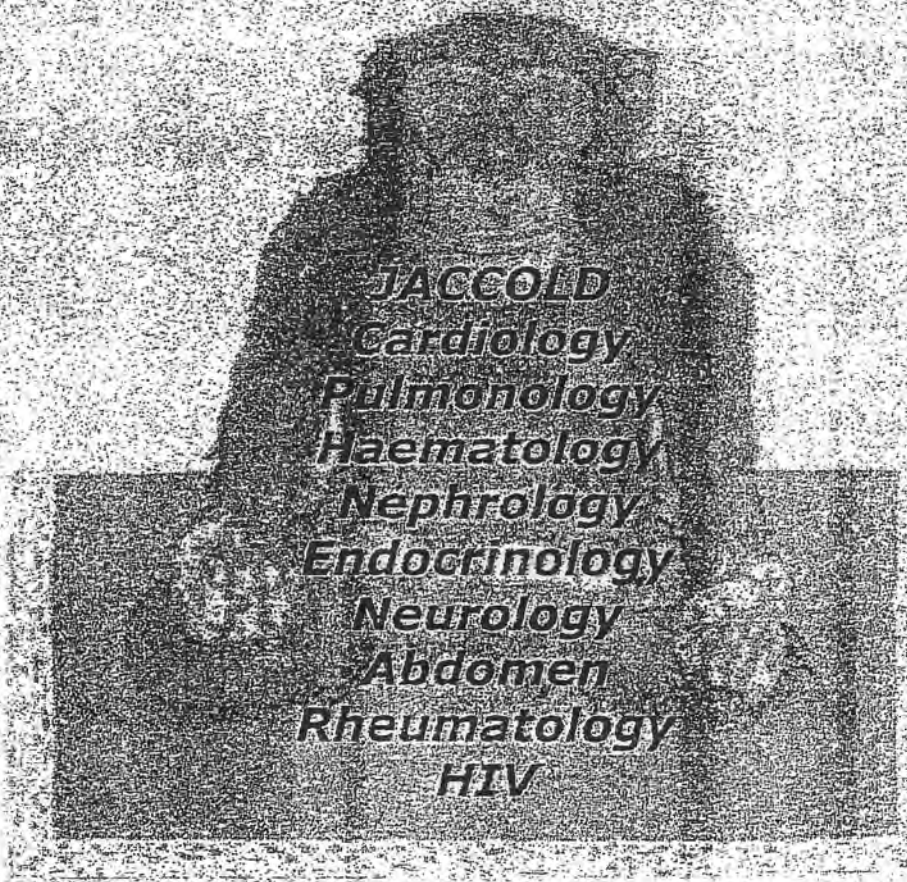
A Desperate Attempt to Pass Internal Medicine

These summaries do not replace any textbook, but honestly, a week before the exam, what do you revise?



JACCOLD

- Jaundice (please see notes on abdomen)
- Anaemia (for approach, please refer to haematology)
- Clubbing
- Cyanosis
- Oedema
- Lymphadenopathy
- Dehydration

Dont study this "Jacold",

not that great.

circular / rotative movement → saw tooth wave → start on warfarin

Atrial flutter @ 150bpm.

but b4 → shot of clexane

any muscle fib → totally irregular

→ aetiology

cardioversion.

- ♥ tachycardia induced failure

ANAEMIA

Anaemia is a reduction in the concentration of haemoglobin:

<13.5g/dl in an adult man

<11.5g/dl in an adult female

Anaemia is not a disease itself, but results from an underlying pathological process.

How is anaemia classified?

- Red blood cells with a low mean cell volume (MCV) appear small **(microcytic)** and pale **(hypochromic)**
- Those with a high MCV appear large and round or oval-shaped **(macrocytic).**
- They may be normal in shape and size **(normocytic, normochromic)** but reduced in number.

Look at the nails, (also koilonychias – dry, brittle, ridged, spoon-shaped nails – can be due to severe iron deficiency anaemia) fingers, tongue, conjunctiva.

Symptoms:

These may be due to the underlying cause or to the anaemia itself.

- Fatigue
- Dyspnoea
- Faintness
- Palpitations
- Headache
- Tinnitus
- Anorexia

Signs:

May be absent even in severe anaemia.

- Pallor
- Signs of a hyperdynamic circulation: tachycardia, flow murmurs (ejection systolic loudest over apex – due to compensatory rise in cardiac output), cardiac enlargement
- Retinal haemorrhages (rare)
- Later, heart failure (if myocardial reserve is reduced): here a rapid blood transfusion may be fatal.

Causes of anaemia:

MICROCYTIC ANAEMIA

Iron deficiency anaemia (iron is essential for haem production)

- Chronic bleeding (usually from gastrointestinal or menstrual loss)
- Malabsorption e.g. gastrectomy, celiac disease
- Hookworm (blood loss)
- Pregnancy (increased demand)
- NB. Dietary inadequacy alone is rarely the sole cause)

Thalassaemia minor (an abnormal haemoglobin)
Sideroblastic anaemia (iron incorporation into haem is abnormal)
Long-standing anaemia of chronic disease

MACROCYTIC ANAEMIA

Megaloblastic bone marrow (oval macrocytes on the blood film)

Vitamin B12 deficiency due to:

- Pernicious anaemia (vit B12 deficiency due to lack of intrinsic factor secretion by an atrophic gastric mucosa)
- Gastrectomy
- Ileal disease, e.g. Crohn's disease, ileal resection (>60%)
- Poor diet (vegans, very rare)

Folate deficiency due to:

- Dietary deficiency, especially alcoholics
- Malabsorption, especially celiac disease
- Increased cell turnover, e.g. pregnancy, leukaemia, chronic haemolysis, chronic inflammation
- Antifolate drugs e.g. phenytoin, methotrexate, sulphasalazine

Non-megaloblastic bone marrow (round macrocytes on the blood film)

- Alcohol
- Cirrhosis of the liver
- Reticulocytosis e.g. haemolysis, haemorrhage
- Hypothyrodism
- Marrow infiltration
- Myelodysplastic syndrome
- Myeloproliferative disease

NORMOCYTIC ANAEMIA

Bone marrow failure:

- Aplastic anaemia (bone marrow fatty or empty), e.g. drugs (such as chloramphenicol, indomethacin, phenytoin, gold, sulphonamides, antineoplastics), radiation, SLE, viral hepatitis, pregnancy, Fanconi syndrome, idiopathic
- Ineffective hematopoiesis (normal or increased bone marrow cellularity), e.g. Myelodysplastic syndrome, paroxysmal nocturnal haemoglobinuria
- Infiltration, e.g. leukaemia, lymphoma, myeloma, granuloma, myelofibrosis

Anaemia of chronic disease:

- Chronic inflammation, e.g. infection (abscess, TB), connective tissue disease
- Malignancy
- Endocrine deficiencies, e.g. Hypothyroidism, hypopituitarism, Addison's disease
- Liver disease
- Chronic renal failure
- Malnutrition

Haemolytic anaemia

- Intracorpuscular defects
  e.g. Hereditary sphaerocytosis, elliptocytosis
  Haemoglobinopathies – sickle cell anaemia, thalassaemia
  PNH (paroxysmal nocturnal haemoglobinuria)
- Extracorpuscular defects
  e.g. Immune – autoimmune incompatible blood transfusion
  Hypersplenism
  Trauma – marathon runners, prosthetic heart valves
  Microangiopathic – DIC
  Toxic – malaria

CLUBBING

Affects fingernails most often but remember to look at the toes.

Cause: Unknown.
Possibly due to an increase in blood flow through multiple arteriovenous shunts in the distal phalanges.

What do you look for?

Some **signs** of clubbing:

1. Shamroth sign: ◇
2. Loss of angle between nail and nail bed (i.e. there is no dip)
3. An exaggerated longitudinal curvature
4. Softening of the nail bed, so the nail feels boggy and there is an increase in *nail bed fluctuation (see-saw nails)*
5. Interphalangeal depth ratio >1
6. Bulbous swelling of the tip of the finger / toe – "Drumstick" appearance. (There is an increased bulk of soft tissues over the terminal phalanges, very advanced clubbing)

☺ Remember, clubbing is a sign of chronic disease, rarely clubbing can develop over several weeks, as in empyema.

How do you elicit the signs?

1. Look across the nail and nail bed at the "nail bed angle". The angle is normally obtuse – but disappears in early stages of finger clubbing.
2. Detect nail bed fluctuation: Place both thumbs under pulp of terminal phalanx and try move the nail within the nail bed using your index finger – "spongy feel".

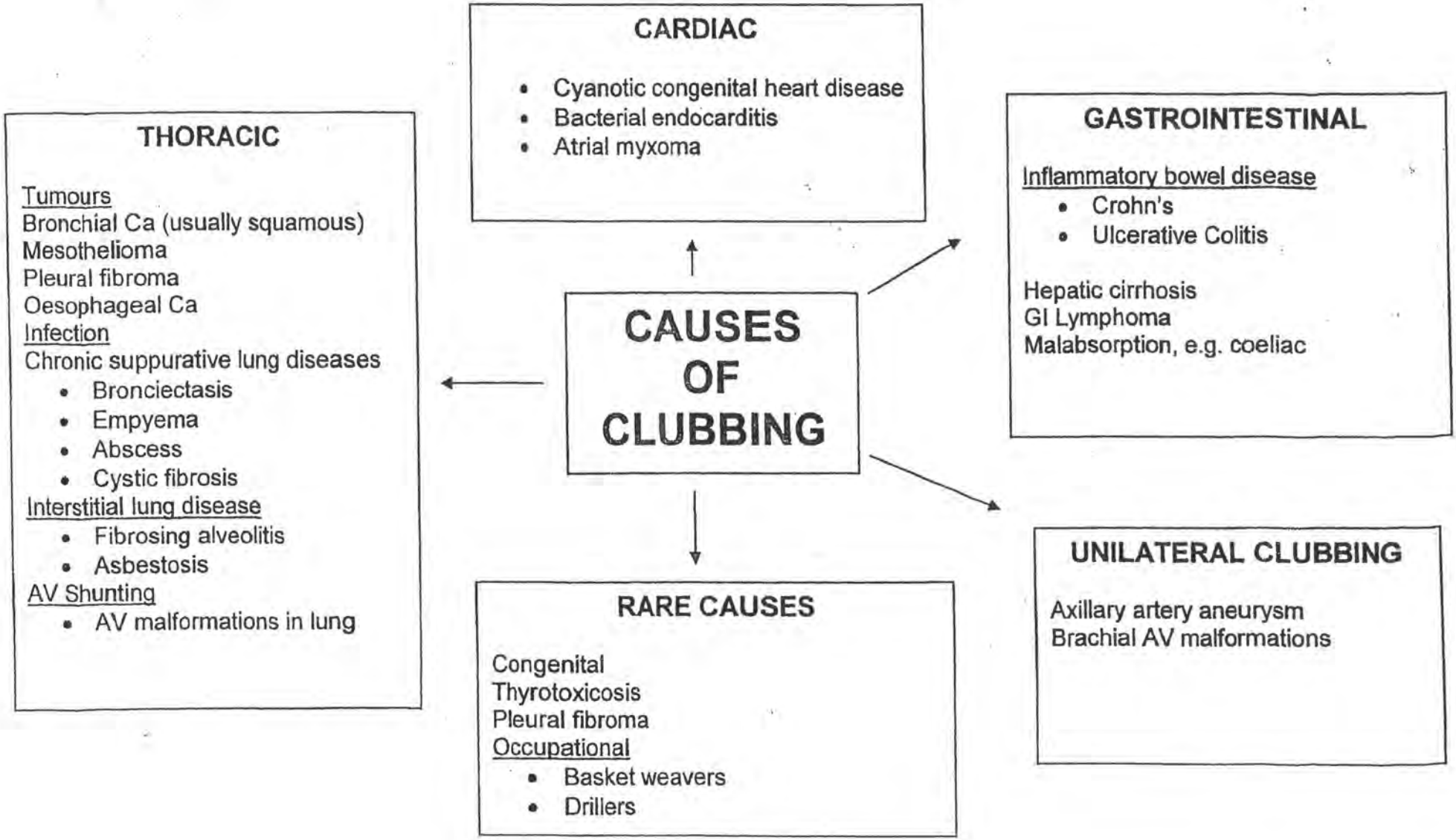
What are the causes of clubbing:

Test yourself first: True or False.

Causes of clubbing include:

- Empyema: T: Cause is unknown, probably the result of chronic hypoxia to the nail bed. It is therefore a feature of chronic hypoxic diseases like central cyanotic conditions, chronic suppurative lung disease and a-v shunting.
- *Cystic fibrosis: T: Due to chronic suppuration.*
- Fibrosisng alveolitis: T: Because of chronic hypoxia.
- Asthma: F: Hypoxia characterised by acute episodes rather than chronic state.
- Lymphoid interstitial pneumonitis: T: As a result of chronic hypoxia.

☺ Note, if the underlying cause is treated successfully, the clubbing may resolve.



CYANOSIS

Cyanosis is an abnormal blue discolouration of skin and mucous membranes; it is due to the presence of deoxygenated haemoglobin in superficial blood vessels.
The haemoglobin molecule changes colour from blue to red when oxygen is added to it in the lungs.
If more than **50g/dl** of deoxygenated haemoglobin is present in the capillary blood, the skin will have a bluish tinge.
Cyanosis **does not** occur in anaemic hypoxia because the total haemoglobin content is low. So therefore cyanosis is easier to detect in polycythaemia.

Central Cyanosis

Look the tongue.
Due to arterial hypoxaemia (there is an abnormal amount of deoxygenated haemoglobin in the arteries and so a blue discolouration is present in parts of the body with a good circulation, such as the tongue).
Always *indicates underlying disease* (most often cardiac or pulmonary) – so focus on the cardio and respiratory exam.
In patients with normal Hb concentration, central cyanosis can be detected when arterial oxygen saturation <90%
Anaemic or hypovolaemia patients rarely have central cyanosis – because severe hypoxia is required to produce the necessary concentration of deoxygenated haemoglobin.
Patients with polycythaemia are cyanosed at higher oxygen tensions.

<u>What are the causes of central cyanosis?</u>

1. Decreased arterial oxygen saturation
   - Decreased concentration of inspired oxygen: high altitude
   - Lung disease: inadequate oxygen transfer (may be correctable by increasing inspired oxygen) e.g. Severe COPD with cor pulmonale, massive pulmonary embolism, pulmonary fibrosis
   - Right-to-left cardiac shunt (cyanotic congenital heart disease) i.e. When desaturated blood enters the systemic circulation without passing through the lungs. E.g. PDA, transposition of the great vessels, VSD with a R-L shunt. *
   - Also left ventricular failure due to pulmonary oedema.
2. Polycythaemia
3. Haemoglobin abnormalities (rare): methaemoglobinaemia, sulphaemoglobinaemia.

* VSD with a R-L shunt = Eisenmenger's syndrome. Congenital heart defect, first L-R shunt, results in pulmonary hypertension and shunt reversal, then cyanosis. (with or without cardiac failure and respiratory infections). Here cyanosis is not reversed by increasing inspired oxygen.

Peripheral Cyanosis

Look at hands and feet.
Occurs when central cyanosis is present, but more commonly seen in poor peripheral circulation i.e. the blood supply to a certain part of the body is reduced and the tissues extract more oxygen than normal from the circulating blood. E.g. the lips in cold weather are often blue, but the tongue is spared.

What are the causes of peripheral cyanosis?

1. All causes of central cyanosis cause peripheral cyanosis
2. Exposure to cold
3. Reduced cardiac output: left ventricular failure or shock
4. Venous or arterial obstruction
5. Raynaud's phenomenon; atheromatous peripheral arterial disease

Causes of **acute** cyanosis:

Impending emergency!

- Asthma
- Foreign body (lumen obstruction)
- Pneumothorax
- Pulmonary oedema
- Hypoventilation due to respiratory depression, e.g. opiate overdose

OEDEMA

'Pitting' oedema reflects increased interstitial fluid – results from the disruption of 'Starling forces'. – dictate fluid transit across capillary basement membranes.
Pitting oedema occurs in cardiac failure unless the condition has been present for a long time and secondary changes in the lymphatic vessels have occurred.

Usually influenced by the effect of gravity on venous hydrostatic pressure and therefore accumulated in the ankles during the day and improves overnight. i.e. 'dependent' oedema.

'Non- pitting' oedema may reflect protein deposition. E.g. myxoedema associated with hypothyroidism.

'Idiopathic oedema' occurs > in women. Typically varies with the menstrual cycle, characterised by marked diurnal variation in weight – reflects variation in capillary permeability rather than extracellular fluid volume.

Clinically:

A substantial volume (litres) of extracellular fluid may accumulate without any clinical signs.
Immobile limbs are often first to be affected, ankle swelling and over the sacrum in bed-bound patients.
Note the upper level of oedema. – It rises higher up the lower limbs with increasing severity. May affect the genitalia and the abdominal wall.
Ascites is common in children, young adults and liver disease.
Pleural effusions are common and can be a feature of any cause of generalised oedema.
Facial oedema on waking – common in adults with low oncotic pressure.
Features of intravascular volume depletion (tachycardia, postural hypotension) may occur when oedema is due to decreased oncotic pressure or increased capillary permeability.

Investigations:

- Do proper cardiovascular examination and abdominal examination.
- Test the urine for protein and measure serum albumin level.
- If there is ascites or a pleural effusion, do an aspiration (measure protein, glucose and microscopy of cells) to confirm the diagnosis.

Causes of oedema:

Low plasma oncotic pressure:

Low serum albumin due to

- Increased loss – nephritic syndrome
- Decreased synthesis – liver failure
- Malnutrition/ malabsorption

Increased capillary permeability:

Leakage of proteins into the interstitium, reducing the osmotic pressure gradient which draws fluid into the lymphatics and blood

- Local – infection/ inflammation
- Systemic – severe sepsis
- Drug – related, e.g. calcium channel blockers

Increased hydrostatic pressure:

High venous pressure / obstruction

- DVT or venous insufficiency – local oedema
- Pregnancy
- Pelvic tumour
- Congestive heart failure
- Intravascular volume expansion (iatrogenic, renal failure, Conn's syndrome)

Lymphatic obstruction

- Infection – filariasis, lymphogranuloma venerum
- Malignancy
- Radiation injury
- Congenital abnormality

A different classification of the causes which may help with the clinical examination:

Pitting lower limb oedema

Cardiac: CCF, constrictive pericarditis
Hepatic: cirrhosis causing hypoalbuminaemia
Renal: nephritic syndrome causing hypoalbuminaemia
GIT: malabsorption, starvation, protein-losing enteropathy causing hypoalbuminaemia
Beri Beri
Cyclical oedema

Pitting unilateral lower limb oedema

DVT
Compression of large veins by tumour or lymph nodes

Non-pitting lower limb oedema

Hypothyroidism
Lymphoedema

- Infectious (e.g. filariasis)
- Malignant (tumour invasion of lymphatics)
- Congenital (lymphatic development arrest)
- Allergy
- Milroy's disease (unexplained lymphoedema which appears at puberty and is more common on females)

Management:

Treat the specific cause
Diuretics are commonly used for oedema
Where there is sodium retention and generalised oedema, restriction of sodium (and sometimes fluid) intake is rational, with diuretic treatment.
Mild fluid retention – will respond to a thiazide or to a low dose loop diuretic, like furosemide.
Oedema caused by venous or lymphatic obstruction or by increased capillary permeability, diuretics may be dangerous. – They will cause hypovolaemia, with a secondary hyperaldosteronism and rebound exaggeration of oedema.
Rather use compression either continuously or intermittently.
Large doses of diuretics, sometimes in combination – in nephrotic syndrome, renal failure and severe cardiac failure.

LYMPHADENOPATHY

Lymphadenopathy can be caused by benign or malignant disease. Enlarged lymph glands may be an important indicator of haematological disease, but are also common in infection and inflammation.

Reactive nodes: expand rapidly and are painful
Nodes due to haematological disease: painless

Localised nodes: look for inflammation in the appropriate drainage area, scalp, ear, mouth, face or teeth for the neck, the breast for the axilla, the perineum or external genitalia for inguinal lymph nodes.

Generalised lymphadenopathy: May be secondary to infection, connective tissue disease or extensive skin disease but is more likely to signify underlying haematological malignancy. (ask about weight loss and night sweats, especially for lymphoma)

Investigations: first a FBC, (to detect neutrophilia in infection or evidence of haematological disease), an ESR and chest x-ray (look for mediastinal lymphadenopathy)
If these findings indicate malignancy, formal cutting neddle or excision biopsy is indicated to confirm diagnosis on histological examination.

Groups of lymph nodes to examine:

1. Cervical and supraclavicular nodes:

Ask the patient to sit and examine the patient from behind. There are **8** groups.
Palpate first the **submental** node – lies directly under the chin
Then the **submandibular** nodes – below the angle of the jaw
Next the **jugular chain** – lies anterior to the sternocleidomastoid muscle
Then **posterior triangle** nodes – posterior to the sternocleidomastoid muscle
Occipital nodes in the occipital region
Then the **postauricular** node – behind the ear
Next the **preauricular** node- in front of the ear
Lastly the **supraclavicular** nodes – in the supraclavicular fossa at the base of the sternocleidomastoid muscle.

2. Axillary nodes:

Raise the patient's arms and palpate as high as possible into the axilla. There are **5** groups.

- Central
- Lateral (above and lateral)
- Pectoral (medial)
- Infraclavicular
- Subscapular (most inferior)

3. Epitrochlear nodes:

Palpate proximal and slightly anterior to the medial epicondyle.
If enlarged, usually indicates pathology. It occurs with local infection, immunocompromised disease, non-Hodgkin's lymphoma or syphilis (rare).

4. Inguinal nodes:

There are 2 groups:

- Along the inguinal ligament
- Along the femoral vessels

Firm, small, mobile nodes commonly found in normal patients.

5. Popliteal fossa

Very occasionally, popliteal nodes may be found in the popliteal fossa.

Characteristics of lymph nodes:

Site:
Localised (local infection, early lymphoma) vs generalised (late lymphoma)
Palpate all the groups as above.

Size:
Large nodes are usually abnormal (>1cm)

Consistency:
Hard: suggest carcinoma deposits
Soft: may be normal
Rubbery: may be due to lymphoma

Tenderness:
Infection or inflammation

Fixation:
Nodes that are fixed to underlying structures are more likely to be infiltrated by carcinoma than mobile nodes.

Overlying skin:
Inflammation of the skin suggests infection, tethering to the skin suggests carcinoma.

Causes of lymphadenopathy:

Generalised lymphadenpoathy

Lymphoma (rubbery and firm)
Leukaemia
Infections
- Viral: Infectious mononucleosis, CMV, HIV
- Bacterial: TB, Brucellosis, syphilis, streptococcal
- Protozoal: Toxoplasmosis
- Fungal: Histoplasmosis

Connective tissue diseases, e.g. Rheumatoid arthritis, SLE
Infiltration, e.g. sarcoid
Drugs, e.g. phenytoin (pseudolymphoma)

Localised lymphadenopathy

Local acute or chronic infection
Metastases from carcinoma or other solid tumour
Lymphoma, especially Hodgkin's disease

Or if you prefer this classification of possible causes:

1. Infective (see above)
2. Neoplastic
   - Primary: lymphomas, leukaemias
   - Secondary: Lung, breast, thyroid, stomach
   - Connective tissue disorders: RA, SLE
3. Sarcoidosis
4. Amyloidosis
5. Drugs: phenytoin

(3)

Pulmonology

- Dyspnoea
- Pleural Effusion
- Asthma
- Pneumonia
- TB
- COPD
- Interstitial lung disease
- Sarcoidosis
- Pulmonary Embolism
- Pulmonary Hypertension
- Lung cancer
- Pulmonary oedema
- Lung abscess
- Bronchiectasis
- Cystic Fibrosis

Approach to Dyspnoea

History:

- Duration of onset
- Severity: NYHA Classification
- Exacerbating factors:
  - nocturnal Sx,
  - positional Sx → Trepopnoea: dyspnoea when lying on one side, suggestive of ipsilateral lung disease
- Associated Sx:
  - Cough, wheeze, haemoptysis, chest pain, stridor, voice change, ankle swelling, constitutional Sx
- Personal and family Hx of lung/ heart disease
- Other Hx:
  - Employment, hobbies, pets, lifestyle
  - Medication, illicit drug use

NYHA Classification of Dyspnoea

I. No limitation of physical activity
II. Slight limitation ordinary activities
III. Marked limitation ordinary activity
IV Sx at rest

Examination:

- GENERAL:
  - Sats, Sx respiratory distress, pulsus paradoxus, cyanosis, paradoxical chest movement
- CVS:
  - ↑ JVP, precordial pulsation, gallop, apex
- RESP:
  - Wheeze, creps, ↓ breath sounds, hyperinflation, tracheal
- EXTREMITIES:
  - Oedema, cyanosis

Special investigations:

- ABG
- CXR
- ECG
- TFT
- FBC,

Arterial Blood Gas

What it tells you about Gas Exchange:

- Amount of ventilation → $PaCO_2$ > 6 kPa under ventilating; → $PaCO_2$ < 4 kPa over ventilating
- Adequate oxygenation → PaO_2 > 7 kPa
- Is there a V/Q mismatch

What it tells you about pH:

- Respiratory component from $PaCO_2$
  - ↑$PaCO_2$ = respiratory acidosis
- Metabolic component from base excess/deficit
  - ↑ base excess = metabolic alkalosis

Causes:

Instantaneous
- PE
- Pneumothorax

Acute (min - hrs)
- Airway disease → asthma, COPD
- Parenchymal disease → pneumonia, pulmon oedema
- Pulmon vascular disease → PE
- Cardiac disease
- Metabolic acidosis
- Hyseria

Subacute (days)
- Pleural effusion
- Lobar collapse
- Acute interstitial pneumonia
- SVC obstruction
- Pulmonary vasculitis

Chronic
- COPD, asthma
- Diffuse parenchymal disease
- Hypoventilation
- Anaemia
- thyrotoxicosis

eg. Pneumonia complicated by pleural effusion.

Pleural Effusion

Definition:
- fluid accumulation in pleural space
  - > 500 ml = stony dull
  - > 200 ml = 1 line on xray

Mechanism:
- ↑ Hydrostatic pressure
- ↓ Oncotic pressure
- ↑ Microvascular permeability
- Lymphatic oedema

TRANSUDATE: HF, constrictive pericarditis, mitral stenosis, Meigs
TRANSUDATE: Nephrotic, ↓ Protein intake, liver cirrhosis.
EXUDATE

Approach:
- History, examination CXR (AP and Lateral)
- Does the patient have heart failure?
  - 75 % cardiac effusions resolve within 48 hrs of diuresis
- Pleural tap
  - Note appearance of fluid: Thin water = Trans; Thick water = Exudate; Milky = Chylothorax (Lymph) Post trauma/Ø/Infection by Ca.; Custard = Empyema (Aus) Drain!
  - Fluid protein and LDH
  - 20ml for cytology → malignant cells + diff count
  - Microbiology → MCS, AFB + culture
  - pH: Ø = Trauma, bleeding tendency, Ca, TB
  - ADA and TB PCR
- Exudate vs. Transudate
  - N S – albumin prot > 30g/l = Exudate and <30g/l = Transudate
  - Abn or borderline S – albumin → use lights criteria
- Further investigations
  - CT chest with pleural contrast → diff benign vs. malignant disease
  - Repeat cytology
  - Further tests → amylase, glu, chol, PGs, Hct, fungal stains
  - Pleural biopsy for TB culture + histology
  - Consider thoracoscopy if persistent undiagnosed pleural effusion

Lights Criteria

For and Exudate:
- Fluid prot/S – prot > 0.5
- Fluid LDH/S – LDH > 0.6
- Fluid LDH > ⅔ upper limit N S - LDH

Causes:

Transudate:

Common
- CHF
- Hepatic Chirrosis
- PE
- Peritoneal dialysis
- Nephritic syndrome
- Atelectasis

Less Common:
- Constrictive pericarditis
- Hypothyroidism
- Meig's Syndrome
- Malignancy (5%)

↑ Hydrostatic P = HF, PE, Constrictive pericarditis, Meigs
↓ COP = Liver cirrhosis, Nephrotic syndrome, ↓ Protein.
Hypothyroidism, Meigs Syndrome.

Exudate: (mostly unilateral.)

Common:
- Para-pneumonic
- Malignancy
- PE
- RA
- Mesothelioma

Massive effusion = TB
RA.

Less Common:
- Empyema
- TB, other infections
- Subphrenic abscess → hepatic, splenic
- Auto-immune disease
- Pancreatitis
- Post Cardiac Surgery/ Radiotherapy
- Drug induced → amiodarone, bromocriptine, methotrexate, phenytoin, nitrofurantoin

TB Effusion:
- Can be massive in volume
- Rx same as for PTB
- Steroids may ↓ fluid volume but don't affect long term outcome
- Dx → pleural thickening and calcification

Bilateral effusion: Pulm. infarct, CCF, Connective tissue d/o's

Effusion in HIV Patient
- Commonest causes → Kaposi Sarcoma, para-pneumonic, TB, PCP, lymphoma
- Diff Dx includes → CCF, fluid overload, PE, drug related, other infections, leukemia, myeloma

Destinction btwn asthma & COPD regarding dyspnoea:
COPD: Better @ night
Asthma: Worse in morning & during night.

Asthma

Definition:
- Reversible AW obstruction
- AW hyper-responsiveness
- Chronic inflammation

Pathology:
- AW obstruction due to → smooth muscle contraction, thickened secretions, AW wall thickening
- May eventually become irreversible due to → basement membrane thickening, epithelial desquamation, collagen deposition → AW remodelling with smooth muscle hyperplasia and hypertrophy

Aetiology:
- Immunologic mechanisms → atopic individuals produce IgE specific B-lymphocytes
- Genetic factors
- Environmental factors
- Hygiene hypothesis

Triggers:
- Dust mites
- Pets
- Smoking exercise
- Cold
- Infection
- Drugs → B Blockers, NSAIDS
- Anxiety
- Pollen

Clinical Features:
- Cough, Expiratory wheeze, SOB, Chest tightness
- Ask about → nasal obstruction, atopic dermatitis, hay fever, food allergy, GORD, triggers, social situation/stressors, aspirin sensitivity, family Hx, NOCTURNAL Sx

Clinical hx + 1 or more:

Diagnosis:
1) • FEV_1 > 15% (200 ml) ↑ after inhalation 200 - 400□g Salbutamol in 15 – 30 mins or 20 % improvement from baseline
2) • FEV_1 > 15% ↓ after 6 min exercise
3) • 20% diurnal variation in PEF on >3 days in a week PEF diary for 2 wks.

B_2 agonist

Aspirin Induced Asthma = Atopic Pt's
- Chronic rhino-conjunctivitis, nasal polyps and asthma
- Mechanism → COX by aspirin with ↑ leukotriene production by Lipo-oxygenase pathway
- ↓ PGE_2

10% of adult asthma is NSAID related.

Non – essential Special Investigations:
- FBC + diff (↑ eosinophils)
- IgE + RAST
- Aspergillus precipitins
- CXR → infection & pneumo.
- Metacholine/ histamine challenge
- Sputum MCS
- Laryngoscopy

we want to exclude infection!

PEF: Before & after 10 mins post b_2 agonist.

Diff Dx
- Upper AW obstruction
- Foreign body aspiration
- SOF
- Tumour (carcinoid)
- Vocal cord dysfunction
- Bronchiolitis
- GORD
- Chronic PE

Classification of New Patients

	Intermittent	Persistent		
	Mild	Mild	Moderate	Persistent (severe)
Day time Sx	< 2 / week	3-4 / week	>4 / week	Continous
Nocturnal Sx	<1 / month	2 – 4 / month	> 4 / month	Frequent
PEF	>80 %	>80 %	60 – 80 %	< 60 %
	SAB_2A No dly preventer No controler	SAB_2A ↓ Dose ICS 250 – 500 □g Beclamethasone	SAB_2A Mod dose ICS +/- LAB_2A LRA	SAB_2A ↑↑ Dose ICS > 1000 □g LAB_2A LRA
		4cc	8cc	8cc
				↓ Oral prednisone

Day Sx
Night Sx
PEF

Management of Chronic Asthma:
Non Pharmacological:
- Allergen avoideance
- Cessation smoking
- Weight reduction
- Immuno-therapy

Avoid trigers
Avoid precip. factors
↓ Weight.

Acute Severe Asthma

→ Never Morphine!!!
Histamine release
↓
AW obstruction.

Risk Factors:

- Previous near fatal asthma
- ≥3 classses of medication
- Large B_2 use
- Brittle asthma → Type 1: wide PEF variability
  → Type 2: sudden severe attacks on background good control

Severity:

Moderate

- ↑ Sx
- PEFR 50 – 75%
- No features of severe asthma
- May be D/C after 1 hour after Rx if PEF > 75% predicted or best

Severe

- PEFR 33 – 50% (< 50% of predicted (N) or best)
- RR ≥ 25
- HR > 110
- Inability to complete sentence in 1 breath

Life Threatening

- PEFR < 33%
- SaO_2 < 92 (need ABG)
- PaO_2 < 8 kPa
- Normal CO_2
- Silent chest
- Cyanosis
- Poor respiratory effort
- Bradycardia/ hypotension/ arrhythmia
- Exhaustion
- Confusion
- Coma

When to Phone ICU

- Worsening PEF despite Rx
- Worsening hypoxia
- Hypercapnia
- ↓pH
- Exhaustion/ poor resp effort
- ↓LOC
- Respiratory arrest

↓ PEF
↑ $PaCO_2$
↓ Ph
↓ LOC
Resp. arrest.

Management:

- Admit immediately
- High Flow O_2 (40 – 60 %)
- IVI access
- Drugs:

Salbutamol 5mg nebs → repeated doses or continous e.g. 5 – 10mg /hr

↓

Atrovent

Add Ipratropium Bromide 0.5mg if if poor response or signs of life threatening asthma

↓

Oral Steroids as effective as IVI → 30 – 40mg prednisone 5 – 7 days or Hydrocrtisone 100mg IVI

↓ If poor response

IVI Aminophylline loading dose 5mg/kg over 20 min → maintenance dose 0.5mg/kg @ (0.5 x kg) ml/hr

or: Salbutamol 3-20 ug/min.
Terbutaline 1,5 – 5,0 ug/min

↓

$MgSO_4$ 1.2 – 2g IVI over 20 mins | Ab if infection

A
B
C
A
B_2
Atrovent
Bronchic
Prednisone or Glucocortes
Aminophyline
$MgSO_4$
Abs.

Discharge When:

- On ↓ B_2A dose
- Off nebs and on inhaled meds > 24 hrs
- PEF > 75% predicted or best
- Minimal PEF diurnal variation

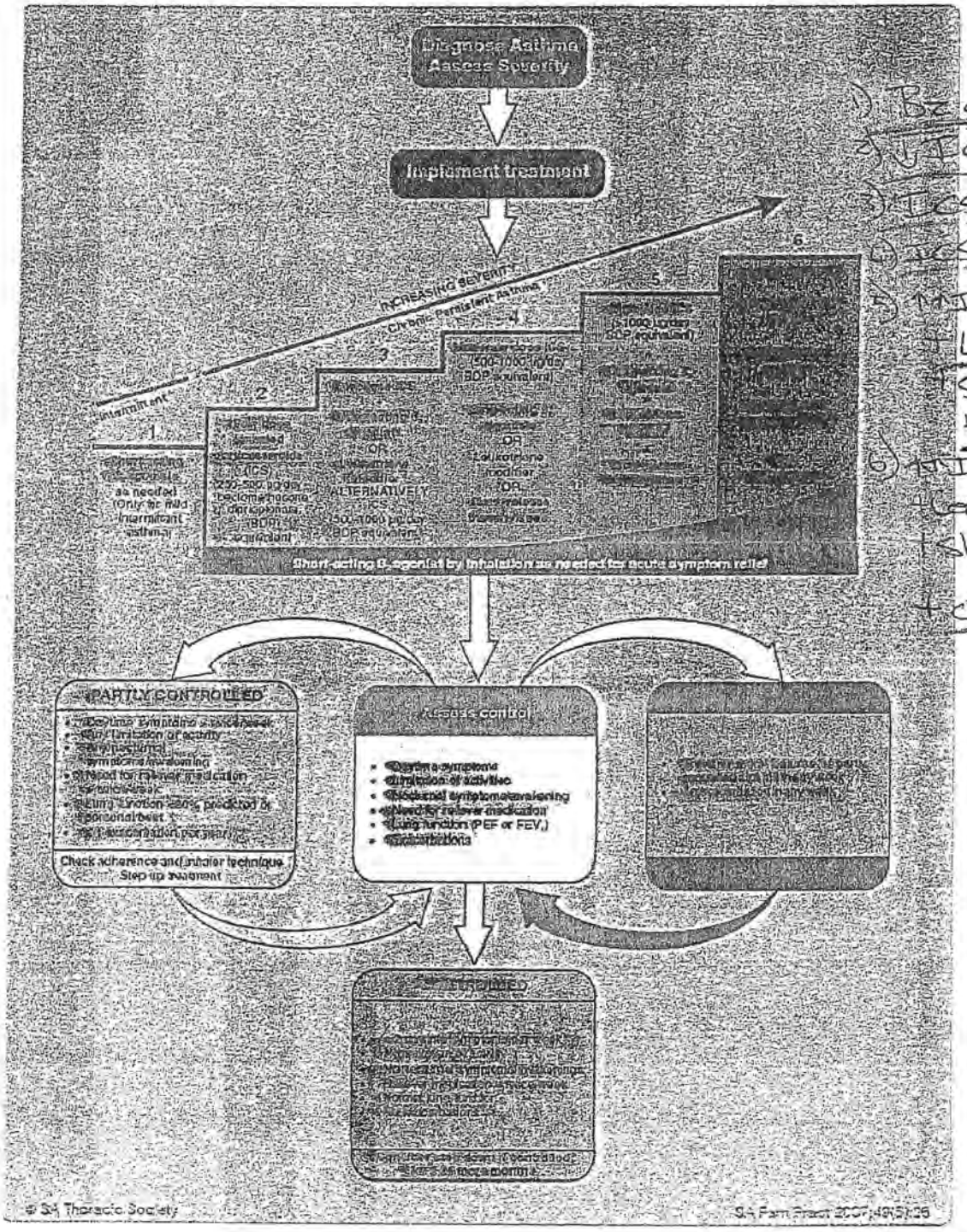
When to ventilate:

- ✓ Coma
- ✓ Resp arrest
- ✓ PaO_2 < 60 mmHg
- ✓ $PaCO_2$ > 45 mmHg
- ✓ Ph ↓ 3 falling
- ✓ Exhaustion, Confusion, drowsiness

Brown, Purple, green, orange

Blue

CONTROLLERS		RELIEVERS
Anti-inflammatory action to prevent asthma attacks	Sustained bronchodilator action but weak for unproven anti-inflammatory effect	For quick relief of symptoms and use in acute attacks as PRN dosage only
Inhaled corticosteroids 1. Beclomethasone 2. Budesonide 3. Fluticasone 4. Ciclesonide	*Long-acting β2 agonists* 1. Salmeterol 2. Formoterol	*Short-acting β2 agonists* 1. Salbutamol 2. Fenoterol 3. Terbutaline
Leukotriene modifiers 1. Montelukast 2. Zafirlukast *Oral corticosteroids* 1. Prednisone 2. Prednisolone 3. Methylprednisone 4. Methylprednisolone	*Sustained-release theophylline preparations*	*Anticholinergics* Ipratropium bromide



1) B2 agonist
2) ↑ ICS
3) ↑ ICS + LABA
4) ↑ ICS + LABA
5) ↑↑ ICS + LABA
+ Leucotrine Ant
+ Slow release theophylline
6) ↑↑ ICS + LABA
+ Leucotrien Ant
+ Slow release theophylline
+ oral corticosteroids

Physical Sg's & Sx's — Confirm Dx — Aetiology — Prog — Cx — Mx.

CxR/sputum/bloods + diff — CAP, NOS, ASP, B Typ/Atypical — Risk factors — Poor prognostic & Cx

Pneumonia

Definition:

- Acute infection of lower respiratory tract with Sx of consolidation

Clinical Features:

- Fever, malaise, cough (productive, non-productive, rusty/green, blood stained)
- Dullness to percussion, ↓ chest movement, bronchial breathing, tachypnoea, crepitations, ↑ vocal fremitus

CAP

Aetiology:

Typical: — previously fit pt.

- S. pneumonia:
  - ↑ age, co-morbidity, acute onset, high fever, pleuritic chest pain
  - Bacteraemic: COPD, alcoholism, DM, dry/ no cough, female
  - Pleural effusion
- H. influenza
- S. aureus
  - Recent influenza like illness
  - Multi-lobar, cavitation, spontaneous pneumothorax

Atypical:

- Legionella spp
  - Younger pts, smokers, > severe infection, no co-morbidity, neuro Sx, SX of multi-system disease
- Chlamydia pneumonia
- Mycoplasma pneumonia
  - Younger pts, previous Ab, ↓ multi-system involvement,
  - Extra-pulmonary involvement: haemoptysis, skin & joint problems
  - Lymphadenopathy
- Klebsiella pneumonia:
  - ↓ plat, leukopenia, male

Risk Factors: — Risk factors/predisposition. — Aspiration pneumonia/Solid oral diet

- Aspiration
- Alcohol — Hospitalized pt's.
- DM
- Oral steroids — COPD/cigarette smoking — oral steroids
- Immune suppression
- HIV — DM
- COPD — Bronchial obstruction/Bronchodilators
- Institutionalisation — Immunosuppression.

CURB – 65

1. Confusion
2. Urea > 7mmol/l
3. RR > 30/min
4. BP S <90, D < 60
5. Age > 65

+ Poor prognostic Sx's: Confusion, Hypoxaemia, Albumin < 35g/l, WCC < 4 or > 20, + Bld culture, Bilat/Multilobar involvement.

Poor prognostic Sx:

> 2 have ↑ risk of death and should be Mx as severe pneumonia

- 65 yrs
- Co-existing disease
- Respiratory rate > 30
- Confusion
- BP: systolic < 90mmHg, diastolic < 60mmHg
- Hypoxemia
- Urea >7mmol/l
- Albumin <35 g/l
- WCC < 4 or > 20
- MCS: +ve blood culture
- Radiology: bilateral or multilobar involvement

CXR Findings:

- Consolidation (most common lower lobes), air bronchograms.
- Interstitial infiltrates
- Cavitation (TB)

Special investigations:

- CXR
- Oxygenation: sats / ABG
- Bloods
  - FBC + diff + plat
  - U&E + LFT
  - CRP
  - Blood culture
- MCS
  - Sputum for TB and general MCS
  - Pleural fluid MCS
  - Viral and atypical antigens
- Specific tests
  - Legionella: urinary antigen, culture, direct immune-florescence, serology/PCR
- CT
  - Only Id Dx doubtful, pt not responding.
  - To exclude abscess / empyema, malignancy, interstitial process

0 = @ Home : amoxil + macrolide

1 = outpt : Co-amoxiclav + Macrolide + Cephalosporine

2 = Inpt : Blactam + macrolide

3 = High care/ICU : Pen + Aminoglycoside Macrolide.

↳ exclude: abscess, Empyema, Ca, Interstitial lung disease.

Management:

General Measures:

- Oxygen
- Fluids
- Analgesia
- Nutrition
- Physiotherapy

O_2 IVI fluids Analgesia Nutrition Physio

Hosptialization Criteria

- Features of severe pneumonia
- Co-morbids illness
- Cyanosis
- Multi-lobar consolidation
- HIV

Antibiotics:

	Preferred	Alternative
Mild	Amoxil 500mg tds po	Erythromycin 500mg qid po OR Clarithromycin 500mg bd po
Moderate	ORAL: Amoxil 500mg tds po + Erythromycin 500mg qid po IVI: Cefuroxime 750mg 8hrly + Erythromycin 500mg 6 hrly	IVI: Ampicillin 500mg 6hrly + Erythromycin 500mg 6 hrly OR Clarithromycin 500mg bd
Severe	IVI: Cefuroxime 1.5g 8hrly + Erythromycin 500mg 6 hrly	IVI: Augmentin 1.2g tds + Erythromycin 500mg 6 hrly OR Clarithromycin 500mg bd
Legionella	Clarithromycin 500mg po / IVI +/- Rifampicin	
Chlamydia	Clarithromycin 500mg po / IVI	Tetracycline if C. Burnetti/ psittaci
Haemphilus	Amoxil, augmentin,	Cefuroxime
Staph aureus	Flucloxacillin 1 – 2g IVI +/- Rifampicin 600mg od/bd po/IVI MRSA: Vancomycin 1g bd IVI	Teicoplanin 400mg bd IVI +/- Rifampicin 600mg od/bd po/IVI

Treatment Failure:

- Slow clinical progress esp. elderly pts
- Incorrect Dx
- Secondary Cx
  - Para-pneumonic effusion
  - Abscess
  - Empyema
  - Extra-pulmonary infection
- Inappropriate Ab
- Atypical pathogen
  - TB
  - PCP
- Impaired immunity
  - HIV
  - Cancer
  - Overwhelming infection

Stay sick
Wrong Dx
Wrong Abx
Atypical Abx's
& Cx
No immunity

How Long to Treat

- 5 days: Uncx pneumonia
- 7 days: severe or undefined
- 14 - 21 days: legionella, staph or G -ve, e.g. Klebsiella.

Vaccinate †Risk Individuals

Influenza:

- Chronic lung disease
- Cardiac, renal, liver disease
- Diabetes
- Immune Suppression
- Age > 65
- Institutionalisation
- Health care workers
- *C/I In EGG ALLERGY*

Pneumococcus:

- Asplenic
- Cardiac, renal, liver disease
- Diabetes
- Immune Suppression

PCP Pneumocystis Jeroveci Pneumonia

Clinical:

- Insuidous / subacute onset
- Progressive dyspnoea
- Dry cough, fever
- Present with Sx of respiratory distress
  - Cyanosis
  - Nasal flaring
  - Use accessory muscles
- CXR + tracheal tug.
  - Bilateral hilar infiltrates
  - Ground glass appearance (but wings appearance!)
- ↑↑↑↑LDH (but nonspecific)

Remember: Pt looks unwell worse than his CXR!!

* Pneumo +
* less distress

Treatment:

- O_2
- Prednisone 40mg dly x 5 days (↑ survival if hypoxic)
- Bactrim 4tabs qid x 21 days > 60 kg, 3 tabs < 60kg
- Do CMV viral load aas if +ve then ↑ mortality

- Other options
- Prophylaxis : Bactrim 2 tabs div till CD4 > 200

Nosocomial Pneumonia

Definition:

- Radiographic infiltrates and onset of new Sx >72 hrs post admission

Aetiology:

- G –ve
- *Pseudomonas*
- Klebsiella
- Bacterodies
- Clostridium

Risk Factors:

- Age ≥ 70
- Chronic lung disease, co-morbidity
- COC, CVI
- Chest or abdominal surgery
- Mechanical ventilation
- NG feeding
- Previous Ab exposure
- Steroids/ cytotoxic drugs
- Poor dental hygiene

Management:

General:

- Pts developing Sx < 48hrs post admission most likely CAP and MX accordingly
- Assess severity
- O_2 and IV fluids
- Clindamycin or ciprofloxacin in penicillin allergy

Antibiotics:

	Preferred	Alternative
G –ve Bacilli	Cefuroxime 1.5g IVI tds	Flouroquinolone IVI **OR** Imipenem 500mg qid IVI **OR** Meropenem 0.5 – 1g tds IVI
Pseudomonas	Ciprofloxacin 500 – 750mg bd po Ceftazidime 2g tds IVI + Gentamycin **OR** tobramycin IVI	Ciprofloxacin 400mg bd IVI Piperacillin 4g tds IVI + Gentamycin **OR** tobramycin IVI
G +ve Cocci	Aminoglycoside + antepseudomonal penicillin IVI **OR** 3rd gen Cephalosporin	

Aspiration Pneumonia

Definition:

- Following aspiration of exogenous material or endogenous secretions into lungs
- ↑ correlation between volume of aspirate and developing pneumonia

Predisposing Factors:

- ↓ LOC
  - Alcohol, drug overdose, post-ictal, massive CVI
- Dysphagia
  - Motor neuron disease, CVI
- Upper GI Tx/disease
  - Surgery to stomach or oesophagus
  - Mechanical impairment of glottic or cardiac sphincter: tracheostomy, bronchoscopy, NG feeding
- Reflux
  - ↑ volume vomiting, ↑ volume NG feeding, feeding gastrostomy, recumbent position
- Nursing home residents

Management:

1. Chemical Pneumonitis
   - General supportive measures, suction if aspiration observed
   - Steroids → controvertial but may befefit ARDS
   - Ab → usually given to prevent 2ndary bacterial inf
     - Cefuroxime + metronidazole **OR**
     - Penicillin + clindamycin
2. Bacterial
   - Ab necessary → Augmentin **OR** penicillin + metronidazole
   - Assess swallowing Fx if no cause found
3. Machanical obstruction
   - Causes include: saline, barium, ingested fluids, gastric contents, drowning, foreign body
   - Mx → tracheal suction

Pulmonary TB

Definition:

- Caused by Mycobacterium Tuberculosis
- Spread from primary focus to hilar and mediastinal LN (primary focus heals spontaneously)
- Direct extension – Primary active TB
- Pleural extension with effusion
- Haematogenous spread – Milliary TB + TB Meningitis

Predisposing Factors:

- Extremes of age
- Primary infection < 1 yr ago
- + TB contact
- HIV
- Silicosis
- Co-morbidity: CRF, DM, Malignancy
- GIT disease assoc with malnutrition

Diagnosis:

- 3 x sputum samples for MCS and AFB (ZN stain)
- OR NGA specimens
- CXR
  - Upper lobe infiltration/ cavitation
  - Fibrous scar tissue and calcification
  - Milliary pattern
  - Hilar/ para-tracheal lymphadenopathy
- PPD → Mantoux
  - Read after 48 hrs
  - use 0.1ml of 1:1000 tuberculin units
  - <5mm negative
  - ≥5mm previous BCG
  - ≥10mm positive
  - ≥15mm strongly positive
  - ≥10 in HIV+ means TB
- Bronchoscopy with bronchoalveolar lavage
- Biopsy from extrapulmonary sites
- HIV Elisa, FBC, U&E, LFT

Management:

New Cases:

- Rifampicin + INH + PZE + ETB daily x 2 months
- Rifampicin + INH daily x 4 months
- > 60kg get 4 tabs rifafour

Retreatment:

- Rifampicin + INH + PZE + ETB + STREPTOMYCIN daily x 2months
- Rifampicin + INH + PZE + ETB daily x 1 month
- Rifampicin + INH + ETB x 5 months

Clinical Features

- Cough productive > 2 wks +/- haemoptysis
- PUO, unresolved pneumonia, night sweats
- ↓ Weight
- Erythema nodosum
- HSM
- Lymphadenopathy, lobar collapse
- Consolidation
- ± pleural effusion
- Cavitation
- Pericarditis

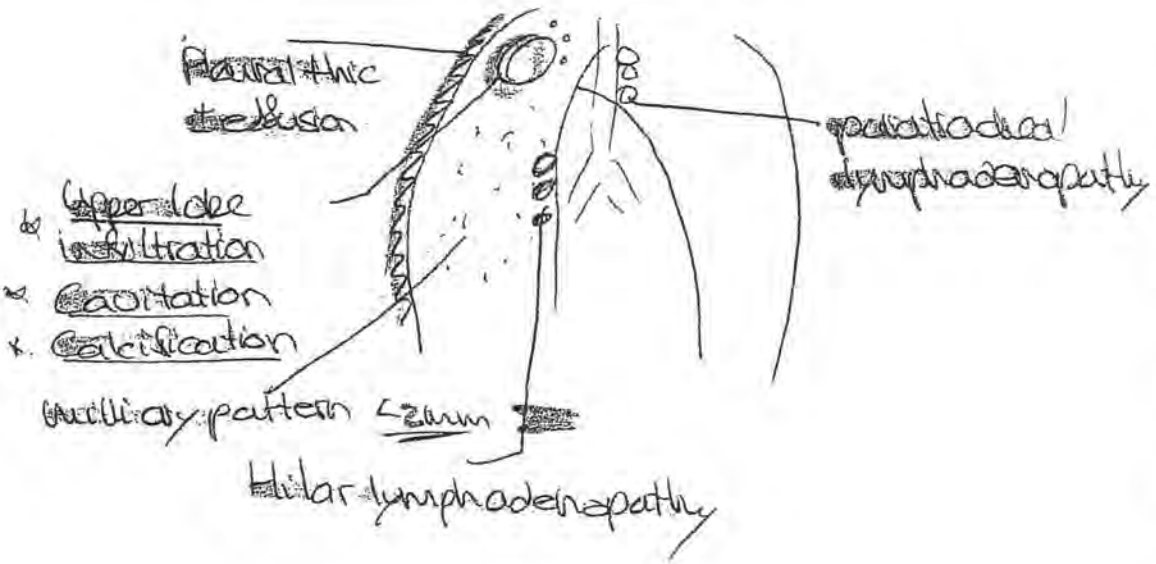
Complications:

Pulmonary:

- Massive haemoptysis
- Cor pulmonale
- Fibrosis, emphysema
- Atypical Mycobacteria Inf, aspergilloma
- Hilar/pleural calcifications
- Pleural effusion
- Bronchiectasis
- Empyema / lung abscess
- Obstructive lung disease

Non-pulmonary:

- Milliary TB
- TB Meningitis
- GU TB
- Pericardial effusion/ constrictive pericarditis
- Pott's paraplegia
- Psoas abscess



MDR-TB

Definition:

- Resistance to RIF and INH (2 or > first line drugs) Resistance to R & I

Mechanisms of Resistance:

- Natural
- Acquired through selection of resistant mutants
  - Inadequate therapy
  - Non-compliance

Risk Factors:

- Previous TB Rx
- HIV co-infection
- Contact with MDR TB
- Rx failure

Previous TB / contact = MDR TB.
HIV

Treatment:

Aminoglycoside	Amikacin Kanamycin	Bactericidal
Pyrazinamide		Bactericidal
Ethionamide		Bactericidal
Fluoroquinilones	Ciprofloxacin Ofloxacin	Weakly Bactericidal
Ethambutol Cycloserine/ Terizidone		Bacteriostatic

6 months intensive phase

12 – 18 months continuation phase

XDR-TB

Definition: (R) & (I) = Fluoroquinolones!

- MDR-TB plus resistance to fluoroquinilones and 1 or > Injectables
  - Kanamycin
  - Capreomycin
  - Amikacin

Treatment:

- Capreomycin
- Ethionamide
- Pyrazinamide
- PAS
- Ethambutol / Cycloserine / Terizidone

6 months intensive phase

12 – 18 months from culture conversion

Sg/Sx → Aetiology (5) → Precipitant ECG/CXR/ → Co (2) → Mx Bactos.

COPD Lung fx.

Definition:
- Chronic progressive AW obstruction including emphysema and chronic bronchitis
- Fixed AW obstruction
- Minimal or no reversibility with bronchodilators
- Minimal variability in day time Sx
- Slowly progressive and irreversible deterioration in lung Fx → worsening Sx
- Chronic Bronchitis: clinically cough sputum most days for 3 consecutive months for 2 consecutive years
- Emphysema: histological Dx of destruction of air spaces distal to terminal bronchiole

mucus production + cough > 3m/year for 2yrs.

Pathology: (goblet cell)
- Mucous gland hyperplasiav (squamous hyperplasia with loss of cilial Fx) → large airways
- Chronic inflammation and fibrosis → small airways.
- Emphysema Centriacinar / Panacinar / Irregular.
- Thickened pulmonary arteriolar wall and remodelling →due to hypoxia → ↑Pulmon VR, Pulmon HT, ↓ gaseous exchange

Aetiology: (5)
- Smoking
- α_1 – Antitripsin deficiency (genetic).
- ↑ familial risk
- Air pollution/ 2nd hand smoke
- Occupational organic / inorganic dust.

Classification NICE 2004
- Mild → FEV_1 50 – 80% predicted, may or may not be Sx (cough, sputum)
- Moderate → FEV_1 30 – 49% predicted, usually Sx
- Severe → FEV_1 < 30% predicted, usually hypoxic with Sx cor-pulmonale

COPD Gold criteria.

Clinical Features:
Symptoms:
- Dyspnoea, ↑ in day, better @ night.
- Cough usually chronic + productive
- Wheeze
- ↓ exercise tolerance

Complications
- Spontaneous pneumothorax
- Cor-pulmonale
- Respiratory failure
- Polycythemia
- Acute exacerbations
- Lung Ca

Signs:
- Tachypnoea
- Use of accessory muscles
- Hyperinflation (barrel chest, hyperresonance, ↓ heart sounds)
- ↑ expiratory time (Exp > 6 secs.)
- Pursed lip breathing (auto PEEP)
- ↓ breath sounds +/- basal crepitations
- Sx of cor-pulmonale (anckle oedema, ↑ JVP, warm peripheries, pleothoric conjunctiva/face, bounding pulse, polycythemia, flapping tremor if acute ↑CO_2)

However: distance liver ↓; ↓ retrosternal

Special Investigations:
- Lung Fx tests → ↑TLC, FRC + RV due to air trapping + ↓ elastic recoil
  → FEV_1 < 80%
  → *Minimal/ no reversibility*
- CXR → Hyperinflation with black lung sign,
  → ↓ posterior ribs, ↓ ant.
  → Bullae
  → Flattened hemi-diaphragms on lat.
- FBC → Polycythemia
- ECG → LVH, LAH
  RVH, RAH, RAD. (downward R in V1).

Diff Dx
- Asthma
- Bronchiectasis
- Bronchiolitis
- LV failure

A – Asthma
B – Bronchiectasis
C – Cystic fibrosis
LV Failure.

Management:
Non-Pharmacological:
- Smoking cessation
- Pulmonary rehabilitation → graded exercise, breathing techniques, education
  → ↑ exercise tolerance, quality of life, ↓ hospital admissions
- Diet → wt loss if obese; supplement if catabolic due to WOB
- Psychosocial support
- Vaccination → prevent inf to prevent exacerbations

Pharmacological:

MILD: SAB_2A or Ipratropium prn

MODERATE: regular Ipratropium or LAB_2A
FEV_1 < 50 add inhaled steroids
Oral Theophylline
(Also if > 2 exacerbations/yr)

SEVERE: Combination Rx Ipratropium + SAB_2A
Oral steroid trial: 30mg x 2wks
Steroid responsive if FEV_1 improves >15%

1) Bz agonist B
Anticholinergics
2) Anti muscarinics A
3) Corticosteroids C
4) Theophylline T
5) Stop Smoking O_2
6) O_2 S

Other:

- LTOT: for pts in resp failure PaO_2 <7.3 or normal with any 1 of:
  - secondary polycythemia
  - peripheral oedema
  - confusion
  - Use for min 15hrs/day
- Vaccinations Pneumococ/Influenza.
- Mucolytics → trial and continue if improvement

Surgery:

- Bullectomy
- lung volume reduction surgery
- lung transplant → young pts with α_1 – Antitrypsin deficiency

ACUTE EXACERBATION of COPD

Aetiology:

- Bacterial/ viral infection
- Rupture of bullae
- MI
- PE

Management:

Controlled O_2 Therapy
24 – 35 % via facemask → keep sats 80 – 90% to balance hypoxia, hypercapnia and pH

↓

Nebulised Bronchodilators
Severely dyspnoeic pts may benefit Salbutamol 5mg 4 hrly +/- Ipratropium bromide

↓

Steroids
Hydrocortisone 200mg IVI stat then all pts get short course Prednisone 30 mg po x 2 wks

↓

Antibiotics
Only if Sx of inf e.g. New CXR changes, pyrexia, ↑ CRP

↓

Antibiotics
Only if Sx of inf e.g. New CXR changes, pyrexia, ↑ CRP

↓

Physiotherapy

↓

No Response
Consider IVI Aminophilline, repeat nebs, consider intermittent CPAP

↓

Still No Response
Consider intubation if pH < 7.26 and $PaCO_2$ increasing

O2
B2
Solucortef
Antibiotics.
Physiotherapy
No Response
↳ Aminophylline.
↓
No Response
↳ Intubate.

Restrictive lung disease!!!

thick wall inflam cell exudate

Interstitial Lung disease

Definition:

- Heterogeneous group of diseases characterised by alveolar wall thickening + inflammatory cells and Exudate
- Slow progressive loss of gaseous exchange
- Progression: ↑ lung stiffness → ↓V/Q → ventilation defects and ↑ exertional dyspnoea → respiratory failure + pulmonary HT

↓ V/Q mismatch ↓ pHT/resp. fail ↓ Corpulmonale

Classification:

Known Aetiology:

- Occupational lung disease: asbestosis, beryllosis
- Drugs: nitrofurantoin, amiodarone, bleomycin, sulfasalazine, methotrexate
- Hypersensitivity reactions: extrinsic allergic alveolitis
- Infections: TB, fungi, viral

Assoc with Systemic Disease:

- Sarcoidosis
- Autoimmune: RA, SLE, systemic sclerosis, mixed CT disease, auto-immune thyroid disease
- Abdominal: Ulcerative colitis, RTA

Idiopathic:

- Idiopathic pulmonary fibrosis
- Organising pneumonia
- Lymphocytic interstitial pneumonia

Whats Important

- Remember to ask about hobbies → birds, mushrooms, exposure to malts
- Occupational Hx
- Other systemic diseases
- Fam Hx

Clinical Features:

- Progressive exertional dyspnoea
- Non-productive paroxysmal cough
- Abnormal breath sounds → inspiratory/expiratory creps!!
- Restrictive pulmonary spirometry
- Abnormalities on CXR or CT

Special Investigations:

- CXR
- ABG, FBC, U&E etc.
- Mainly dictated by clinical findings

Cx: Cor Pulmonale!! (metalic creps + blue!!)

Sarcoidosis

Definition:

- Multisystem granulomatous disease of unknown origin

Pathology:

- Non-caseating epitheloid granulomas
- Resolve spontaneously
- Manifestations related to specific organ involvement
- Ca metabolism may be disturbed:
  - Hypercalcemia
  - Hypocalcemia
  - Nephrocalcinosis
- Metabolic activity of macrophages causes ↑ S-ACE

Diff Dx – Granulomatous Lung Disease

- Sarcoidosis
- TB
- Wegner's Granulomatosis
- Leprosy
- Brucellosis
- Primary billiary cirrhosis
- Hypogammaglobulinemia
- Fungal infections
- Schistosomiasis
- Lymphoma
- Chron's disease
- De Quervain's Thyroiditis

Clinical Features:

- Asymptomatic:
- Brain:
  - SOL
  - Pachymeningitis
  - Diabetes insipidus
- Head:
  - Anterior uveitis
  - Sicca syndrome
  - Lupus pernio: bluish tinge to nose, cheeks and ears → assoc with chronic disease
  - Lymphadenopathy
  - Lacrimal/parotid enlargement
  - CN palsy
- Lungs:
  - Löfgren's Syndrome: mild acute disease, usually non-progressive, fever, bilateral hilar lymphadenopathy, arthalgia, erythema nodosum. Resolves spontaneously and completely in 80% in 1 – 2yrs. Minority develop lung disease
  - Persistent Progressive Infiltrative Lung Disease: hilar/ mediastinal lymphadenopathy, exertional dyspnoea, lung infiltrates, clubbing, cyanosis
- Heart:
  - Arrhythmia

- Heart block
- Sudden death

- **Abdomen:**
  - Granulomatous liver disease
  - Splenomegaly
  - Nephrocalcinosis / kidney stones
  - Hypercalcuria
- **Bones:**
  - Osteoporosis
  - Arthropathies
  - Phalangeal bone cysts
- **Other:**
  - Peripheral neuropathies
  - Skin plaques
  - Scar infiltration
  - Mononeuritis multiplex
  - Erythema nodosum

Staging

0.	Normal
I.	Hilar Lymphadenopathy
II.	Hilar Lymphadenopathy + parenchymal infiltrates
III.	Parenchymal infiltrates
IV.	Progressive Fibrosis, honey-combing, pleural involvement

- Onset either Acute: arthropathy, uveitis, hilar Lymphadenopathy, lethargy, fever
  Chronic: paroxysmal non-productive cough, exertional dyspnoea, extra-pulmonary features

Special Investigations:

Clinical Approach:

- MAKE Dx: clinical pic + HTCT +/- biopsy
- ASSES SEVERITY: CXR, ECG, PFT, BLOODS:
  - U&E, FBC, LFT
  - Immunoglobulins
  - ACE

} Can be ↑ in Active Sarcoidosis

Ca^{2+} & ACE

- STABLE VS PROGRESSIVE: CXR, PFT, oximetry, ACE, Urea,
- OTHER:
  - Tuberculin test (-ve in ⅔)
  - Broncho-lavage ↑ lymphocytes
  - Radionucleotide scan

Causes Bilateral Hilar LA

Infection:
- TB
- Mycoplasma
- Coccidiomycosis
- Histoplasmosis
- Recurrent Infections

Malignancy:
- Lymphoma
- Mediastinal Tumours
- Leukemia

Dusts:
- Silicosis
- Berylliosis

Other:
- Extrinsic allergic Alveolitis
- hypogamaglobulinemia

MANAGEMENT:

STAGE I & II:

- Seldom require Rx, may resolve spontaneously
- Severe systemic features: short course steroids +/- NSAIDS

STAGE III & IV:

- Systemic steroids → 40mg prednisone dly for active disease x +/- 4 wks till response then ↓
- Maintenance dose → 5 – 15mg taper off slowly over few months, long term therapy over 6 – 12 months

OTHER DRUGS:

- Methotrexate → 10 – 25mg wkly x 6 months
- Azothiaprine → neuro-sarcoidosis and SII/III pulmonary Sarcoidosis
- Cyclophosphamide → neuro-sarcoidosis unresponsive to steroids, limited use due to toxicity
- Antimalarials → skin and hypocalcemia chloroquine, hydroxychloroquin 200mg dly

LAST RESORT → Lung transplant

Indications for Immune Suppressive Rx:
- Cardiac Sarcoidosis
- Hypercalcemia
- Increasing Sx
- Neuro-sarcoidosis
- Splenic/ hepatic/ renal
- Sight threatening ocular sarcoidosis
- Lupus pernio

PULMONARY EMBOLISM

	ACUTE MASSIVE PE	ACUTE SMALL/ MED PE	CHRONIC PE
PATHOPHYSIOLOGY	Major hemodynamic effects: ↓ CO; acute RH failure; disordered V/Q ratio	Occlusion of segmental pulmonary artery → infarction ± effusion	Chronic occlusion of pulmonary microvasculature; pulmonary hypertension, RH failure.
SYMPTOMS	Sudden dyspnoea, faintness, central chest pain, apprehension, fever, hypoxia	Pleurisy, restricted breathing, haemoptysis	Exertional dyspnoea, late – exertional syncope, Sx of RV failure
SIGNS CVS	Major circulatory collapse, tachycardia, hypotension, ↑JVP, gallop rhythm P_2 wide split	Tachycardia	May be minimal in early disease Late RVH, heave, loud split P_2
RESP	Severe cyanosis, no local signs	Pleural rub, raised hemidiaphragm, crepitations, effusion (usually blood stained)	Terminal – Sx RV failure
OTHER	↓cardiac output	Low grade fever	
INVESTIGATIONS CXR	Often subtle, oligemic lung fields, slight ↑ hilar shadows	Pleuropulmonary opacities, pleural effusion, linear shadows, raised hemidiaphragm	Enlarged pulmon artery trunk, enlarged heart, prominent RV
ECG	$S_1Q_3T_3$, ↓wave ↕ in V_1-V_4, RBBB, PO_2 ↕ PCO_2	Sinus tachycardia	Dx RVH and Strain
ABG		↓PCO_2	Exertional ↓ PO_2 or desaturation on formal exercise testing
V/Q SCAN	Major areas of ↓ perfusion	Perfusion defects not matched on ventilation scan	May be no abn
PULMON ANGIOGRAPHY	Definitive Dx	Definitive Dx	Usually Dx, may need lung biopsy to confirm

Diff Dx:
- Aortic Dissection
- Cardiac Tamponade
- MI

Radiological Features:
- Wedge shaped opacity
- Horizontal linear opacities
- Pleural Effusion (usually blood stained)
- Pulmonary opacities any size/ shape
- Raised hemi-diaphragm

Clinical Features:
- Tachycardia, tachypnoea
- AF
- ↓ Chest movement (due to pain)
- Pleural rub
- Loud P_2 & splitting S_2
- Hypoxia with N PaO_2
- Low grade fever
- Sx of DVT
- Sx of RHF

Risk Factors for VTE

Major
- Surgery
  - major abd/pelvic, ortho, post-op ICU care
- Pregnancy
  - late trimester, C/S, PET
- Malignancy
  - pelvic/abd, advanced or mets
- Lower limb problems,
- Mobility

Minor
- CVS
  - Cong HD, CCF, HT, CVP, superficial venous thrombosis
- Oestrogens
  - COC, HRT
- Miscellaneous
  - Malignancy, neuro disability, thrombotic d/o, obesity, IBD, nephritic syndrome, myeloproliferative disorders, dialysis

Special Investigations:
- investigations add wt to clinical suspicion thus must asses probability of Dx including clinical plc and risk factors
- CXR
- ECG
- ABG
- Spiral CT, V/Q, Doppler leg veins
- D-Dimer:
  - If probability ↓ then –ve result excludes PE
  - If probability ↑ then +ve result needs further investigation
  - –ve result unhelpful in ↑ probability cases
- Do not send unstable pt for Dx investigations. Rather Rx.
- Echo is first line before CT, but do not delay Rx by >1hr

CONSIDER IN PTS WITH
- Unexplained SOB
- Collapse
- New onset AF
- Sx RHF
- Pleural Effusion

Risk Assessment

- Clinical Features compatible with PE
  - ↑↑RR
  - +/- haemoptysis
  - +/- pleuritic chest pain
- Plus 2 other factors
  1. Absence of another reasonable explanation
  2. Presence of major risk factor

- 1 + 2 → HIGH pre-test probability
- 1 or 2 → INTERMEDIATE pre-test probability
- Alone → LOW pre-test probability

Management:

General:

- O_2 100%
- IV access, baseline bloods (inc clotting profile)
- ECG
- Analgesia → opiates but beware Hypotension
- Mx Cardiogenic Shock with inotropes if Massive PE causes ↓ RV filling

Anticoagulation:

- IVI heparin
  - 5000 – 10 000 IU or 80IU/kg as bolus
  - Maintenance dose 1300 IU/hr or 18IU/kg/hr

Thrombolytic Therapy:

- Indicated if hypotensive, Sx of RHF, acute collapse
- Streptokinase 250 000 U over 20 mins with 100 000 U/hr for 24 hrs
- Give hydrocortisone to prevent circulatory collapse
- Stop heparin during thrombolysis and restart later
- C/I in active bleeding, recent Hx of ICH

Hypotensive/RHF/collapse.

Embolectomy:

- Rarely done,
- For acute life threatening massive PE

Caval Filters:

- Recurrent PE despite adequate Rx
- Anticoagulation Rx C/I → neurosurgery
- Filter placed below renal arteries in IVC

Pulmonary Hypertension

Definition:
- PAP >25mmHg @ rest or >30mmHg during exercise

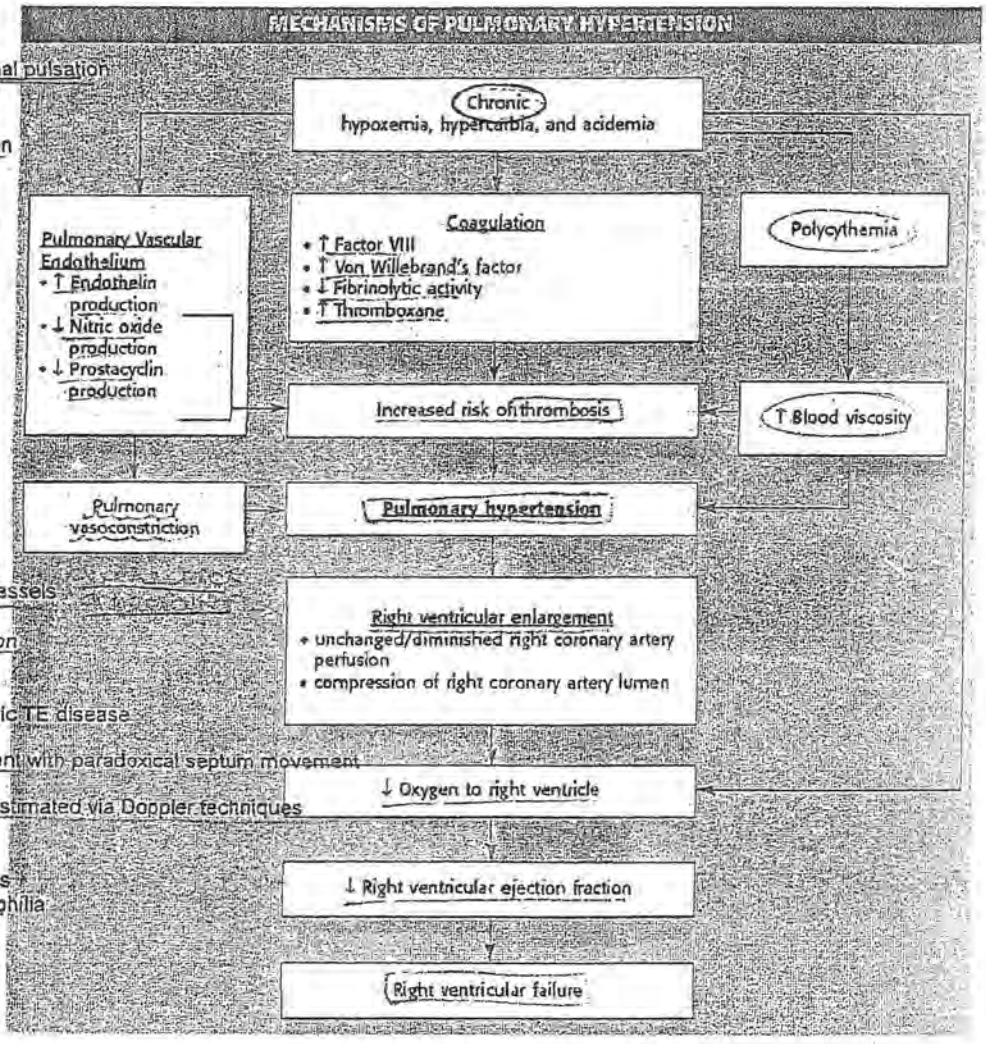
Classification:
1. Pulmonary Arterial HT:
   - Primary pulmonary HT (familial, sporadic)
   - Related Conditions: HIV, collagen vascular disease, portal HT, Drugs + toxins
2. Pulmonary Venous HT:
   - Left sided Heart or Valvular disease
   - Extrinsic compression of pulmonary veins
3. Due to Respiratory Disease or Hypoxemia:
   - COPD, ILD, sleep disordered breathing, chronic exposure to ↑ altitudes,
4. Chronic Thrombolic Disease:
   - PE, sickle cell disease
5. Disorders directly affecting Pulmonary Vasculature:
   - Sarcoidosis, Schistosomiasis,
   - Pulmonary capillary haemangiomatosis

Clinical:

Signs:
- Palpable P_2
- Epigastric or parasternal pulsation
- Tricuspid insufficiency
- Early satiety
- Pulmonary regurgitation
- Distended JVP
- Hepatomegaly
- + Hepatojugular reflux
- Ascites, Anasarca

Symptoms:
- Exertional Dyspnoea
- Fatigue
- Anginal chest pain
- Orthopnoea
- Syncope
- Haemoptysis

Special Investigations:
- CXR
  - ↑ pulmon a.
  - ↑ RH shadow
  - ↓ peripheral vessels
- ECG
  - R axis deviation
  - RVH
- V/Q Scan
  - Exclude chronic TE disease
- Echo
  - RH enlargement with paradoxical septum movement
  - TR
  - PA pressure estimated via Doppler techniques
- PFT
- Bloods
  - Auto-antibodies
  - HIV, Thrombophilia
  - TSH, S-ACE
  - ABG



Management:

General:
- Anticoagulation
- O_2
- Digoxin and diuretics
- Contraception and immunizations: *influenza, pneumococcus*

Primary - Sp... - Familial

CAUSES AND MECHANISMS OF SECONDARY PULMONARY HYPERTENSION

	Causes:	Mechanisms:
PULMONARY DISEASE	A) Chronic obstructive pulmonary disease • Chronic bronchitis, emphysema B) Cystic fibrosis C) Interstitial lung disease • Idiopathic pulmonary fibrosis, pneumoconiosis, radiation, chemotherapy agents D) Recurrent aspiration pneumonitis E) Atelectasis F) Pneumonia G) Neonatal lung disease H) Severe asthma I) Bronchiectasis	1) Pulmonary vasoconstriction from alveolar hypoxemia, hypercarbia, and acidemia 2) Pulmonary vascular bed destruction 3) Increased cardiac output from increased blood viscosity secondary to polycythemia 4) Compression of pulmonary vessels from increased lung volumes (COPD)
CARDIAC DISEASE	A) Congenital heart disease • Atrial septal defect, ventricular septal defect, patent ductus arteriosus B) Left-sided heart abnormalities • Cardiomyopathies, mitral stenosis, left atrial myxoma, aortic regurgitation/stenosis/coarctation, constrictive pericarditis, ball-valve thrombus C) Pulmonary vein obstruction • Mediastinitis, tumor/adenopathy D) Eisenmenger's syndrome	1) Increased left to right flow **OR** 2) Impairment of pulmonary venous return 3) Pulmonary vasoconstriction from arterial hypoxemia, hypercarbia, and acidemia
THROMBOTIC/ EMBOLIC DISEASE	A) Chronic pulmonary thromboembolism • Thrombus, tumor, ova, parasites, foreign material (talc) B) In situ thrombosis C) Sickle cell disease D) Factor deficiencies • Protein C, protein S, antithrombin III	1) Obstruction of proximal or distal pulmonary vasculature 2) Hypoxemia leading to pulmonary vasoconstriction
VASCULAR DISEASE	A) Collagen-vascular disease B) Scleroderma C) CREST syndrome D) Rheumatoid arthritis E) Pulmonary vasculitis • Wegener's disease, polyarteritis, Takayasu's arteritis F) Sarcoidosis G) Schistosomiasis	1) Perivascular infiltration and fibrosis leading to compression of vessels and formation of thrombosis 2) Pulmonary vascular bed destruction 3) Hypoxemia leading to pulmonary vasoconstriction
HYPOVENTILATION DISORDERS	A) Marked obesity B) Sleep apnea disorder C) Kyphoscoliosis D) Neuromuscular disease • Multiple sclerosis, muscular dystrophy E) Chronic exposure to high altitude	1) Decreased respiratory excursion resulting in hypoxemia 2) Decreased ventilatory drive
LIVER DISEASE	A) Cirrhotic liver disease B) Noncirrhotic liver disease	1) Failure of liver to metabolize vasoactive substances resulting in shunting into pulmonary circulation and pulmonary vasoconstriction

Some 3 muscular causes

1° = Familial / Sporadic.

2° = LHD / Pulmonary disease / Vessels / Liver

Pulmonary disease: Restrictive → Interstitial → Obstructive lung disease

Vessels: → RA, SLE, SCI, Sarcoid, Amyloid.

Liver: thromboembolic → viscosity → chronic pulm embolism; cirrhosis, Hepatopulm

Lung Cancer

Classification:
Non-small Cell:

- Squamous:
  - most common type
  - may present as single lesion on CXR, but may form multiple cavitatory lesions
  - often present with Hypercalcemia
- Adenocarcinoma:
  - Not only *smoking related, can occur in scars or fibrosis*
  - May be primary or 2ndary from other sites
- Alveolar cell carcinoma:
  - Rare
  - Fluffy air space shadow on CXR,
  - ↑↑↑↑↑↑↑ sputum production

Small Cell:

- 20 – 25% of all lung Ca
- Usually not amendable to surgery, chemo/radio sensitive
- Untreated extensive SCLC has mean survival +/- 6wks
- SIADH

→ Lambert Eaton Syndrome.

Metastases:

- To the lungs: breast, kidney, uterus, testes, ovary, thyroid...
- From the lungs: liver, bone, brain, adrenals, skin

Clinical Features:

Local Tumour effects:

- Cough: persistent or change from previous
- Haemoptysis
- Chest pain
- Un-resolving pneumonia or lobar collapse
- Wheeze or stridor
- Shoulder pain
- Pleural effusion
- Shoulder pain
- Dysphagia
- Pancoast tumour: Horner's syndrome and weakness of hand muscles

Metastatic Tumour effects;

- Cervical/supraclavicular lymphadenopathy
- Palpable liver edge
- Bone pain
- Neurologic sequelae

Paraneoplastic Syndromes:

- Cachexia and wasting
- Clubbing:
  - More common in squamous and adeno, but can occur in any
- SIADH
  - Hyponatraemia hypo-osmolality, urine osmolality ↑↑↑↑↑
  - Causes include: HIV, Post major surgery, carbamezepime, Fluoxetine, pneumonia, stroke, psychosis SCLC
  - Management: Fluid restriction, Demeclocycline 450mg bd (tetracycline derivative, blocks ADH in Distal tubule, *may be used long term*)
- Ectopic ACTH:
  - Pts present with Cushing's syndrome, but due to rapid development the biochemical changes predominate
  - Mainly in SCLC
- Hypertrophic Pulmonary Osteo-arthropathy:
  - Thickening of periosteum esp. tibia, fibula, radius, ulna
  - Any cell type, mostly in squamous and adeno
- SVCO:
  - Malignant causes: Lung Ca and lymphoma
  - Benign causes: granulomatous disease, intra-thoracic goitre, CVP, pacemaker wires.
  - Clinical Features:
    - face and upper body oedema with pleothora and cyanotic appearance
    - venous distension of upper body and face
    - Pemberton's Sign: facial plethora, distress and stridor after lifting arms above head for few mins.
    - Dyspnoea
    - Headache worse on lying down or bending forward
    - Other Sx of malignancy
  - Manage according to underlying cause

Special Investigations:

- CXR
  - Unilateral hilar enlargement
  - Peripheral pulmonary opacity
  - Lobar/segmental collapse
  - Pleural effusion
  - Broadening of mediastinum

- ↑ cardiac shadow
- Elvation of hemi-diaphragm
- Rib destruction

- Bloods:
  - U&E, CMP, LFT,
- Sputum cytology
- Dx pleural tap
- FNA of LN
- CT/MRI
- Bone Scan
- PET scan

Looking for mets

- Diagnostic tests:
  - Bronchoscopy
  - Radiologically guided lung biopsy if
    - Newly enlarging mass not amendable to Bronchoscopy
    - Multiple nodules in pt not known with malignancy
    - Persistant undiagnosed single or multiple pulmonary infiltrates
    - Hilar mass

C/I to Resection

- Distant mets
- Invasion of central mediastinal structures
- Malignant effusion
- Contralateral nodes
- $FEV_1 \leq 0.8L$
- Severe unstable cardiac or med d/o

Diff Dx of Coin Lesion in Lung

- Malignancy
- Abcess
- Granulomas
- Carcinoid tumour
- Pulmonary harmatoma
- AVM
- Encapsulated Effusion
- Cyst
- Foreign body
- Skin tumour

Staging:

NSCLC:

- Staged using TNM system

SCLC:

- Staged as limited (ipsilateral hemi thorax and supraclavicular LN) or extensive

Management:

NSCLC:

- Stage I and II usually amendable to surgery
- Chemotherapy and Radiotherapy usually reserved for inoperable patients

SCLC:

- Limited SCLC may benefit from surgery
- Chemotherapy mainstay of Rx, may increase survival to 14months in limited disease
- Radiotherapy also used.

Pulmonary Oedema

Definition:

- fluid accumulation in the interstitium of the lung
- dependant oh hydrostatic and oncotic forces

Aetiology

Direct lung injury:

- Chest trauma, pulmonary contusion
- Aspiration
- Smoke inhalation
- Pneumonia
- O_2 Toxicity
- PE / reperfusion injury

CVS Causes:

- LVF post MI or IHD
- MS
- Arrhythmias
- Malignant HT

Injury in ↑ Hydrostatic Pressure:

- High altitude
- Neurogenic
- Re-expansion injury

Haematogenous Lung Injury:

- Sepsis
- Pancreaitis
- IVI drug use eg. heroin
- Cardiopulmonary bypass
- Multiple transfusions (fluid overload)

Clinical

Symptoms:

- Dyspnoea
- Orthopnoea
- Pink frothy sputum

Signs:

- Distressed, pale, sweaty
- ↑ pulse, tachypnoea
- Pulsus alternans
- ↑ JVP, gallop rhythm
- Fine creps
- Wheeze (cardiac asthma)

Special Investigations:

- CXR
  - Cardiomegaly, bilateral small shadowing of costo-phrenic angles, kerley B lines, fluid in fissures
- Bloods
  - U&E, S-Alb, Pro-BNP, Cardiac Enzymes
- ABG
- Echo

Management:

First Line:

- O_2 and intubation if necessary
- Nitroglycerine SL x 2 tabs if SBP > 100mmHg
- Furosemide 40 – 80mg IVI (may need more in renal failure)
- Morphine 2 – 4 mg IVI
- ECG and Rx arrhythmias

Second Line:

- Dopamine if SBP 70 – 100mmHg and Sx of shock
- Dobutamine if SBP > 100mmHg and no Sx of shock

Once Stable:

- Daily weight, BP and pulse 6 hourly.
- Repeat CXR
- Change to oral Furosemide
- ACE-I if in LVF, also consider BB and spironolactone
- Warfarin and digoxin in AF

Lung Abscess

Definition:
- Cavity lined by chronic inflammatory tissue containing a collection of pus

Causes:
- Inadequately Rx pneumonia
- Bronchial obstruction
- Pulmonary infarction
- Septic emboli
- Sub-phrenic abscess
- Hepatic abscess
- Aspiration

Predisposing Factors:
- Dental disease
- Diabetes
- ↓ LOC
- Bronchus Ca
- Pneumonia
- Immunocompromised
-

Clinical Features:
- Swinging fever, wt loss, malaise
- Cough with purulent sputum
- Pleuritic chest pain
- Haemoptysis
- Anaemia, crepitations, clubbing

Special Investigations:
- CXR
  - Walled cavity
  - Air/fluid level
- Sputum MCS
- CT scan
- Bloods
  - FBC, U&E, CRP, ESR, Blood culture, LFT

Management:
- Antibiotics
  - Amoxyl 500mg Bd
  - Metronidazole 400mg tds
  - Rx 4 – 6 wks until clinically and radiologically resolved
  - Clindamycin if penicillin allergy
  - Augmentin if G –ve organisms suspected
- Postural drainage
- Surgical excision if
  - no response to Rx
  - very large > 6cm
  - resistant organisms
  - haemorrhage
  - recurrent disease

Diff Dx for Cavitating Mass
- Cavitatory Ca
- Cavitatory TB
- Wegner's Granulomatosis
- Infected cyst or bullae
- Aspergilloma
- Pulmonary infarct
- Rheumatoid nodule
- Sarcoidosis
- Pulmonary infarct

Empyema

Definition:
- Pus in pleural space

Causes:
- Usually as a complication
- Pneumonia, Chronic Inf e.g. TB
- Rupture of sub-phrenic abscess through hemi-diaphragm

Clinical Features:
- ↑↑↑ and remitting fever
- Rigors, sweating, malaise, ↓ wt
- Polymorph leukocytosis, ↑↑ CRP
- Pleural pain, dyspnoea
- ↑↑↑ purulent sputum if ruptures into a bronchus
- Sx of fluid in pleural space

Management:
- Surgical drainage via chest drain
- Ab as for lung abscess can be given

Bronchiectasis

Definition:
- Abnormal dilation of one or more bronchi
- Chronic airway inflammation
- Associated recurrent chest infections, purulent sputum and airflow obstruction

Causes:

• **Genetic**	Cystic Fibrosis, Kartagener's
• **Congenital**	pulmonary sequestration
• **Post infective**	whooping cough, TB, severe pneumonia
• **Immune deficiency**	HIV, CLL, Nephrotic syndrome
• **Toxins**	aspiration, inhalation gasses/chemicals
• **Mechanical insults**	foreign body, extrinsic compression by LN, intrinsic compression by tumour
• **Associations**	SLE, Ulcerative colitis, Chron's, Marfan's

Clinical Features:

Symptoms:
- Chronic cough ↑↑↑↑↑↑↑ sputum production with halitosis, worse in morning
- Recurrent haemoptysis
- Dyspnoea
- Intermittent Pleuritic chest pain
- Lethargy/malaise, wt loss, low grade fever

Signs:
- Coarse insp and exp creps
- Airflow obstruction with wheeze

Clubbing!

Special Investigations:

Essential:
- CXR
  - *Tramlines, ring shadows, thickened airway walls*
- High Res CT
- Sputum MCS
- PFT
- Ig A, E, M, G
- Aspergillus — NB

Second line:
- CF sweat test
- Auto antibodies
- Barium swallow *if suspect recurrent aspiration*

Management:

General Principles:
- Rx underlying condition
- ↓ Bacterial load and prevent 2ndary infection
  - Intermittent during exacerbations
  - Long term in severe disease
  - ↑ Dose for longer periods
- Colonization:
  - S.aureus → H. Influenza → M. Catarrhalis → Pseudomonas spp.
- Prevent exacerbation:
  - Keeping airways clean → physio
  - Breathing techniques
  - Exercise regime
- Other:
  - Optimize nutrition
  - Refer for surgery if disease limited to one segment
  - Lung transplantation

Exacerbation:
- **Mild disease:**
  - Ciprofloxacin 750mg bd if suspect pseudomonas x +/- 2weeks
  - If early recurrence consider long term antibiotic Rx amoxil 500mg bd or doxycycline 100mg dly
- **Severe Disease:**
  - Chronic suppressive Rx to prevent progression
  - Long term therapy with nebulised aminoglycoside to ↓ levels of pseudomonas

Congenital
CF
Ciliary dysfx syndrome
1° Hypogammaglobulinaemia

Acquired-children
Pneumonia
1° TB
Inhaled foreign body

Acquired-Adults
Suppurative Pneumonia
Pulm TB
Bronchial tumour

Most common fatal autosomal recessive disease in young caucasians.

Cystic Fibrosis

Definition:
- Mutation is autosomal recessive on long arm Chr 7 → chloride channel mutated
- Ciliary dysfunction

Diagnosis:
- Diagnosed in neonates and small children

Clinical features:
- Often Fam Hx
- Failure to thrive, meconium plugs, rectal prolapse
- Resp:
  - Cough, wheeze, Bronchiectasis, respiratory failure, cor-pulmonale, recurrent infections
- GIT:
  - Pancreatic insufficiency (DM, steatorrhoea), distal intestinal obstruction, gall stones, cirrhosis
- Other:
  - Male infertility, osteoporosis, vasculitis, arthritis, nasal polyps, sinusitis, HPOA

Special investigations:
- Genetic screening for CF
- Sweat test > 60mmol/l
- Faecal elastase useful screening test for pancreatic insufficiency

Management:
General Principles:
- Lung function
  - Maintaining good lung Fx
  - Aggressive Rx of infections
  - Refer for transplant when and if necessary
- Nutrition
  - Nutritional support
  - Monitor weight
  - Supplement enzymes
- GIT
  - Annual screening for portal HT and Cirrhosis
- Endocrine
  - Screening and managing DM and osteoporosis
- Fertility advice
- Psychosocial support

(Cystic fibrosis transmembrane conductance regulator)
Mutation in gene coding for Cl^- channel responsible for $Cl^- \& H_2O$ movement across epithelial membranes
Resp epithelium relatively dehydrated ⇒ ↑ resp infections & ciliary dys fn

Lung (N) @ birth → Bronchial infect
↓
Bronchiectasis
↓
Recurrent exacerbations
↓
lung damage
↓
Resp failure
↓
Death

Cardiology

- AF
- Infective Endocarditis
- Rheumatic Fever
- Pericardial Disease
  - -Acute Pericarditis
  - -Constrictive Pericarditis
  - -Pericardial Effusion
  - -Pericardial Tamponade
- Syncope
- Valvular lesions
  - -Aortic Stenosis
  - -Aortic Incompetence
  - -Mitral Stenosis
  - -Mitral Incompetence
  - -Pulmonary Stenosis
  - -Pulmonary Incompetence
  - -Tricuspid Stenosis
  - -Tricuspid Incompetence
- Heart Failure
- Hypertension
- Disease of Heart Muscle
  - -Dilated cardiomyopathy
  - -Hypertrophic cardiomyopathy
  - -Restrictive cardiomyopathy
  - -Myocarditis
- Atherosclerosis
- Congenital Heart Disease
- Chest pain

Atrial Fibrillation Don't miss it in exam!!!!!

Def: AF = chaotic, irregular atrial rhythm @ 300 – 600bpm. The AV node responds intermittently – thus irregular ventricular rate. Most common sustained arrhythmia.

Clin importance =
a) loss of atrial contraction
b) inappropriate fast ventricular response
c) loss of atrial appendage contractility and emptying – risk of thromboembolism.

Dx for irregular pulse:

- il Flutter with
  ble heart block
- rial /ventricular ectopic
  eats
- kenbach heart
  k(2nd, type 1)

APPROACH:

1) **Dx it clinically!**
2) **Do ECG**
3) **Find cause:**
   - Hx – alcohol? Thyroid sx?
   - Exam – pale? Murmur?CCF? embolic phenomena?
   - Vitals (esp.BP)
   - Bld – UCE/TFT/Cardiac markers
   - ECHO – left atrial enlargement, mitral valve disease, structural abnormalities, poor LV Fx.
   - CXR – dilated heart? Infection?
4) **Mx arrhythmia (rate vs rhythm control)**
5) **Mx cause**
6) **Screen for and prevent Cx**
7) **Explain to pt**

Sx: asymptomatic, chest pain, palpitations, dyspnoea
Sg: Irregular rate, Irregular volume
S1 variable intensity
Pulse deficit > 10.

ECG changes:
1)Absent P waves
2)Irregular R-R interval

Causes: ARITHMATIC
A – Alcohol
R – Rheumatic valve disease
I – Ischaemic heart disease
T – Thromboembolic = PE
H – Hypertension/HF/Hyperthyroid
M – Mitral valve disease/MI
A – Atrial myxoma/Anaemia
T – Trauma = Post-op
I – Infection = Pneumonia/Enodcarditis
C – Cardiomyopathy/Constrictive pericarditis/Congenital heart disease

Cx:
1)embolic stroke!!
2)tachycardia-mediated cardiomyopathy. } due to ↑ HR
3)greater irregularity of ventricular response.

Risk factors for stroke:
-previous stroke/TIA
-Hypertension/DM/CCF
-mitral sten/age>75
-atria>5cm/left vent dysfx
= = Anticoagulants

AF (< 48hrs)	Chronic AF (> 48hrs)	Paroxysmal AF
sociated illness rmonia). ry ill/haemodynamically le:O2>UCE>Sedate>Emergency rsion (do not delay in order to ticoagulation) anticoag – heparin 5000- 0U IV (if DC cardioversion but time is running out). ol ventricular rate: 1st choice – n/verapamil/metoprolol. oice – digoxin/amiodarone.	1)Rate control vs rhythm control - No diff in mortality/morbidity.(RACE and AFFIRM trail). 1st choice: b-blocker/rate limiting Ca-blocker. 2nd choice: digoxin/amiodarone. Don't give b-block & ca-block together = bradycardia risk. 2)Anticoagulate – warfarin (INR 2-3) Alternative – Aspirin, esp if < 65 + no risk factors.	1)Pill-in-pocket (eg.flecainide PRN), if: infrequint, SBP>100 mmHg, no past LV dysfx. 2) If above not appropriate – regular b-blocker. 3)Anticoagulate

Warfarin = Bleeding diathesis
Plts < 50 x 10^9/L
BP > 160/90
Compliance issues
Pt choice

If AF continues despite above:
AV node ablation, pulm vein ablation, pacing

Explain to pt:
-Part of your heart (the small heart chamber) is not contracting well, thus blood can clot there/or it can move and block vessels elsewhere in your body, even cause your death. It is thus very important to drink your heart meds, as well as your bld thinners. Your INR must be maintained (btwn 2-3) inorder to prevent bld clotts, thus you MUST follow up at the clinic.

Fever + changing murmur = Do bld cultures x3 think IE!!!

Infective Endocarditis – Infection of endocardial surface of heart, may be acute or subacute.

Fever + new/changing murmur = IE until proven otherwise
Pathogenesis = [Bacteraemia + Abnormal cardiac endothelium]
Portal of entry (oropharynx/iv drug abuser/nosocomial infect) – Bacteraemia – Turbulent flow over diseased valve – deposition of bacteria – vegetation(clump of fibrin,plts,wbc,bacteria) – Endocarditis – Septic emboli.

Classification:

Acute (50% on normal valves)	Sub-acute (abnormal valves)
Severe febrile illness Prominent/changing murmur Petechiae Absent typical clinical Sg's Cx = Embolization, Cardiac failure/Renal failure	Stigmata of IE

Valve involvement: MV>>AV>TV>PV
Risk: High risk = Prosthetic valves, previous IE, congen heart disease
Moderate risk = HOCM, mitral valve prolapse, mitral regurge, thickened leaflets

Stigmata of IE

1) Sx's: Fevor, rigors, chills, night sweats, flu-like sx's, chest pain, dyspnoea, cough.
Recent surgery? IV drug abuser? Poor dental hygiene?

2) Sg: *General* – clubbing (10%)
Cardiac – Murmur (90%)
CCF (50%)
Athralgia
Pyrexia (90%)
Skin lesions: Oslers nodes (15%) – 'ouch' raised, painfull 3-15mm on Soles/palms.
Janeway lesions – 'pain away' 1-2cm, painless. Soles/palms/fingers/toes
Splinter haemorrhages (10%) – proximal nailbed
Petechia (50%) – mucous membranes/skin
Eyes – Roth spots (5%) – emboli
Splenomegally (40%)
CNS – emboli (20%) – focal sg's. Mycotic anearisms (10%)
Renal – Haematuria (70%)
Embolic Phenomena – emboli – abscesses in organs (brain, heart, kidney, spleen, GIT, Lung(right sided endocarditis))

APPROACH:

1) Hx
2) Exam
3) S/I and Organism Isolation
4) Dukes Criteria
5) Mx – Admit to hosp + bedrest
   Antibiotics
   Surgery – valvoplasty
6) Explain to pt.
7) Prophylaxis
8) Prevent Cx

) *Bld culture* – 3 specimens, @ different times/sites.
5-10% culture negative
ld – FBC = normocytic normochromic anaemia
Thrombocytopenia
ESR/CRP = increased (for assessing purposes)
UCE/LFT/CMP
rine analysis = microscopic haematuria
CG – dysrhythmias (conduction defect - abscess/infarct)
Prolonged P-R interval, ST elevation in AvR
XR – cardiomegally
CHO – vegetations if > 2mm

Organisms
Strep Viridans – commonest, prosthetic valve
Staph Aureus – break in skin (IV drug abusers/catheters/sepsis)
Staph Epidermidis – prosthetic valve
Enterococcus (group D)
Gram –ve HACEK organisms – *Haemophilus, Actinobacillus, Cardiobacterium, Eikenella, Kingella Candida*
Pseudomonas – IV abusers

∴ MCSS + HACEK + pseudomonas!

4)Dukes criteria:
2 Major/1 Major + 3 minor/5 Minor
Major:
+ve blood culture
*typical organism in 2 cultures
*3 +ve cultures> 12hrs apart
Endocardium involved
*+ve ECHO
* new valvular regurge
Minor:
Predisposition (Cardiac lesion/iv drug abuser)
Vasculr/immunoligical sg's
+ve bld culture that do not meet major criteria
+ve ECHO that do not meet major crit

(Stamford Rx criteria)

Mx:
tibiotics: Empirical Rx = benzylpenicillin + Genta
Enterococ = amoxicillin
Streptococ = benzylpenicillin (2-4 wks) then amoxicillin
Staph = fluclox + genta
Coxiella = doxy + rifampacin
Fungi = flucytosine followed by fluconazole
rgery: HF due to valve damage
Antibiotic failure
Large left valvular lesion with embolic risk
Valve ring abscess
Valve perforation
Unstable prosthesis
Mycotic aneurism

Culture –ve IE:
5-10%
Cause = Prior antibiotics
Organism that fail to grow in culture =
*coxiella burnetti (Q fever)
*clamydia
*bartonelle Malthusia
*legionella

7)Prophylaxis:
Dental/oral/resp/oesophageal procedures:
Amoxill 2g 1 hr prior
GU/GIT: High risk – Amoxil + Genta
Moderate risk – Amoxil/Ampi

8)Cx:
CCF (valve insufficiency)
Systemic emboli
Mycotic aneurism formation
Intracardiac abscess formation
Renal failure – glomerulonephritis due to immune complex deposition

+ Antibiotic failure
+ HF due to valve damage

✓ Embolic strokes
✓ CCF
✓ Renal failure
✓ Absess/Aneurism formation.

heart, skin, joints, CNS

Rheumatic Fever – Inflam disease, due to an autoimmune reaction, triggered by molecular mimicry btwn the cell wall M proteins of the infecting strep pyogenes and cardiac myosin and laminin.

Epidemiology: children and young adults (5-15yrs)
Aetiology: 3% of untreated group A b-haemolytic streptococ pharyngitis develop acute rheumatic fever.
Pathology: *Affects heart, skin, joints, CNS*
All 3 layers of heart may be affected
Rheumatic carditis — *Aschoff nodules* — granulomatous lesion with central necrotic area
Small valvular vegetations may develop
Synovial membranes acutely inflamed ----- subcutaneous nodules

S/I:
Throat swab
Bld - ASOT – increased titre or > 200 units in adults
Dnase B titre – increase
WCC – leucocytosis
CRP/ESR – increase
CXR – cardiomegally/pulm. Congestion/effusion
ECG – AV block/features of pericarditis
ECHO – cardiac dilatation/valve abnormalities

Viral!!

ufection?
RF?
ll joints?

APPROACH
1) Hx and Exam
2) S/I
3) Dx – Jones Criteria
4) Mx
5) Cx

Modified Jones Criteria (1992)
Evidence of recent strep infect + 2 major/1 major + 2 minor

Evidence of strep infect = recent strep infect, hx of scarlet fever, +ve throat Swab, ASOT>200, increase DNase B titre.

Major=
Polyarthritis (large joints – painfull, swolen, tender)
Erythema Marginatum (Pink rash 20%, Mostly trunk)
Subcutaneous Nodules (painless, pea-size,hard,over tendons,joints)
Chorea (Sydenhams chorea/St. Vitus dance – spasmodic/unintentional/ Choreiform,develop late)
Carditis – new/changing murmur
Cardiomegally/CCF
Pericardial effusion
1st degree AV block
Diastolic mitral murmur (due to valvulitis) – Carey-Coombs murmur

Minor=
Previous rheumatic fever
Fever
Arthralgia
CRP/ESR increase
Leucocytosis ↑ PR interval.

rditis=
irest (6wks if carditis)
ortive rx – CCF rx
rin 60mg/kg/day
icosteroids (prednisone) until ESR decrease
Anti strep rx=
a)immediate=Benzathine pen. 1,2 MU IMI stat
Phenoxymethyl pen. 500mg bd x10days
Macrolide for for pen allergy
b)prophylaxis= Phenoxymethyl pen. 500mg/day x5 years after last attack
mobilize joints in severe arthritis
loperidol/diazepam for chorea

Cx:
*60% with carditis = chronic rheumatic heart disease.
Mitral (70%), Aortic (40%), Tricuspid (10%), PV (2%)
*Recurrence – precipitated by pregnancy, other strep infections, use of Pill.

Pericardial Diseases

Pericardium = 2 layers: Visceral and Parietal
↓
Reflects back apon itself @ great bld vssels and join the parietal pericardium – forming a sac.
≈ 50 ml in normal heart

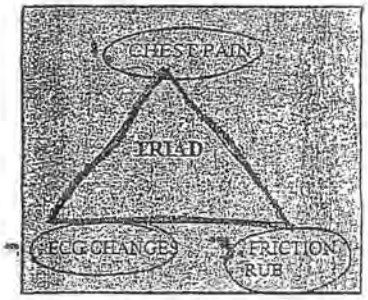
4 diseases:
> Acute Pericarditis
> Constrictive Pericarditis
> Pericardial Effusion
> Cardiac Tamponade

*You don't want to miss a [illegible] (that's why Hx,ECG and Blds are NB)
*Other Pericardial diseases

Acute Pericarditis – *Inflam of pericardium, primary or secondary to systemic disease.*

Sx: *Chest pain* – better when sitting up and leaning forward, worse with deep breathing and supine position. *Fever, malaise*
Sg: *Friction rub* – Best @ lower left sternal edge, end expiratory, pt lying forward

ECG = diagnostic: ST elevation (saddle shape; smiley face), in ant/lat/inf leads > then ST resolution > T flattening > T inversion > normal T. ST depression in AvR. PR segment depression in ant/lat/inf leads.
Blds = FBC,ESR,CRP,Cardiac markers (trop I may be raised), Viral serology, bld cultures, autoantibodies if indicated, fungal precipitants, TFT.
CXR = pulm infiltrates/cardiomegally – pericardial effusion?
ECHO = If pericard effusion suspected



APPROACH:
1) Hx & Exam
2) Confirm dx and find cause
   >ECG!!
   >Blds
   >CXR
   >ECHO
3) Mx - rx cause and analgesia
4) Cx – watch out!, it's a TRRAP!!!!!!

Mx =
1)Rx underlying cause
2)Analgesia - NSAIDS (ibuprofen 400mg/8h)
3)Steroids/immunosuppressants if relapse occur

Cx = TRRAP
*Tamponade
*Recurrence
*Residual constrictive pericarditis
*Atrial arrhythmias
*Pericardial effusions

Etiology = Fibrous material deposited in pericardial space - effusion often follows.
Idiopathic most common
Infectious = *Viral* (coxsackie, mumps, herpes, HIV)
Bacterial (Staph,Strep,Pneumococ,Meningococ,H.influenza)
TB
Fungal (Histoplasmosis,Candida)
Post MI = *Acute* (1-7 days) – 20% of MI pts, common in ant MI
Dresslers syndrome (2-10 wks) – autoimmune response to cardiac damage. Antimyocardial antibodies found
Neoplasms = *primary tumours* of heart (mesothelioma)
Metastatic pericarditis (breast, lung, hodgkin's lymphoma, leukaemia, melanoma)
Uraemic Pericarditis = 6-10% of chronic *renal failure* pts —— DIALYSIS!!!
Collagen vascular = RA/SLE/Systemic sclerosis
Drugs = *Hydralazine/Isoniazid*
Infiltrative = *Sarcoid*

Constrictive Pericarditis – Chronic pericarditis resulting in fibrosed, thickened, adherent and/or calcified pericardium
Changes are chronic = body time to compensate = not immediately life threatening

Constrictive Pericarditis vs. *Restricte Cardiomyopathy*
Similar in presentation
Treatable — Most cases not treatable

Sx = Abdo pain/Fatigue/Dyspnoea/Palpitations
Sg = Mimics CCF – ascites/hepatosplenomeg/oedema
Increased JVP, Kussmauls sg, Friedrich sg (y descent> x Descent), soft, diffuse apex, soft S1&S2, S3, pericardial Knock (early diastolic sound), pulsus paradoxus, AF (30%)
Thus —- don't miss irregular pulse!!

APPROACH:
1) Hx & Exam
2) Confirm dx and find cause
   >ECG!!
   >Blds
   >CXR
   >CT/MRI
   >ECHO
   >Endomyocardial biopsy
3) Mx - Rx Cause
   Surgical – resection of pericardium
   Diuretics & Salt restriction

ECG = small QRS, inverted T or flat, AF, ~~elect~~
CXR = small heart, pericardial calcification
CT/MRI = if no calcification on cxr, do ct -- if still none – cardiomyopathy?
Endomyocardial biopsy = pericarditis vs. cardiomyopathy
ECHO = Thichened/calcified wall. Decreased ejection fraction.
Blds = Same as acute pericarditis

Causes: Same as acute pericarditis

Diff for Sg's of RHF
Cor pulmonale? ——— Sg's of lung patholohy? Hx? Lung fx test
CCF? ——— Freimingham criteria
Constrictive pericarditis? ——— kussmaels? Knock? Calcification on CXR/CT/MRI?
Restrictive cardiomyopathy? ——— non of above, biopsy?
Isolated RHF ——— rare (heart fails in sincitium)

Pericardial Effusion – Accumulation of fluid in pericardial sac, often complicate acute pericarditis.

- none/similar to
- carditis/dyspnoea/cou
- phrenic irritation
- raised JVP, soft
- apex
- alpable friction
- early),
- wart's sg = effusion
- press base of left
- – dull to percuss
- w angle of left
- capula

APPROACH:

1) **Hx & Exam, monitor vitals!!!!!**
2) **Confirm dx and find cause**
   - >ECG
   - >Blds
   - >CXR
   - >ECHO – procdure of choice!
   - >Dx tap : Transudate/exudates/malignant cells/bacteria
3) **Mx - Rx Cause**
   - Most resolve spontaneously
   - mild= serial ECHO, anti-inflam meds
   - severe= pericardiocentesis (sonar guided)
   - In malignancy – reaccumulation common— Pericardial window
4) **Continue to monitor pt** (tamponade?)
5) **Cx** – (tamponade!)

ECG = low voltage QRS
Electrical alternans
Flat T
CXR = Enlarged, globular heart
ECHO = echo-free zone around heart
Blds = same as for acute pericarditis, albumin
Dx tap= MCS, malignant cells, WCC, ANA, glucose, total prot, albumin

Etiology=
Transudate – CCF, low albumin, hypothyroid
Exudate – Causes similar to acute pericarditis. May develop secondary to hemopericardium (trauma, post MI rupture)

Cardiac Tamponade – Cx of effusion. CLINICAL Dx!!! = **MEDICAL EMERGENCY**
Pathophys: Increased pericardial pressure – decreased venous return – decreased diastolic ventricular filling – decreased CO – hypotension + venous congestion. Main problem= **CIRCULATORY COLLAPSE.** ——Common cause for **CARDIAC ARREST**

2) Airway – Intubate and ventilate if resp failure
   Maintain open airway
   Breathing – 100% 02 (non-rebreather mask)
   Intubate – ventilate
   Monitor SATS, RR
   Circulation – 2xIV 1L cristalloids to temporarily Increase the CO
   Draw same blds as for effusion
   Monitor BP, HR, ECG, temp, urine excretion

1) Sx = *Dyspnoea, flushed, syncope, sweating*
   Sg = *Tachycardia*
   Becks triad = Distended neck veins
   Muffled heart sounds
   Hypotension
   Classical quartet = Distended neck veins
   Hypotension
   Tachycardia
   Pulses Paradoxus
   Kussmauls sg (increased JVP during insp)
   Friedreich sg
   Impalpble apex
   Electrical alternans

u already drawn should be sent
y for same tests as effusion.
ericardial fluid away for same
well.

APPROACH

1) Pick it up!!! (dx)
2) ABC
3) Tap it (pericardiocentesis)
4) Find cause
5) Further Mx

3) Do emergency pericardiocentesis.
Preferably guided by ultrasound, but do not wait for sonar machine!!!!!!!! Just do it!
(Use CVP set, so fluid can be tapped through it)
When the needle is in, in will move as the heart contracts – don't freak out.
The blood/fluid aspirated should not clot.
Confirm placement by sonar/when finished.

5) Rx underlying cause.
Contact physician & cardiothoracic surgeon ASAP.
Pericardiotomy if effusion recurrent.

Constrictive pericarditis vs Cardiac tamponade

	Constrictive pericarditis	Cardiac tamponade
Kussmaul	+	JVP to increased to see
Pulsus Paradoxus	1/3 cases	Always
Pericardial knock	+	-
BP	Decreased	Very decreased

Syncope- Sudden, transient loss of consciousness due to decreased cerebral bld flow with spontaneous recovery.

Aetiology = **Cardiac** vs. **Extracardiac**

Electrical
*Tachy = VT, Torsades, SVT, rapid AF
*Brady = Sick sinus syndrome, 2/3 degree AV block
*Pacemaker failure

Mechanical
*Obstructive
L=AS, MS, LA myxoma
Carotid stenosis
R= PS, PE, PHT
*Tamponade
*Myocardial dysfx
CAD, Lv dysfx

1)Neurally mediated vasomotor
-Vasovagal (50%)
-Visceral: micturition syncope, cough syncope, Valsalva, ocular pressure
-Carotid sinus syncope
-Psychiatric: panic/anxiety

2)CNS
-TIA/Stroke
-subarachnoid haemorrhage
-cervical spondylosis

3)Orthostatic hypotension
-drugs: anti-hypertensives(escp. ACEI)
-venous poling (postural)
-autonomic neuopathy
*primary = Shy-Drager
*secondary = DM
-hypovolaemia

4)Metabolic
-hypoxia ↓O2
-hypoglycaemia ↓gluc
-hypocapnia Hyperventilation.

Seizure vs Syncope

	Seizure	Syncope
Facial colour	Cyanotic ✓	Pale
Tongue bitting	Common ✓	Rare
Aura	Sometimes ✓	No
Nausea	Uncommon	Common
LOC	May be longer ✓	Brief
Reorientation	Minutes ✓	Seconds
Todd's paresis	Sometimes ✓	No
Attacks	Repeated	Infrequent
Age	<35	Variable
CK	Increased	Normal
+ve EEG	Sometimes	No

Urinary incontinence ✓ (−)

Get co-lateral info → Tonic/clonic?

APPROACH

1)**Hx and Exam** = Exclude seizure. Question witness. CVS and CNS exam. Focal CNS sg's?
2)FBC/CMP/UCE/CK/GLUCOSE
3)Normal exam------vasovagal--------Tilt test if recurrent
Abnormal CVS exam/hx---------cardiogenic---------ECG/ECHO/Carotid dopler/24hr ECG Holter
Orthostatic---------Exclude meds ✓
---------Normal CNS exam-------post ganglionic autonomic insufficiency---heartbeat Variability testing
---------Abnormal CNS exam-----Periheral neuropathy (DM), Shy-Drager syndrome, CT/MRI –if focal CNS sg's

Clin problem is that of a heart valve lesion.

Valvular Heart Disease

When you mention a murmur – comment on 9 things:
1) Timing (systolic\diastolic)
2) Location (where it is heard the loudest)
3) Radiation (where else can you hear it)
4) Duration (pan/early/late)
5) Intensity (1-6)
6) Shape (crescendo/decrescendo)
7) Pitch (low – bell of stet; high – diaphragm)
8) Variation with manuvers
9) Added sounds?

(L) → Exp.
(R) → Insp.

Intensity
1 = soft,soft (optimal conditions needed)
2 = soft but audible
3 = louder, no thrill
4 = loud, palpable thrill
5 = loud, but still need stet + thrill
6 = no stet needed

Benign Murmur:
>Soft
>Mid-systolic
>No radiation
>No added sounds
>Heard @ left sternal edge

Cx of valve lesions
>HF
>Pulm.HT
>Dysrrhythmias (esp..AF)
>Infective Endocarditis
>Stroke

5 !!!

Clinical pearls: In *multiple murmurs* ----- which 1 is dominated by clinical sg's?
Severity of murmur------Determined by duration and not loudness! NB
Loud S1----------Always think of MS

Failing to hear murmur in:
AI: Listen all down left sternal edge with pt sitting up @ end expiration.
MS: Turn pt on left later side, listen around & @ apex.

NB: Peripheral pulse · [illegible]
Carotid pulse: Volume/character.

Aortic Stenosis – *Most common fatal valvular lesion (ventricular dysrrhythmias/ sudden onset LHF)*

Def: Narrowed valve orifice (normal= 3-4cm²)
Severe= <1.0cm²
Critical= <0.75cm²

Pathophys:
*Obstruction —— Pressure overload——increase in LV end diastolic pressure——concentric LVH——subendocardial ischaemia——angina/arrhythmias/LVHF
*Outflow obstruction = fixed CO
*LVHF——Pulm oedema (acute sten)/Pulm Ht (chronic sten)——CCF

NB: Not all LV outflow obstruction = AS.
*Supravalvular obstruction – congenital fibrous diaphragm above aortic valve + Mental retard + Hypercalcaemia ==Williams syndrome.
*Subvalvular diaphragm – congenital fibrous ring
*Hypertrophic cardiomyopathy – septal muscle hypertrophy HOCM.

Aetiology:
Congenital = flow through abnormal valve (bicuspid) – calcify
Acquired = degenerative calcified AS "wear & tear" – elderly
Rheumatic heart disease – progressive fusion, thickening & calcification, 40% aortic involvement

APPROACH
1) Dx it!!!
2) S/I and Aetiology
3) Mx
4) Prognosis
5) Cx
6) Explain to pt!

Sx's= ASD – Angina,syncope, Dyspnoea
Angina: exertional, due to fixed CO & subendo-Cardial ischaemia. < 5yr survival.
Syncope: Fixed CO/arrhythmia. <3yr survival
Dyspnoea: LV failure, systolic & diastolic dysfx
Pulm oedema. < 2 yr survival

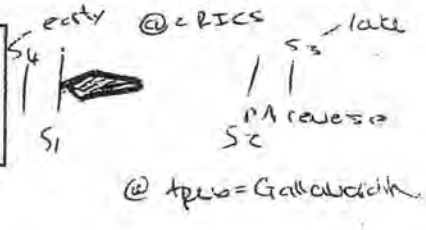
Sg's=
Peripheral – Pulsus parvus et tardus (slow upstroke) Carotid
Small volume pulse
Cardiac – *palpation*—Apex not usually displaced,
May be heaving
Palpable S4
Systolic thrill (2nd right ICS)
Auscultation –
Time: ejection systoli/mid-sytolic
Location: 2nd right ICS
Radiation: to neck NB
Duration: longer as disease progress
Intensity: grade…
Shape: Crescendo-Decrescendo
Pitch: harsh, high pitch, musical quality @ apex (Gallavardin phenomena)
Heart sounds: reverse splitting
Soft S2/absent A2
S4 (early in disease)—LV hypertrophy
S3(later in disease)-LV dilate

…osis:
…ptomatic pt – good survival
…tomatic, untreated pt –
…ngina<5
…yncope<3
…pnoea<2

ECG (12 lead): LVH/strain/AF/LBBB L Axis.
CXR: Post stenotic aortic root dilatation, calcified valve, LVH
ECHO: TEST OF CHOICE Measure valvular area and Pressure gradient. Jet flow/leaflet abnormalities
Fever? —exclude infective endocarditis
Previous RF?

Mx:
Asymptomatic – monitor
Serial echo's
Supportive\medical – avoid exersion
-IE prophylaxis
-Avoid nitrates/ACEI
Symptomatic – surgery (AV replacement/open or balloon valvuloplasty)
Indications: Angina/Syncope/Dyspnoea
LV dysfx NB
Cx of surgery: reduced CO, bleeding, AV block, stroke.

Cx:
>IE
>AV block
>Ventricular dyssrhythmias
>Sudden LV failure



Aortic regurge (AR)

Pathophys: AR——Bld flow back into LV——Volume overload——LV dilatation——increased SV——increased SBP & decreased DBP——1)increased wall tension (due to increased SBP & LV dilatation)——pressure overload——LVH [dyspnoea, PND]
——2)decreased coronary perfusion (due to decreased DBP)——increased myocardial O2 demand [syncope, angina]

VITALS = esp. BP
ATHEROSCLEROSIS? = I.H.D
MI workup if acute. Fever – IE workup.
ECG (12 lead) = LVH, LA enlargement
CXR = LV enlargement, LA enlargement, Aortic root dilatation
ECHO = GOLD STANDARD
Bldg – baseline, exclude autoimmune, syphilis (RPR/VRDL etc).

Aetiology:
Most common= IE &RF
Supravalvular (aortic root disease with dilatation of ascending aorta)=
-atherosclerotic dilatation and aneurism
-cystic medial necrosis (Marfan, Ehlers Danlos)
-dissecting aortic aneurism
-systemic HT
-syphillis
-other connective tissue disorders (SLE,RA, Reiters, ankylosing spond.)
Valvular : (cusp).
-Congenital abnormalities (bicuspid AV)
-Connective tissue disorders
-RF, IE, prosthetic valve
ACUTE AR = Acute rheumatic fever, IE, aortic dissection, trauma, failed prosthetic valve.

Prognosis:
Mild to moderate – few sx's
Symptomatic – prognosis worse
Severe acute AR – 10-30% live>1yr after dx

Cx:
>CCF
>IE
>Arrhythmias

APPROACH
1) Dx it!
2) S/I & aetiology
3) Mx
4) Prognosis
5) Cx

Sx's: dyspnoea, orthopnoea, PND, fatigue, palpitations, syncope, angina
Sg's:
(Peripheral sg's of chronic AR (due to hyperdynamic circulation):
1.Pulsating pupil = **Gandolfi sg**
2.Pulsating uvula = **Mueller sg**
3.Head bobbing = **DeMusset sg**
4.Distended neck veins during systole = **Corrigan's pulse**
5.**Bounding pulse**
6.**Waterhammer pulse** (large PP)
7.**Pulses Bisfiriens** (only if AR + AS)
8.Pulsetile blushing of nail bed = **Quincke's sg**
9.**'Pistol shot'** sound over femoral artery
10.Systolic-Diastolic femoral murmur = **Duroziez's murmur**
11.Pulsating liver = **Rosenbach sg**
12.Pulsating spleen = **Gerhard sg**

Cardiac sg's:
Palpation = heaving apex (hyperdynamic)
Can be displaced
Auscultation = pt sitting forward with hands straight
S1 = soft
S2 = soft/absent
S3 = severe AR
3 murmurs: @ aortic area (2nd (R) ICS) = ejection systolic murmur
@ apex = Diastolic rumble (Austin flint)
@ (L) lower sternal border = decrescendo early diastolic = Aortic root disease or
@ (R) lower sternal border = decrescendo early diastolic = Cusp disease
Hill's test = Femoral-brachial SBP difference:
10-20mmHg = mild
20-40mmHg = moderate
>40 mmHg = severe

Mx:
Asymptomatic = -serial ECHO, assess LV size
-afterload reduction with nifedipine/ACEI
-IE prophylaxis
Symptomatic= -restriction of activities
-Rx CCF
-Surgery (AV replacement/repair) if:
Sx severe
Progress to LV dilatation
LVEF<55% @ rest
Acute AR= Stabalize with IV vasodilators before surgery

Mitral Stenosis (MS) – fixed CO Don't miss it in exam!!!
Normal Mitral Valve (MV) = 4-6cm²
Haemodynamically significant MS = MV < 2cm²

Pathophys: MS-----LV inlet obstruction-----Left atrial enlargement-----increase in LA pressure-----Pulm HT----increase in RV pressure-----RHF

NB: Atrial contraction crucial for LV filling. Thus, in AF/Tachy/Pregnancy = decrease in CO!! (shortened diastolic filing time)

Aetiology:
Congenital – rare
Acquired – Rheumatic heart disease most common

APPROACH
1) Dx it!
2) S/I & aetiology
3) Mx
4) Prognosis
5) Cx

Sx: 2-5yrs frm onset of serious sx'x to death
Early – dyspnoea/cough during exertion or increased CO states
Late – resting dyspnoea/orthopnoea, Haemoptysis, activity limitation
Hx of RF, 15-20yrs ago?
Sg: General – Mitral facies (flushed)
Hepatomeg, ascites, oedema, crackles
Pulse - ± irregular/irregular (AF)
JVP – giant a-waves = Pulm HT
Absent a-waves = AF
Precordial palpation – Tapping apex
Palpable S1
Palpable P2 (pulm HT)
L parasternal heave (RVH)
Auscultation – (loud S1) (No S1 in calcified valve)
Loud P2 (wide split S2)
Opening snap (lost if calcified)
Mid diastolic rumble (low pitched), @apex
Pulm regurge (graham steell)
Other murmurs ± MR,TR

ECG – P mitrale (LAE)
CXR – LA enlargement (double contour, spraying of Carina, pulm congestion)
Kerley B lines, MV calcification, flattened-Left heart border
ECHO – GOLD STANDARD
Thickened valve, fusion of leaflet, LAE, Ejection fraction.

Cx:
*AF!!!!! (an atrium that dilate will fibrillate)
*Emboli
*Acute resp decompensation
*IE
*pulm haemorrhage

Mx:
Avoid factors that increase LA pressure (exercise, [illegible], fever)
Medical: Rx AF (anticoag, rate control)
IE prophylaxis
Rate control – b-blocker
Diuretic
Surgery indications: MV area<1cm2 + sx's
NYHA III/IV
Worsening Pulm HT
IE
Systemic emboli
Surgery options: Balloon valvuloplasty
Open commisurotomy
MV replacement

The rest of MS

Mitral Regurge (MR) Dilated LV → CCF.

Pathophys: Chronic MR---gradually increase flow across MV into LA during systole---progressive LEA---decreased fraction of SV flows forward---LV dilate (to increase SV & maintain CO)---increase in LV wall tension---CCF

Acute MR ---increase in LA pressure---increase Pulm artery pressure---Pulm oedema---RV failure (acute onset CCF)

MR causes LV dilatation---causes annulus dilatation---worsens MR!!!

ECG = LAE, LVH
CXR = LVH, LAE, Pulm HT
ECHO = CHOICE!
Etiology – flail leaflets, vegetations
Severity – regurge volume/fraction
Orifice area.
LV fx – increased LV/LA size, EF
Colour flow shows abnormal jet

Sx: Few sx's initially due to gradual LAE
Later – dyspnoea, PND/orthopnoea, fatigue, Lethargy, palpitations
Hx of rheumatic heart disease, MI etc.
Sg: *Pulse* – rappid (unless LVF)
Palpation – apex displaced, enlarged due to LV dilatation
Auscultation – S1=soft/absent
S3=usually present
Pansystolic murmur radiating
To axilla & back

S1 S2 S3
Dilated LV (Floppy)

Etiology:
Dilated = LV dilatation (CCF, Dilated CM, Myocarditis)
Leaflets = congenital (eg.cleft leaflet)
Myxomatous degeneration (MVP, marfan)
IE, rheumatic heart disease
Chordae = trauma/tear, acute MI, IE
Papillary muscles = ischaemia, infarct, rupture, Aneurism, HCM

APPROACH
1) Dx it!
2) S/I & aetiology
3) Mx
4) Cx
5) Explain to pt.

Cx:
>AF
>CCF
>Pulm HT
>Pulm oedema
>IE

S1 S2 S3.

Mx:
Medical:
Asymptomatic – ECHO's to monitor progression
IE prophylaxis
Symptomatic – decrease preload (diuretics)
Decrease afterload (ACEI)
Surgery
Indications =
Acute MR
Persistent sx'x despite optimal medical Rx
Onset of LV dysfx/increase in LV volume when asymptomatic

Options =
Valve repair or replacement

Mitral Valve Prolapse (MVP) – 3-5% of population (♀ > ♂) Barlow's syndrome

Leaflets displace into LA during systole

Aetiology:
>Myxomatous degeneration of chordae & leaflets which are thinned, voluminous & redundant (too big for orifice)
>alone, or with connective tissue disease (eg. Marfan)
>May e associated with pectus excavatum, straight back syndrome, other skeletal abnormalities.

ECG – non-specific T wave changes
ECHO!! – systolic prolapse of MV leaflet into LA
-Assess severity of MR
CXR – same as MR

Sx's: apical chest pain (prolonged, non exertional, stabbing)
Dyspnoea, hyperventilation, anxiety, palpitations, presyncope, fatigue
± sx'x of MR
Sg's: Click-murmur syndrome (Barlow syndrome)
-Mid-systolic click = tensing of redundant valve tissue, Billowing of post. leaflet in mid-systole.
-Mid to late systolic murmur (regurge after prolapse), Crescendo.
-Manuevers to change LV volume =
Squad to stand, valsalva ---decrease venous return---decrease vent.filling---earlier click & louder & longer murmur

APPROACH
1) Dx it!
2) S/I & aetiology
3) Mx
4) Cx
5) Explain to pt.

Mx:
Asymptomatic without MR = excellent prognosis
β-block for palpitations, pain, anxiety
Anticoag – if systemic embolus
For MR - IE prophylaxis, standard indications for MV repair

Cx:
Depend on degree of MR
>Sever MR
>IE
>Arrhythmias
>Thromboembolism
>Sudden death

Tricuspid valve disease – Tricuspid regurge (TR) and Tricuspid stenosis (TS)

Aetiology:
TS – Rheumatic, Congenital, Carcinoid syndrome, Fibroelastosis
TR – RV dilatation (commonest cause), Rheumatic, IE, Ebstein Anomaly, Carcinoid, Trauma

Sx: RHF
-fatigue, pedal oedema, abdo pain (liver congestion), ascites, dyspnoea (may reflect RH forward failure)
Sg: Carotid pulse = irregular in AF
JVP = increased
Prominent a-waves in TS
Large v-waves in TR (cv-waves)
+ve Hepatojugular reflux in TR
Precordial = L parasternal heave in TR (RV)
Palpation
Auscultation = All R-sided sounds louder on inspiration except pulm ejection click!
TS – Diastolic rumble 4th ICS
TR – Pansystolic murmur along L-lower sternal border = Carvallo's murmur
RV S3 – L-lower sternal border
ABDO – Hepatomegally with systolic pulsations in TR, Ascites
PEDAL OEDEMA

ECG = TS – RAE (P-pulmonale)
TR – RAE, RVH, AF
CXR = TS – Dilatation of RA without Pulm artery involvement
TR – RA & RV enlargement
ECHO = Diagnostic

APPROACH
1) Dx it!
2) S/I & aetiology
3) Mx
4) Cx
5) Explain to pt.

IE, CCF, Dysrrhythmias, thromboemboli

Mx:
Supportive – preload reduction (diuretics), IE prophylax.
TV surgery usually indicated by need for other interventions.

Pulmonary valve disease – less commonly involved

Aetiology:
Pulm Sten (PS) = congenital, rheumatic
Pulm Regurg (PR) = 2° to dilatation of valve ring
= Pulm HT (MS!!!, COPD, PE)
= rheumatic, IE

Sx: chest painm syncope, dyspnoea, leg oedema
Sg: PS = systolic murmus (2nd LICS), pulm ejection click
Normal/loud/soft P2, Right S4
PR = early diastolic murmur @ base
Graham steel murmur (diastolic) @ 2nd/3rd LICS
Increase with insp, no peripheral stigmata

APPROACH
1) Dx it!
2) S/I & aetiology
3) Mx
4) Cx – as TS/TR
5) Explain to pt.

ECG = RVH
CXR = prominent Pulm. arteries if pulm HT, Enlarged RV
ECHO = Diagnostic – RVH, RV dilatation
PS/PR by doppler

lx:
E prophylaxis
R = rarely requires Rx (well tolerated if systemic vascular sistance = normal)
= Valve replacement if severe

S = Balloon valvuloplasty, depending on severity

So basically : ~~[illegible]~~ Insufficient CO to perfuse tissue & organs.

Heart Failure

What is heart failure?-----"a Clinical syndrome of effort intolerance due to a cardiac abnormality, usually accompanied by neurohormonal adaptations resulting in sodium and water retension" (Packer,M.1989)

Neurohormonal adaptation = Heart cannot maintain an adequate CO – Neurohormonal activation (RAAS, vasopressin, endothelin) – Na nd H2O retention and vasoconstriction – increase afterload & intravascular volume – increase BP & cardiac work – myocyte loss – BACK TO SQUIR !!

APPROACH

1)Dx it!!!!!!
2)S/I
3)Stage heart failure
4)Drugs that reduce symptoms
5)Drugs that reduce mortality
6)Aetiology-------Rx
7)Precipitant------RX
8)Risk reduction & prevention of Cx
9)Classify according to NYHA
10)Explain to pt!!!!!

RHF	LHF
-Increased JVP	-Pulm oedema (cough, dyspnoea, PND)
-Hepatomeg	-Cardiomegally
-Ascites	-Pleural effusion
-Peripheral oedema	-S3
-Right S3	-pulses alternans
-HJR sustained	-peripheral cyanosis
	-syncope

1)Framingham criteria for Dx of CCF (65% sensitivity)
@ least = 1 Major & 2 Minor

Major	Minor
>PND	>Peripheral oedema
>Possitive HJR	>Pleural effusion
>Acute Pulm.oedema	>Night cough
>Rales	>Dyspnoea on exertion
>Cardiomegally	>Hepatomegally
>Increase venous pressure	>HR>120
>Neck vein distension	>Vital capacity < 1/3rd of normal (L Fx)
>G - S3	

AHA & ACC

taging of HF (American heart association & American ollege of cardiology)

High risk with no Sx's – *Rx: prevent remodelling;Rx metabolic syndrome.DM-ACEI/ARB*
Structural heart disease, no sx's – *A + B-blocker & ACEI*
Structural heart disease, previous/current Sx's – *B + diuretic + aldosterone antagonist ± digoxin, + salt < 2g/day*
Refractory Sx's (on max Rx) – *C + inotropes/LVAD/transplant Salt < 1g/day*

2)UCE/Hb/Thyroid fx/ECG/CXR – help to establish nature & severity & Cx
Brain natriuretic peptide (BNP) – elevated, used as screening in pt's with Dyspnoea + Oedema

ECHO – all pt's!!
-determine aetiology
-valvular diseases (eg.MS)
-EF >65 %
-monitor progression of disease

chamber size
valve defects
vegetations
structural abs's
EF

4)Drugs that reduce Sx's:

1 = **Diuretics:** Loop diuretic (for peripheral/pulmonary oedema)
Regarded as 1st line in symptomatic CCF
Furosemide – 40mg bd, increase according to diuretic response & BP

2 = **Digoxin:** DIG trial – long term Rx reduce Sx's & hospitalization
New studies – impact negatively on survival
Still in most guidelines

5)Drugs that reduce mortality:

1 = **ACEI:** Improves survival in all stages of HF
Start low: Captopril – 6,25mg tds, increase to 50mg tds
Enalapril – 2,5mg bd, increase to 10mg bd

2 = **B-blocker:** In haemodinamically stable pt – reduce mortality (carvedilol, metoprolol, bisoprolol)
Copernicus trial – 35% reduction in mortality when carvedilol, 25mg bd was used in pt's with LVEF<25%.
They are not rescue therapy for bedridden pt's
Start low!!!! Monitor BP!!! Carvedilol 3,125 mg bd – 25-50mg bd)

3 = **ARB's:** As effective, or less, than ACEI.
CHARM-Added study - ARB + ACEI together = better. Seldom done due to cost.

4 = **Aldosterone antagonists:** Spironolactone 25-50mg/day added to ACEI and diuretic = reduce mortality, in pt's with NYHA III-IV.

6)Aetiology:
1.**Ventricular outflow obstruction** = HT,AS,Pulm HT,PS
2.**Ventricular inflow obstruction** = MS, TS
3.**Ventricular volume overload** = ⊙ LV overload: AR, MR ⊙RV overload: ASD, VSD ⊙ Increased CO (hyperdynamic causes, eg anaemia etc)
4.**Reduced contractility** = MI/Myocarditis/Cardiomyopathy/I.H.D
5.**Arrhythmias** = AF, complete heart block, tachycardia cardiomyopathy
6.**Diastolic dysfx** = Constrictive pericarditis, restrictive cardiomyopathy, LVH & fibrosis, cardiac tamponade

Systolic vs diastolic dysfx.
(Pump failure) (filling problem of ventricle)

7) ID Precipitant ——— RX:
H- Hypertension
E-Endocarditis
A-Anaemia/Alcohol/Atherosclerosis
R- Rheumatic fever
T- Thyrotoxicosis
F- Failure of complaince
A- Arrhythmias
I- Ischemia/Infarction
L- Lung disease: pleural effusion/COPD
E- Endocrine: Cushings/Pheo/aldosterone ↑
D- Diet: increase NaCl intake

8)Risk reduction (metabolic syndrome), and prevent CX:
>Impaired liver Fx (due to congestion)
>Renal Failure (hypoperfusion)
>Thromboembolism (stasis)
>Arrhythmias
>Remoddeling
-occurs in: MI,HT,Cardiomyopathy,Valvular disease
-Includes: Hypertrophy,Myocyte loss, Fibrosis, Dilatation
-Rx:"reverse remodelling" - ACEI/B-blockers

9) Classify according to NYHA
I = No Sx's
II = Some Sx's on exertion
III = Marked Sx's on exertion
IV = Marked Sx's @ rest

10)Explain to pt his condition!!

Cor Pulmonale – RHF secondary to lung disease (be aware of the blue pt in HF!!)

Pulm.HT + Hypoxia----RV hypertrophy
----Hypoperfusion of kidneys-----RAAS----Volume overload-----RHF

Sx = Chest pain, dyspnoea, syncope, CYANOSED (if not blue, then not cor pulmonale) NB look under tongue!
Sg = L parasternal heave (RVH)
Palpable P2 (Pulm HT)
R Ventricular S4
Mid-systolic ejection murmur
Early diastolic murmur due to PR
Tall a-wave
TR = All sg's
ECG = RVH – Right axis deviation and dominant R in V1
Tall P (P-pulmonale) in II, and V1/V2 – Right Atrial Enlargement (RAE)
APPROACH = same as Heart failure

Go look for the lung pathology (most common COPD, chronic PE, Pulm fibrosis, severe kyphosis)

ABCC
PE
Acute
Chronic
Obstructive
Restrictive (interstitial)
Drugs
Recurrent PE
Musculoskeleta (kyphosis/scoliosis)

> 140/90 Hypertension
110-120 } NORMAL
60-80

BP = CO x PVR
S D
Sympathetic system, ABG II,
SV x HR
Preload, Afterload, Contractility

1)Sx: Headaches
Nausea/Vomiting
Poor Vision
Convulsions
Transient paralysis
Coma
Epistaxis
Sg: Fundoscopy TOD
CVS – LVH, Tamboric A2, S4
Cranial nerves – stroke?
Abdo – bruit, large kidney, renal bruit, R-F delay
Urine Dipstix!!!! – protein/bld

APPROACH
1)Sx's/clinical clues
2)Dx HT
-Hx/Exam
-Is HT sustained
3)Screen for other CVS risk factors
4)Exclude secondary causes
5)Detect Target Organ Damage
6)Mx it!

metabolic syndrome

2)Assessment of BP: ~ 40
Method:

	SBPmmHg	DBPmmHg
1)Clinical (office): for Dx, repeat 3 seperate visits =	140	90
2)Ambulatory BP – to exclude white coat HT =	125	80
3)Home (pt monitors own BP) =	135	85

Is HT sustained: 3 separate visits and would pt benefit frm Rx?
Blds – baseline + specific test guided by clinical clues (eg. aldosterone etc), Fasting glucose/lipogram,
ECG, CXR, BMI

3)Recommended BP values:
Uncomplicated HT: <140/90
Indications for target BP <130/80:
Risk factors for atherosclerosis (DM, Smoking, Dyslipid, Obesity)
Chronic kidney disease
Secondary prevention of stroke/TIA
LVH

4)Primary (Essential) > 90%
Secondary < 10%
1) -Renal disease
-renal vascular
-renal parynchymal disease
2) -Endocrine
-Cushings
-Pheochromocytoma
-Conn's – Aldosterone
-Hyperparathyroidism
-Acromegally
-Primary hypothyroidism
-Thyrotoxicosis
3) -Coarctation
4) -PET
5) -Obstructive sleep apnoea
6) -Drugs: COC, NSAIDS, glucocorticoids, *Sympathomimetics*

Detect Target Organ Damage
art – LVH, MI, HF, Arrhythmias
ain – Stroke (ischemic/haemorrhagic), Dementia
dney – Microalbuminuria/proteinuria, Renal failure
ripheral artery – Aortic aneurism, Gangrene
tina: Grade 1 = Copper wiring of artery walls (silver wiring)
Grade 2 = AV "nipping" – narrowing of vessels
Grade 3 = Ischaemia – Flame shape haemorrhages, cotton wool spots
Grade 4 = Papilloedema

REVERSING 2° AX HPT WILL NOT IMPROVE HPT IN 95% OF CASES.

Suspected Diagnosis	Clinical Clues	Diagnostic Testing
nal parenchymal hypertension	Estimated GFR<60 ml/min/1.73 m2	Renal ultrasonography
	Urine albumin-to-creatinine ratio > 30mg/g	
novascular disease	New elevation in serum creatinine, marked elevation in serum creatinine with initiation of ACEI or ARB, refractory hypertension, flash pulmonary oedema, abdominal bruit	Magnetic resonance or CT angiography, invasive angiography Sonar
retation of the aorta	Arm pulses>leg pulses, arm BP>leg BP, chest bruits, rib notching on chest radiography, R-F delay	MRI, aortography
imary aldosteronism (Conn's)	Hypokalaemia, refractory hypertension	Plasma renin and aldosterone, 24-hour urine potassium, 24-hour urine aldosterone and potassium after salt loading, adrenal CT, adrenal vein sampling
Cushing's syndrome	Truncal obesity, wide and blanching purple stria, muscle weakness	Plasma cortisol, urine cortisol after dexamethasone, adrenal CT
acocromocytoma	Headaches, paroxysmal hypertension, palpitations, perspiration and pallor, diabetes	Plasma metanephrine and normetanephrine, 24-hour urine catechols, adrenal CT
bstructive sleep apnea	Loud snoring, daytime somnolence, obesity, large neck	Sleep study
Preeclampsia/eclampsia		
Miscellaneous endocrine: Hypothyroidism	Coarse hair, thick lips and tongue, puffy eyelids	Thyroid function
Hyperthyroidism	Exophthalmos, lid retraction, goiter	

)Mx:

Other risk factors OD or disease	Blood pressure (mmHg) Normal SBP 120–129 or DBP 80–84	High normal SBP 130–139 or DBP 85–89	Grade 1 HT SBP 140–159 or DBP 90–99	Grade 2 HT SBP 160–179 or DBP 100–109	Grade 3 HT SBP≥180 or DBP≥110
o other risk factors	No BP intervention	No BP intervention	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes (immediate drug treatment)
1–2 risk factors	Lifestyle changes	Lifestyle changes	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	Lifestyle changes for several weeks then drug treatment if BP uncontrolled	[illegible]
3 risk factors, MS or OD	Lifestyle changes	Lifestyle changes and consider drug treatment	Lifestyle changes	Lifestyle changes	[illegible]
Diabetes	Lifestyle changes	Lifestyle changes Drug treatment	Drug treatment	Drug treatment	[illegible]
Established CV or renal disease	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]

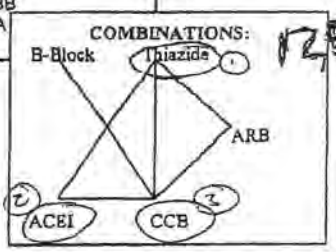
Subclinical organ damage
-LVH: ACEI, CA, ARB
-Asymptomatic atherosclerosis: CA, ACEI
-Microalbuminuria: ACEI, ARB
-Renal dysfunction: ACEI, ARB

Clinical event
-Previous stroke: Any BP-lowering agent
-Previous MI: BB, ACEI, ARB
-Angina pectoris: BB, CA
-Heart failure: Diuretics, BB, ACEI, ARB, anti-aldosterone agents
-Atrial fibrillation:
Recurrent: ARB, ACEI
Permanent: BB, non-dihydropiridine CA
ESRD/proteinuria: ACEI, ARB, loop diuretics
Peripheral artery disease: CA

Condition
-ISH (elderly): Diuretics, CA
-Metabolic syndrome: ACEI, ARB, CA
-Diabetes mellitus: ACEI, ARB
-Pregnancy: CA, methyldopa, BB
-Black individuals: Diuretics, CA

7 GROUPS OF HT
1 DIURETICS
2. ACE-I
3. B BLOCKER
4. VASODILATOR
5 CA CHANNEL BLOCKER
6 α BLOCKER
7. CENTRAL ACTING.

DAC



12,5

Diseases of Heart Muscle

1)Dilated Cardiomyopathy (DCM)
2)Hypertrophic Obstructive Cardiomyopathy (HOCM)
3)Restrictive Cardiomyopathy (RCM)
4)Myocarditis

First exclude disease secondary to CAD, valvular heart disease, congenital heart disease, pericardial disease before making a Dx.

Dilated Cardiomyopathy – Once CCF: 50% 5 yr survival

Aetiology: Idiopathic (risk factor = male, black, fam hx) 25%
Alcohol
Collagen vascular disease
Infectious (post-viral (Coxsackie), HIV etc), myocarditis
Metabolic (uraemia, nutritional deficiency)
Toxic (cocaine, heroine, glue sniffing)

Clin pic: CCF, Systemic/Pulm emboli, arrhythmias, sudden death

Investigations: *ECG* = ST-T wave abnormalities
Poor R wave progression
Arrhythmias
CXR = global cardiomegally

ECHO = 4-chamber enlargement
Depressed ejection fraction
MR/TR secondary to dilatation
Endomyocardial biopsy = rule out Rx-able cause

Mx: Rx underlying cause, eg.stop Alcohol
Rx CCf, arrhythmias
Antigoagulate (prevent thromboemolism) when EF < 20%, or AF, or hx of emboli.
Immunize – Influenza, pneumococ
Surgery = Cardiac transplant, LVAD, cardiomyoplasty (latissimus dorsi wrap)

Hypertrophic Obstructive Cardiomyopathy – unexplained ventricular hypertrophy

Clin pic: Asymptomatic, dyspnoea, angina, CCF, arrhythmias, sudden death

Sg: Pulses: Rapid upstroke pulse
Bifid pulse
Precordial palpation: Heaving apex, double impulse
Precordial auscultation: Normal/Reversed split S2
S4
Systolic murmur @ LLSB, enhanced by squat-to-stand/valsalva

Investigations:
ECG = LVH
Prominent Q, tall R in V1
ECHO = LVH
MR
Diastolic dysFx
LAE

Cx: AF, VT, CCF, Sudden death

Mx:
Avoid extremes of exertion
IE prophylaxis
Medical – B-block
Surgical – (drug-refractory Sx's)
-Surgical myomectomy
-septal ethanol ablation
-dual-chamber pacing
Rx of arrhythmias – amiodarone, intra-cardiac defibrillator
Screen pt's 5yrly.

Restrictive Cardiomyopathy – infiltration of myocardium → decreased ventricular compliance → diastolic dysFx

Aetiology = Infiltrative (amyloidosis)
Non-infiltrative (scleroderma)
Storage diseases (haemochromatosis)
Endomyocardial (fibrosis, Loeffler's endocarditis)

Clin pic:
>CCF
>Arrhythmias

S/I: ECG = low voltage
Non-specific ST-T wave changes
Non-ischaemic Q waves
CXR = mild cardiac enlargement
ECHO = normal pericardium
slightly decreased systolic fx
diastolic dysFx
Biopsy = distinguish etiology

Poor prognosis

Mx:
Exclude constrictive pericarditis
Rx underlying cause
Rx CCF
Anticoagulate
Transplant

Myocarditis – Inflam of myocardium, NB cause of DCM, usually self-limiting

Aetiology: Iiopathic
Infectious: Coxsackie B, HIV, Mumps, S.Aureus
Acute Rheumatic fever
Collagen vascular diseases
Sarcoid

Clin pic:
>Constitutional illness
>Acute CCF
>Chest pain
>Emboli
>Sudden death
>Arrhythmias

S/I: ECG = ST-T wave changes
Conduction defects
BLDS = increased CK, Trop I, LDH, AST with myocardial necrosis
± increased WCC, ESR, ANA, Rheumatoid factor
Blood culture for mycoplasma
CXR = Enlarged cardiac silhouette
ECHO = dilated chambers
Segmental wall motion abnormalities

C: DCM
Death in young adults (24-48 hrs)
Recurrent or chronic

Mx: Supportive
Restrict physical activity
Rx CCF
Rx arrhythmias
Anticoagulate
Rx underlying cause

ATHEROSCLEROSIS – Multifocal fibroproliferative immunoinflammatory disease of medium and large size arteries, fuelled by lipids. Cause = coagulative necrosis. Consequence = Ischaemia/necrosis

evision:
iseases of bld vessels:
therosclerosis
ypertensive vascular disease
-Atherosclerosis
-Arteriosclerosis
neurisms & dissections
-Atherosclerosis
-Syphilitic
-Abnormalities of connective tissue
- Marfan)
asculitis (inflam. disease)

So how do we recognize atherosclerosis?

1) Clinical event (MI/Stroke)
2) Risk factor assessment (BP, Lipids, Smoking, DM)
3) Invasive testing (Angiography)
4) Non invasive testing (Exersice ECG, Sonar, Heart Ca^{2+} scan, MRI, CT, PET scan)

The Story of King Atherosclerosis

Risk Factors (↑ with age, > males, Hypertension, Dyslipidaemia, Abnormal glucose, smoking, obesity, inactivity, high resting pulse)
↓
Impaired NO bioactivity
↓
Endothelial dysFx
↓
Clinical Sequelae (Ischaemic Heart Disease):

1) Sudden death
2) Heart Failure
3) Dysrrhythmias
4) Chest Pain =

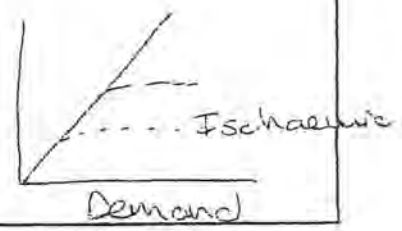
MI
Sx = Chest pain > 20 min, radiates to Arms (L), throat, jaw, back
Anxiety
Cold, clammy, pale (Sympathetic NS)
Dyspnoea, Syncope
Sg = Sympathetic – pallor, ↑HR, sweating
Vagal – vomiting
↓BP, ↓ urine excretion, cold
Inflam Sx/Sg - ↑WCC, ↑temp
ECG = STEMI/NON STEMI
Cardiac markers (Trop, CK)

effort → CHRONIC STALE ANGINA
@ rest → ACUTE CORONARY SYNDROME

STEMI	NON-STEMI	UNSTABLE ANGINA
+ve cardiac markers	+ve cardiac markers	-ve cardiac markers

CHRONIC STALE ANGINA
Fixed Stenosis (PLAQUE)
-demand led stenosis
-related to effort
-predictable
-Sx's over long term
-Sx's on minimal exertion
Exercise testing:
*duration of exercise
*degree of ECG changes
*Abnormal BP response
Stable plaque:
*thick fibrous cap
*little inflame.cells
*small lipid core

ACUTE CORONARY SYNDROME (THROMBOSIS ON PLAQUE)
Dynamic Stenosis
-supply-led ischaemia
-sx's at rest
-unpredictable
-sx's over short term
-frequent or nocturnal sx's
-ECG changes at rest
-ECG changes with sx's
-elevation of troponin
-Unstable plaque:
*thin fibrous cap
*high inflame.activity
*large lipid core
*risk of rupture – thrombosis/arteriospasm



Mx – Hx, ECG, Cardiac markers

Rx of chronic stable angina :

1) Reduce sx's ------ improve quality of life.
   - B-blockers
   - CCB
   - Nitrates - eliceryl trinitrate (sublingual).
2) Reduce MI/Death
   - Antiplatelet drug, ACEI, B-blocker, Statin
   - Reduce risk factors
   - Revascularization

Rx of ACS:

1) General myocardial oxygenation
   - O2.
   - Aspirin — inhibit Thromboxane A2
   - Clopidogrel (Plavix) Inhibit ADP
2) Analgesia: Morphine
3) Decrease myocardial energy consumption: B-blocker
4) Coronary Vasodilation: Glyceral trinitrate
5) Plaque stabilization/Ventricular remodelling: Statin & ACEI

PLUS FOR NON-STEMI

- Antithrombin: LMWH
- Glycoprotein IIB/IIIA inhibitors: Abciximab

PLUS FOR STEMI

- Thrombolysis: Streptokinase/ Alteplase/ Reteplase

Acute

All survivors of MI:

- A = Aspirin
  ACEI
  Alcohol in moderation
- B = BP - B-blocking
- C = Cholesterol – Statin
  No cigarettes
- D = Diet
  Rx Depression
- E = Exercise

NIFEDIPINE drug of choice in Prinzmental angina

Bhomnreth sign.

ANGINA → Chest pain due to ischaemic heart disease

↳ RISK FACTORS : MAJOR → SMOKING, DM, HT, family Hx, DYSLIPIDAEMIA
79% of pts will have at least 1 Major

→ INVESTIGATIONS : ECG, CXR.
↳ exclude PE, Dissecting aorta.
pH manometry → Reflux
↳ Barium swallow.

Chest Pain

Diff Dx:

CENTRAL:

- *-Cardiac:* MI
  Myocardial Sischaemia
  Mitral valve prolase
  Myocarditis
  Pericarditis
- *-Aortic:* Aortic dissection
  Aortic aneurism
- *-Oesophageal:* Oesophagitis
  Oesophageal spasm
  Maliory-Weis syndrome
- *-Massive PE*
- *-Mediastinal:* Tracheitis
  Malignancy

PERIPHERAL:

- *-Lungs/pleura:* Pulm.infarct
  Pneumonia
  Pneumothorax
  Malignancy
  TB
  Connective tissue disease
- *-Musculoskeletal:* Osteoarthritis
  Costochondritis (Teitze's disease)
  Rib fracture
  Intercostal muscle injury
  Epidermic myalgia
- *-Neurological:* Prolapsed disk
  Herpes zoster
  Thoracic outlet syndrome

Investigations: Hx, ECG, CXR and take it from there

REMEMBER: Common cardiac symptoms = Chest pain, dyspnoea, palpitations, syncope, oedema. So know your approaches to them!!

Congenital Heart Diseases

ACYANOTIC CONGENITAL HEART DISEASE (for cyanotic heart diseases, please refer to paediatrics)

1. LEFT TO RIGHT SHUNT LESIONS
- extra blood is displaced through a communication from the left to the right side of the heart, resulting in increased pulmonary blood flow
- shunt volume dependent upon three factors: size of defect, pressure gradient between chambers or vessels, peripheral outflow resistance
- untreated shunts can result in pulmonary vascular disease, right ventricular hypertension (RVH), and R to L shunts

Atrial Septal Defect (ASD)
- three types
  - ostium primum - common in Down syndrome
  - ostium secundum - most common type (50-70%)
  - sinus venosus - defect located at entry of superior vena cava (SVC) into right atrium
- often asymptomatic in childhood
- murmur: often grade 2/6-3/6 pulmonic outflow murmur with widely split and fixed S2
- ECG: right axis deviation (RAD), mild RVH, right bundle branch block (RBBB)
- CXR: increased pulmonary vasculature
- natural history: 80-100% spontaneous closure rate if ASD diameter < 8 mm
- if remains patent, congestive heart failure (CHF) and pulmonary hypertension can develop in adult life
- management: elective surgical or catheter closure (low risk procedures) between 2-5 years of age

Ventricular Septal Defect (VSD)
- most common congenital heart defect (30-50%)
- small VSD (majority)
  - asymptomatic, normal growth and development
  - murmur: early systolic to holosystolic, best heard at left lower sternal border (LLSB)
  - ECG and CXR are normal
  - most close spontaneously, do not need surgical closure even if remain patent
- moderate to large VSD
  - delayed growth and development, decreased exercise tolerance, recurrent URTIs or "asthma" episodes, CHF
  - murmur: holosystolic at LLSB with thrill, mid-diastolic rumble at apex, size of VSD is inversely related to intensity of murmur
  - ECG: left ventricular hypertrophy (LVH), left atrial hypertrophy (LAH), RVH
  - CXR: increased pulmonary vasculature, cardiomegaly, CHF
  - natural history: secondary pulmonary hypertension, CHF by 2 months of age
  - management: treatment of CHF; surgical closure

...tent Ductus Arteriosus (PDA)
- patent vessel between descending aorta and pulmonary artery
- ...ctional closure within first 1-15 hours of life, anatomical closure within first ...ys of life
- 5-10% of all congenital heart defects
- common in premature infants (1/3 of infants < 1750 grams)
- may be asymptomatic or have apneic or bradycardic spells, poor feeding, ...ssory muscle use
- ...ssociated tachycardia, bounding pulses, hyperactive precordium, wide pulse ...ssure
- murmur: continuous "machinery" murmur, best heard at left infraclavicular area
- ECG: may show LVH, RVH
- CXR: normal to mildly enlarged heart, increased pulmonary vasculature
- ...iagnosis by echocardiography (ECHO)
- ...atural history: spontaneous closure common in premature infants, less ...mmon in term infants
- ...anagement: indomethacin, surgical ligation, or catheter closure
- ...igh risk of SBE, antibiotic prophylaxis required until 6 months after closure

Coarctation of the Aorta
- narrowing of aorta almost always at the level of the ductus arteriosus
- commonly associated with bicuspid aortic valve (50%)
- few have high BP in infancy (160-200 mmHg systolic) but this decreases as collaterals develop
- if severe, presents with shock in the neonatal period when the ductus closes
- often asymptomatic with upper extremity systolic pressures of 140-145 mm Hg
- weak pulses, decreased blood pressure in lower extremities, radial-femoral delay
- if associated with other lesions (e.g. PDA, VSD), can cause CHF
- ECG: RVH early in infancy, LVH later in childhood
- murmur: absent or systolic with late peak at apex, left axilla, left back
- management: balloon arterioplasty or surgical correction
- complications: essential hypertension

CYANOTIC CONGENITAL HEART DISEASE
- systemic venous return re-enters systemic circulation directly
- most prominent feature is cyanosis (O 2 sat < 75%)
- differentiate between cardiac and other causes of cyanosis with hyperoxic test (if improvement of PaO2 , less likely cardiac cause)
- survival depends on mixing via shunts (e.g. ASD, VSD, PDA)

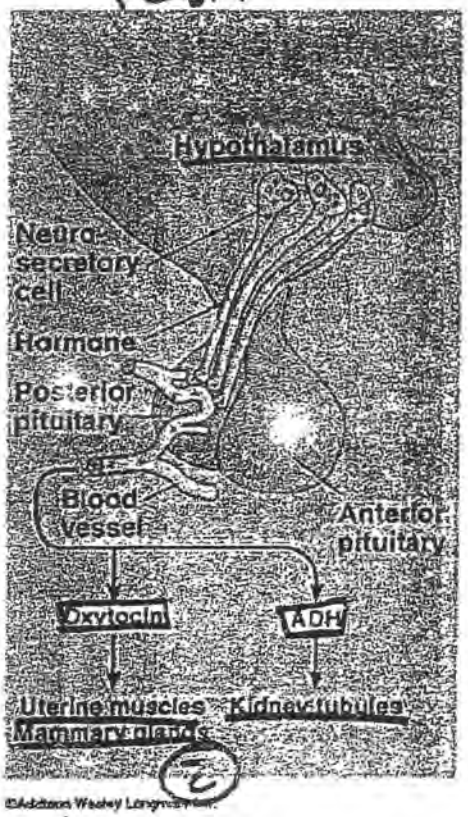
Endocrinology

- Pituitary Gland
- DM
- Adrenal Gland
  -Addison's disease
  -Hyperaldosteronism
- Diabetes Insipidus
- Pheochromocytoma
- Hyperprolactinaemia
- Thyroid Gland
- Cushings Syndrome
- Parathyroid hormone
- Hypercalcaemia
- Hypoparathyroidism
- Endocrine Emergencies

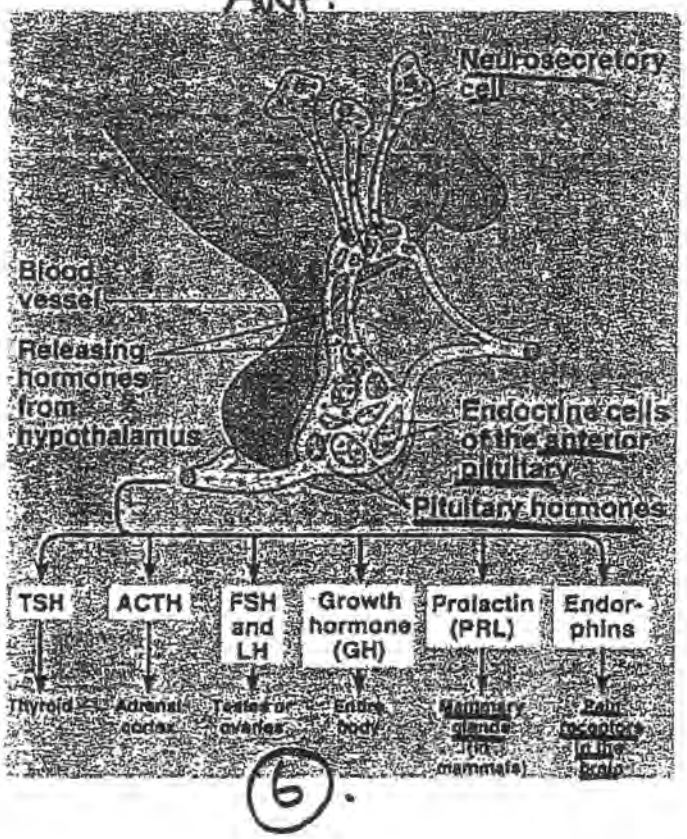
Endocrine

Ptuitary Gland

Post.



Ant.



SPOT diagnosis: Endocrinopathies

1. Thyrotoxicosis: Hair loss, pretibial myxoedema, onycholysis, buldging eyes (exophthalmos)
2. Hypothyroidism: Hair loss, eyebro loss, cold pale skin, characteristic face
3. Cushing's syndrome: Central obesity and wasted limbs, moon facies, buffalo hump, supraclavicualr fat pads, purple abdominal striae.
4. Addison's disease: Hyperpigmentation (face, neck, palmae creases).
5. Acromegaly: Acral (distal) and soft tissue overgrowth, big jaws (macrognathia) hands and feet, thick coarse skin, Coarse facial features.
6. Hyperandrogenism: Hirsutism, temporal balding, acne
7. Hypoptuitarism: Pale, yellow thinned skin resulting in fine wrinkles around the eyes and mouth making the pt look older.
8. Pseudohypoparathyroidism: Short stature, neck and 4th and 5th metacarpals.
9. Hypoparathyroidism: Dry, scaly, puffy skin, brittle nails, coarse, sparse hair

Pituitary adenoma.

Ptuitary tumours: Mostly benign adenomas

< 1cm = microadenoma

>1 cm = Macroadenoma

The anterior pituitary secretes a number of hormones including:

- Growth hormone (GH)
- Prolactin (PRL)
- Thyroid-stimulating hormone (TSH)
- Adrenocorticotropic hormone (ACTH)
- Melanocyte-stimulating hormone (MSH)
- Follicle stimulating hormone (FSH)
- Luteinizing hormone (LH)

+ Endorphins

8.

Although theoretically a tumour could secrete any of these hormones, the common tumours secrete *growth hormone* (acromegaly), *prolactin* (prolactinoma and hyperprolactinaemia), mixed secretions or no secretion at all.

There are 3 histological types:

1. Chromophobe: (70%) – Non-secretory but cause hypoptuirarism, most secrete PRL, a few secrete GH or ACTH. Local pressure effects in 30%
2. Acidophil (15%) – Secrete PRL or GH. Local Pressure effects in 10%
3. Basophil (15%) – Secrete ACTH. Pocal pressure effects rare.

Patient presentation:

Local Pressure effect symptoms: Headache, visual field defects

On examination:

1. BITEMPORAL HEMIANOPIA DUE TO OPTIC CHIASM COMPRESSION
2. CN palsy III, IV, VI due to pressure or invasion of the cavernous sinus.
3. DI
4. Disturbance of the hypothalamic centres of Temperature control, sleep and appetite.
5. Erosin through the floor of the sella tursica causing CSF rhinorrhoea.

SI:

1. MRI /CT scans
2. Visual field examination

3. Blood tests for the hormones are important diagnostic tools- PRL, IGF- 1, ACTH, Cortisol, TFT's, LH, FSH, testosterone levels in males, short Synacthen test.
4. Glucose tolerance test if acromegaly suspected.
5. Over night Dexamethasone suppression test if Cushings disease suspected.
6. Water deprivation test if DI suspected.

Most tumours are benign but are quite serious because of their position close to important brain structures.

Treatment includes:

1. **Hormone replacement as needed: Ensure stroids given before thyroxine as it can induce an adrenal crisis.**
2. Surgical removal: **For prolactinoma:** Bromocriptine before surgery. Give hydrocirtisone 100mg IV/IM pre-op. Repeat ptuitary function test to assess replacement needed. 6-8 weeks post-op repeat dynamic tests for adrenal function.
3. Ablation by radiotherapy: Post-op if complete removal of tumor wasn't possible.
4. Post-op: Discuss fertility, as this is decreased due to decreased gonadotrophins.

Rapid pituitary enlargement

Ptuitary apoplexy – Bleeding into tumour

Rapid ptuitary enlargement due to haemorrhage into a tumour – causes a sudden mass effect, cardiovascular collapse due to hypopntuitarism and death.

Hx:

1. Headache

Ex:

1.Meningism ✓

2.↓GCS ✓

3. Ophthalmoplegia ✓

Visual field defects ✓

Differential: It presents like a subarachnoid bleed.

Treatment: involves urgent steroids (Hydrocortisone 100mg IV) and surgery.

Steroids > ∅

HYPOPITUIRISM

It is the diminished secretion of the anterior pituitary hormones and is most commonly caused by a pituitary macroadenoma. The hormones are affected in the following order:
Growth Hormone, Gonadotrophins: FSH and LH, Prolactin, Thyroid-stimulating hormone(TSH), ACTH. Panhypopituirism is deficiency of all anterior hormones, usually caused by irradiation or surgery.

Common symptoms and signs:
Decreased GH
Lethargy, central obesity, atherosclerosis, muscle weakness, dry wrinkly skin, osteoporosis, decreased Cardiac output and glucose.

Decreased Gonadotrophins
Female: Amenorrhoea, decreased libido, osteoporosis, decreased fertility, hari loss, breast atrophy, dyspareunia
Male: Erectile dysfunction, decreased libido,gynaecomastia,hair loss, hypogonadism.
Chronic anaemia may also occur.

Decreased TSH
Leads to secondary hypothyroidism. This contributes futher to apathy and cold intlolerance. In contrast to primary hypothyroidism, frank myxoedema is rare, probably because the thyroid retains some autonomous function.

Lack of ACTH
Results in symptoms of cortical insufficiency.
In contrast to primary adrenal insufficiency, aldosterone sectretion maintains normal K-levels. The patient doesn't become pigmented because ACTH decreases and there is lack of stimulation of melanocytes.
Lethargy, Postural hypotension, dilutional hyponatraemia, Pallor, Hair loss.

Lack of Prolactin
Rare-failure of lactation

Causes:
Structural- Primary pituitary tumour, esp adenoma.
Craniopharyngioma
Meningioma
Congenital deficiencies- GnRH(Kallmann's syndrome
Functional- Chronic systemic illness, Anorexia nervosa, Excessive exercise
Head injury, Para-sellar surgery or radiotherapy.

Hypothalamus- Kallmann's syndrome, tumour, inflammation, infection (e.g. meningitis), ischaemia.
Pituitary stalk: Trauma, surgery, mass lesion(craniopharyngioma, meningioma.
Pituatary: Tumour, irradiation, surgery, inflammation, infiltration(Haemachromatosis, Amyloidosis etc).Sheehan syndrome(pituitary necrosis after postpartum haemmorage)

Investigations:
- In acutely unwell patients, the priority is to diagnose and treat cortisol deficiency.
- MRI or CT
- ACTH def. - Short ACTH stimulation test or Insulin tolerance test(CI: epilepsy, heart disease, adrenal failure.)
- LH/FSH def - male - random serum testosterone, LH and FSH
  - Pre-menopausal women - ask if menses is regular
  - Post menopausal women - measure FSH and LH. Should be >30mU/L.
- TSh def - measure random serum thyroxine. TSH is often detectable in 2ary hypothyroidism, due to inactive TSH isoforms in blood.
- Arginine and GH releasing hormone test.
- Glucagon stimulation test when ITT is contraindicated.

Treatment:
Involves hormone replacement and treating the underlying cause
- Hydrocortisone for 2ary adrenal failure
- Thyroxine if hypothyroid
- Hypogonadism(for symptoms and to prevent osteoporosis). Males: testosterone enanthate 250mg IM every 3 weeks, daily topical gels or mucoadhesive tablets. Female(premenopause): Oestrogen.
- If GH deficiency is suspected refer to an endocrinologist.can give Somatropin (GH).

Acromegaly

The disease is due to the hypersecretion of of growth hormone from a pituitary rumour in > 99% of cases and is rarely associated with ectopic production of growth hormone eg a carcinoid tumour.Prevalence is 1:1 and it mainly presents between 30-50 years. Growth hormone stimulates soft tissue and skeletal growth through increased secretion of Insulin-like growth factor and its secretion is inhibited by somatostatin.

Clinical signs:

The most common complaints are headache and sweating.Other:

Coarsening of facial features:

- frontal bossing
- prominent supraorbital ridge
- enlargement of lips, nose and tongue.
- mandibular enlargement with prognathism macroguathia
- widened space between the lower incisor teeth

- thickened skin
- In children and adolescents, initiation of GH hypersecretion prior to epiphyseal long bone closure is associated with development of pituitary gigantism

Soft tissue swelling results in

- increased heel pad thickness
- increased shoe or glove size.
- ring tightening
- characteristic coarse facial features and a large fleshy nose.

Other commonly encountered clinical features include

- Hyperhidrosis
- deep and hollow-sounding voice
- oily skin, arthropathy, kyphosis
- carpal tunnel syndrome
- proximal muscle weakness and fatigue
- obstructive sleep apnoea (soft tissue swelling in the larynx)

Generalized visceromegaly occurs, including:

- Cardiomegaly
- Macroglossia
- thyroid gland enlargement
- hepatomegaly

Can also present with Local tumor effects

Pituitary enlargement

Visual-field defects

Cranial-nerve palsy

Headache

Complications:

- Impaired glucose tolerance (40%), DM (20%), as growth-hormone is counter regulatory to insulin.
- Vascular: Hypertension, left ventricular hypertrophy, cardiomyopathy. There is an increased risk of ischaemic heart disease and stroke, due to the increased BP and insulin resistance.
- Malignancy - increased risk of colonic polyps that may develop into colon cancer - guidelines suggest a colonoscopy at 50.

Investigations:

- Random Growth hormone measurements are not helpful as GH is secreted in a markedly pulsatile manner. GH is increased in stress, sleep and puberty. Decreased in puberty.
- Serum IGF-1 is used as a screening test for Acromegaly
- The clinical diagnosis must be confirmed by measuring Gh during an oral glucose tolerance test. Usually GH is inhibited by a rise in glucose and Gh should be undetectable(<0,5). In Acromegaly there is a failure to suppress GH. False positives is seen in puberty, pregnancy, hepatic and renal disease, anorexia nervosa and DM.
- Prolactin levels may be elevated.
- MRI of pituitary fossa
- Test pituitary function for hypopituatarism
- ECG
- Visual field and acuity
- Old photos to compare with

Treatment

- Trans-spenoidal surgery is usually the treatment of choice. Cure rate - 80% in microadenomas and 40% in macroadenomas. 3 months post-op', repeat special investigations to assess GH. If GH remains high, adjuvant medical or radiotherapy may be needed.
- Medical: Somatostatin analogues (octreotide given monthly IM) and lanreotide. Dopamine agonist are less helpful but help in patients with prolactin excess. Pegvisomant, a recombinant GH analogue acts as a GH receptorantagonist.It suppress IGF-1,Gh in
- Radiotherapy: If surgery inappropriate or as adjuvant therapy. It may take years to work.

- It is important to do yearly follow ups - GH. IGF-1 measurement, OGTT, visual fields, CVS etc. Aim is to keep GH<5mU/L.

Hirsutism

Is excessive and increased hair growth on female humans in locations where the occurrence of terminal hair normally is minimal or absent. For example, a beard or chest hair. Hirsutism is a symptom rather than a disease and may be a sign of a more serious medical indication, especially if it develops well after puberty.

The cause of hirsutism can be either an increased level of androgens (male hormones) or an oversensitivity of hair follicles to androgens. Male hormones such as testosterone stimulate hair growth, increase size and intensify the growth and pigmentation of hair.

Cutaneous manifestations:

1. Acne
2. Male pattern balding(androgenic alopecia)
3. Virilisation -condition where androgen levels are high enough to cause additional signs. Virilisation can suggest a possible ovarian or adrenal neoplasm:

- Deepening of voice
- Breast atrophy
- Increased muscle bulk
- Clitoromegaly
- Increased libido
- Some women also have menstrual dysfunction

Causes:

- Polycystic ovary syndrome
- Idiopathic hirsutism
- Drugs - Danazol
- Congenital adrenal hyperplasia (most often 21-hydroxylase deficiency)
- Hyperthecosis
- Ovarian tumors
- Adrenal tumors
- Severe insulin resistance syndromes
- Hyperprolactinemia
- Cushing's syndrome
- Obesity

Special investigations:

- Blood tests may show elevated androgen levels.
- CT scan, MRI, pelvic ultrasound -- used to identify cysts or tumors on the ovaries or adrenal glands

Treatment(Depends on how severe the problem):

Determine the cause eg.

- If on medication that can cause Hirsutism - stop meds
- Tumour - surgery
- Obesity - lose weight

If no underlying cause is found, a combination of self-care strategies and hair-removal techniques may be used. Psychological support may also be helpful since hirsutism is often a frustrating and embarrassing condition.

Eat healthy, exercise and maintain an adequate weight.

Meds

- Oral contraceptives— ypically choose an OC that contains a progestin with low androgenicity (or an antiandrogen such as cyproterone acetate or drospirenone)
- Anti- androgens: Spironolactone,flutamide. and cyproterone acetate -- blocks androgen receptors in the body
- Insulin lowering drugs - metformin, rosiglitazone.Doesn't really help significantly.
- Eflornithine (Vaniqa) is a prescription cream that treats unwanted facial hair. It slows new hair growth but doesn't get rid of existing hair. Hair comes back if you stop using the cream

Cosmetic methods

OTHER
MODY
Action in
- TYPE A insu
- Lepecha
Dmss
Exec
- Infect
- Genet.

Diabetes Mellitus (DM)

DM results from a lack or diminished effectiveness of endogenous Insulin.

Type 1 DM: Insulin deficiency due to selective destruction of Insulin secreting pancreatic B cells. → No insulin.

Type II DM: Insulin deficiency as well as Insulin resistance occurs. — Fat, liver, muscle.

Risk factors for type 2 diabetes:

1. Increased age
2. Glucose intolerance
3. Family history of diabetes
4. Physical inactivity and calorie excess
5. increased waist circumference
6. Increased BMI/Obesity

7. HDL<0.9 TG>2.8
8. PCOS
9. GDM / Macrosomic bab
10. Die IGT, IFG Hi 5.6-6.4

Insulin Resistance Syndrome/ Syndrome X (Metabolic Syndrome)

Indicates and increased risk for DM Type 2 and Atherosclerotic disease.

1. Hyperinsulinaemia
2. Increased waist circumference
3. Impaired glucose tolerance > 5,6
4. Hypertension > 130/55
5. Increased TGL 1,7
6. Decreased HDL <1,03
7. Gout

BMI > 30

Prevention of Syndrome X: Exercise more, control individual vascular risk – decrease weight, use Statins, Antihypertensives, Hypoglycaemics (glitazones)

Classification of DM

1. Impaired glucose tolerance (IGT) FBG <7mmol/L and OGTT 2h glucose >7.8-11.1mmol/L - Risk of developing DM.
2. Impaired fasting glucose (IFG) FBG 6.1 - 7.0mmol/L. DO a OGTT to exclude DM
3. Type I
4. Type II

Metabolic Ahw → Fasul in Hyperglycaemia

CAUSES OF KUSSMAUL BREATHING

K : Ketoacidosis
U : Uraemia
S : Salicylates
M : Methanol
A : Alcohol
L : Lactoacidosis

E : Ethylene glycol
Others : Paracetamol
INH.

Diagnosis

Normal FPG = <5.6 mmol/L
Impaired Fasting Glucose (IFG) = 5.6-6.9 mmol/L (pre-diabetic state, increased risk of developing DM)

Presenting symptoms of hyperglycaemia

1. Polyuria, frequency and glucosuria
2. Polydipsia and dry mouth, thirst
3. Weight loss- insulin deficiency
4. Nocturia
5. Polyphagia
6. Blurry vision
7. Burning feet
8. Fatigue
9. Kussmaul's breathing [deep sighing respiration]
10. FUNGAL INFECTIONS esp. Candida, UTI's, ABSCESSES

+

Random Plasma Glucose > 11.1 mmol/L

OR

FBG > 6.9mmol/L [draw in the morning after overnight fast]

OR

2-hour Post oral glucose tolerance test (OGTT) >11.1 mmol/L

[OGTT =75g glucose ingested, measure Plasma glucose @ ~~0 and 2~~ hours!!!]

OR

Raised venous glucose on 2 separate occasions (Random plasma glucose, FBG, 2-hour Post OGTT)

If there is any doubt – use the oral glucose tolerance test (OGTT)

Classification of Diabetes Mellitus (DM)

	TYPE 1 (Insulin Dependent)	TYPE 2 (Non-Insulin Dependent)
Etiology	• idiopathic • Autoimmune **Destruction of B-cells**	• genetically-linked
Onset	• usually before age 30 Young and acute	• usually after age 40
Genetics	• associated with HLA DR3 DR4 and DQ alleles • 40% concordance in monozygotic twins	• greater heritability than Type 1 • non-HLA-associated • 80-100% concordance in monozygotic twins
Pathophysiology	• completely insulin-deficient	• abnormal insulin secretion

		tissues likely due to receptor and post-receptor abnormalities • increased hepatic gluconeogenesis
Risk Factors	• personal history of autoimmune e.g. Graves' disease, myasthenia gravis, Addison's disease, pernicious anemia	• obesity • family history • prior abnormal glucose tolerance • hypertension • hyperlipidemia • gestational diabetes mellitus (GDM)
Body Habitus	• typically normal to wasted	• typically overweight
Pharmacological	• Absolute insulin required	• combination of oral hypoglycemic agents +/- insulin
Circulating Islet Cell Antibodies	• 50-85%	• < 10%
Other Aspects	• prone to ketoacidosis	• not prone to ketoacidosis but prone to hyperosmolar coma HHS
	NOT ALL PATEINTS WITH LATE ONSET DM HAVE TYPE 2	Not excluded with keto-acidosis 20% of patients have DM complications at diagnosis

Diabetes Secondary to Specific Etiologies

1. Genetic
- Down syndrome, Turner's syndrome, Huntington's disease, Porphyria, Klinefelter's syndrome, Pradar – Willi syndrome
genetic defects in B-cell function and insulin action

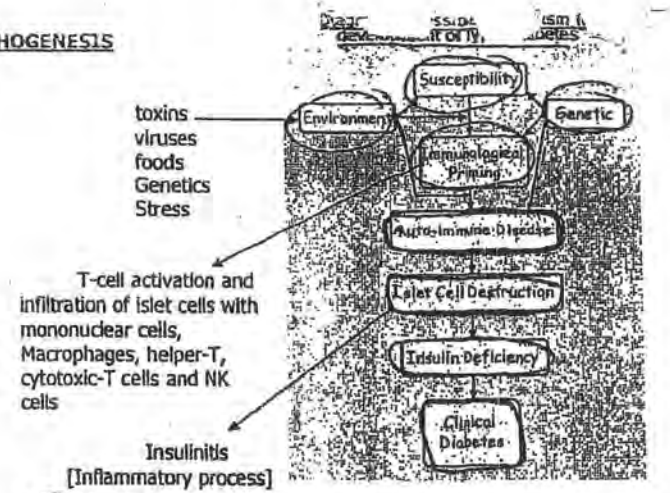
2. Diseases of the endocrine/exocrine pancreas
- pancreatitis esp. alcoholic, neoplasia, cystic fibrosis (CF), hemochromatosis (bronzed diabetes), Pancreatectomy(if >90% of pancreas removed)

3. Endocrinopathies
- acromegaly, Cushing's syndrome, glucagonoma, hyperthyroidism, Hyperthyroidism, Pheochromocytoma, Aldosteronoma

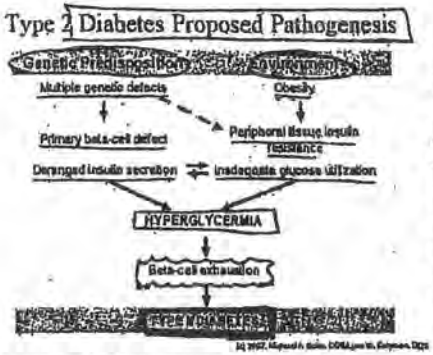
4. Drug-induced
- ß-agonists, glucocorticoids, thiazides, phenytoin, Protease Inhibitors

5. Infections
- cytomegalovirus (CMV), congenital rubella, Mumps, Coxsackie

PATHOGENESIS



- ~20% of B-cells left will present clinically as diabetes. Very slow process.
- Complex and poorly understood interaction between environmental and genetic factors.



Reduced B-cell mass due to genetic defect or amyloid deposits – injured B-cells!

Insulin resistance in adipose tissue, liver and fat [due to obesity, renal failure, TB drugs, Cushing's, Acromegaly, Cystic Fibrosis, PCOS, Werner's syndrome, aging and sedentary lifestyle, genetics, and high FFA levels or metabolic syndrome, Pregnancy, glucose toxicity] + pancreatic B-cell failure leads to impaired glucose tolerance and hyperglycaemia. If the insulin response is adequate = euglycaemic. If not = TYPE 2 DM!!!

esterified fatty acids causing post-receptor defects in Insulin's action.
2. Mutation of genes encoding insulin receptors
3. Circulating autoantibodies to extracellular domain of the insulin receptor.

Lab tests in DM:

Diagnostic	Assessment of Glycaemic Control
OGTT FBG	RBG HBA1C Fructosamine

COMPLICATIONS OF DIABETES
- ~~Neuropathy~~
- **Infections**
- **Macrovascular**
- **Microvascular** [intracellular hyperglycaemia of vascular endothelium causing abnormal endothelial functioning, this causes increased vessel wall protein accumulation and microvascular cell loss together with vessel occlusion].

Aggravating factors: poor glycaemic control, inadequate control of hypertension and cholesterol, smoking, high fat diet

Macrovascular

Accelerated atherosclerosis leading to
1. IHD and coronary artery disease (CAD),
2. CVD, stroke,
3. pulmonary vascular disease (PVD)
4. Peripheral vascular disease [amputation, gangrene

Most common cause of death in type 2 DM. Once macrovascular disease develops in a diabetic, they have a poorer prognosis for survival than normoglycaemic patients with macrovascular disease.

In [illegible] years of DM, following the activation of RAAS.
- In Type 2 patients it is mostly present at diagnosis and follows activation of the SNS secondary to insulin resistance and hyperinsulinaemia.
- The TARGET is lower for diabetic patients namely: 130/85 mmHg!!!!
- Target lipid values in diabetics: LDL < 2.6, HDL > 1.15 and TGL <2.5 mmol/L

Infections:

1. CAP
2. Acute bacterial cystitis and pyelonephritis
3. Emphysematous pyelonephritis
4. Perinephrinic abscess
5. Fungal cystitis
6. Necrotizing fasciitis
7. Invasive otitis externa
8. Rhinocerebral MUCORMYCOSIS
9. Cholecystits

Microvascular
- **Retinopathy**
- **Nephropathy**
- **Neuropathy**

- major chronic complication of type 1 and type 2 DM
- pathognomonic lesion is **basement membrane thickening**
- classically causes **retinopathy, nephropathy and neuropathy**
- can involve many other organs, including heart and skin

Eye complications:
1. **Glaucoma**
2. **Cataracts**
3. **Retinopathy**
4. Glycation of the lens protein with cross linking
5. Osmotic swelling of the lens

Retinopathy stages:

1. **Background/non-Proliferative:**
   - Micro aneurisms
   - Scattered exudates (hard, yellow) = leaking vessels
   - Haemorrhages (flame shaped, dot and blot)
   - Cotton wool spots (<5) = dead/ischaemic vessels
   - Venous dilations and looping

2. **Pre-proliferative:**
   - Amount of micro aneurisms increase
   - Multiple haemorrhages
   - Cotton wool spots (>5)
   - Venous beading, looping and duplication
   - Intra-retinal micro aneurism (IRMA)
3. **Proliferative/ Rubeosis Iridis**
   - New vessels everywhere
   - Fibrous proliferation
   - Haemorrhages
4. **Advanced diabetic eye disease** ADED.
   - Retinal detachment
   - Rubeosis iridis
   - Neovascular glaucoma
5. **Maculopathy**
   - Macular oedema
   - Exudates within 1 DD of the fovea
   - Circinate around the macula
   - Sudden, quick loss of vision < 6/12

Annual eye screening mandatory:
1. Visual acuity
2. Eye examination (ophthalmoscopy through dilated pupils)

When to refer?
1. Severe non-proliferative/proliferative retinopathy
2. Macular oedema or exudates in close proximity to the macula
3. Cataract
4. Unexplained reduction in Visual acuity

- present in 50% of patients after 10 years with DM, 80-100% after 20y.
- one of the leading causes of blindness

Nephropathy

Especially common in Type 1 diabetes

STAGES:
1. Increased glomerular filtration rate (GFR) and kidney hypertrophy
2. microalbuminuria (30-300 mg/24h)
3. Overt nephropathy (>300mg/24h, positive urine dipstix)
4. End Stage Renal Disease [↑BUN and Creatinine, ↑ K and fluid overload]

Progresses to cause hypertension, persistent proteinuria (macroalbuminuria), nephrotic syndrome and renal failure. Microalbuminuria is an indication for

decrease CVD risk.

Annual screen for nephropathy:
1. u-albumin:creatinine ratio (spot sample)
2. 24h u Albumin excretion rate
3. Early morning albumin concentration
4. Dipstix for microalbuminuria

Prevention and Treatment of Diabetic nephropathy:
- tight glucose control
- tight blood pressure control – ACE inhibitors (Shown to reduce nephropathic complications) and calcium channel blockers (CCB)
- limit use of nephrotoxic drugs and dyes
- restriction (controversial)
- Stop smoking

Neuropathy

- common in both type 1 and type 2 DM
- Pathophysiology: metabolic defect thought to be due to increased sorbitol and/or decreased myoinositol (exact mechanisms not understood)

Classification of Diabetic Neuropathy

1. Poly neuropathy: Sensorimotor neuropathy
   - Feet > hands
   - Asymptomatic, numbness, parasthesia (pins and needles), allodynia (pain on noc-noctious stimulus) or pain.
   - Sensory neuropathy mostly predominates with the Cx: Ulceration (painless), Neuropathic oedema, Charcot arthropathy, Callosities
   - distal symmetric "glove and stocking" polyneuropathy
2. Autonomic neuropathy: (30% of diabetics)
   - GIT: Gastroparesis, Constipation, Intermittent Diarrhoea
   - Cardiovascular Dysautonomia: orthostatic hypotension, Resting Tachycardia, Prolonged Qt interval
   - Genitourinay: impotence, voiding difficulties – urinary retention with overflow incontinence
3. Mononeuropathy [entrapment, spontaneous, external pressure]
   - Entrapment neuropaties:
     - Carpal Tunnel Syndrome (median n),
     - Ulnar nerve compression syndrome,

- Meralgia paresthetica (lat cut n of thigh),
- Lateral popliteal nerve compression (drop foot)
- Eye: Lateral rectus
- Radial nerve – atrophy
- Thoracoabdominal radiculopathy

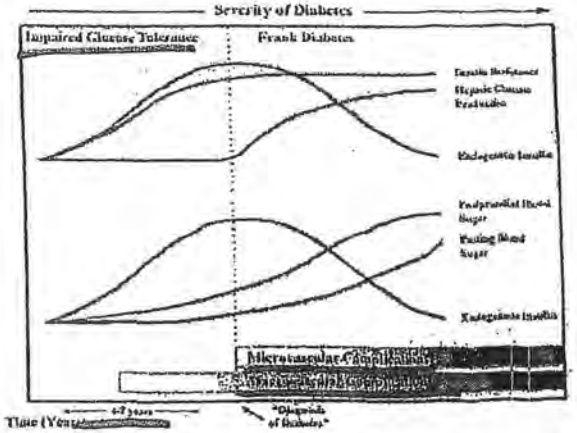
4. Proximal motor neuropathies
   - Amyotropathy: especially proximal neuropathy affecting the quadriceps muscles with weakness and arthropathy.

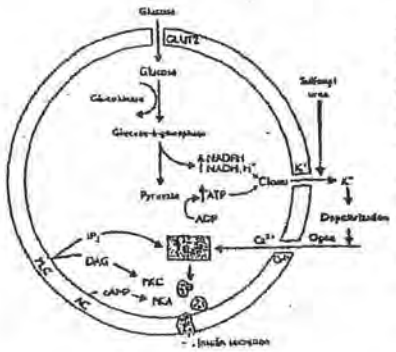
**Screen for neuropathies by using 128 Hz tuning fork for vibration testing and 10g monofilament.

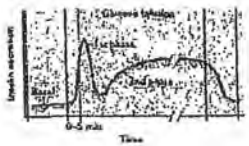
Management of Neuropathies:
- tight glucose control
- anti-depressants (e.g. amitriptyline), capsaicin, and anti-epileptics (e.g. Tegretol, Neurontin) for painful neuropathic syndromes
- erythromycin and domperidone for gastroparesis
- foot care education: Check feet daily, Wash feet daily, Keep toenails short, Protect feet, Always wear shoes, Look inside shoes before putting them on, Always wear socks, Break new shoes gradually
- Alpha lipoic acid and Gamma Linolenic acid

4. Other Complications
- skin disease
- bone and joint disease

TREATMENT OF DIABETES







Diabetes Control and Complications Trial (DCCT) (1993) demonstrated a 50-70% decrease in microvascular complications in type 1 DM in an intensively treated group as compared to a conventionally treated group as well as a marked decrease in vascular complications in those with well-controlled blood pressure

Type 2 DM: Insulin secretion Defects:
1. Blunted/Absent first phase of insulin response to glucose
2. Hyperglycaemia fails to trigger insulin response.
3. Decreased insulin secretion capacity.

Aim of Tx: Maintain near normal glucose while avoiding hypoglycaemia.
Targets for glucose control:

Current recommendations by ADA!

FBG (before breakfast)	5.0 – 7.2 mmol/L
Postprandial plasma glucose (2H after a meal)	<10 mmol/L
HBA1C	< 7 %

1. Non-pharmacological Interventions

1.1 Diet

Lifestyles changes to prevent a patient with IGT to develop Type 2 Diabetes: (58% reduction)

5 pillars of a healthy diet:

- Reduce saturated fat and sugar intake
- Increase fiber intake
- NB Low GI carbs (starch carbs)
- Limit salt intake
- Avoid alcohol consumption and stop smoking.

1.2 Exercise

- 25-30min aerobic exercise 3-4x per week
- Target heart rate of 60 -70% of maximum
- Exercise improve glycaemic control and insulin sensitivity
- Improve lipid profile: ↓TGL, ↓ LDL, ↑HDL.
- Decrease BP
- Increase metabolism and helps with weight reduction

2. Pharmacological Interventions

Type 1 DM pt invariably need Insulin
Type 2 DM Managed initially with diet and exercise alone – progress to need for oral hypoglycaemic agents and then insulin depending on Glycaemic control.

2.1 Oral hypoglycaemic agents

- **INSULIN AUGMENTING AGENTS [INCREASE INSULIN SECRETION]**
- **ASSISTING AGENTS [REDUCE INSULIN RESISTANCE]**
- **INSULIN SELF**

Principles:

1. Combining drug = more effective than stopping one agent and introducing another.
2. Adding a 2nd agent > than increasing dose of one agent already near maximum dosage
3. 3 drug combinations may be useful but lack experimental testing
4. Failure of 2 oral agents calls for Insulin alone or in combination with oral agents.
5. In pt with severe hyperglycaemia: Insulin may be started from the beginning, when toxicity resolves= reduce or withdraw it!

INSULIN AUGMENTING AGENTS [INCREASE INSULIN SECRETION]

1. **Sulfonylurias: Gliclazide (Diamicron),** Glibenclamide, Glipizide, Chlopropamide, Tolbutamide.
2. **Metglitinides: Repaglinide (Novonorm)** Nataglinide (Starlix)

Sulfonylurias:

Stimulate release of endogenous insulin by blocking K-ATPase channels → Open Ca channels → Ca influx→Insulin release! NB: You need functioning B – cells!

S/E: NB!! **hypoglycemia**, nausea, GI discomfort

C/I:

- Type 1 DM – no functioning B- cells left!
- Pregnancy
- hepatic or renal impairment. [Metabolized in Liver (CYT P450 enzyme) and active metabolite excreted by kidneys.] – will ↑ risk for Hypoglycaemia.
- Also C/I in pt on Warfarin. Warfarin induces CYT p450 enzyme thus decrease metabolism of SU and increase its level in blood – HYPOGLYCAEMIA!
- Can't combine with other SU/ Metglitinides
- NB: SU 1 receptor, SU 2A and B receptors as well on cardiac muscle! SU will occupy ALL of these receptors causing Ca influx and thus causing a TACHYCARDIA. It aggravated cardiac ischemia = called **Cardiac Ischemic preconditioning!**

Indications:

- Use with other Oral Hypoglycaemic agent

Meglitinides: postprandial Glucose Regulators

Stimulate release of endogenous insulin by binding to ATP dependent K-channel on B- cells. Not SU receptor. (rapid-acting, better post-prandial glucose control)

It is ___ at me ___ 's an: ics th ... ologi ... in pe

S/E: hypoglycemia (less frequent than with sulfonylureas)

C/I: hypersensitivity
diabetic ketoacidosis (DKA)

ASSISTING AGENTS [REDUCE INSULIN RESISTANCE]

Insulin

1. **Biguanides: Metformin**
2. **Thiazolidinediones: Pioglitazone, Rosiglitazone**
3. **Alpha-glucosidase Inhibitors: Acarbose**

Biguanides: Metformin (Glucophage)

1. Reduce gluconeogenesis in liver
2. Increase Insulin mediated glucose utilization
3. Reduce glucose absorption through gut
4. Increase splanchnic glucose utilization
5. Activate Insulin receptors and GLUT 4 receptors. When you exercise – you move GLUT receptors to cell membrane and make them fuse with the cell membrane at a permanent level.

Advantages:

1. Weight loss and slight anorexic effect
2. No Hypoglycaemia
3. Decrease thrombotic risk as it decrease platelet aggregation and decrease plasminogen activator inhibitor (PAI-1)
4. Positive effect on lipid profile
5. Safe in pregnancy

S/E:

- lactic acidosis
- anorexia, nausea
- diarrhea
- GI discomfort

↓ Biz Absorption.

C/I:

- hepatic or renal impairment due to lack of Lactic acidosis.
- alcoholism
- advanced age
-

Thiazolidinediones: rosiglitazone (Avandia)

1. Increase peripheral insulin sensitivity, decreases peripheral Insulin resistance by enhancing insulin action on glucose and lipid metabolism
2. reduce gluconeogenesis

Take ... eeks ... Lactic

4. MOA: activate PPAR-¥ (nuclear receptor) → Stimulate gene expression of regulators of lipid and glucose metabolism → Increase GLUT-4 production with improved glucose transport → increased hepatic glucose disposal and decreased glucose production
5. Decrease TGL and increase HDL (decrease visceral fat by increase peripheral fat)

S/E:

- Increased TG
- weight gain
- hepatotoxicity
- anemia (decrease hb)
- fluid retention

C/I:

- liver disease (NB do to ALT regularly)
- congestive heart failure (CHF)

Alpha-Glucosidase Inhibitors: Acarbose (Prandase)

Decrease/delays the digestion/absorption of carbohydrates by preventing the conversion of poly- and disaccharides to monosaccharides (thus decreasing postprandial rise of glucose).
Only use it as monotherapy!!!

S/E: flatulence
Abdominal cramping
Diarrhea

C/I: hypersensitivity, DKA,
Inflammatory bowel disease (IBD)

Thus: MOA of antihyperglycaemic agents:

1. GIT: decrease digestion of complex sugars – Alpha-Glucosidase Inhibitors (Acarbose)
2. Pancrease B-cells: Increase Insulin secretion – SU, non-SU secretaloques
3. Liver: Decrease hepatic glucose production – Biguanides, Thiozolidinediones
4. Increase glucose uptake in muscles - – Biguanides, Thiozolidinediones

Step care in DM Type 2:

STEP 1: Nutrition – Diet, Exercise, Lifestyle changes
Training in self-Mx and self-monitoring of glucose
STEP 2: Add oral agents (monotherapy or combined)
STEP 3: Add or change to Insulin
STEP: Intensify Insulin Therapy

What for WHO?

High postprandial glucose	-	ACARBOSE, MEGLITINIDES
Obese pt	-	METFORMIN if BMI >25, if BMI <25 use metformin/SU. GLITAZONES can also be used.
Recently dx type 2 DM	-	SU
Insulin resistance	-	GLITAZONES

NB: How to decide what to give:

- BMI >25 = metformin
- BMI < 25= Metformin/SU – if this fails – combine metformin and SU and Insulin thereafter if still no response.

2.2 Insulin

When to start? HBA1C routinely > 7% indicated pt might benefit from Insulin. 3 monthly HBA1c monitoring is NB!

Indications for Insulin in type 2 DM:

- After **failure on Oral Hypoglycaemic agents** (OHA) alone [mono or combined tx], combination Insulin + OHA can improve glycaemic control with less weight gain.
- **Persistent hyperglycaemia** with OHA.
- Persistent **weight loss** in Type 1 DM
- **LATENT AUTOIMMUNE DISEASE IN ADULTS** (skinny type 2's)
- OHA S/E or allergic reactions reducing acceptability or compliance
- Pt on **multiple medications**
- Pt with **renal or hepatic** impairment
- Women planning pregnancy
- Gestational Diabetes
- Intercurrent events: MI, CVA, Acute illness, surgery

NB: Patients should be educated to self-adjust their insulin dose in light of exercise and calorie intake to achieve normoglycaemia.

Subcutaneous Insulin Analogues (100u/mL)

Insulin regimens should:

1. Mimic Insulin profiles of healthy id. (post prandial spikes and basal levels)
2. Maintain effective glycaemic control and avoid complications.

Administration:

- subcutaneous injections: Lateral thighs, Abdomen, not umbilicus, Lateral upperarm! Not forearm.
- continuous subcutaneous insulin infusion pump
- IV infusion (regular insulin only)

NB:** Lipodystrophy: S/E if only inject at the same spot everytime – due to the fact that insulin has got Growth hormone properties. Absorption from this area is very poor!

Preparations:

TREATMENT	ACTION	ONSET OF ACTION (H)	PEAK (H)	DURATION (H)
CONVENTIONAL HUMAN INSULIN				
NPH	Intermediate	2-4	4-6	12-16
Lente	Intermediate	2-4	4-12	12-18
Ultralente	Long-Acting	6-10	10-16	18-20
Regular	Rapid (dose dependent)	30-60 min	2-4	6-8
ANALOQUES				
Glarginine	Long	2	Flat	24
Detemir	Long	2	Flat	14-16
Lispro (Humalog)	Ultra-rapid	5-15 min	60 min	4-5
Aspart (Novolog) (Novorapid)	Ultra-rapid	5-15 min	60 min	4-5
Glulisine (Apidra)	Ultra-rapid	5-15 min	60 min	4-5

Also: Soluble Insulin Humulin S or Actrapid

@ b ar ly DM.

ADMINISTRATION: daily 0,5-1 units/kg → DM1. 0,2-0,4 kg → DM2.

1. Estimate of total daily insulin requirement when starting an adult type 1 diabetes patient on insulin = 0.5 – 1.0 units/kg and when starting an adult with type 2 diabetes = 0.2-0.4 units/kg. OR 1 unit insulin for every 1 unit of BMI.
   Athletes and pt near there ideal body weight will require less insulin than obese pt.
   Be aware of the honeymoon period!
2. Design a regimen to suit pt lifestyle

Insulin regimes

Traditional once or twice daily	*Flexible Basal bolus*
No longer recommended Appropriate: 1. Initial tx. 2. Pt with poor understanding of the disease	Basal and at meal times Requires an intelligent an motivated pt 4 injections required daily

Twice daily regime

Total daily dose

- **2/3 morning:** 2/3 intermediate + 1/3 short acting
- **1/3 evening:** 2/3 intermediate + 1/3 short acting

Flexible Basal Bolus regime

Total daily dose

- **Basal Bolus:** 40% of dly dose. NPH/Glargnine once or twice dly
- **Meal time bolusses:** 60% in 3 divided dosages Regular/ Lispro/Aspart within 30 min before meals

40%	20%@ meal	20%@ meal	20%@ meal

s afh bas (sory

1. **Site of injection:** Good site = thighs, abdomen, upper arm)
2. **Depth of injection:** In subcutaneous tissue not in muscle
3. **Insulin concentration:** 100U/ml
4. **Insulin dose:** higher dose, slower absorption
5. **Insulin mixing:**
6. **Heat application or massage:** Increase absorption. Pt should not rub/massage because we don't want to accelerate absorption. NB
7. **Exercise:** will increase absorption due to vasodilatation.
8. **Illness increases Insulin requirements despite reduced food intake.**

Sliding scale:

Patient takes fixed doses of intermediate-acting insulin (N) but varies doses of fast-acting insulin (Regular or Humolog) based on blood glucose reading at time of dose

Pre meal glucose	Insulin dose	Lag time	Comments
2.8 mmol/L	↓2 U	Inject during meal	Include > 10g simple CH
2.8-4.4	↓1 U	0	
4.4-7.2	No change	0	
7.2-8.3	↑1 U	0	
8.3-11.1	↑2 U	10 min	
11.1-13.9	↑3 U	15 min	
13.9-16.7	↑4 U	20 min	Test u-ketones
16.7-19.4	↑5 U	25 min	

Insulin sliding scale example for 3 daily injections				
Blood glucose (mmol/L)	Insulin nr of Units			
	Breakfast		Dinner	Bed
	Regular/Humolog	NPH	Regular/Humolog	NPH
< 3	-2	25	-2	18
3.1-3.9	-1		-1	
4-8 (target)	12		9	
8.1-12.0	+1		+1	
12.1-17.0	+2		+2	
>17	+3		+3	

- pt must be taught to count the grams of CH they anticipate eating, the dose of Insulin is adjusted according to this.
- **NB*** 1U Lispro/Aspart for every 15g CH. This should be individualized!**

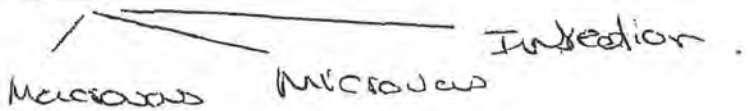
Glucose Monitoring

- frequent self-monitoring and recording of blood glucose is now standard management – pt should keep a record of home fingerprick glucose records to detect patterns of hyper- or hypoglycaemia.
- hemoglobin A1c (HbA1c or glycosylated hemoglobin) percentage indicates level of plasma glucose over past 3 months
  Extremely useful for monitoring patient's long-term diabetes control
  Goal is to maintain HbA1c within < 7% or <6.5% if patient is at increased arterial risk e.g. previous stroke or MI.
- Fructosamine levels reflect control over 2-3 weeks.

Patients coming for F/U. What to do?

1. Educate and give lifestyle advice; Promote exercise, healthy eating and weight reduction.
2. Find out about problems/ SE experienced
3. Assess vascular risk:

- BP (target <140/80)
- Dipstix, UKE [creatinine, microalbuminuria]
  Patients with renal disease: BP <125/75
- Encourage to stop smoking
- Check cholesterol
- Check Insulin injecting sites for infection or lipodystrophy and advice on rotating sites.
- Look for Cx!



Remember: Foot Care.

Diabetic Keto-acidosis

Symptoms patient presents with:

1. Polyuria, Polydipsia
2. Weight loss
3. Weakness
4. Nausea and vomiting
5. Leg cramps
6. Blurred vision
7. Abdominal pain

Signs:

1. Dehydration
2. Hypotension
3. Tachycardia tachypnoea
4. Kussmaul's breathing
5. Smell of acetone
6. Metabolic acidosis
7. Hypothermia
8. Confusion, drowsiness, coma

Causes and precipitating factors:

1. New presentation of Insulin Dependent DM
2. Known Insulin dependence DM +
   - Inappropriate reduction in Insulin
   - Co-existing infection
   - Surgery
   - MI
   - Emotional stress

Differential diagnosis:

Suspect HONK when hyperglycaemic without high urine ketones. HHS.

Diagnostic criteria:

1. GLUCOSE > 13 mmol/L
2. Arterial pH < 7.3
3. Urine Ketones >/= 2 +
   (Remember 3's)

Mx:

1. ABC
2. Fluid deficit:

[0.6 x wt(kg) x (s-Na/140)]-[0.6 x wt]= 4-6L

Replace 3 L from ECF with 0.9% NaCl

Replace 3L from IVF with dextrose

3. Glucometer reading
4. Confirm reading with formal blood glucose
5. Urine testing for ketones
6. If elevated Blood Glucose positive - give **50 U of soluble Insulin in 50ml N Saline [1 U/ml]. Administer IV @ a rate of 6 ml/hr.** Blood glucose usually falls by 5 mmol/hour.
   Persistent ketonuria – give 10% dextrose as fluid replacement of choice combined with Insulin @ 6U/hour
7. Catheterize in no urine passed for 3 hrs.
8. NGT to empty stomach in unconscious/semi-conscious pt.
9. CVP if CVS compromised
10. plasma expander if BP not respond with N Saline
11. Antibiotic if suspected no Primary cause found: Ceftriaxone 1g
12. Monitor blood glucose hourly for 3 hours and therafter every 2-4 hours.
13. Once Blood sugar < 15mmol/L – change to soluble Insulin tds or start with N regime and ensure adequate calorie intake.
14. fluid replacement:
    - 1 L N Saline over 30 min.
    - Second Liter over 1 hour.
    - Then followed by L bags over 2, 4, 8 hours.
15. Once glucose < 15 mmol/L change to 10% dextrose, except when hypovolaemic
16. K replacement: NOT in FIRST 2 L of fluid. Thereafter administer K as follows:
    - < 3 mmol/L give 40mmol K
    - < 5 mmol/L give 20 mmol K

Hypokalaemia is a potential cause of death in pt being treated for DKA!!!

17. pH < 6.9 – give 50ml Bicarbonate over 30 min. NB

A raised WBC count in a pt with DKA doesn't indicated underlying inf.

18. Heparin anticoagulation as these pt are at increased risk for developing Thromboembolism

Cx:

1. Cerebral oedema if you ↓ Glucose too rapidly or when hypotonic fluids are given (Rx with mannitol and O2)
2. ARDS
3. Thromboembolism
4. DIC
5. Acute Circulatory failure

NB: When do you change from Insulin Infusion to Subcut Insulin?

Continue IV infusion until ketones – Continue IV infusion until 60 min after 1st subcut dose.
Start of with a short acting insulin tds before meals. Thereafter (24h), determine the patients total daily insulin requirement and administer 2/3 before breakfast and the remainder before supper. The insulin given should comprise ½ soluble and ½ intermediate acting Insulin.
Take glucometer readings before B-fast, Lunch and dinner and adjust Insulin accordingly.

ADRENAL GLANDS

Adrenal insufficiency : ADDISON'S DISEASE AND CRISIS

Addison's disease = Chronic adrenal insufficiency (1^0 and 2^0 adrenal insufficiency)
Addison's crisis = Acute adrenal insufficiency = **ER!!!** Inability to secrete increased cortisol/ACTH in response to stress (Infection, dehydration, surgery) leading to hypovol. shock, fever, extreme weakness, decreased LOC, nausea, vomiting, hypoglycaemia!

Hypothalamus
↓
CRF
↓
Pituitary
↓
ACTH
↓
Adrenal Cortex ← 1^0
↓
Cortisol and Aldosterone

Destruction of the adrenal cortex leads to cortisol and aldosterone deficiency!

Causes:
1^0

1. **80% DUE TO AUTOIMMUNE DISEASE**
2. **Metastases** from (Breast Ca, lung Ca, Renal Ca, Lymphoma) to adrenals
3. Opportunistic infections in HIV (CMV, Mycobacterium Avium)
4. **Adrenal haemorrhagic infarction** (Waterhouse Friederichsen syndrome in children, coagulopathy in adults)
   SLE, Antiphospholipid AB syndrome)
5. **Granulomatous disease**: Sarcoidosis and **TB** of adrenals (Commonest cause worldwide)
6. Congenital (late onset congenital adrenal hyperplasia)

2^0

1. Pituitary or Hypothalamic disease [no hyperpigmentation as ACTH intact, aldosterone synthesis normal]/
2. Iatrogenic: Chronic corticosteroid usage with suppression of pituitary-adrenal axis, now suddenly steroid withdrawal.

**** NB Waterhouse Friederichsen syndrome:***
Bilateral adrenal cortex haemorrhage esp. occurring in rapidly deteriorating meningococcal sepsis.

- **Purpura**
- **Meningitis**
- **Coma**
- **DIC**

Also Pseudomonas, H. Influenza, S. Aureus, Pneumococcal, Streptococcal sepsis.
No Cortisol ⇨ decrease vascular tone, No aldosterone ⇨ extracellular fluid volume not maintained.
Thus: Adrenal failure ⇨ Shock.
Mx: AB: Cefriaxone
Adrenal Support: Hydrocortisone 200mg/4 h IV
ICU

Approach:

Clinical Presentation:
1. Fatique, myalgia, arthralgia, fainting, weakness, Anorexia, weightloss
2. Abnormal GIT fx. UNEXPLAINED GIT DYSFX!!!
   - Nausea, Vomiting, Abd pain, Diarrhoea, Constipation -
3. Personality Changes, Depression, Psychosis
4. **Pigmentation** in unexposed skin areas: Lips, Creases of hands, Scars, Buccal Mucosa due to ACTH secretion and its cross reaction with Melanin. – in PRIMARY, NOT SECONDARY!!!
5. **Dehydration and salt craving.** – in PRIMARY, NOT SECONDARY!!!
6. Decease pubic and axillary hair in females.
7. **Hypotension NOT responding to pressors, NB!!!!**
8. Vitiligo

↓

Lab Investigations:
1. ↓Na, ↑K (due to ↳Aldosterone)
2. ↳Glucose (due to↳Cortisol)
3. UKE: Uraemia/ BUN/ Creatinine
4. FBC and Diff Count: Eosinophilia and Anaemia (normocytic, normochromic)
5. Increased Ca 2+.

↓

Diagnosis:

1. **ACTH Stimulation test : PRIMARY**
   Take plasma Cortisol before and 30min after tetracosactide (Synacthen) 0.250mg IM. [synthetic ACTH]
   Failure of cortisol to rise > 553mmol/L after 30min = Addison's
   NB: This test will be falsely + in pregnancy and in pt on contraceptive pills due to an increase in the cortisol binding protein.
2. **Basal ACTH** will be ↑ **primary** Addison's. 9am ACTH will be ↑ addison's.
3. **21-hydroxylase antibodies** + in autoimmune disease.
4. **AXray/CXray/ CT abdomen:** ↑ enlargement of adrenals in adrenal haemorrhage, active TB or Metastatic Malignancy. Signs of past TB = upper zone fibrosis or calcification.
5. In SECONDARY: LOW CORTISOL, LOW ACTH, NORMAL K+/ BUN/ CREATININE

↓

Precipitating factors:

1. Omission of medication
2. Illness – Severe infection, MI, CVI, Severe trauma, surgery without adrenal support
3. Withdrawal of steroid tx in a pt on long term steroid tx.
4. Administration of drugs impairing adrenal hormone synthesis e.g. KETOCONAZOLE.
5. Drugs increasing steroid metabolism e.g. Phenytoin and Rifampicin.

↓

Treatment of Addison's crisis!!! ER!!!

1. Hydrocortisone 100mg IV stat then 50mg 4 hrly for 24 hours
2. Tamper slowly over next 3 days.
3. Change to oral replacement therapy when oral feeds are tolerated
4. OVERLAP FIRST ORAL AND LAST IV DOSE!
5. 5% Dextrose in N Saline IV/ N Saline IV in large volumes!
6. If Aldosterone insufficiency give fludrocortisone when shift to oral tx.
7. Treat the precipitant.

Treatment of Addison's Disease

1. Replace Steroids: 15-25mg hydrocortisone daily in 2-3 devided doses. Not late in day –INSOMNIA!
2. Fludrocortisone daily po when signs of aldosterone deficiency present.
3. If no response to tx – Consider autoimmune cause.
4. Always warn pt. on just abruptly stopping steroid usage and increase steroid dose in times of illness or surgery!

Adrenal Cortex

Zona:

- glomerulosa → Aldosterone (Salt)
- fasciculata → Cortisol (sugar)
- Reticularis → Androgens (sex)

Hyperaldosteronism

Excess production of aldosterone independent of the RAAS system causing ↑ Na and H2O retention and a ↓renin release.

Patient presentation:

1. Usually Asxs
2. Hypertension – Esp. @ a young age.
3. Hypokalaemia – weakness, cramps, parasthesia, occasionally paralysis, polyuria, polydipsia, latent TETANUS!
4. Alkalosis
   In a patient NOT on a diuretic!
5. Na "mildly↑/N

Differential diagnosis:

1. Excessive diuretic usage: Rule out. If patient not on a diuretic – consider this diagnosis first!

SI:

1. UKE (pt must ideally not be on a diuretic, hypotensive, steroids, K, laxatives for 4 weeks)
2. Do not rely on a ↓K as >20% can be normokalaemic.
3. **Aldosterone/Renin Ratio (ARR):** Pt sits upright for 2 hours. Antihypertensives withheld for 2 weeks (Spironolactone for 6 weeks). Alpha blockers can be used as it does not affect the test. A ↑ ratio (↑Aldosterone) indicates hyperaldosteronism.
4. MRI/CT scan of the adrenals to localize the cause: Only done if hyperaldosteronism is proven. If unilateral adenoma shown – excision. If no nodules or bilateral nodules are seen a trial of Glucocorticosteroids (GCS) may be used to test for GRS. In GRA the GCS ↓ACTH production by negative feedback and therefore ↓ aldosterone production.
5. If the above are inconclusive: Adrenal vein sampling may be done. Venous blood sampled from both adrenals and if one side demonstrates increased aldosterone an adenoma is likely.
6. Adrenal scintigraphy can alternatively be used. If it shows an increased unilateral uptake of the isotype, adenoma suspected.

Causes:

1° **Hyperaldosteronism (Conn's syndrome).**

(Think of Conn's in: *HYPERTENSION ASSOCIATED WITH HYPOKALAEMIA!!! * Refractory HT depsite 3 antihypertensives * Hypertension before 40years of age (esp. Women))

1. 2/3 Conn's adenoma
2. 1/3 Bilateral adrenal hyperplasia
3. Glucocorticoid-remediable raldosteronism (GRA)
   (ACTH regulatory gene element of the 11 B-hydroxylase gene fuses to the aldosterone synthase gene, increasing aldosterone production, and bringing it under the control of ACTH.

2° **Hyperaldosteronism [Due to high renin from ↓renal perfusion]**

1. CCF
2. Liver chirrosis +ascites
3. Nephrotic syndrome
4. Renal artery stenosis
5. Sodium losing nephritis
6. Barter's syndrome [congenital cause – defective NaCl channel in the loop of Henle causing a leak]
7. Renin-secreting tumours

Non-aldosterone mineralocorticoid excess:

1. Ectopic ACTH syndrome
2. Liquorice
3. 17 Alpha-hydroxylase/11B-hydroxylase deficiency
4. Liddle's syndrome

Mx:

Conn's syndrome: Laparoscopic adrenalectomy. Give Spironolactone up to 300mg per 24h po 4 wk pre-op to control the BP and to treat the hypokalaemia.

Hyperplasia: Spironolactone or Amiloride or Eplerone(does not cause gynaecomastia like other 2)

GRA: Dexamethasone 1mg,24h po for 4 wks. If Bp still ↑ after this treatment- swithch to Spironolactone as alternative

Adrenal carcinoma: Surgery +/- post-op adrenolytic therapy with mitotane – poor prognosis!

↓ADH (Post. Pituitary).

Diabetes Insipidus

↑volume of diluted urine (>3L/day) due to impaired H2O absorption as result of ↓ADH secretion from Posterior pituitary gland.

Cranial DI: ↓ ADH production by the posterior ptuitary gland.

Nephrogenic DI: Renal tubules are unresponsive to ADH.

Patient complaints:

- Polyuria
- Polydipsia
- Dehydration
- Patient passes 5-20L H2O/day
- Patient complains of excessive thirst- drinking EVERYTHING!!!

SI:

1. UKE
2. Ca
3. Glucose (exclude DM)
4. Serum and Urine osmolalities: Plasma osmol >300mOsmol/kg and Urine osmol <400mOsmol/kg.
5. Serum Na ↑. Polydipsia might cause a duilutional hyponatraemia.
6. **WATER DEPRIVATION TEST:** Used to establish Dx of DI and differentiate cranial from nephrogenic DI.
   Normal: Urine osmol > 600mOsmol/kg
   Primary polydipsia: Urine concentrates, but less than normal, e.g. >400-600 mOsmol/kg
   Cranial DI: Urine osmol increases to > 600 mOsmol/kg after desmopressin.
   Nephrogenic DI: No increase in urine osmol after desmopressin.

Differential Diagnosis:

Diabetes, Diuretics, Lithium, Primary Polydipsia (Caused by psychiatric disease: SZP/Mania)

Causes:

Cranial:

- Structural Hypothalamic lesion or high stalk lesion (trauma/hypophysectomy)
- Infection
- Vascular: Sheehan syndrome (infarction seen after severe hypotension e.g post partum haemorrhage)
- Ideopathic
- Genetic defect: Dominant
  Recessive: DIDMOAD syndrome: Diabetes Insipidus Diabetes Optic Atrophy and Deafness (Wolfram's Syndrome)

Nephrogenic :

- Genetic: V2 receptor mutation, Aquaporin -2 mutation, Cystinosis
- Metabolic Abn: Hypokalaemia, Hypercalcaemia
- Drug Therapy: Lithium, Demeclocycline
- Poisoning: Heavy metals
- Chronic Kidney Disease: PCKD, Sickle cell anaemia, Infiltrative disease.

Treatment:

Cranial DI:

1. Find the cause: MRI
2. Test anterior ptuitary function
3. DDAVP (Desmopressin) and analoque of ADH via the nasal mucosa. Dose 10-20 microgram/12-24 hours, usually, 5 microgram in the morning and 10 micrograms @ night.

Nephrogenic DI:

1. Thiazide diuretics e.g. bendroflumethiazide 2.5-5 mg/day po.
2. NSAIDS: (e.g. Indometacin 15 mg 8 hrly) as it lowers Prostagladins. Prostaglandins inhibit the action of ADH locally. [SE: Reduced GFR].

ER Management:

1. Urgent UKE and serum and urine osmolalities.
2. Monitor urine output and check UKE twice dly.
3. Do not lower NA too quickly – risk of Cerebral oedema and brain injury. If Na >170 use 0.9% Saline and reduce Na at a rate of less than 12mmol/L per day. The use of 0.45% Saline can be dangerous.
4. Desmopressin 2 micrograms IM (lasts 12-24 hours)

Hyperprolactinaemia

Hyperprolactinaemia is the most common disturbace of the ptuitary gland. MB

- It presents earlier in females than males due to menstrual disturbances.
- Prolactin stimulates lactation and antagonize sex steroids periphally. Raised levels of Prolactin lead to secondary hypogonadism, infertility and osteoporosis as it inhibits Gonadotrophin releasing hormone (GRH) secretion – leading to a low testosterone, estrogen, FSH and LH level.
- serum prolactin levels > 300 µg/L (300 ng/mL) virtually diagnostic of prolactinoma
- prolactin-secreting tumours may be induced by estrogens and may grow during pregnancy

Patient presents with following complaints:

FEMALES

1. Amenorrhoea or Oligomenorrhoea
2. Infertility
3. Leaking breasts
4. Decreased libido
5. Weight gain
6. Dry Vagina
7. Osteoporosis
8. Local pressure effects: Headache

MALES

1. Impotence
2. Reduced facial hair
3. Leaking breasts
4. Osteoporosis
5. Local pressure effects: Headache

Examination:

FEMALES and MALES

1. Galactorrhoea
2. Hypogonadism
3. Local pressure effects: Visual field defects (Bitemporal hemianopia), CN palsies (III, IV, VI)

Differential Dx:

Secretion of Prolactin (PRL) stimulated by :

1. Physiological: Pregnancy, Breat-feeding, stress e.g. post-seizure, Sleep, hypoglycaemia, mid-menstrual cycle, TRH, sexual activity
2. DRUGS: Phenothiazines, estrogens, psychotropics (e.g. haloperidol, risperidone), antihypertensives (e.g. reserpine, verapamil), alpha -methyldopa, opiates, high-dose estrogens, metoclopramide, domperidone, cimetidine
3. Diseases: Prolactinoma (micro/macroadenoma)
   Stalk damage: Ptuitary adenomas, transection, trauma
   Hypothalamic disease: Craniopharyngioma, other tumours
   Other: hypothyroidism (due to ↑TRH), chronic renal failure (↓clearance and excretion), liver cirrhosis.

(CRANIOPHARYNGIOMA) Develpos from Rathke's pouch – situated between the ptuitary and the 3rd ventricle. Commonest childhood intracranial tumour, 50% presents in childhood with Growth failure and with amenorrhoea, ↓ libido, hypothalamic symptoms – DI, hyperphagia, sleep disturbances- in adulthood. Treatment is surgery)

Tests:

1. Basal PRL: Do a non-stressful venepuncture between 9 am and 4 pm.
   Causes of basal PRL secretion (>390 mU/L): Secreted from the anterior ptuitary. Release is inhibited by Dopamine produced in the Hypothalamus.
   Hyperprolactinaemia causes:
   1. Increased production from ptuitary (Prolactinoma)
   2. Disinhibition by compression of the ptuitary stalk reducing the Dopamine levles
   3. Administration of a Dopamine antagonist
2. Pregnancy test
3. TFT
4. UKE
5. MRI of ptuitary if no other causes found.
   Any level of PRL >5000 probably indicates a prolactinoma.
   Macroadenoma (>10cm): PRL levels 10.000-100.000

Treatment includes

1. bromocriptine or carbegoline (long-acting dopamine agonist),
2. surgery. Compl: Permanent hormone def, recurrence so reserved for 2nd treatment.
3. +/–radiation
   - these tumours are very slow-growing and sometimes require no treatment

MACROADENOMAS	MICROADENOMAS
▪ Tumour >1 cm in diameter on MRI ▪ Initially tx with Bromocriptine ▪ Surgery indicated if visual symptoms, pressure effects which fails to respond to medical tx or when pregnancy is contemplated – 25% of macroadenomas expand during pregnancy. ▪ Post-surgery: Radiation or Bromocriptine.	▪ Tumour <1 cm ▪ 25% of population have asymptomatic microprolactinomas. ▪ Bromocriptine will - ↓PRL, restore menstrualting cycles and ↓ tumour size. Dose titrated up: 1.25 mg dly, then increase wkly by 1.25-2.5mg/d until 2.5mg/12h. SE: Nausea, Depression, Postural hypotension. If pregnancy planned – use barrier methods until 2 periods have occurred, if pregnancy occurs, stop bromocriptine after 1st missed period. Alternative = Carbegoline ▪ Surgery if intolerant to Domapine agonist.

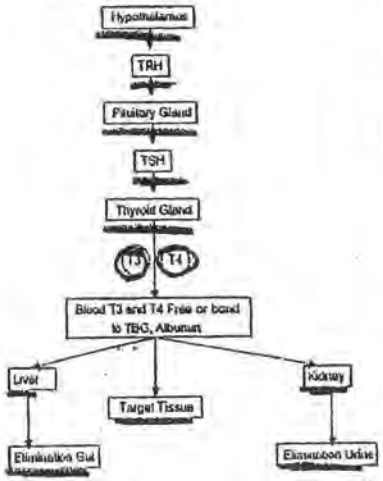
Hypoprolactinemia

- Inability to lactate ⟶ MB
- may be the first sign of Sheehan's syndrome (postpartum pituitary hemorrhage)

Hypoprolactinaemia DI.

Thyroid

Thyroid System Diagram



TRH: Thyroid releasing hormone
TSH: Thyroid stimulating hormone
secreted by the anterior pituitary gland. (glycoprotein)
T4: Thyroxine
T3 Triiodothyronine
TBG: Thyroid binding globulin
[redacted] (not bound to TBG or Albumin) is the ACTIVE part!
T3 and T4 fx: Increases cell metabolism thus vital for growth and development, also increases catecholamine effects.

Thyroid functions:
Serum T4 and T3: To measure free portions are more useful than to measure the total levels.
TBG capacity: Unreliable because pregnancy and hormone replacement therapy increases the levels of TBG falsely. Cough mixtures containing iodine falsely increase TBG as well. TBG decreased when using androgens, corticosteroids and phenytoin, also low in chronic liver disease and acromegaly.

T3 resin uptake test: Measures the unoccupied receptors. Are thus at its lowest when hormone levels are high.

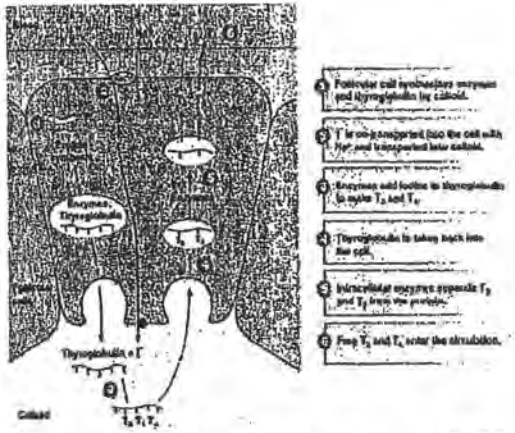


Fig. 23-9

Radioactive Technesium 99 (T99) or iodine I 131 or I 132: measures the function of the gland as well as the pattern of uptake.

TSH levels: no rise in hyperthyroidism due to negative feedback from T4 an T3. In hypothyroidism, TSH levels will be elevated.

Tests:
1. Antithyroid peroxidase (TPO) and antithyroglobulin antibodies raised in autoimmune thyroid disease: HASHIMOTO's THYROIDITIS or GRAVE's DISEASE.
   If + in Grave's: HIGH risk of developing hypothyroidism later!
2. TSH receptor antibodies: ↑ in GRAVE's (useful in pregnancy)

When to screen a patient for thyroid functions NBIII***
1. Patients with AF
2. Patients with hyperlipidaemia (4-14% will have hypothyroidism)
3. Diabetes Mellitus – annual review
4. Women with DM in 1st trimester and post-delivery (3 fold rise in incidence of post partum thyroid dysfunction)
5. Patients in LITIUM and AMIODARONE
6. Patients with DOWN's or TURNER's syndrome or Addisons disease.

Essential clinical features of an enlarged thyroid:
1. Midline swelling
2. Moves on swallowing
3. Diffuse or nodular
4. Central trachea?
5. Lymphnode enlargement
6. Retro-sternal extension

Causes of an enlarged thyroid:

DIFFUSE:
1. Physiological — Pregnancy/Puberty
2. Grave's disease
3. Thyroiditis
   - Hashimoto's
   - Acute suppurative
   - Subacute: (de Quervain's thyroiditis – painful)
   - Riedl
   - Drug induced
   - Subacute thyroiditis
   - Non-toxic:

NODULAR:
1. Multinodular goiter
2. Single nodule:
   - Benign: Adenoma
   - Malignant: Papillary (60%)
     Follicular(17%)
     Anaplastic
     Medullary
     Lymphoma

Causes of Hyperthyroidism:

Most Common:
1. Grave's Disease
2. Toxic multinodular goiter
3. Autonomously functioning goiter

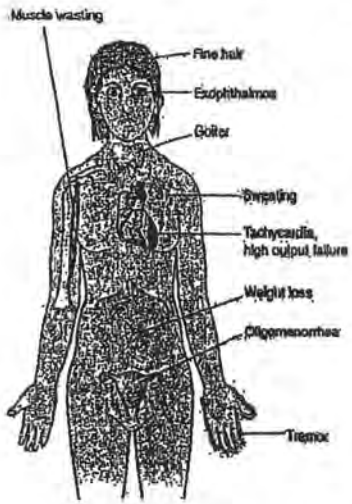
Rarer causes:
1. Thyroiditis or other causes of destruction
2. Thyrotoxicosis factitia
3. Iodine excess (Jod-Basedow phenomenon)
4. Struma ovarii
5. Pituitary tumour (TSH secr.)
6. HCG stimulation (Hydatiform mole/Choriocarcinoma)
7. Ovarian teratoma (Contains thyroid tissue)
8. Metastatic differentiated CA of thyroid

Physiological goitre:
Simple diffuse
- 5 – 15yr (esp. pregnancy)
- Tight sensation in neck esp. upon swallowing
- Soft & symmetrical
- 2-3x normal size
- No tenderness, lymphadenopathy or overlying bruit
- T3/T4 and TSH normal
- No Thyroid antibodies
- No treatment required → most regress
- Cx: May transform → multinodular simple goitre (due to hyperplasia/involution over 10-20 years)

Simple Multinodular:
- Rare before middle age
- Slowly ↑ size
- Pain caused by hemorrhage into nodule or cyst
- Nodular or lobulated on palpation and may extend retrosternally
- Very large ones → Mediastinal compression → stridor/dysphagia/SVC obstruction/Hoarseness due recurrent laryngeal nerve involvement (More likely in CA)
- T3/T4 and TSH normal (OR upper limits with TSH undetectable)
- Radiographs: Tracheal displacement/compression; intrathyroidal calcifications; retrosternal extension
- Small: No Rx with annual review (→ toxic multinodular goitre)
- Large: Partial thyroidectomy (mediastinal compression/cosmatically unattractive)
- Recurrence 10-20 years later no uncommon and cannot be prevented

Hyperthyroidism:

Symptoms patient presents with:



AS well as
- Weight loss despite a healthy appetite.
- Heat intolerance,
- Diarrhoea
- Polyuria
- Irritability
- Emotional liability
- Psychosis
- Itching
- Eye discomfort and DOUBLE VISION
- Fatique and Weakness
- Loss of Libido

Signs:
1. Tachycardia
2. AF
3. Warm peripheries
4. Fine Tremor
5. Warm,moist skin
6. Palpitations
7. Palmar erythema
8. Hair thinning
9. lid lag (eyelids lag behind eye' s decent as patient watches your finger descend slowly)
10. lid retraction (sclera exposed above iris causing a stare)
11. Nervousness
12. Anxiety, Hyperactivity, Dysphoria
13. +/- a goiter
14. +/- thyroid bruits
15. Proximal muscle weakness
16. Gynaecomastia

Laboratory investigations:
- Ask for T3 and T4 as well as TSH
- All will have ↓ TSH except for rare case of TSH-secreting pituitary adenoma)
- Most will have ↑ T4, 1% will only have ↑ T3

- [illegible]
- [illegible]
- Often at other sites such as [illegible] and [illegible]
- [illegible] with [illegible] [illegible]
- It is associated with [illegible]os and [illegible].
- [illegible]
- Often [illegible] or [illegible] or carbimazole.

Special investigations

1. [illegible] and [illegible]
2. [illegible] (<0.5)
3. ↑ I 131/ T99 uptake with a diffuse uptake pattern.
4. [illegible] Thyroid autoantibodies
5. [illegible]
6. [illegible]
7. [illegible] (ass. With DM)

Patients with exophthalomos have an [illegible] with [illegible], Infiltration by lymphocytes and macrophages and deposits of [illegible], fat and oedema.

THYROID EYE DISEASE:

Present in 70 % of patients with Grave's disease:

1. [illegible]
2. [illegible]
3. [illegible] and [illegible]
4. [illegible] – protruding eyes
5. [illegible]is – eyes protrude beyond the orbit
6. [illegible]
7. [illegible]
8. [illegible]
9. [illegible]
10. [illegible] esp. of upward gaze) due to fibrosis and muscle swelling

Treatment of opthalmopathy:

1. [illegible]
2. [illegible]
3. [illegible]
4. [illegible] (corneal ulceration)
5. [illegible] (Diplopia)
6. [illegible] (decreased acuity, papilloedema)

Patient can be hypo-, eu- or hyperthyroid on presentation. Eye signs can be present +/- Grave's Disease but is caused by an autoimmune process similar as found in this condition.

[illegible] and [illegible]

[illegible]

1. [illegible]
   - Nodular goiter
   - No eye signs
   - No pretibial myxoedema
   - No Thyroid stimulating globulin

If [illegible] in a [illegible] = [illegible]

2. [illegible]

3. [illegible]: Radioactive iodine is not increased.

4. [illegible]: Transient hyperthyroidism caused by iodine intake.

5. [illegible]

Choriocarcinoma, hydatiform mole as is secretes gonadotrophin which binds to the TSH receptors and stimulates thyroid tissue.

Management:

1. [illegible]: Propranolol for rapid control of symptoms
2. [illegible] Esp. in young patients, mild hyperthyroidism and a slightly enlarged goiter, during pregnancy.
   Thionamides: Thiourea, Propyl-thiouracil (PTU) and neomercazole or imidazole group (carbimazole).

   Carbimazole 40-60mg/24h in devided doses for 4 weeks reducing it to 20-40mg/day in devided doses for the next 1-2 months.Reduce further according to TFT every 1-2 months until maintainance of 5-20mg/day.
   Or give carbimazole and thyroxine simultaneously.
   SE:
   - Enlargement of goiter esp. when meds cause hypothyroidism [prevent by giving thyroxine simultaneously, but not together with PTU]
   - Agranulocutosis: leadign to life-threatening sepsis. If pt develops signs of infection, skin rask, pharyngitis, fever mouth ulcers treatment must be stopped and WBC count performed immediately.
   - Dermatitis, joint pains, myalgia, jaundice, fever, lympadenopathy.

1. Toxic ADENOMA (autonomically functioning adenoma)
   - Single nodule producing T3 and T4
   - Isotope scan (T99) shows a HOT nodule and the rest of the gland is suppressed
   - Tx: Radioiodine

Hyperthyroidism
CAUSES

2. Toxic multinodular goiter (Secondary hyperthyroidism)
   = Plummer disease

SEEN IN ELDERLY PT and Iodine deficient areas!

- Cervical swelling. Thyroid nodules secreting thyroid hormones.
- Heavy sensation when swallowing
- Kinking of the trachea – pt awakens at night with dyspnoea
- Haemorrhage into a nodule can cause respiratory distress.
- NO EYE SYMPTOMS
- Px: IODISED SALT
- MX: Exogenous thyroid hormone: 0,2 mg thyroxine dly. Or radioactive iodine
- **Indications for surgery:**
  1. Pressure symptoms: Dysphagia or dyspnoea
  2. Cosmetic considerations
  3. Fear of malignancy (Esp. When one dominant nodule palpated)
- When Surgery has to be performed:
  SUBTOTAL THYROIDECTOMY
  Patient prepared with bedrest, controlling of cardiac failure if present and a short course of lugol iodine. Add a beta-blocker when cardiac failure under control. Perform a sub-total thyroidectomy.
  If cardiac failure is uncontrollable – Tx with radioactive iodine with doses higher than for Grave's.

3. GRAVE's/ BASEDOW's disease (Primary Hyperthyroidism) – 60-80 % of thyroitoxicosis!

- Common in ages 20-50 years old, females > males
- Autoimmune disease caused by Stimulating TSI receptor antibodies which also reacts with orbital autoantigens.
- Diffuse thyroid enlargement
- Hyperfunctioning/hyperthyroidism
- Associated with other autoimmune diseases: Vitiligo, Type 1 DM, Addison's disease

Symptoms:

a. Anxiety and tremor
b. Tachycardia
c. Sweating and heat intolerance
d. Dry mouth and thirst
e. Weight loss despite a healthy appetite
f. Muscle weakness
g. Dyspnoea
h. Frequency
i. Diarrhoea

Signs:

a. Restless
b. Anxious
c. Hyperactive
d. CARDIOVASCULAR: Tachycardia and AF, sometimes an ejective systolic murmur present. Pulse pressure increased. Peripheral vasodilatation with palmar erythema.
   In older patients cardiac failure present
e. Sweating hands, onycholysis
f. Diffuse enlarged thyroid often asymmetrical +/- a brult
g. EYE SIGNS: 70% have eye signs.

- No signs or symptom
- Only signs (Lid Retraction and Lag)
  No signs
- Soft tissue involvement (Peri orbital oedema)
- Staring gaze
- Rare and grittiness
- Widening of palpebral fissure
- Discomfort and photophobia
- Proptosis (eye protrusion of > 20mm) becoming pronounced with exophthalmos later – this leads to corneal ulceration due to the inability of the eyes to close properly.
- Extra-ocular muscle involvement (Diplopia and Loss of convergence due to muscle weakening esp. of sup. rectus muscle.
- Corneal involvement: Keratitis
- Sight loss (compression of the optic nerve)
- Lid lag when eyes look downwards
- Chemosis
- Inflammation

Primary Hypothyroidism

1. Autoimmune hypothyroidism (Hashimoto's atrophic thyroiditis)
2. Iatrogenic (Radioactive iodine treatment, thyroidectomy, external irradiation of the neck)
3. Drugs: Iodine excess-causes hypothyroidism causes a goitre in patients with underlying auto-immune thyroiditis, lithium, antithyroid drugs, Amiodarone
4. Iodine deficiency
5. Infiltrative disorders of the thyroid – amyloidosis, Sarcoidosis, Haemochromatosis, scleroderma.

Secondary Hypothyroidism is very rare.

NB: Association with hypothyroidism disease:

- Turner's syndrome
- Down's Syndrome
- Cystic fibrosis
- Primary Billiary Chirrosis
- POEM's syndrome [Polyneuropathy, Organomegaly, Endocrinopathy,M-protein band from plasmacytoma and Skin pigmentation/leiherioc].

Treatment:

1. **Levothyroxine**
   If no residual thyroid function 1.5 microgram/kg/day
   Patients under age 60 without cardiac disease can be started on 50 – 100 micrograms/day and the dose adjusted according to TSH levels.
   In elderly especially those with CAD the starting dose should be much less (12.5 – 25 micrograms/day)

NB: Long term effects of thyroxine = Osteoporosis and Accelerated Artherosclerosis.

Subclinical Hypothyroidism:

RAISED TSH WITH NORMAL T4 → Antibody +
→ Previous treatment for Grave's
→ Other organ specific autoimmune disease
→ TSH > 10

If YES: Thyroxine treatment until TSH in N range
If NO: 6 -12 monthly TSH measurement. If symptomatic a trial of Thyroxine.

Euthyroid sick syndrome

- ↓T4 and T3
- Inappropriately normal/↓ suppressed TSH
- In the context of starvation or severe illness
- Not a primary thyroid disease
- Unclear if any benefit from thyroid therapy

Thyroiditis

Acute: Rare, due to suppurative infection of the thyroid
Subacute: De Quervians thyroiditis/ granulomatous thyroiditis – mostly viral
Chronic: Mosly autoimmune (Hashimoto's)

Acute:

1. Bacterial: Staphs/Streps
2. Fungal: Aspergillus, Candida, Histoplasma, Pneumocystis
3. Radiation
4. Amiodarone: Normal thyroid function, ERS raised, Painful thyroid.

Subacute:

Viral (granulomatous) – mumps, coxsackie, influenza, adeno and echovirus

- Mostly affects middle aged females
- 3 phases:
  - Painul,
  - enlarged thyroid
  - Complete resolution
- Tx: NSAIDS and glucocorticoids when necessary

Chronic:

1. **Hashimoto's thyroiditis:** MOST COMMON CAUSE OF HYPOTHYROIDISM!

   Autoimmune disease as above plus initial goiter due to lymphocytic and plasma cell infiltration, fibrosis and follicular cell hyperplasia.
   Later- very little thyroid tissue left.
   Rarely associated with pain. Common in females 20-60 years.
   Antibody titres are very high.
   T4 Normal and TSH moderately increased.
   It has an insidious onset and progression.

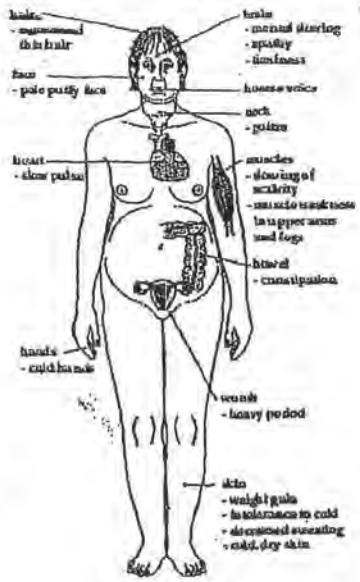
2. Reidel's: Rare, middle aged women. Painless and insidious course. Symptoms are due to compression. A dense fibrosis develops. There is usually no thyroid function impairment.

ernal TU: [illegible] of absorbed iodine. 2. Inhibits incorporation of iodine into iodothyrosine and iodothyronine and inhibits the bonding of iodothyrosines. 3. Inhibits conversion of l-thyroxine to L –tri-iodothyronine (t3) in peripheral tissues.

3. Radioactive iodine (I 131) Cx: hypothyroidism
4. Thyroidectomy Indications: Pressure symptoms already present, fear of malignancy, failed medical management, cosmetic reasons, pregnancy, Young patients Cx: Damage to Recurrent L nerve – hoarseness and hypoparathyroidism.

Clinical presentation:

1. Tiredness and weakness
2. Depression
3. Dry skin
4. Feeling Cold
5. Hair loss
6. Difficulty in concentrating and poor memory
7. Constipation
8. Myalgia
9. Weight gain and poor appetite
10. Hoarse voice
11. Menorrhagia, later oligo- and amenorrhoea
12. Paresthesia
13. Impaired hearing



Symptoms of hypothyroidism

Examination:

- **General:** Dry skin and cool extremities
  Puffy face, hands and feet- Toad like face! [NON-PITTING OEDEMA]
  Diffuse Alopecia
  Dry coarse hair
  Hoarse voice
- **Cardio:** Bradycardia
- **Respiratory:** Serous Cavity effusions
- **Musculoskeletal:** Delayed, slow relaxing tendon reflexes
  Carpal tunnel syndrome
- **Neurological:** Cerebellar ataxia, peripheral neuropathy,
- +/- a goiter, signs of CCF or pericardial effusion

Dementia in elderly pt! Check thyroid first!

SI:

1. TSH↑, free T4↓. But in secondary hypothyroidis: T4 ↓ and ↓/N TSH due to lack of the ptuitary
2. U/S and Scintigraphy are of little value
3. Anti TPO Antibodies +
4. S-CK↑, S-Chol ↑, s-TGL ↑
5. Normochromic or macrocytic anaemia
6. ECG: Bradycardia with small QRS complexes

CUSHING SX

Also called hyperadrenocorticism or hypercorticism. Caused by high levels of cortisol in the blood.

Causes:

Exogenous (ACTH ↓ due to – feedback)

1. Iatrogenic: Glucocorticosteroids as medication for e.g. Asthma, RA, immunesuppresion after organ transplant. – MOST COMMON

Endogenous

1. Tumours producing cortisol or ACTH
2. Cushings disease: Bilateral adrenal hyperplasia due to an ACTH secreting non-cancerous pituitary adenoma (microadenoma) – 85% OF ENDOGENOUS CAUSES (↑ ACTH)
3. Adrenal adenoma or carcinoma (carcinoma may be associated with abdominal pain and virilization in females. (↓ACTH)
4. Adrenal nodular hyperplasia (↓ACTH)
5. Hyperplastic adrenal glands (↓ACTH)
6. Ectopic ACTH production: *Paraneoplastic cushing's syndrome with small cell lung cancer and carcinoid tumours.* (↑ ACTH)

Cushing's syndrome can also be sub-classified according to whether or not the excess cortisol is dependent on increased ACTH.

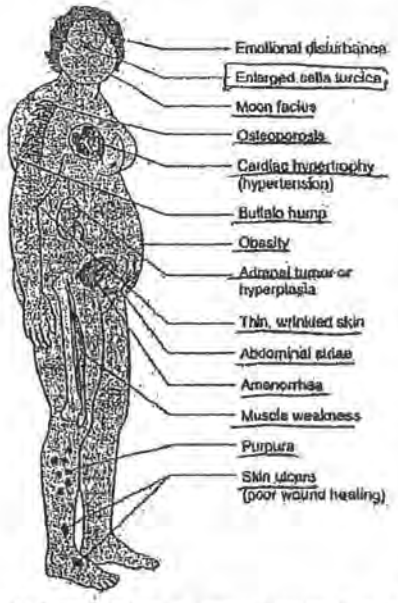
- *ACTH-dependent* Cushing's syndrome is driven by increased ACTH and includes exogenous ACTH administration as well as pituitary and ectopic Cushing's.
- *ACTH-independent* Cushing's syndrome shows increased cortisol, but the ACTH is not elevated but rather decreased due to negative feedback. It can be caused by exogenous administration of glucocorticoids or by adrenal adenoma, carcinoma, or nodular hyperplasia.

Untreated Cushing's syndrome can lead to heart disease and increased mortality.

Pseudo Cushing's:

1. Alcohol excess – stimulates adrenal glands.
2. Major depression – Increases stress response
3. Obesity: Simple or as part of Metabolic syndrome

1. PATIENT PRESENT TO YOU WITH:



1. Weight gain – central obesity (trunk and face and sparing the limbs)

2. Buffalo hump and supraclavicular fat distribution: Fat pad growth along collar bone and back of neck – lipodystrophy

3. Moon face

4. Sweating

5. Telangiectasis (dilation of capillaries)

6. Thinning of skin – easy bruise, dryness esp. of the hands and other mucous membranes.

7. Purpura

8. Purple striа (the weight gain in Cushing's syndrome stretches the skin, which is thin and weakened, causing it to hemorrhage) on the trunk, buttocks, arms, legs or breasts)

9. Proximal muscle weakness (hips, shoulders)

10. Gonadal dysfunction: females: Hirsutism, Acne, Irregular menses, amenorrhoea, infertility, reduced libido. Males: Impotence. Hirsutism is a male-pattern hair growth in a female, and/or cause hair to become extremely dry and brittle. Oligomenorrhea (decreased frequency of menstruation) due to elevations in androgens (male sex hormones), normally at low levels in women.

11. Hypercalcaemia: leading to skin necrosis.

12. Osteoporosis (+/- fractures), persistent hypertension due to cortisol's enhancement of adrenaline's vasoconstrictive effect

12. Glucose intolerance/ Insulin resistance or overt DM leading to increased infections and slow wound healing. Also Polyuria and polydipsia

13. Psychological disturbances: Euphoria, irritability, Depression, Psychosis, Anxiety.

14. Hyperpigmentations: Cushing's due to increased ACTH (POMC → ACTH and Melanocyte stimulating hormone).

EYE SIGNS ⇒ INFECTIONS ⇒ keratitis,
⇒ Cataracts, retinal detachment

HYPERTENSION ⇒ Na ⇑ K retention.

Polycythaemia,

Zona glomerulosa – Aldosterone.
Zona Fasciculata – cortisol.
Zona Reticularis – Androgens.

15. Cortisol's can exhibit mineralocorticoid activity in high concentrations worsening hypertension and leading to hypokalaemia (common in ectopic ACTH secretion).

16. Gastrointestinal disturbances, opportunistic infections and impaired wound healing (cortisol is a stress hormone, so it depresses the immune and inflammatory responses).

17. Cushing's may cause sore and aching joints, particularly in the hip, shoulders, and lower back.

SPECIAL INVESTIGATIONS: DO NOT PERFORM RANDOM CORTISOL LEVELS – OF NO VALUE!

1. Confirm the diagnosis
2. Localize the source by using laboratory investigations and imaging studies

When suspect Cushing's Syndrome:

A. Overnight dexamethasone suppression test: Give the patient 1 mg dexamethasone @ midnight, check serum cortisol < and > 8 am.

In normal patients: High dose of cortisol causes – feedback and thus ↓ ACTH and ↓ Cortisol to < 50nmol/L.

In Cushing's syndrome: Failure to suppress cortisol secretion. Thus high levels of cortisol detected

OR

B. 24 h urinary free cortisol (N value < 280nmol/24h)

FALSE + : (Pseudocushing's) seen in Depression, Obesity, Alcohol excess, and inducer of liver enzymes such as phenytoin, phenobarbital, Rifampicin as it increases the rate of cortisol metabolism.

2.Localize the lesion

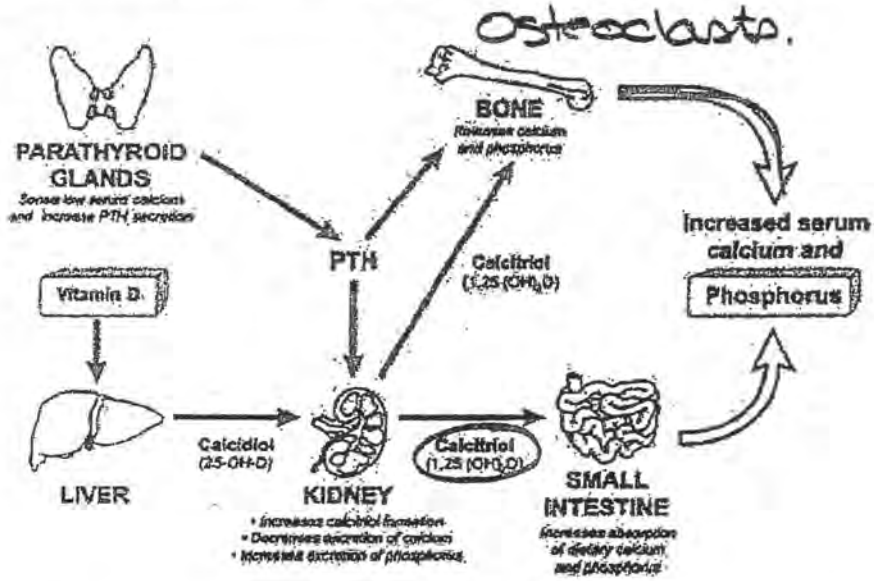
- Do plasma ACTH – if undetectable, adrenal tumor likely.
- Do physical examinations to determine any visual field defect if pituitary lesion is suspected?
- CT scan of adrenals and MRI of pituitary gland to detect presence of adenomas.
- Scintagraphy of the adrenal gland with Iodocholestrol scan.

TREATMENT:

1. Carefully taper off and eventually stop medication e.g. steroids, causing symptoms
2. Adrenal adenoma may be removed by surgery
3. ACTH-secreting corticotrophic pituitary adenoma should be removed after diagnosis.
4. Medications: Ketoconazole, metyrapone, aminogluthimide
5. Removal of the adrenals in the absence of a known tumor is occasionally performed to eliminate the production of excess cortisol. This occasionally removes neg feedback from previously occult pituitary adenoma which starts growing rapidly and produces extreme levels of ACTH leading to hyperpigmentation = this is called NELSON's SYNDROME!

Parathyroid hormone (PTH) and hyperparathyroidism

If ↓Ca 2+ in the blood → PTH ↑ in response. Secretion inhibited by low serum Mg.
Not influenced directly by PO43- (except by PO4 effect on the ionic calcium levels)
PTH secreted by 4 parathyroid glands situated posterior to thyroid.



PTH actions:

1. Increase osteoclast activity (bone resorption) releasing Ca 2+ and PO4 3- from the bones.
2. Increases Ca 2+ and Mg absorption and decreases PO4 3- and HCO3 absorption in the renal tubules.
3. Increase active 1.25dihydroxy-cholecalciferol (Vitamin D3) production.
4. Increased Ca 2+ and PO 4 absorption from gut
5. NET EFFECT: increased serum Ca 2+ —> increased vit D, decreased PO 4

Patient presents with:

1. Asymptomatic with ↑Ca2+ on routine tests.
2. Symptoms related to ↑Ca2+
    - Weakness
    - Tiredness
    - Depression
    - Polyuria and Polydipsia
    - Renal STONES
    - Abdominal pain
    - Bone resorption effects: pain

On examination:

1. Dehydration
2. Pancreatitis
3. Ulcers (duodenal:gastric = 7:1 MEN 1 causes ↑PTH and Zollinger Ellison syndrome)
4. osteopenia and osteoporosis, #'s
5. ↑BP and when untx – cardiovascular risk and mortality

Associated with MEN! (multiple endocrine neoplasia)

Causes and differential dx:

Primary hyperparathyroidism(↑Ca2+, ↑PTH)	80-85% = solitary adenoma, 15-20% = hyperplasia and <0.5% = carcinoma.
Secondary:(↓Ca2+, appr ↑ PTH)	Same as for hypocalcaemia = Malabsorption, Osteomalacia, Rickets, Low Vit D intake, chronic renal failure.
Tertiary:(↓Ca2+, inappr ↑↑ PTH)	After prolonged secondary hyperparathyroidism causing glands to act autonomically having undergone hyperplastic or adenomatous changes. Ca2+ increases unlimited by feedbaxk control. Seen in chronic renal failure.
NB: Malignant hyperparathyroidism:	Parathyroid related protein (PTHrP) produced by some squamous cell lung cancers, breast and renal cell carcinomas. This mimics PTH resulting in ↑Ca2+ but ↓PTH as PTHrP not detected in the assay

Investigations:

1. **↑PTH, ↑Ca2+**
   [Diefferetials with these tests: Lithium, Thiazides, Familial hypocalcuria, Hypercalcaemia, tertiary hyperparathyroidism.
2. **↓PO43-** (unless renal failure)
3. **↑ALP levels** from bone activity
4. 24h **urinary Ca2+↑**
5. **DEXA bone scan** to assess osteoporosis
6. OSTEITIS FIBROSIS CYSTICA = BM fibrosis and cyst formation due to severe resorption : **Brown tumours, Subperiosteal erosions of distal phylanges on hand Xrays, pepper-pott skull on skull Xrays.**

Treatment:

Surgery prevents #'s and peptic ulcers.

Indications for surgery [excision of all 4 hyperplastic glands or adenoma:

1. High serum or urinary Ca2+
2. Bone disease
3. Osteoporosis
4. Renal calculi
5. Decreased renal function'age <50 years

CX of surgery:

- Hypoparathyroidism
- RLN damage (hoarse voice)
- Post-op symptomatic ↓Ca2+ - check Ca2+ for 14 days post-op.

Mild symptoms does not validate surical removal:

1. Advise – Increase fluid intake to prevent stones
2. Avoid thiazides or high Ca2+ and Vit D intake
3. Review in 6 months
4. Cincalcet (Increases Parathyroid cells to Ca2+ thus ↓PTH secretion
   S/E: Myalgia, decreased testosterone.

Hypercalcaemia

Serum Ca 2+ is about 50% protein bound (mostly albumin) and not exchangeable and alterations in protein content of the blood for any number of reasons may affect the total serum Ca 2+ without altering the ionized form.

Normal total serum Ca 2+ range is 2.25-2.62 mmol/L

Definition of Hypercalcaemia = Total corrected serum Ca 2+ > 2.62 mmol/L (10.5 mg/dL) OR Ionized Ca2+ > 1.35 mmol/L (5.4 mg/dL)
It is a medical emergency!

Sources of ECF Ca 2+ : diet and resorption from bone
Loss of Ca 2+ from ECF space via: GI losses, renal excretion and deposition in bone matrix
Calcium regulated mainly by two factors: parathyroid hormone (PTH) and Vitamin D
And its actions is mainly on three organs: GI tract, bone, and kidney

Vitamin D
Necessary for Ca 2+ and PO 4 absorption from GI tract
Production of 1,25 Dihydroxy-Vit D *is enhanced* by PTH and low PO4 levels

Calcitonin
- Polypeptide secreted by thyroid C cells
- secretion enhanced by Ca 2+ , GI hormones, pentagastrin
- major actions: Decreased osteoclastic bone resorption, increased renal PO 4 and Na+ clearance

ACUTE NET EFFECT: decreased serum Ca2+ when given in pharmacologic doses

Magnesium
major intracellular divalent cation
Ca 2+ is resorbed from the kidney with Mg, and thus Ca 2+ balance is difficult to maintain in Mg deficiency

Phosphorus
Found in all tissues and necessary for most biochemical processes as well as bone formation

Parathyroid Hormone (PTH)
Increased Ca 2+, vit D
decreased PO 4

Vitamin D
Increased Ca 2+, PO 4

Calcitonin
decreased Ca 2+ (In pharmacologic doses)

PATIENT PRESENTATION: **BONES, STONES, MOANS AND ABDOMINAL GROANS**

- STONES (kidney):Polyuria, polydipsia, Renal colic
- MOANS (mental)Lethargy, Depression, Drowsiness, Decreased cognitive function
- ABD GROANS(GIT)Anorexia, Nausea, Dyspepsia, Constipation, Peptic ulcer
- BONES:Hypotonia, bone pain.
- Primary Hyperparathyroidism:

1. Asxs ·
2. Renal calculi ,
3.Hypertension ·
4. Acute dehydration ·
5.Tumours never palpable ·
6.Arrhythmias ·

Pathophysiology
Increased bone resorption
Increased gastrointestinal absorption
Decreased renal excretion

Causes:
With Normal or ↑PTH levels:
> 90% of hypercalcemia is caused by either parathyroid disease or malignancy.
1. Primary or tertiary Hyperparathyroidism
2. Lithium induced hyperparathyroidism
3. Familial hypocalciuric hypercalcuria

With ↓PTH levels:
1. Malignancy: Lung, Breast, Renal, Ovarian, Colonic, Thyroid Multiple myeloma
2. ↑ 1,25(OH)2 Vit D due to intoxication e.g Sarcoidosis
3. Thyrotoxicosis
4. Paget's Disease with immobilization
5. Milk-alkali syndrome
6. Thiazide diuretics
7. GlucoCS deficiency

Investigations:
1. Serum Ca 2+ , PO4 , PTH, diagnostic imaging for renal calculi and osteopenia

Treatment of Hypercalcemia

Treat acute, symptomatic hypercalcemia aggressively with rehydration and calciuresis
- IV NS infusion (**usually requires 4-6 L of fluid)**
- Only after adequately rehydrated, **promote calciuresis with a loop diuretic, i.e. furosemide**
- **bisphosphonates** is the treatment of choice as it inhibits osteoclast activity. It is indicated in malignancy-related hypercalcemia. **Pamidronate** is most commonly used via IV route since poorly absorbed from the GI tract. It takes several days until full effect but effect is long-lasting. Mithramycin is effective when patient can not tolerate large fluid load (dangerous - hematotoxic and hepatotoxic)
- **Calcitonin:** inhibits osteoclastic bone resorption and promotes renal excretion of calcium. Combination of calcitonin and steroids may prolong reduction in calcium
- **Steroids:** anti-tumour effects. useful in vitamin D-related hypercalcemia (including sarcoidosis) and hematogenous malignancies (myeloma, lymphoma). Slow to act (5-10 days); need high dose
- **Prostaglandin inhibitors**

Surgical treatment if indicated
Avoid immobilization

HYPOPARATHYROIDISM

Primary:

Clinical presentation:

1. Tetany
2. Depression
3. Perioral parasthesia
4. Trousseau's sign [wrist flexion, fingers drawn together if brachial artery occluded with BP cuff]. for 3 mins

5. Neuromuscular excitability e.g. tapping over the parotid (facial n.) causes facial muscles to twitch [Chvostek's sign].
6. Chronic Hypocalcaemia = Cataract
7. ECG: prolonged QT interval.

Investigations:

1. ↓Ca2+
2. ↑ PO43-/N
3. Normal ALP

Causes:

1. Autoimmune [associated with other autoimmune diseases].
2. Congenital – Di george syndrome

Tx: Alfacalcidol

Secondary:

Due to radiation, surgery (thyroidectomy/parathyroidectomy), hypomagnaesemia.

Pseudohypoparathyroidism:

Failure of target cells to respond to PTH.

SIGNS: Short metacarpals (esp. 4th and 5th), round face, short stature, mental retardation.

SI:

1. ↑PTH
2. ↑/N ALP
3. ↓ Ca2+

Tx: The same as for primary.

Endocrine Emergencies:

*Thyroid 'storm'

-Severe Thyrotoxicosis, [mortality = 10%]
-Most commonly caused by infection in an undiagnosed/improperly treated hyperthyroidism

-Clinical sx's
-fever,agitation,confusion,tachycardia,AF,cardiac failure(older pt's)

-Treatment Neo comazole
-IV fluids 10% GLUCOSE, VITAMINS, CORTISONE,
-Broad spectrum ab
-B-blockers(Propanalol)80mg/6hours p/o or 1-5mg/6hours IV
-Radiographic contrast(Sodium Idopate)500mg daily p/o will normalise T3 levels within 48-72 hours by inhibiting the release of thyroid hormone + reducing conversion of T4 to T3
-Dexamethasone 2mg/6hours or Amiodorone have similar effects
-Carbimazole 40-60mg daily p/o inhibits the synthesis of new thyroid hormone
After 10-14 days the pt can be managed on carbimazole alone.

*Myxodoema Coma

-Rare presentation of hypothyroidism [mortality = 50%]
-Usually in elderly pt's who appear myxoedematous

-Clinical sx's
-decreased LOC,temp as low as 25,convulsions,increase in CSF pressure and proteins

-Treatment
-Throxine IV(not usually available)
-Triidothyronine IV bolus 20 ug followed by 20ug/8hours until clinical improvement

*Hypoglycaemia

-BG<3.5 mmol/l [mortality 2-4% in insulin treated pt's]
-Usually due to overtreatment of DM(usually insulin)

-Clinical sx's
-Autonomic sx's: sweating, trembling, anxiety
-Neuroglycopenic sx's: Confusion, drowsiness, inability to concentrate, speech difficulty
-Non-specific sx's: nausea, headache

-Risk factors for developing hypoglycaemia
-strict glycaemic control
-age (very young and very old)
-sleep

-longstanding diabetes
-Hx of previous hypoglycaemia
-renal impairment

-Treatment
-Oral carb treatment (able to swallow)
-[adults]30-50ml of 20-50% dextrose or glucagon 1mg IM
-[children]IV dextrose 0.2g/kg
-Where intermediate/long acting medication is used, relapse may occur after initial treatment
-Relapse:10%dextrose infusion, titrated to pt's BG
-Consciousness not regained: suspect cerebral oedema = mannitol + oxygen
-Adjust future pharmacotherapy to prevent future episodes

**Adrenal insufficiency*

-inadequate secretion of cortisol and/or aldosterone
-Secondary(more common) = 1.]withdrawal of glucocorticoid therapy
2.]hypothalamic or pituitary disease

-Primary(rare) =1.]Addisons disease(due to autoimmune,HIV,TB,malignancy
2.]Congenital adrenal hyperplasia

-Tests for glucocorticoids
-ACTH stimulation test to differentiate between primary and secondary
-Administer 250ug ACTH IM: if cortisol levels fail to respond=adrenal insufficiency
-Decreased ACTH = secondary ; increased ACTH = primary

-Clinical sx's
-can present with: circulatory shock with severe hypotension, hyponatremia, hyperkalemia, and in some instances hypoglycaemia and hypercalcaemia.
-muscle cramps, nausea, vomiting, diarrhoea, fever
-Vittiligo in 10-20% of pt's with auto-immune Addisons

-Treatment
-Cortisol(hydrocortisone)15mg @ waking and 5mg @ 18:00 p/o
-Individual dosages and responses may vary
-Adrenal crisis is however an EMERGENCY!
-IV hydrocortisone succinate 100mg + IV fluids(saline + 10% dextrose for hypoglycaemia)
-IV hydrocortisone should continue @100mg/6hours until GIT symptoms go away

Manage of glucocorticoid treatment
(see clinical features of cushing disease)

-Treatment

-Cortisol(hydrocortisone)15mg @ waking and 5mg @ 18:00 p/o
-Individual dosages and responses may vary
-Adrenal crisis is however an *EMERGENCY!*
-IV hydrocortisone succinate 100mg + IV fluids(saline + 10% dextrose for hypoglycaemia)
-IV hydrocortisone should continue @100mg/6hours until GIT symptoms go away

-Hazards of glucocorticoid treatment

-(see clinical features of cushin's disease)

4

Haematology

The Red cell
- Erythropoiesis & Haemoglobin
- Anaemias:
  - -Approach
  - -Iron deficiency
  - -Anaemia of chronic disease
  - -Sideroblastic anaemia
  - -Thalassaemia
  - -Haemolytic anaemias
  - -Aplastic anaemia
  - -Megaloblastic anaemia
- Myeloproliferative disorders
- The Spleen

The White cell
- Neutrophil
- Eosinophil
- Basophil
- Lymphocyte
- Monocyte

The Platelet & Bleeding disorders

Leukaemia

Lymphomas

Multiple myeloma

DVT