Contents

CVS REVISION - 1

----- Active space -----

Aortic Valve Disorders :

- Ⓝ Aortic valve
  - 3 leaflets/cusps → if → ↓ → ↑ risk of stenosis; ↑ → ↑ risk of regurgitation
  - 3 commissures
  - 1 fibrous annulus

Aortic Stenosis (AS)

00:04:37

Pathophysiology :

Degeneration/calcification of aortic valve + Inflammation (a/w atherosclerosis) → Aortic sclerosis → Gradient + → Aortic stenosis.

- Young : Bicuspid valve (BAV).
- Elderly : Degeneration & calcification.

Features :

- BAV → Young patients :
  - NOTCH 1 defect.
  - Associated with aortopathies (Mandatory CT aortogram).
- Tricuspid valve : > 60 y/o.

Note → Rheumatic etiology :

- Uncommon for AS.
- Rheumatic fever + Valvulitis (MR > MR + AR) → 15 – 20 y → RHD (MS + MR > MS + AR > AR + AS.)

Hemodynamics :

- Aortic valve opens at the end of isovolumetric contraction.
- Ⓝ gradient b/w LV & aorta is zero (LV = 120 mmHg, Aorta = 120 mmHg).
- AS : Valve does not open completely → Gradient ⊕ ∝ Severity of disease.

Note : Gradient = Mean transvalvular pressure gradient (MTPG).

Severe AS : Given by 40/4/1 rule :

- MTPG > 40 mmHg (In sclerosis < 20 mmHg).
- Peak flow velocity > 4 m/s (Across valve).
- Surface area of valve < 1 cm^2 (Normal : 3 – 4).

Compensatory mechanism : To maintain cardiac output.

Concentric LV hypertrophy → ↑ LV mass + ↓ cavity size.

Mild/Moderate AS : Asymptomatic	Severe AS : Symptomatic	Very severe AS : LV failure (Poor prognosis)

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Clinical Features :

	Angina	Syncope	Dyspnea
Poor prognosis if untreated after	5 yrs	3 yrs	2 yrs

Angina :

- ↑ LV mass → ↑ O_2 demand.
- ↓ capillary density (w.r.t. wall thickness).
- Tachycardia → ↓ perfusion time.
- Atherosclerosis.

Syncope : D/t LV outflow obstruction → Fixed cardiac output state even when ↑ demand.

Dyspnea : D/t ↑ filling pressure (LVEDP).

↑ LVEDP → ↑ LAP → ↑ PCWP → Fluid escapes into pulmonary interstitium.

Exacerbating factors :

A - Fib :

- Contribution of atria to cardiac output ↑ (25 → 40%).
- Thus, A-fib is fatal in AS.

Systemic HTN :

- Masking of severe AS :
  ↑ SBP → ↑ Aortic pressure → ↓ Gradient (Falsely low).
- Thus, strict BP control needed.

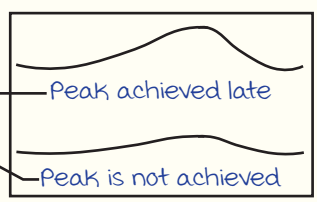
Diagnosis :

1. Transthoracic Echo : To look for 40/4/1 rule.
2. Angiogram : Mandatory (To rule out atherosclerosis).
3. CT aortogram.
4. Dobutamine stress echo : To differentiate b/w
   LV failure d/t AS (vs) Mild AS with Pre - existing LV failure
   Low flow low gradient.

Examination Findings :

Pulse : Slow rising pulse

- Severe AS : Pulsus tardus.
- Very severe AS : Pulsus parvus et tardus.



BP : D/t LVH → Masks AS.

JVP : Only elevated in terminal patients (Not relevant).

Apex : Laterally displaced Heaving apex (High amplitude sustained apex).

Heart sounds :

- S1 : (N) (Ejection click → mistaken for loud S1).
- S2 (A2) →
  - Loud : BAV (Young).
  - Soft : Elderly (Calcified valve).
  - Reverse/paradoxical split (P2 → A2) : Severe AS.

- S3 : Ⓝ/Less than Ⓝ filling of a non – compliant dilated ventricle. → Pathological : LV failure (Very severe AS). OR Ⓝ/more than Ⓝ filling of a hypercompliant ventricle. → Physiological.

----- Active space -----

- S4 : Specific to AS — d/t healthy LA contraction ⊕ → Non – stenosed mitral valve (No MS). / Hypertrophied, non-dilated LV (no MR, AR).
- Murmur :
  - Harsh ejection systolic murmur with late systolic accentuation.
  - Best heard in aortic area & sitting position.
  - Mixed frequency → Low freq : Loud → Carotids. / High freq : Soft blowing, musical → Apex (Gallavardin phenomenon).

Management :

1. Aortic valve replacement (AVR) :
   a. Done in Severe AS.
   b. Bioprosthetic valves (No anticoagulation needed).
   c. Asymptomatic severe AS : Follow-up → Gradient > 50mmHg OR Symptoms → AVR.
   Note : AS has a risk of sudden cardiac death.
2. Transcatheter Aortic Valve Implantation (TAVI) : If surgery is C/I.
   Not open surgery; no ICU stay.

Aortic Regurgitation (AR)

00:34:33

CHRONIC REGURGITATION

Etiology :

Root issue : Ⓥⓢ Valve leaflet issue :

- Syphilis
- Marfan's syndrome
- Ehler Danlos syndrome
- Takayasu arteritis
- Behcet's disease
- IgG4 related disease
- Cogan's syndrome

(Specific)

- Rheumatic cause
- Quadricuspid valve
- Takayasu arteritis
- Ankylosing spondylitis

Pathophysiology :

Hemodynamics :

- Ⓝ diastolic gradient between LV (10 mmHg) & aorta (80 mmHg) : 70 mmHg → Favours regurgitation.
- No backleak d/t competent aortic valve.

----- Active space -----

Exacerbating factors :

- Nocturnal angina : Bradycardia at night → more filling → Prolonged diastole → ↑ Regurgitation → ↓ Blood to coronary circulation → Angina
- Systemic HTN : ↑ Aortic pressure → ↑ Gradient → ↑ Regurgitation.

Relieving factor : Exercise/NTG/Nitroprusside.

Vasodilatation → ↓ Aortic pressure → ↓ Gradient → ↓ Regurgitation.

Compensatory mechanism : Eccentric hypertrophy with dilatation.

Clinical Features :

Mild/moderate AR :

- Asymptomatic (Since ejection fraction is ↑↑).
- Occasional palpitation.
- LVEDP & ESV (End systolic volume) is (N).

Severe AR :

- LV failure (Ejection fraction is (N) to low).
- LVEDP ↑↑ : Dyspnea.
- ESV ↑↑ : S_3 (+) ve.
- ↑ SBP & ↓↓↓ DBP (Almost zero) → Wide pulse pressure → Hill's sign : Lower limb BP exceeds upper limb BP by 20 mmHg.

Examination Findings :

Pulse :

1. Collapsing pulse : High volume (+) → Rapid upstroke & downstroke. / Ill – sustained peak.
2. Bisferiens pulse (AR/AR + mild AS/HCM) → Two peaks in systole.

Note : Pseudocollapsing pulse (Seen in MR) → (N) volume + Rapid upstroke/downstroke + well sustained peak.

BP : Wide pulse pressure.

JVP : Changes only in terminal disease.

Apex : Hyperdynamic apex, down & out.

Heart Sounds :

- S1 : Soft S1 (Premature closure).
- S2 : Delayed A2 / ↑ Blood in LV (+) → Root issue : Loud S2. / Leaflet issue : Soft S2.
- S3 : Heard in failure.

For S1 :

- Premature : Soft closure.
- Delayed : Loud closure.

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- S4 : Not heard.
- Murmur : EDM (End diastolic murmur).
  - High pitched, soft blowing.
  - Decrescendo.
  - Austin – Flint murmur : Low pitched d/t displacement of anterior mitral leaflet.
    ↓
    Cole Cecil murmur : Radiates to axilla.

Management :

AVR :

- Done in symptomatic severe AR.
- Asymptomatic patient with 55/50 rule → Ejection fraction ≤ 55 %.
  → LV end systolic diameter > 50 mm.

ACUTE REGURGITATION

Presentations :

Acute pulmonary edema (D/t sudden ↑ LVEDP → ↑PCWP) ± Cardiogenic shock.

Causes :

- Infective endocarditis.
- Aortic dissection : Acute AR + chest pain.
- Rupture of sinus of Valsalva : Acute AR + Right heart failure symptoms.
  - Immediate Mx : NTG/Nitroprusside.
  - Definitive Mx : AVR.

Mitral Stenosis (MS) 00:52:28

Mitral Valve :

- 3D structure.
- Surface area : 4 – 6 cm^2.
- Parts :
  - Annulus.
  - Leaflets with commissures.
  - Chordae.
  - Papillary muscles.
  - Adjacent LV myocardium.

Types of MS :

1. Progressive MS : > 1.5 cm^2
2. Severe MS : < 1.5 cm^2 → Asymptomatic / Symptomatic
3. Very severe MS : < 1 cm^2

Etiopathogenesis :

Main etiology : Rheumatic origin.

Main pathology : Commissural fusion → Fish mouth abnormality.

ARF —(15 – 20yrs)→ RHD → MS + MR (m/c).
RHD → MS + AR.

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Hemodynamics & compensation :

- Normal : Ventricular filling is passive > active & occurs across an open valve.
- In MS :
  - ↑ LAP at rest for ventricular filling.
  - On exertion → ↓ diastole time → ↑↑ LAP for ventricular filling.
  - Very severe MS : LV failure.

↑↑ LAP for ventricular filling. → ↑PCWP
↑PCWP —moderate MS→ Dyspnea
↑PCWP —severe MS→ ↑Pulmonary artery EDP → Pulmonary hypertension

- Dyspnea at rest
- RVH
- Hypertensive tricuspid regurgitation

First symptom of :
- AS : Angina
- AR : Palpitation
- MS : Dyspnea on exertion

Clinical Features :

- Pulmonary hypertension related symptoms.
- Pulmonary edema (In tachycardia).
- A – fib.
- Hemoptysis : D/t pulmonary capillary apoplexy.
- Ortner's syndrome : D/t compression of RLN.
- Hoarseness of voice.
- Dysphagia : D/t compression of esophagus.

Examination Findings :

Pulse : Normal.

BP : Normal.

JVP : Elevated (D/t RVH).

Apex : Tapping apex (Loud, ill-sustained S1).

Heart Sounds :

- S1 : Loud S1 → ↑ Velocity of valve closure.
  → Downward position of leaflets (D/t inadequate LV filling).
  → Delayed closure.
- S2 :
  - Loud, palpable P2 d/t Pulmonary HTN.
  - A2 – P2 widening : Pulmonary HTN with RV failure.
- Opening snap (OS) :
  - Seen in organic MS.
  - D/t ↑ LAP.
  - Severity of MS → Long duration of murmur.
    → Short S2 – OS gap.
- S3, S4 : Not seen.
- Murmur :
  - Low pitched, mid diastolic (MDM).
  - Presystolic accentuation (Absent in A – fib).

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Management :

1. Pulmonary edema → Control heart rate → β - blockers / Verapamil/Diltiazem
2. Anticoagulation : Oral vitamin K antagonists
3. Surgery : Percutaneous mitral balloon valvotomy /commissurotomy
   Upon failure : Mitral valve replacement.
   (1st line for : Calcific MS +/ mod/Severe MR/LA clot)
   ↓
   Dx : Trans esophageal echo

Mitral Regurgitation (MR) 01:10:38

Acute MR :

- D/t posteromedial papillary muscle rupture.
- Seen in inferior wall MI (RCA involvement).

Chronic MR :

1° MR :

- RHD : MS + MR (m/c).
- MVP : Developed countries.
- SLE/Rheumatoid arthritis.

2° MR (Innocent bystander mechanism) :

MR begets MR : LV dysfunction → Annular dilatation. → 2° MR. → LV remodelling → LV dysfunction

Pathogenesis :

Hemodynamics : Reduction in afterload.

LV - LA gradient >>> LV - Aorta gradient.

(LA = 10mmHg; LV = 120mmHg; Aorta = 120mmHg).

↓

Regurgitation into LA.

- Worsens with hypertension (↑ aortic pressure).
- Relieved by Nitrates : Vasodialation (↓ pressure).

LVEDP Ⓝ / LV ESV Ⓝ / Ejection fraction Ⓝ.

Compensation : Eccentric hypertrophy with dilatation of LV.

Clinical Features :

- Mild/Moderate MR : Palpitation/Asymptomatic.
- Severe MR : LV failure → Ejection fraction Ⓝ/ ↓ ↓ + LVEDP/LVESV ↑ ↑.

Examinations Findings :

Pulse : Pseudocollapsing pulse.

BP : Normal.

JVP: Normal.

Apex : Hyperdynamic apex; displaced down & out.

Heart sounds :

- S1 : Soft S1 d/t → Poor coaptation of leaflet. / ↓ ↓ dp/dt of isovolumetric contraction.
- S2 : Early A2 + Normal P2 → Wide split S2.

Pulse in LV failure :

- Pulsus alternans
- Pulsus dicroticus

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- S3 : Heard (Even without failure).
- S4 : Not heard.
- Murmurs : Pansystolic murmur.
  - High pitched.
  - Soft blowing.
  - Seen in the apex.
  - Radiates to axilla.

Myxomatous Degeneration :

MVP ± MR.

MVP

Click & murmurs : Non ejection click

- Dynamic auscultation (Valsalva & standing).
- ↓↓LV cavity size → ↓↓chordae stretch → ↑↑Prolapse → Click moves closer to S1 : Long duration murmur.
- All murmurs ↓on dynamic auscultation except :
  - HCM : ↑ intensity.
  - MVP : ↑ duration.

Management :

- Symptomatic : Surgery (Repair $\xrightarrow{\text{fails}}$ Replacement).
- Asymptomatic with 60/40 rule :
  - Ejection fraction ≤ 60%.
  - LV End Systolic diameter ≥ 40mm.

CVS REVISION - 2

----- Active space -----

Basics of Pulse

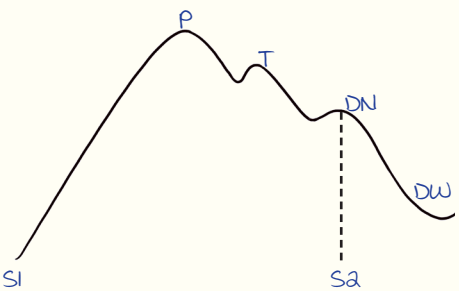
00:00:13

Features :

- Pressure wave.
- Origin : Aorta.
- Velocity : 5 m/s.
- Assesses LV contractile performance.

Pulse Wave :

1. Normal wave :



P : Pressure wave

T : Tidal wave (Aortic recoil)

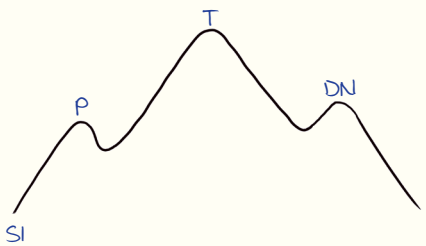
DN : Dicrotic notch

DW : Dicrotic wave (Reflected wave)

↓

Determined by : Peripheral resistance

2. Stiff/non-compliant vessels :



Cushioning effect of vessels lost

↓

↑ Pulse wave velocity

↓

Augments the T wave (DW arrives early)

↓

↑ Central SBP (CSBP) : Best marker for target organ damage

Abnormalities of Pulse

00:04:43

Relative Bradycardia :

- Rate of heart rate rise is < 10 beats per 1°F rise in temperature.
- Causes :
  - Non - infectious : Lymphoma, drug fever.
  - Infectious : Typhoid, brucella, Q-fever, dengue, leptospirosis, malaria. (Rare)

Rhythm Abnormalities :

Irregularly irregular : A - fib.

Regularly irregular : Ventricular premature contractions (VPC).

Volume Abnormalities :

Low volume (↓ Stroke volume)

1. Hypokinetic : LV failure
2. Pulsus tardus : Severe AS
3. Pulsus parvus et tardus : Very severe AS

High Volume (↑ Stroke volume)

1. Collapsing : AR
2. Pseudocollapsing : MR

----- Active space -----

Contour Abnormalities :

1. Pulsus bisferiens	2. Pulsus dicroticus	3. Pulsus alternans	4. Pulsus bigemini
2 peaks in systole	1 peak in systole 1 peak in diastole	Regular alternating high & low volume pulse	Irregular alternate high & low volume pulse
1. P > T HCM (with SAM) 2. P < T, P = T Severe AR ± mild AS	LV systolic failure	LV systolic failure	VPC

SAM : Systolic anterior motion

Note : Brockenbrough sign → ↓ Pulse volume post VPC (In HCM).

Variation with Respiration :

Pulsus paradoxus/
Normalis Aggregans :

- SBP ↓ ses by > 10 mmHg on inspiration.
- Causes :
  - i. Cardiac tamponade (m/c).
  - ii. Constrictive pericarditis (1/3rd cases).
  - iii. Hyperinflated lung.
  - iv. SVC obstruction.
  - v. Pulmonary embolism.
  - vi. RCM (Rare).

Reverse pulsus paradoxus :

- SBP ↑ses with inspiration.
- Causes :
  - a. Intermittent positive pressure ventilation (IPPV).
  - b. HCM.

Jugular Venous Pulse 00:14:00

Features :

- Height of column of blood above the sternal angle at 45°.
  Semi – recumbent position → ≥ 3 cm H_2O is elevated.
- Assess right heart filling → IJV used (Directly reflects right atrial pressure).
- RAP = 5 cm + IJV (Normal = 8 cm H_2O).

Causes of elevated JVP :

Pulseless elevation : SVC obstruction.

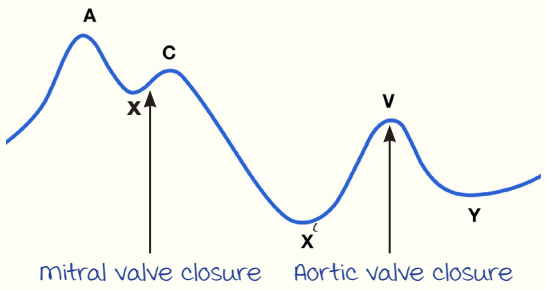
Pulsatile elevation :

1. Circulatory overload.
2. Tricuspid valve pathology (TS/TR).
3. Pulmonary artery pathology (Pulm HTN/embolism)
4. RV pathology (RVH).
5. Pulmonary valve pathology (PS/PR).
6. Right atrial pathology.

JVP Waveform :

----- Active space -----

Waves	Interpretation
a	Rt Atrial contraction (Presystolic)
x, x'	Atrial relaxation
c	Upward tricuspid bulge (Coincides with S1)
v	Atrial filling (Coincides with S2)
y	Atrial emptying (70% of ventricular filling)



Abnormalities :

Abnormal wave		Condition
a wave	1. Prominent	Tricuspid valve obstruction/RVH/Pulm HTN
	2. Giant/Cannon	AVNRT/Junctional rhythm/Complete heart block/VT with AV dissociation
	3. Absent	A-fib/Hyperkalemia
x descent	Prominent/Rapid	Cardiac tamponade/RCM/Chronic constrictive pericarditis (CCP)
	Absent	Tricuspid regurgitation (TR)/RV failure
v waves	Diminished	Hypovolemia
	Prominent	↑ Vena cava pressure : CCP/RV failure 2nd route : ASD/TR (Lancisi sign)
y descent	Prominent	CCP
	Slow	Tricuspid stenosis (TS)

Kussmaul's sign :

- Inspiration → ↑JVP.
- Causes : CCP/RCM/TS/RV MI.
- Not seen in cardiac tamponade.

Abdominojugular reflex : > 3cm/ > 15s → Impending right heart failure.

Heart Sounds

00:34:40

Low pitched heart sounds	Low pitched murmurs
• S3 • S4 • Tumour plop	• MS • TS • Austin Flint murmur

A. S1 :

- Cause : Closure of AV valves.
- Occurrence : Atrial contraction → (S1) → Isovolumetric contraction.
- Loud S1 : MS.
- Soft S1 : AR, MR, Good filling of the heart.

----- Active space -----

B. S2 :

- Split into A_2 → P_2 : Dlt hangout interval (A_2 : 30ms^{-1}; P_2 : 80ms^{-1}) → ∝ Pressure beyond valve.
  → ∝ $\frac{1}{\text{Distensibility of vessel}}$

	A2	P2
Loud	• BAV – AS • Root pathology	Pulm. HTN (Palpable P_2)
Soft	• Elderly AS • Valve pathology in AR	Pulm. stenosis

Wide variable split	Wide fixed split	Paradoxical split
• Early A2 / Delayed P2. • Cause : MR.	• Split does not move with respiration. • Causes : RV failure, ASD.	• Loud P_2 → A_2 • Causes : AR, AS.

Note : MS → Single loud P2.

C. S3 :

- Pathology : Ⓝ/Less than normal filling of a non-compliant dilated ventricle.
- Seen in :
  - AS/AR with failure.
  - MR with/without failure.

D. S4 : Seen in AS.

Added Diastolic Sounds :

O P Time

Early :

- Opening snap.
- Pericardial knock.
- Tumour plop.

3 → Mid → S3

4 → Late → S4

Systolic Clicks :

1. Ejection clicks :
   - Aortic ejection click : BAV.
   - Pulmonary ejection click (Does not ↑ on inspiration).
2. Non – ejection click : MVP

CVS REVISION - 3

----- Active space -----

Heart failure (HF) - Basics

00:00:20

Structural/functional impairment in the ability of the ventricles to pump out blood or fill itself.

Types of HF :

a. HFrEF : Ejection fraction < 40%.

b. HFpEF : Ejection fraction > 50%.

c. HFmEF : Mid range ejection fraction (40–50%).

Stages of HF :

A	B	C	D
Only risk factors eg : DM/HTN	A + Structural abnormality	B + Symptoms (Present/prior)	Advanced heart disease

m/c/c of mortality : Sudden cardiac death — Pump failure

NYHA Classification :

I	II	III	IV
Symptoms on exertion	Symptoms on ordinary activity	Symptoms on less than ordinary activity	Symptoms at rest

NYHA : Only for angina, dyspnea & palpitation (Not syncope).

Heart Failure (HF) - Symptoms

00:06:04

LV systolic failure

- Cachexia (TNF-α)
- ↓ Urine output (Cardio-renal syndrome)
- Altered sensorium
- Cold extremities
- O/E : Narrow pulse pressure, S3, cardiomegaly

↑LVEDP

- ↑LAP → ↑PCWP → Dyspnea → Pulm. edema → Orthopnea & PND
- O/E : Rales, S4

↑RVEDP

- ↑Abdomino jugular reflex (Impending failure)
- ↑ JVP (>3cm)
- Ascites
- Edema
- Hepatomegaly

Framingham's Criteria (Major) :

1. Dyspnea.
2. Acute pulmonary edema.
3. Rales.
4. S3.
5. JVP.
6. Abdominojugular reflex.
7. Cardiomegaly.

----- Active space -----

Dyspnea :

Due to ↑LVEDP → ↑LAP → ↑PCWP.

Bendopnea
• Dyspnea on bending forward • Advanced Lt & Rt HF • A/w ↑JVP & ↑PCWP

Trepopnea
• Dyspnea while lying on one side • Pleural effusion (more on right side)

Crepitations :

HF :	COPD :
• Fine gravitational crepts	• Non-gravitational
• Cold extremities	• Warm extremities

Other Symptoms :

1. Angina : D/t ↑LV mass, LVOT, microvascular disease.
2. Palpitation : D/t cardiomegaly.
3. Syncope : D/t LVOT obstruction.
4. Sinus tachycardia : ↑mortality.

Decompensation :

Factors precipitating acute HF :

1. Non compliance (Diet/drugs).
2. Infections (Eg : Infective endocarditis).
3. Anemia.
4. Arrhythmia (Eg : A-fib).
5. MI.
6. NSAIDs & β-blockers.

Heart Failure (HF) - Management

00:16:18

Investigations :

1. ECG :
   - Low voltage in limb leads.
   - High voltage in chest leads.
   - Poor R-wave progression.
2. ECHO : For ejection fraction.
3. Cardiac MRI : Gold standard.

Treatment Guidelines – HFrEF :

Drugs used (Fantastic 4) :

1. SNS blockers : β-blockers
   - Metoprolol.
   - Carvedilol.
   - Bisoprolol (Best : β_1 selective).
   - Started at lowest dose.
   - Patient should be dry (No edema).
2. RAAS blockers :

ARNI > ACEi > ARBs

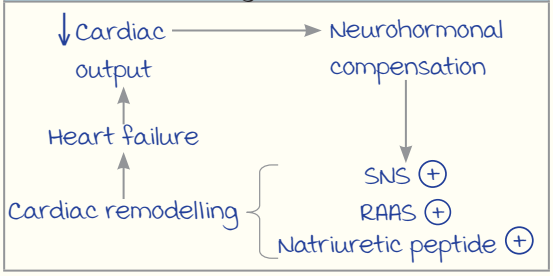
↓

AT – II inhibitor (Valsartan) + Neprilysin inhibitor (Sacubitril).

Note :

- HFpEF : Comorbidity mx.
- HFrEF : Guideline based mx.

Vicious cycle of HFrEF :



3. Mineralocorticoid receptor antagonist (MRA) :
   - Spironolactone/eplerenone/finrenone.
   - S/E : Hyperkalemia, gynecomastia.
4. SGLT2 antagonist : Dapagliflozin/Empagliflozin.

Mortality benefit
β-blocker > ARNI > ACEi > ARB > Hydralazine + Nitrate

Hydralazine : Used in renal failure with HF.

Add on drugs :

- Diuretics : Symptomatic relief.
- Ivabradine : Used if HR > 70 bpm + β-blockers max dose.
  - Inhibits funny currents.
  - S/E : Visual field abnormalities.

Ventricular Dysfunction

00:29:32

Types :

Systolic dysfunction	Diastolic dysfunction
Pumping issue	Filling issue
LV defect	RV > LV defect
F/b diastolic dysfunction	may have Ⓝ systole

Diastolic dysfunction seen in → Constrictive pathology : CCP
→ Restrictive pathology (more severe) : RCM

Symptoms of Diastolic Dysfunction :

1. ↑RVEDP → ↑RAP → ↑Pressure in Vena Cava → Rt HF.
   - Ascitis precox
   - Edema
   - ↑JVP
   - Hepatomegaly
2. Systole Ⓝ ; chamber size Ⓝ.
3. ECG : Low voltage complexes.
4. Kussmaul's sign ⊕ : CCP, RCM, TS.

Acute Pericarditis

00:34:00

Causes : Post viral/uremia.

Clinical features : Chest pain.

ECG :

1. Global ST elevation (Except V1).
2. Concave ST elevation.
3. No reciprocal changes.
4. PR depression.

D/d : MI
1. Localised ST elevation
2. Convex ST elevation
3. Reciprocal changes ⊕
4. No PR depression

----- Active space -----

CCP vs RCM

00:39:10

	Chronic Constrictive Pericarditis	Restrictive Cardiomyopathy
Pathology	Multiple relapses : Acute pericarditis ↓ Rock like pericardium : Rigid, calcific, thickened, fibrous pericardium with adhesions	Stiff, hypertrophic, non-compliant, non-dilated ventricle
	→ Diastolic dysfunction ←	
Causes	Post viral > TB	1. Intercellular accumulation : Amyloidosis (m/c) 2. Intracellular accumulation : a. Hemochromatosis (Iron) b. Fabry's disease (Glycosphingolipids) c. Pompe's disease (Glycogen) 3. No accumulation : DM/Scleroderma
JVP	• Rapid x-descent • Rapid y-descent : Friedreich's sign • Square root sign ⊕	• X-descent is not prominent • No y-descent • No square root sign
	↑On inspiration : Kussmaul's sign	
Elevation & Equalisation of pressures	After 1/3rd of diastole (Pericardial Knock ⊕)	Absent
Other features	• Cachexic & malnourished patient • Pulsus paradoxus (1/3rd of patients) • Pericardial Knock ⊕ • Broadbent sign : Systolic retraction of apex (11th/12th rib indrawing)	• S3 ⊕ • No pulses paradoxus • No pericardial Knock • ↓Transmyocardial filling pressure
	ECG : low voltage complexes	
Ix	MRI (IOC)	ECHO
Rx	Pericardiectomy	Medical management

Cardiac Tamponade

00:57:03 ----- Active space -----

Cause :

Post-traumatic ⟶ Acute rise in intrapericardial pressure.

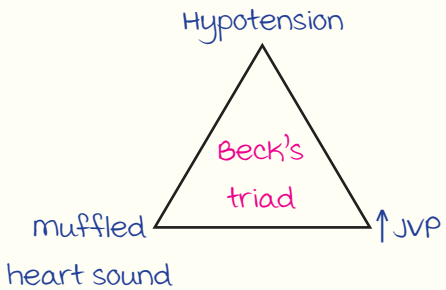
Features :

- Holodiastolic elevation & equalisation of pressures ⟶ No filling.
- Small chambers.
- Diastolic dysfunction.

Clinical Features :

Obstructive shock :

- Hypotension.
- Shock.
- Disproportionate dyspnea.
- Tachycardia.



On Examination :

- JVP :
  - Prominent x-descent (Coupled constraint : Heart acts as one chamber).
  - No y-descent.
  - No square root sign.
- No pericardial knock.
- No Kussmaul's sign.
- Pulsus paradoxus (Inspiration ⟶ SBP decreases > 10 mmHg).

Management :

Investigations :

1. ECG : Electrical alternans (low voltage complexes).
2. ECHO.

Treatment : Emergency pericardiocentesis.

----- Active space -----

CVS REVISION - 4

Dilated Cardiomyopathy (DCM) 00:02:40

Pathology :

Large, dilated, thin walled LV → Poor contractile → Poor relaxation.

Clinical features :

1. Systolic failure : ↓ cardiac output.
   - Cachectic (TNFα).
   - Cold extremities.
   - Altered sensorium.
   - Renal failure (CRS).
   - O/E : Narrow pulse pressure.
     S3 ⊕.
     Cardiomegaly.
2. Diastolic failure : Dyspnea (↑LVEDP → ↑PCWP).
3. Right heart failure : ↑JVP, ascites, edema, hepatomegaly.

Etiology :

1. Genetic : Autosomal dominant → Truncated variant titin mutation (m/c).
   → myh7 (myosin heavy chain 7) mutation.
2. Peripartum cardiomyopathy :
   - Best prognosis.
   - D/t antiangiogenic factors : SFLT 1.
   - R/F :
     - ↑Age.
     - HTN.
     - Multiple pregnancies.
3. Alcohol induced :
   - Good prognosis.
   - A/w ACE polymorphisms.
   - Precipitated by deficiency of :
     a. Selenium : Keshan's disease.
     b. Thiamine.
     c. Mg^{2+}.
4. Drug induced : Anthracyclines (Worst prognosis).
5. Autoimmune :
   - Sarcoidosis.
   - Hemochromatosis.
6. Endocrine :
   - Pheochromocytoma.
   - Thyrotoxicosis.
   - Acromegaly.

7. Acute post inflammatory DCM :	
myocarditis in the infection/post infection period.	
New onset HF : • Hypotension. • Chest pain. • Tachycardia.	• ↑↑Trop I. • m/c/c : HHV6 > Chagas. • Mx : Supportive.

----- Active space -----

Investigations :

1. ECG : Triad → Low voltage in limb leads.
   - → High voltage in chest leads.
   - → Poor R-wave progression.
2. Echo : Global LV hypokinesia.
3. Cardiac MRI : Ischemia vs infarct; ejection fraction (Gold std).
4. Angiography.

Restrictive Cardiomyopathy

00:14:30

Seen in amyloidosis of the heart.

1. Primary.
2. Secondary : No cardiac involvement.
3. Transthyretin induced :
   a. Senile systemic (Wild type) : Elderly patient with carpal tunnel syndrome.
   b. Familial amyloid polyneuropathy (Mutant) : Severe ANS symptoms + Cardiac involvement.

Features :

1. Biatrial enlargement.
2. Biventricular hypertrophy.
3. Interatrial septal thickening.
4. Low voltage complexes.

} Cardiac MRI : IOC.
Glittering/sparkling myocardium → Bad prognosis

ECG : Pseudo infarct pattern.

Takotsubo Cardiomyopathy

00:17:10

AKA stress induced cardiomyopathy/neurogenic myocardial stunning/ transient apical ballooning.

Cause : Sympathetic overactivity → M/C in middle aged females.

Features : ACS like presentation →
- ST elevation.
- ↑Trop I (Not as high as ACS).
- ↑↑NT Pro BNP.

Angiography →
- Normal coronary arteries.
- Hypercontractile base.
- Bulging apex.

Prognosis :

- Short term : Like MI.
- Long term : Good.

----- Active space -----

Hypertrophic Cardiomyopathy

00:20:12

m/c genetic CVS disease.

- AD.
- Mutation : Myosin heavy chain > Myosin binding protein C.

Males = Females
↳ Poorer prognosis (more progressive disease).

95-99% → Stable course

1-5% → Complications :

1. Progressive HF.
2. Arrhythmias (A-Fib).
3. Risk of sudden cardiac death.

D/D : Pompe's disease.

Hypertrophy :

Concentric, inappropriate, asymmetrical hypertrophy.

Concentric,
LV thickness ≥ 15mm
↓cavity size
↑LVEDP

inappropriate,
- No cause.
- No dilatation.

asymmetrical
Left side :
Septum + Anterior wall >> Posterior wall.

Clinical Features :

1. Dyspnea (m/c) : D/t diastolic dysfunction.
2. Angina with normal coronaries (2nd m/c) : D/t microvascular dysfunction.
3. Systolic Anterior Motion (SAM) :
   - D/t asymmetrical septal hypertrophy.
   - Leads to 2° MR.
4. A-fib : D/t ↑LAP.
5. LVOT obstruction → Angina, Syncope, Dyspnea

Note : Most patients are asymptomatic.

Obstruction in HCM

- 1/3rd : Fixed obstruction.
- 1/3rd : No obstruction.
- 1/3rd : Dynamic obstruction (Depends on cavity size).

SAM pathophysiology

Septal hypertrophy
↓
LVOT obstruction
↓
↑velocity of blood across obstruction
↓
Anterior mitral leaflet sucked into septum (mid-late systole)
↓
↑obstruction

Examination Findings :

Pulse : Pulsus bisferiens (P>T).
BP : Normal.
JVP : Normal.
Apex : Double apex/triple apex.

S1 : Normal.
S2 : Normal/reverse split.
S3 : ±
S4 : ±

----- Active space -----

Murmurs :

- Lower left sternal border → Ejection systolic murmur (D/t SAM).
- Apex → Pansystolic murmur (D/t 2° MR).

Biopsy : Myofibre disarray.

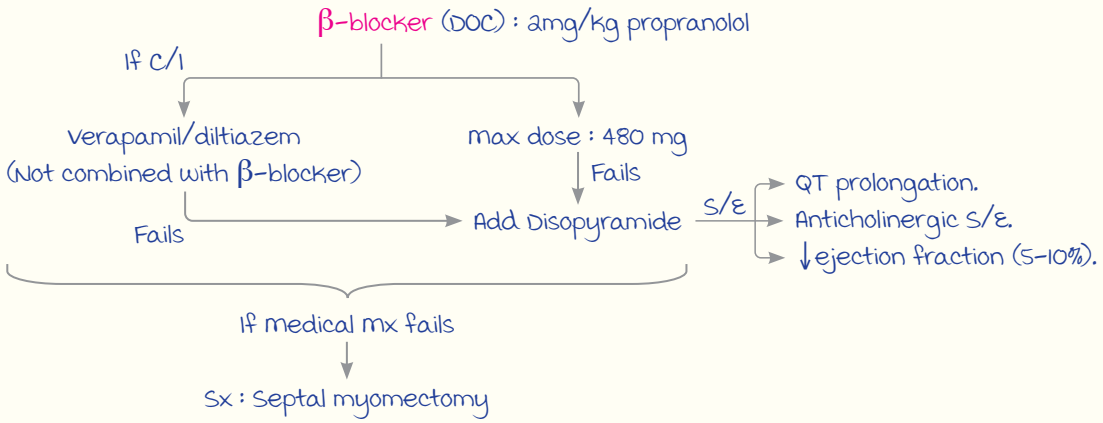
Dynamic auscultation :

- Intensity of murmur ∝ LVOT obstruction.
- Valsalva, standing
  (↓Preload and afterload)
  - ↑Intensity of murmur in HCM.
  - ↑Duration of murmur in MVP.
- Brockenbrough sign :
  ↓Post-VPC pulse volume in HCM (D/t SAM).

Factors affecting LVOT obstruction	
↑Preload ↑Afterload ↓ ↑cavity size ↓ ↓obstruction	↑Force of contraction (Amyl nitrate, isoproterenol) ↓ ↓cavity size ↓ ↑obstruction

Note : MVP and HCM are exceptions. Valsalva/standing ↓ all other murmurs.

Treatment :



Indications for ICD (Implantable cardioverter defibrillator) :

- Family h/o sudden cardiac death.
- H/o spontaneous sustained VT.

----- Active space -----

CVS REVISION - 5

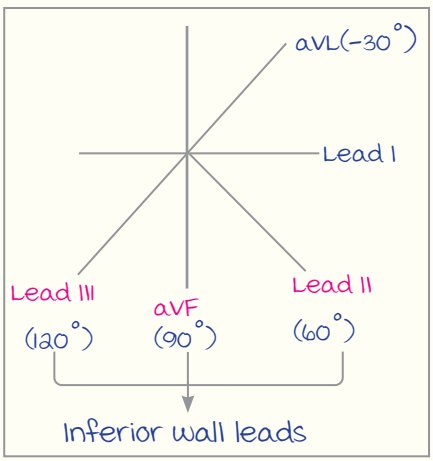
Inferior Wall MI (IWMI)

00:00:35

Dominance of Coronary Circulation :

Depends on supply of PIVA/PDA

- RCA → Right dominant (80%)
- LCx → Left dominant (20%)



Arteries Supplying Inferior Wall :

RCA OR LCx

- RCA → Proximal OR Distal

Landmark : Acute marginal A. (Only branch supplying RV free wall)

Note :
1. RVMI : V3r, V4r, V5r
2. PWMI : V7, V8, V9

RCA Branches :

1. SA nodal branch
2. Atrial branch
3. Acute marginal artery

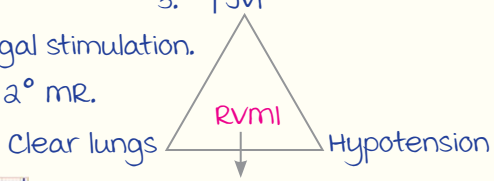
→ Anterior branches —Block→ IWMI + RV-MI ± PWMI

4. AV nodal branch → Posterior branch —Block→ IWMI (No RVMI) ± PWMI.

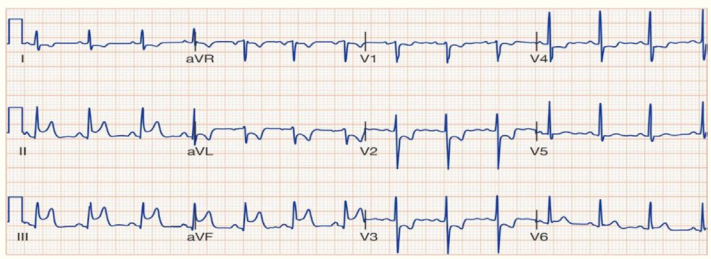
LCx block : IWMI + PWMI.

Features of RCA block :

1. Bradycardia : D/t SA nodal branch block, vagal stimulation.
2. Posteromedial papillary muscle rupture → 2° MR.
   (Single blood supply → RCA)
3. ↑JVP



Rx : Hydration



Occluded artery :

	ST ↑	ST ↓
RCA	Lead III > II	aVL > aVR
LCx	Lead II > III	aVR > aVL

IWMI : ST ↑ in lead II, III, aVF
+
RVMI (Proximal RCA) : V1 ST ↑/Discordance with V2,V3,V4

Anterior Wall MI (AWMI)

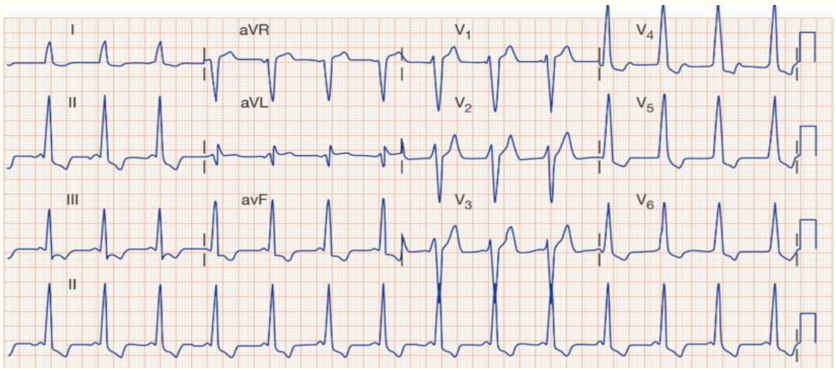
00:09:37

----- Active space -----

LCA → LAD.
→ LCx.

Blood supply (In order)	Area	ECG leads
LAD (D_1) or LCx	High lateral wall	I, aVL
LAD (S_1)	Septum	V1 >> V2
LAD (D_2)	Anterior wall	V2, V3, V4
LAD (D_4) or LCx	Lateral wall	V5, V6

Note : D → Diagonal ; S → Septal



Extensive antero high lateral MI (Above DI, SI, D2, D3) :

- ST ↑ in V2, V3, V4.
- Reciprocal changes in II, III, aVF.
- V1 ST ↑.
- ST ↑ in I & aVL.

ACS Management

00:14:02

Acute Coronary Syndrome :

myocardial injury
↓
↑ Cardiac troponin (> 99th percentile)
&
Rise & fall of troponin

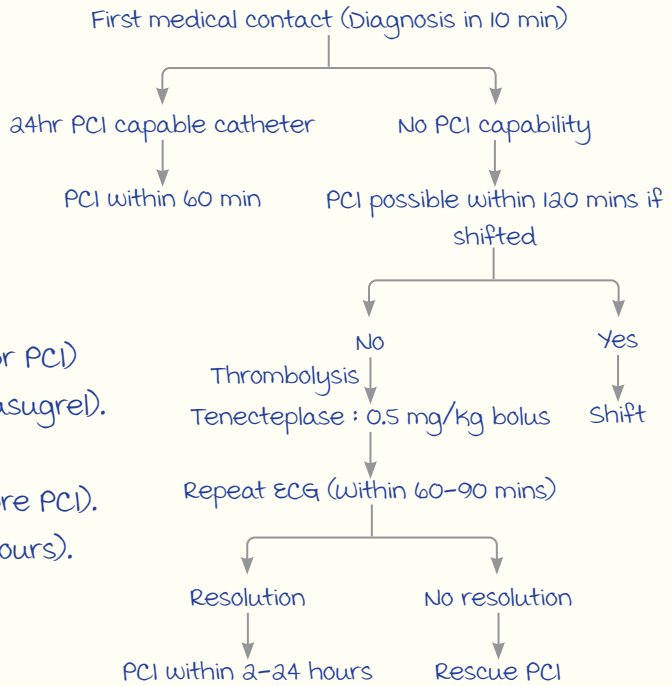
+

1 out of 5 :
1. Clinical evidence of ischemia
2. ECG evidence of ischemia
3. Pathological Q-waves
4. Echo changes
5. Angio changes

----- Active space -----

ACS Protocol :

Golden hours : 6 hours.



medical Mx after Stabilising Pt :

1. Aspirin 300 mg.
2. Clopidogrel 300 mg (600 mg for PCI)
   (If PCI planned : Ticagrelor/Prasugrel).
3. Statin 20-40 mg.
4. Anticoagulant 30 mg s/c (Before PCI).
5. ACEi & β-blockers (within 24 hours).
6. Lifelong aspirin & statins.
7. Antiplatelet for 1 year.

Arrythmia

00:19:43

Mechanisms of Arrhythmias :

1. Abnormal enhanced automaticity : Focal/MAT; Junctional tachy; Ischemic VT; Digoxin toxicity.
2. Triggered activity : Long QT syndromes; Catecholamine induced tachy.
3. Re-entry : AVNRT; A. Fib; Brugada Sx; AVRT & A. Flutter; Scar VT.

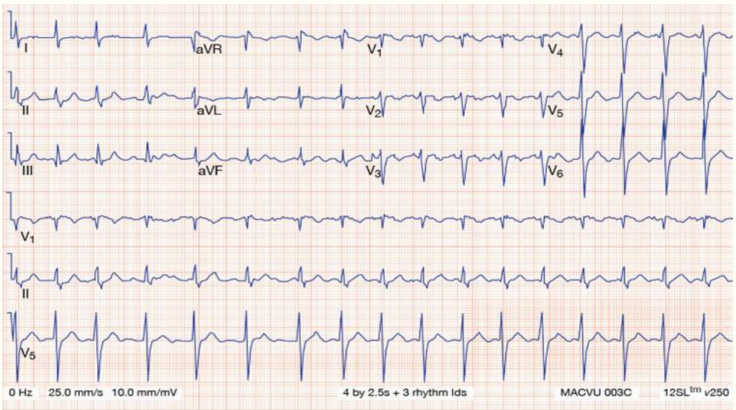
TYPES OF TACHYARRHYTHMIAS

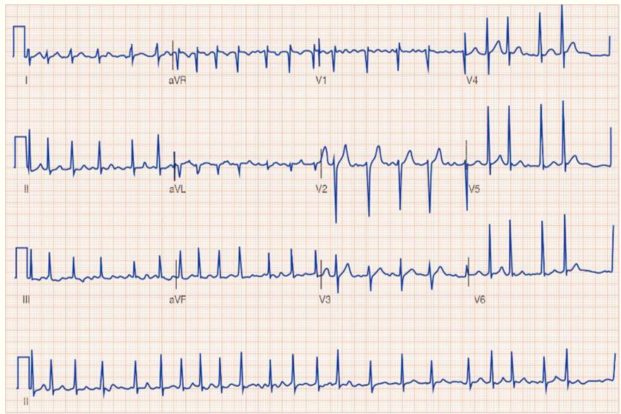
	Narrow QRS	Slightly wide QRS	Wide QRS
QRS interval	< 0.12 seconds	0.12 – 0.16 seconds	> 0.16 seconds
Origin	Above Bundle of His bifurcation	Above Bundle of His bifurcation + Bundle branch block	Ventricles
Examples	• Atrial tachycardia • Junctional tachycardia • AVNRT, AVRT, A-fib, atrial flutter	-	• Polymorphic VT; • Monomorphic VT; • Torsades de pointes

Narrow QRS Tachycardia :

Regular R-R interval	Irregular R-R interval
1. AVNRT : – No P-waves OR – P wave after QRS complex with short RP & long PR interval. 2. AVRT : P wave after QRS complex with short RP (>80-100 ms) & long PR interval 3. Focal atrial tachycardia : – Long RP, short PR interval (P before QRS). – Abnormal P-wave.	1. Atrial fibrillation 2. Multifocal atrial tachycardia (MAT) : 3 distinct P-wave morphology seen

----- Active space -----





Atrial tachycardia

Management :

1. AVNRT :
   - Adenosine.
   - COPD : Verapamil —Fails→ metoprolol.
   - Synchronized DC cardioversion.
2. Atrial Tacycardia
3. MAT (A/w COPD Rx with theophyline)

} Rate lowering agents (verapamil, β–blockers)

Note : Indications for unsynchronized cardioversion → Pulseless VT; V. Fib.; Polymorphic VT.

Atrial Fibrillation :

Features :

1. Irregular R-R interval.
2. Fibrillary waves.
3. No identifiable P-wave.

Types :

1. Paroxysmal : <7 days.
2. Persistent : >7 days.

} → Reverts spontaneously OR With drugs

3. Permanent : LA dilatation >4 cm

↓

Cannot be reverted back to normal.

Complications : Thromboembolism.

Risk factors :

1. Age.
2. HTN.
3. Associations :
   - Structural heart/lung disease.
   - OSAS.
   - Thyroid patients.
   - Psoriasis.
4. Mitral stenosis, prosthetic valve : Valvular A-fib.

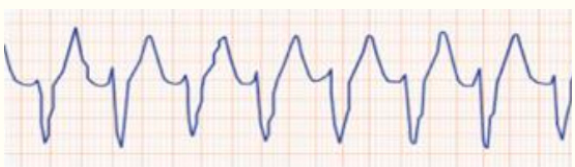
----- Active space -----

Management :

- Hemodynamically stable → Transthoracic Echo
  - LA dilated > 4cm (Structural heart disease) → Rate control : CCB
  - LA (N)
    - > 48 hrs (Or) unknown duration → TEE/Cardiac CT
      - Clot (+) → Anticoagulation X 3wks → Rhythm control (Drugs > DC cardioversion) → Anticoagulation X 4wks
    - < 48 hrs → Rhythm control :
      - Ibutilide
      - Amiodarone (Structural heart disease)
- Hemodynamically unstable → DC cardioversion (100J x 2)

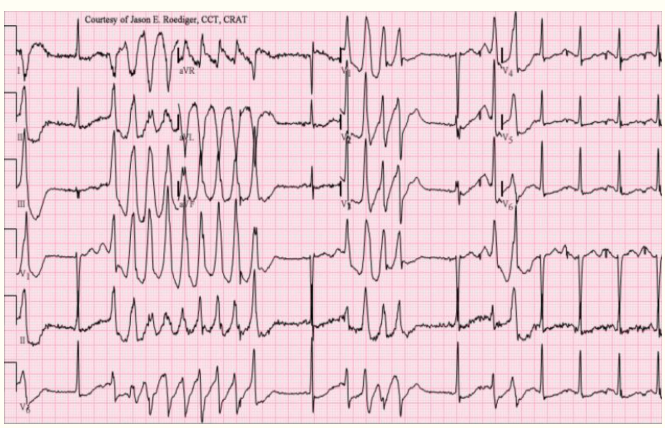
Wide QRS Tachycardia :

1. Monomorphic Ventricular Tachycardia :
   - Sustained VT + rate >100/min.
   - ≥3 VPC.
   - Capture beat/fusion beat (±).
   - Management :
     - Unstable → Synchronised DC cardioversion (360J)
     - Stable :
       1. Procainamide.
       2. Amiodarone (Structural heart disease).
       3. Lignocaine : Post MI.



Monomorphic VT

2. Torsades de Pointes/Polymorphic VT :
   - Polymorphic VT + QT prolongation.
   - Precipitating factors :
     a. Antiarrhythmics : Class Ia, Ic, Class III.
     b. Terbinafine, macrolides.
     c. Hypokalemia, hypocalcemia, hypomagnesemia.
     d. Hypothermia.
   - Mx : Defibrillation (200J) + 2g MgSO4 I.V.



Polymorphic VT

Hyper/Hypokalemia

00:45:20 ----- Active space -----

Hyperkalemia :

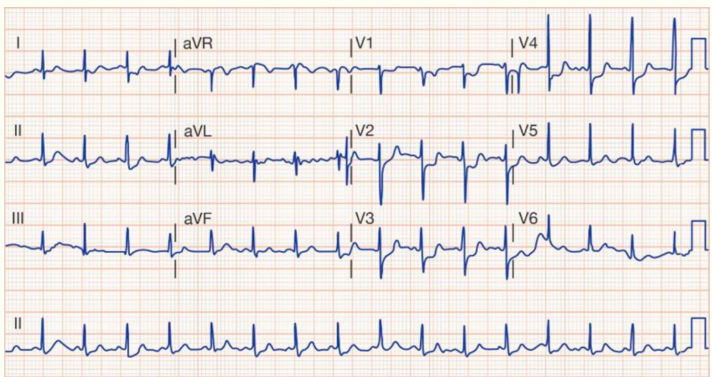
Causes :

1. CKD/AKI (m/c).
2. Hypoaldosteronism.
3. Pseudohypoaldosteronism : RTA type IV.
4. Spironolactone.

ECG changes :

- Tall T-waves : 6-7 mEq/L.
- ↓ST, ↑PR : 7-8 mEq/L.
- Wide QRS : 8-9 mEq/L.
- Absent P-wave : >9 mEq/L.

Mx : IV Calcium gluconate.



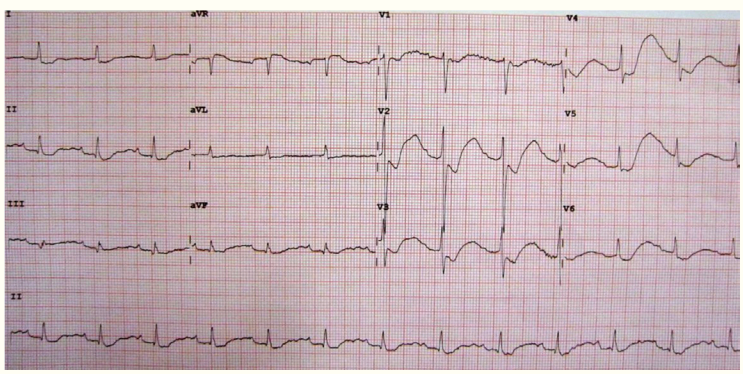
Hyperkalemia

Hypokalemia :

ECG changes :

- Sagging ST segment.
- Prominent U-waves.

Management : IV KCl.



Hypokalemia

----- Active space -----

RS REVISION - 1

Weibel's generation of airways :

- 23 airway generations
  - First 16 : Upto terminal bronchiole → Conducting zone.
  - Last 7 :
    - Respiratory bronchiole
    - Alveolar ducts
    - Alveoli

  → Respiratory zone /acinus

Approach to Lung Diseases

00:02:47

CLASSIFICATION

	Diseases	Pathophysiology
Obstructive lung diseases	Chronic obstructive pulmonary disease (COPD) : 1. Chronic bronchitis 2. Emphysema 3. Small airway disease (Airways < 2mm diameter).	Larger & smaller airways + Parenchymal + Vascular involvement. 1. Lung parenchyma involvement Causes : a. Type 2 RF b. Pulmonary hypertension c. Cor pulmonale 2. Alveolar capillary membrane ↓ Type 1 RF
	• Bronchial asthma (BA) : Pure airway disease.	-
	• Bronchiectasis - Exception : Traction bronchiectasis	-
	• Bronchiolitis	-
	• Cystic fibrosis	-

----- Active space -----

<table>
<tr><th colspan="2"></th><th>Diseases</th><th>Pathophysiology</th></tr>
<tr><td rowspan="2">Restrictive lung diseases</td><td>Intraparenchymal</td><td>Interstitial lung disease (ILD) :
• Diffuse lung parenchymal fibrosis
• Oxygen diffusion affected</td><td>Stages :
• Early : Hypoxia → Type I RF
↓
Pulmonary hypertension
• Late : Hypercarbia + hypoxia
↑ parenchymal damage
↓
Type 3 RF</td></tr>
<tr><td>Extraparenchymal</td><td>• Neuromuscular (NM) :
– Myasthenia gravis
– Amyotrophic lateral sclerosis (ALS)
– Guillain-Barré Syndrome (GBS)
• Chest wall :
– Kyphoscoliosis
– Ankylosing spondylitis
– Obesity</td><td></td></tr>
<tr><td colspan="2">Vascular lung diseases</td><td>• Pulmonary hypertension (PHTN)
• Pulmonary thromboembolism</td><td></td></tr>
<tr><td rowspan="5">Filling/ pleura related diseases</td><td rowspan="3">Filling disorder</td><td>Pneumonia</td><td>Due to exudate</td></tr>
<tr><td>Diffuse alveolar hemorrhage (DAH)</td><td>Due to blood</td></tr>
<tr><td>Acute respiratory distress syndrome/ARDS (Non-cardiogenic)</td><td>Due to fluid</td></tr>
<tr><td>Filling disorder + parenchymal destruction</td><td>Lung abscess/necrotizing pneumonia</td><td></td></tr>
<tr><td>Pleural disorder</td><td>Pleural effusion</td><td></td></tr>
</table>

Note :

Lung parenchyma → Alveoli + alveolar interstitium + vascular interstitium.

----- Active space -----

Respiratory Failure

00:18:32

Types :

	Physiology	Pa O_2	Pa CO_2	P(A-a)O_2	Examples
Type 1	Diffusion failure	↓	Normal	↑	• Alveolar filling disorders : – Pneumonia – DAH – ARDS • ILD • Vascular disorders • Emphysema
Type 2	Ventilatory failure	↓	↑	Normal	Pump : Neuromuscular disorders chest wall issues Effector organ : Chronic bronchitis Generator : Brainstem disorders
Type 3	Combined diffusion & ventilatory failure	↓	↑	↑	• ILD (Type 1 → Type 3) • Type 2 → Type 3 RF is rare

Spirometry

00:21:17

Standard Lung Volumes & Capacities :

Lung volumes	Lung capacities
• Tidal volume : 500 mL • Inspiratory reserve volume (IRV) : 3000 mL • Expiratory reserve volume (ERV) : 1000 mL • Residual volume (RV) = 1200 mL	• Inspiratory capacity = TV + IRV = 3500 ml • Functional residual capacity (FRC)/Equilibrium/ Relaxation Volume = RV + ERV = 1/2 FVC = 2200 mL • Forced vital capacity = TV + TRV + ERV = 4.5L • Total lung capacity = TV + IRV + ERV + RV (TLC) = 5–6 L

Note :

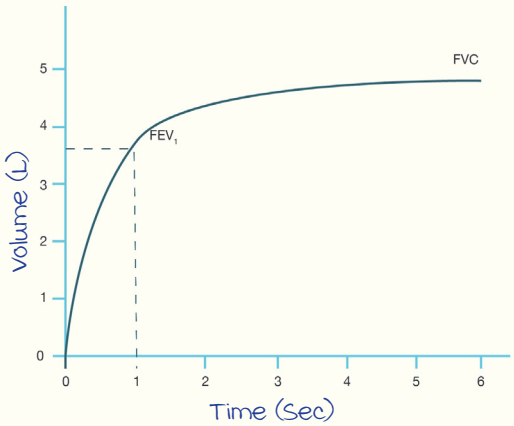
Total body plethysmography : measures RV, FRC, TLC (Spirometer can't measure them).

FEV_1/Forced expiratory volume in 1 second :

Amount of FVC exhaled in 1st second.

- FVC = 5L
- FEV_1 = 4L
- $FEV_1/FVC \geq 80\%$

} Normal values.



----- Active space -----

Lung Volumes in Lung Pathologies :

Elastic recoil pressure (ERP) :

- Obstructive lung disease :
  - ↓ ERP (D/t loss of alveolar attachments) → Hyperinflation → Dynamic compression of airways.
- Restrictive lung disease : ↑ ERP (D/t fibrosis) → ↓ inflation of alveoli.

Interpretations in lung pathologies :

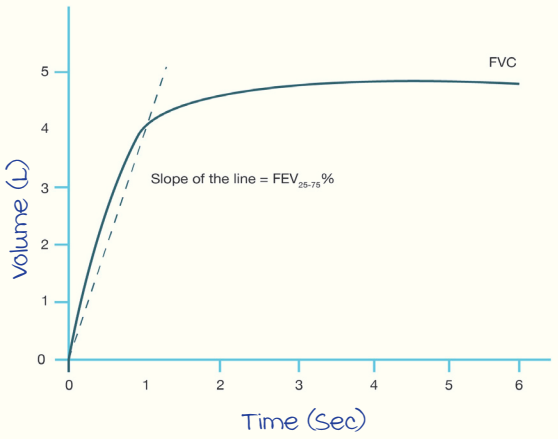
	Obstructive lung diseases		Restrictive lung diseases			Vascular lung diseases
	Hyperinflation phase	Air trapping phase	Intra Parenchymal	Extra parenchymal		
FEV_1/FVC	↓↓	↓↓	Normal to ↑			Normal
FEV_1	↓↓	↓↓	Normal			Normal
FVC	Normal	↓↓	↓↓			Normal
DLCO	Normal Exception : Emphysema ↓↓		↓	Normal		↓↓
RV				NM disorders	Chest wall	
	↑↑	↑↑	↓	Normal	Normal	Normal
TLC	↑↑	Normal	↓↓	↓↓	Normal	Normal
RV/TLC	-	-	-	↑↑	Normal	-

Note : DLCO helps with early diagnosis & prognosis of ILD.

----- Active space -----

Smaller Airway Disease :

- FEV_1/FVC : Normal
- Forced expiratory flow rate 25–75% (FEF 25–75)/
  Maximal mid expiratory flow rate (MMEFR) is used for diagnosis.



DLCO

00:45:30

- Measurement of lung's ability to transfer gas (O_2) across alvelo-capillary membrane.
- Normal value : 20–30 mL/min/mmHg or 70–140%.

DLCO Measurement :

- Gas used : Carbon monoxide (CO).
  - ↑↑ hemoglobin affinity.
  - Diffusion limited gas.
  - Negligible amounts in blood.
- Technique : Single breath technique.

Note :

Alveolocapillary membrane (Diffusion occurs) :

- Components :
  - Alveolar epithelium + Basement membrane.
  - Interstitium
  - Capillary endothelium + Basement membrane.
- Surface area : 70 m^2.
- Thickness : 0.2 – 0.5 micrometre.

Factors Affecting DLCO :

----- Active space -----

Factors :

Increased DLCO	Decreased DLCO
• ↑ Blood volume : – Supine position – ↑ Cardiac output – Congestive cardiac failure – Polycythemia • ↓ PaO_a : High altitude • Exercise & obesity • Left to right shunts	• Valsalva maneuver • Smoking (↑ carboxyhemoglobin) • High flow O_a • Anemia

Disorders with altered DLCO :

Diseases with ↑ DLCO	Diseases with ↓ DLCO
• DAH : – Goodpasture's disease – Wegener granulomatosis – Microscopic polyangiitis • Bronchial asthma (Normal/↑)	• Rheumatological disorders prone to ILD : – Rheumatoid arthritis (RA) – Scleroderma – Mixed connective tissue disease – Dermatomyositis • Pulmonary vascular diseases : – P. Hypertension – P. Thromboembolism • Bleomycin toxicity • Emphysema

Pleural Fluid Analysis

01:00:42

Significance of Pleural Fluid :

Pleural fluid	Detected by
≥50 mL	Ultrasound
≥60–80 mL	Chest X-ray lateral view
≥200 mL	Chest X-ray PA view
≥300 mL	Clinically

Note : Normal pleural fliud volume : 10–30 mL.

----- Active space -----

PLEURAL EFFUSION

Exudative v/s Transudative Effusion :

Light's criteria :

1. Pleural fluid protein/Serum protein ≥ 0.5.
2. Pleural fluid LDH/Serum LDH ≥ 0.6.
3. Pleural fluid LDH ≥ 2/3rd of upper limits of normal serum LDH.

Features :

	Exudative effusion	Transudative effusion
Diagnostic criteria	• Light's criteria : Any 1 of 3 • Pleural fluid protein > 2.9 g/dL • Pleural fluid cholesterol ↑↑	Light's criteria : All 3 absent
Causes	• Pneumonia, TB • Drugs • Malignancy • Connective tissue disease • Esophageal rupture	• Congestive cardiac failure, SVC obstruction • Cirrhosis, Nephrotic syndrome, Hypoalbuminemia, Budd Chiari syndrome • Peritoneal dialysis • Hypothyroidism • Urinothorax

Drugs causing exudative effusion :

- Nitrofurantoin.
- Dantrolene.
- Amiodarone.
- Methysergide.
- Bromocriptine.
- Tyrosine Kinase inhibitors.

Note :

Methotrexate causes :

- Hypersensitivity pneumonitis (m/c).
- Effusion (very rare).

Diseases causing both exudative & transudative effusion :

- Chronic constrictive pericarditis.
- Pulmonary embolism.
- Pulmonary infarction.
- Acute pancreatitis.

----- Active space -----

Components of Pleural Fluid :

	Normal	Empyema	Rheumatoid arthritis
Cells	1700 cells/μL : • 75% macrophages • 25% lymphocytes • <1% mesothelial cells	Neutrophils	• Macrophages. • Multinucleate giant cells (Tadpole)
LDH	<50% of serum LDH	>1000 U/L	-
Protein	1-1.5g/2L	-	-
Glucose	>60g/dL	30-60 g/dl	• <30g/dL (Pathognomic) • Can be 30-60g/dl also
pH	-	<7.2	<7.2

In malignancy, glucose levels : 30-60 mg/dL.

Eosinophilic Effusion :

>10% eosinophils in pleural fluid.

Causes :

- Hemothorax/Pneumothorax.
- Parasitic : Paragonimus westermani.
- Fungal : Coccidioidomycosis, histoplasmosis.
- Asbestosis, drugs.
- Eosinophilic granulomatosis with polyangiitis (EGPA).
- Pulmonary infarction.

Community Acquired Pneumonia A/W Pleural Effusion :

	Pathophysiology	Investigations
Simple parapneumonic effusion	Inflammation ↑ ↑pleural membrane permeability	• LDH • Culture • Glucose • pH } Normal
Complicated parapneumonic effusion	Simple parapneumonic effusion + Bacterial invasion → Fibrin deposition + septation	• LDH ↑↑ • Culture ⊕ • Glucose ↓↓ • pH < 7.2

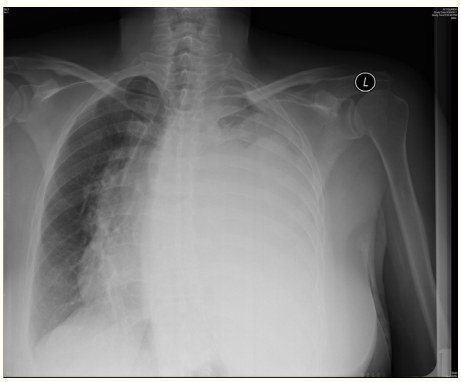
----- Active space -----

Empyema :

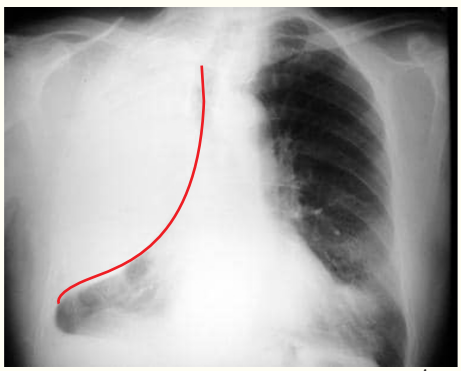
Complicated parapneumonic effusion + macroscopic pus.

- Clinical features :
  - Fever unresponsive to antibiotics (Even after 3 days).
  - Pleuritic pain, tenderness.
  - Tachycardia, clubbing.
- Treatment : Intercostal drainage (ICD).

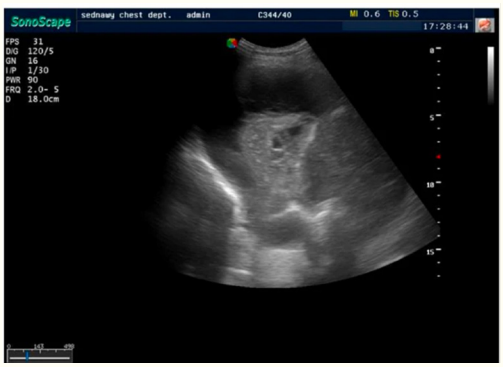
  Indications of ICD :
  - Empyema (Absolute).
  - Pleural fluid pH <7.2.
  - Organism in culture.
  - Loculated pleural effusion.
  - Massive effusion.



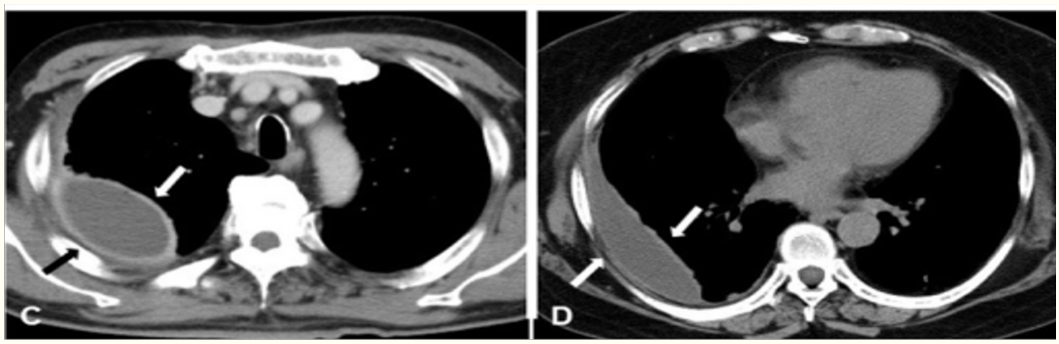
Massive pleural effusion



Radiograph : D sign on empyema/ pregnant belly sign



Ultrasound : Septations in empyema



CECT : Split pleura sign

Note : Split pleura sign : Differentiates empyema from necrotizing lung abscess.

----- Active space -----

Pleural TB :

- Pleural TB $\xrightarrow{\text{Can progress within 5 yrs}}$ Pulmonary/Extrapulmonary TB.
- Pleural biopsy (medical thoracoscopy/VATs guided) : Conclusive.
  - Gene XPERT/CBNAAT/Pleural fluid ADA levels & culture : Inconclusive.

Adenosine deaminase (ADA) :

Pleural fluid ADA	Interpretation
<40 U/L	Not suggestive of TB
>70 U/L + Lymphocytes + Exudative effusion	Highly suggestive of TB
40 to 70 U/L	TB, lymphoma, empyema, malignancy, brucellosis

Note :

- Mesothelial cells : <5% in TB (Normal : < 1%).
- Pleuritis ± effusion → Suggestive of connective tissue disorder (SLE, RA).

Chylous v/s Pseudochylous Pleural Effusion :

	Chylous pleural effusion	Pseudochylous pleural effusion
Cause	Trauma	RA/TB
Features	• Triglycerides : ↑ • Chylomicrons : ⊕ • Milky lymphocytic exudative effusion • Normal glucose • Low LDH	Cholesterol crystals

----- Active space -----

RS REVISION - 2

Pulmonary Thromboembolism

00:00:22

Sites of Thrombosis :

Deep veins :

- m/c : Femoral vein (Supra popliteal).
- In pregnancy : Pelvic veins.

Note : Deep veins of calf → m/c site of deep vein thrombosis.

Causes :

Inherited : Factor V leiden mutation (m/c).

Acquired :

- Antiphospholipid antibody syndrome (m/c).
- Nephrotic syndrome (Urinary loss of antithrombin III/Protein C/S).
- Post-orthopedic surgery.
- Malignancy (Adenocarcinoma).
- COPD.

Types :

	Massive	Submassive	Non-massive
Hypotension	⊕	⊖	⊖
Features	Right ventricle(RV) dilatation ↓ Small left ventricle (LV) ↓ ↓ Cardiac output ↓ Hypotension ↓ Shock	RV dilatation + Markers of RV ischemia : • NT pro BNP, Trop I : – Both ↑ → High risk – One ↑ → Low risk	• Recurrent pneumonia • No RV dilatation/markers

Clinical Presentation :

----- Active space -----

Symptoms :

- Unexplained dyspnea (m/c).
- Syncope.
- Chest pain (Pleuritic).
- Cough with hemoptysis.
- Sudden cardiac death.

Signs :

- Tachycardia, S_3, ↑ JVP
- Clear lung fields, Tachypnea, ↓breath sounds, rales.

Note :

Cor pulmonale : RV hypertrophy + RV failure ⟶ S_3, ↑ JVP.

Investigations :

ABG :

- Hypoxemia.
- Respiratory alkalosis.
- Widening of (A-O) oxygen gradient.

ECG :

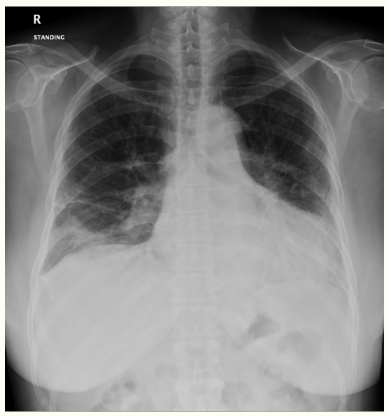
- T inversion in V_1 to V_4 ⟶ Correlates with severity.
- $S_1Q_3T_3$: No sensitivity/specificity.

Echo :

- Findings
  - Right atrium & RV dilatation.
  - Septal push.
  - Small LV.
- To rule out cardiac tamponade.
- McConnell's sign : Hypocontractile RV free wall + Hypercontractile apex.

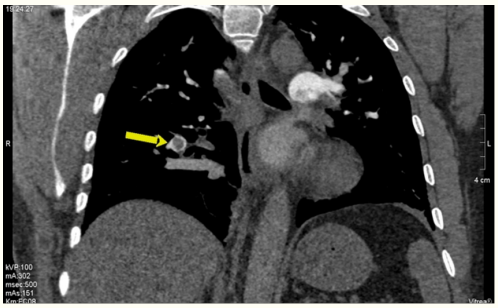
Imaging :

- CT pulmonary angiography (CTPA) : IOC.
  - Findings
    - Clot.
    - Pulmonary artery dilatation.
    - RV dilatation.
  - Polo mint sign : Thin rim of contrast around Central filling defect d/t thrombus.

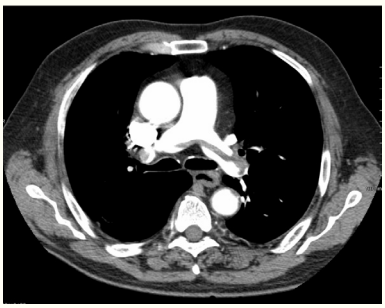


CXR : Long linear band of atelectasis

----- Active space -----



Polo mint sign



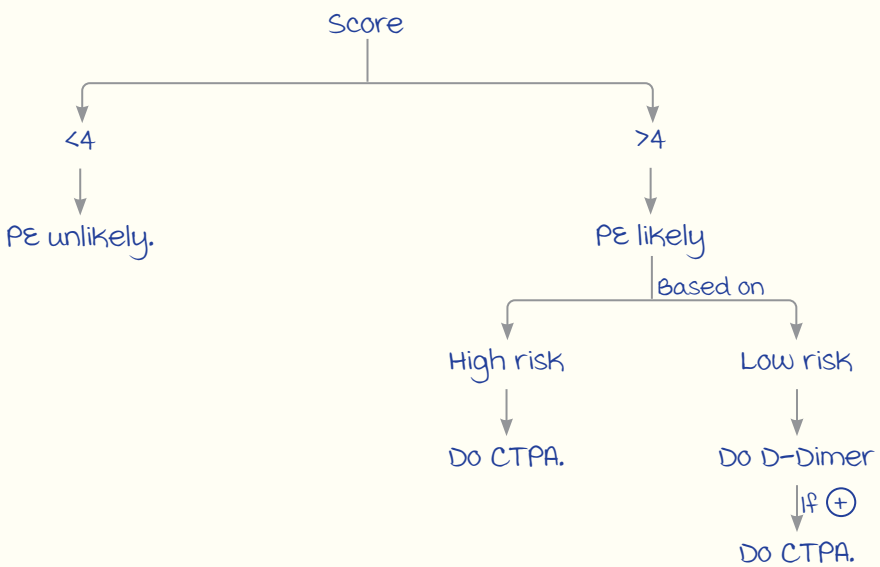
CTPA : Saddle thrombus

Management :

Well's score

Parameter	Score
Clinical signs of DVT	3
Alternative diagnosis less likely than pulmonary embolism (PE)	3
Heart rate >100/min	1.5
Recent surgery/immobilization	1.5
Previous PE/DVT	1.5
Hemoptysis	1
Malignancy	1

Management based on score :



Treatment Algorithm :

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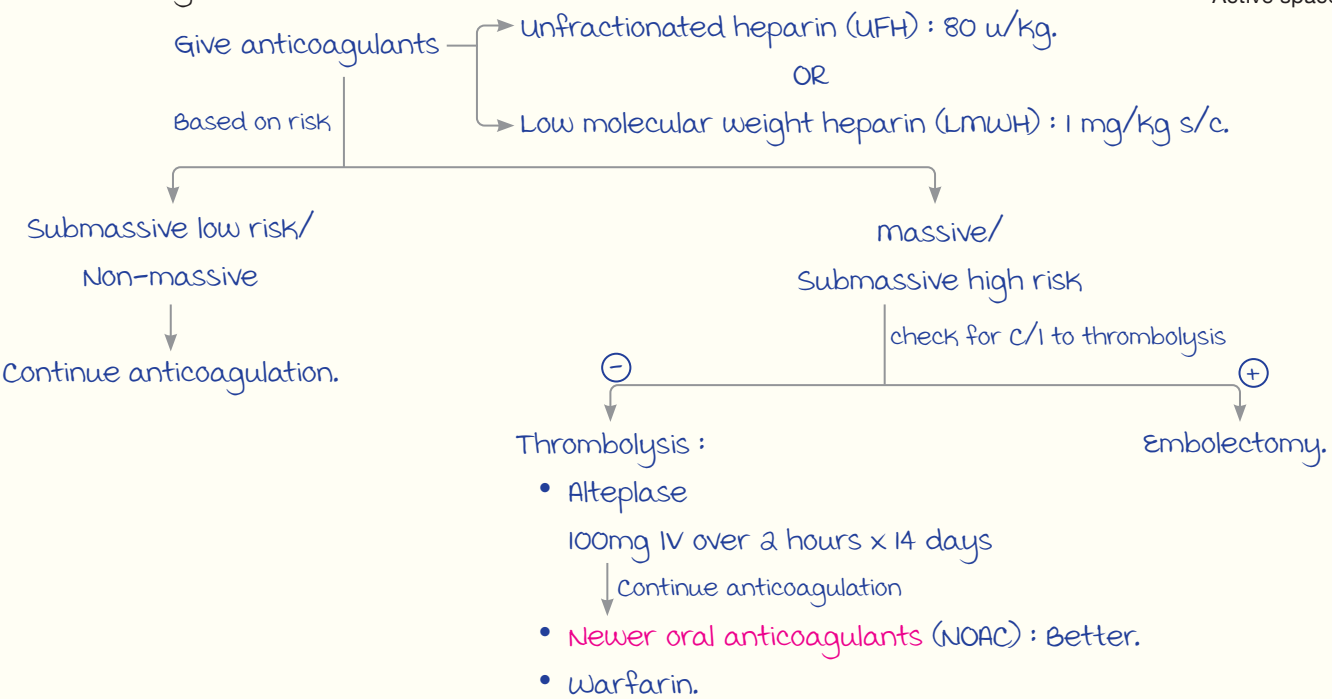


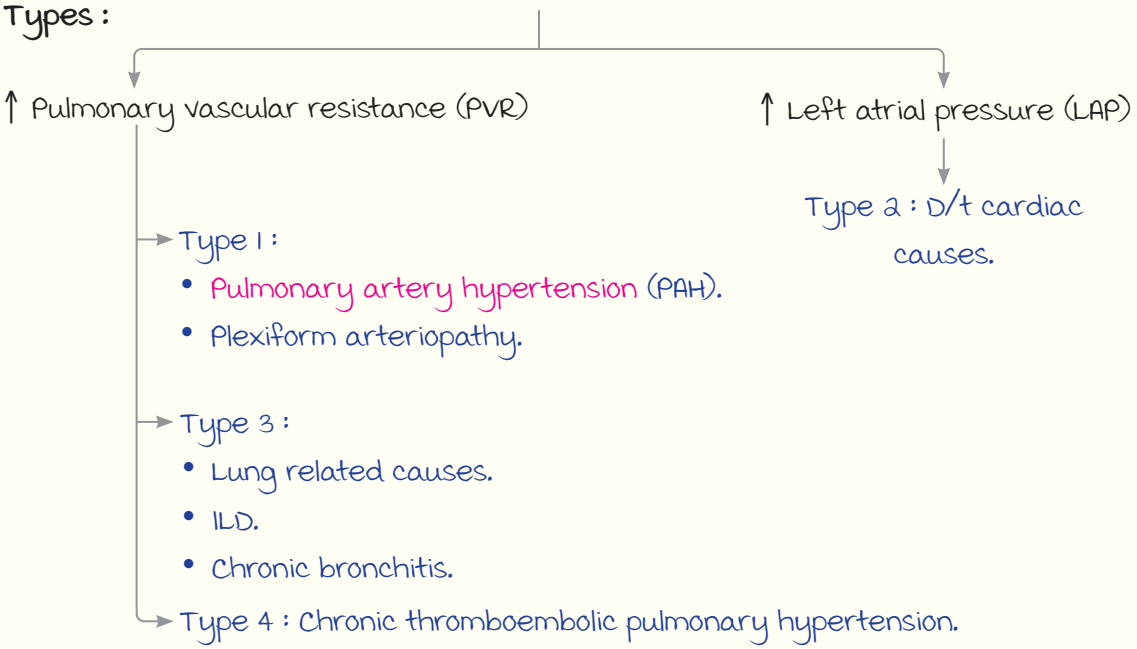
If anticoagulation C/I : Inferior vena cava (IVC) filter.

Pulmonary Hypertension

00:19:28

Resting mean pulmonary artery pressure ≥20 mmHg.

Types :



PVR :

- Change in pressure/flow.
- $\frac{\text{Rt. heart pressure} - \text{Lt. heart pressure}}{\text{Cardiac output}}$
- PVR < 3 wood units : Type 2.
- PVR > 3 wood units : Types 1,3,4.

----- Active space -----

TYPE I : PAH

Causes :

- Idiopathic (m/c).
- Limited systemic sclerosis.
- Toxins : Rapeseed oil.
- Serotonergic substances : Fenfluramine.
- BMPR-2 mutation.
- Infections : HIV, Schistosomiasis.
- Portal hypertension.

Molecular Pathogenesis :

- ↑ Endothelin.
- ↓ Nitric oxide.
- ↓ Prostacyclin.

Clinical Presentation :

Symptoms :

- Fatigue (m/c).
- Breathlessness.
- Chest pain (D/t RV ischemia).

Signs :

- Loud, palpable P_a.
- Parasternal heave.
- Pulsations : Epigastric & 2nd intercostal space.
- Murmurs
  - Pansystolic (Secondary to PAH) : Hypertensive tricuspid regurgitation.
  - Early diastolic (D/t pulmonary regurgitation/artery dilatation) : Graham Steell murmur.

Investigations :

Echo :

- Pulmonary artery dilatation.
- RV function.
- Tricuspid regurgitation.

PFT :

- FEV1/FVC : Normal.
- FVC : Normal.
- DLCO ↓.

Polysomnography & HRCT : To rule out obstructive sleep apnea & ILD.

V/Q scan : To rule out chronic thromboembolic PAH (Rx : Pulmonary endarterectomy).

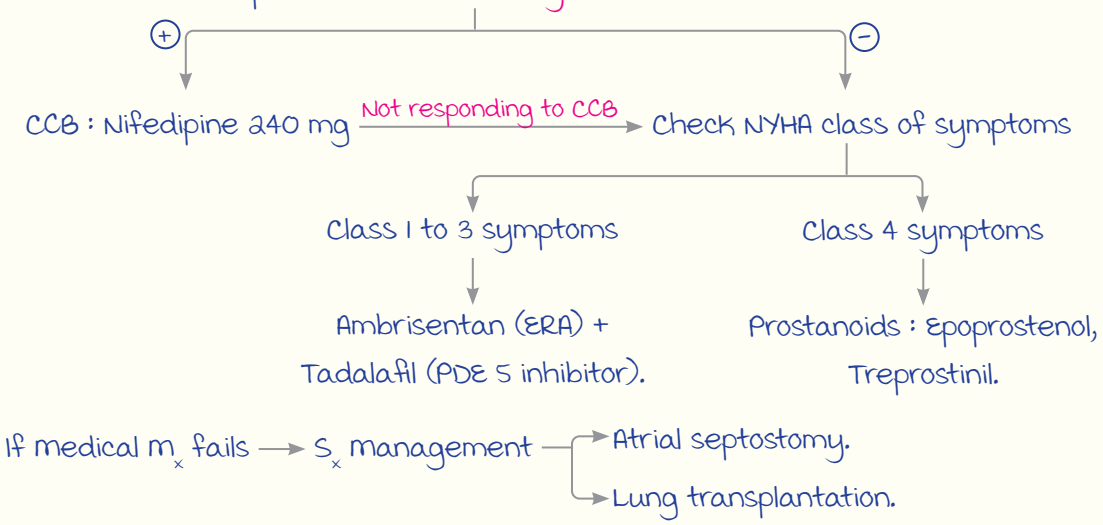
6 minute walk test : Predictor of survival.

----- Active space -----

Management :

Supportive care	Specific therapy
• Avoid pregnancy • Oral anticoagulants • Long term oxygen therapy • Diuretics for right heart failure	• Calcium channel blockers • Endothelin receptor antagonists (ERA) • Phosphodiesterase (PDE) 5 inhibitors • Prostanoids • Guanylyl cyclase stimulants

Rx is based on response to vasoreactivity test.



If medical m_x fails → S_x management → Atrial septostomy.
→ Lung transplantation.

Interstitial Lung Diseases (ILD) 00:36:38

- Diffuse parenchymal lung fibrosis.
- Mediators : TGF-β > PDGF.
- Inherited forms of ILD : Tuberous sclerosis, Neurofibromatosis.

Idiopathic Interstitial Pneumonia/ILD :

Types :

1. Idiopathic pulmonary fibrosis (IPF) :
   - m/c.
   - Usual interstitial pneumonia (UIP) : Histological counterpart.
   - Males > Females.
   - Poor prognosis : Pulmonary hypertension.
2. Non-specific interstitial pneumonia (NSIP).
3. Cryptogenic organising pneumonia (COP).
4. Respiratory bronchiolitis associated ILD (RB-ILD).
5. Desquamative interstitial pneumonia (DIP).
6. Diffuse alveolar damage (Histological counterpart) :
   - Acute interstitial pneumonia (Covid).
   - Poor prognosis.
7. Lymphocytic Interstitial pneumonia (LIP).

----- Active space -----

Note :

ILD a/w Smoking :

- RB-ILD.
- Langerhans cell histiocytosis (LCH).
- DIP.
- Rheumatoid arthritis associated ILD (RA-ILD).

Patterns of ILD :

Pattern	Seen in	Onset	Treatment
UIP	• Idiopathic : Majority • RA • Males > Females	Chronic	Anti PDGF (Platelet derived growth factor) : Nintedanib
NSIP	• Connective tissue diseases (CTD) • Drugs	Subacute	Steroid + MMF (mycophenolate mofetil)
COP	• Polymyositis • Dermatomyositis • Anti-synthetase syndrome	Subacute	Steroid + MMF
LIP	• Sjogren's Syndrome • HIV	-	-

CTD a/w ILD :

- Diffuse systemic sclerosis
- Mixed connective tissue disease (MCTD)
- Sjogren's syndrome
- Polymyositis
- Dermatomyositis
- IgG_4 related disease

} Lower lobe ILD.

- Ankylosing spondylitis (Upper lobe ILD).

Inherited causes of ILD :

- Tuberous sclerosis : A/w lymphangioleiomyomatosis.
- Neurofibromatosis.

Clinical Manifestations :

Signs :

- Clubbing.
- Velcro crackles (Bilateral, Fine, End inspiratory).
- Hypoventilation (Type 3 respiratory failure).

Symptoms :

- Exertional dyspnea.
- Dry, non-productive cough.

Investigations :

PFT :

- FEV1/FVC : ↑.
- DLCO : ↓.

Chest x-ray (CXR) :

B/L, Bibasal, Subpleural reticulonodular infiltrates.

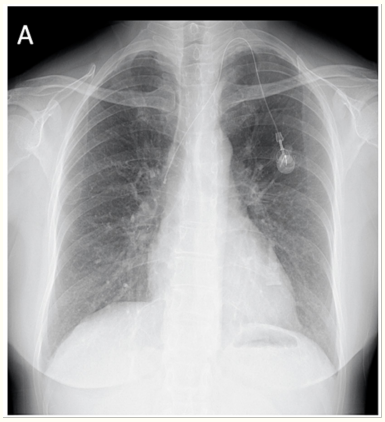
HRCT:

- IOC.
- Findings : Reticular & linear shadows.

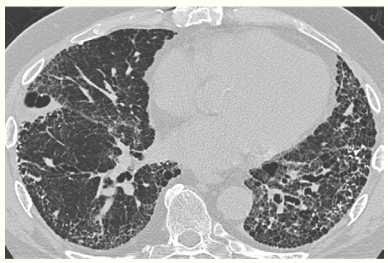
Pattern	HRCT findings
UIP	• Honey combing • Cystic spaces • Loss of lung architecture • Traction bronchiectasis
NSIP	Ground glass opacities (GGO)
COP	• Consolidation • Reverse halo sign : GGO Surrounded by consolidation
LIP	NSIP + Nodules + Cysts

Note :

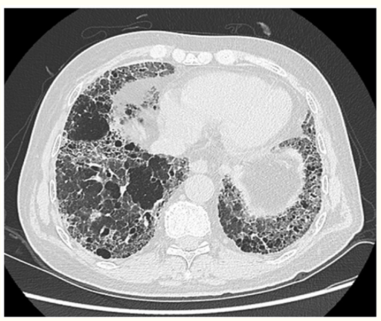
Halo sign : Consolidation surrounded by GGO → Invasive aspergillosis.



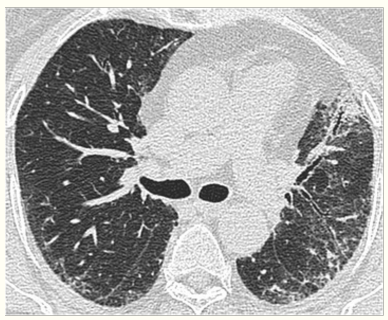
CXR : ILD



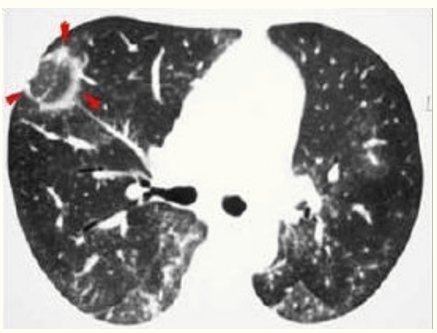
UIP : Honey combing



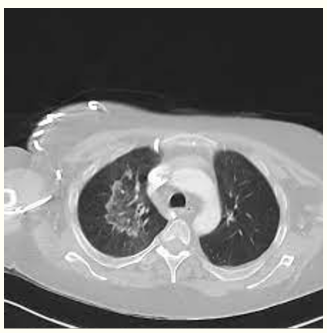
UIP : Honey combing



NSIP Pattern



COP : Reverse halo sign



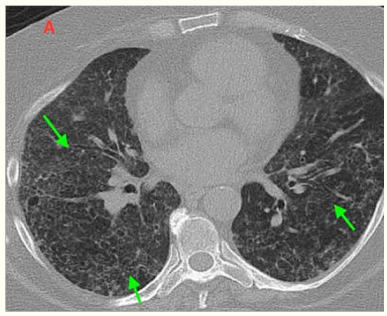
COP : Reverse halo sign

----- Active space -----

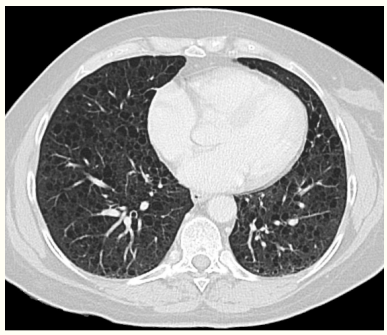
----- Active space -----

Conditions Causing Cysts in Lungs :

1. Langerhan cell histiocytosis (LCH) :
   - Young male smoker.
   - Upper lobe ILD : Nodules + Cyst.
   - A/w diabetes insipidus.
   - Birbeck granules :
     - CD_{1a} cells ≥5%.
     - Tennis racquet appearance.
   - Pneumothorax.
2. Lymphangioleiomyomatosis (LAM) :
   - Young females with tuberous sclerosis.
3. LIP.

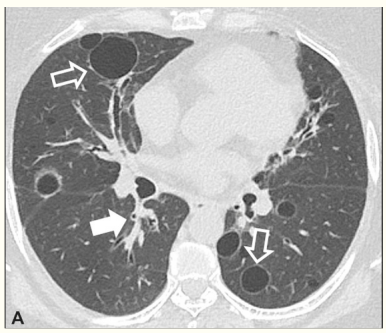


LCH


LAM

Causes of Upper Lobe ILD :

- Ankylosing spondylitis.
- Sarcoidosis.
- Silicosis.
- Coal worker's pneumoconiosis.
- ABPA : Allergic bronchopulmonary aspergillosis.
- Hypersensitivity pneumonitis.
- Berylliosis.
- TB.
- LCH.



LIP

Drug Induced ILD :

- Amiodarone.
- Bleomycin.
- Busulfan.
- Cyclophosphamide.
- Mitomycin.
- Bromocriptine.
- Methotrexate
- Anti-TNFα drugs

} Rare causes.

Note : Methotrexate causes hypersensitivity pneumonitis.

Occupational Lung Diseases

01:11:26

- Silicosis (m/c).
- Coal worker's pneumoconiosis (CWP).
- Asbestosis.

} Complicated.

- Berylliosis → Uncomplicated.

Silicosis :

----- Active space -----

Silicon dioxide/SiO_2 (Quartz) :

- Industries : Rock/Slate cutting, blasting & mining.

	Acute Silicosis	Chronic silicosis
SiO_2 exposure	Large exposure within 2 years	10-30 years
Symptoms	Dyspnea on exertion	Dyspnea & cough
Findings	• PAS positive macrophages • Milky white bronchoalveolar lavage • CT : Crazy pavement pattern (GGO + Nodules + Septation) Note : Crazy pavement pattern is also seen in : • Diffuse alveolar hemorrhage • Pulmonary alveolar proteinosis	Affected cell : Pulmonary alveolar macrophage (PAM) → Reactivation of TB : • Pleural involvement : Nil • Parenchymal involvement : – Upper lobe (UL) ILD • Radiological findings : – Angel wing sign – Egg shell calcification (D/t Hilar lymphadenopathy) – Cavitation ±
Additional features	Poor prognosis	• A/w Scleroderma • Spirometry : Mixed Pattern • Lung Signs in 25%

CWP :

Affected cell : PAM (No risk of TB reactivation).

A/w autoimmune conditions :

Caplan's syndrome : RA + Active synovitis + Nodules + IgA rheumatoid factor ⊕.

Pleural involvement/Malignancy : Nil.

Parenchymal involvement :

- Nodules.
- Upper lobe fibrosis.
- Cavitation ±.
- No hilar lymphadenopathy/Egg shell calcification.

Berylliosis :

- Ceramic industry.
- D/D : Sarcoidosis.

Pleural involvement/Malignancy : Nil

Parenchymal involvement :

- Upper lobe infiltrates → Fibrosis
- Non caseating granulomas
- Thickening of bronchovascular bundles
- Hilar adenopathy

} Features also seen in sarcoidosis.

- NSIP pattern.

----- Active space -----

Asbestosis :

Two types of fibres → Amphibole → Crocidolite.
Amphibole → Serpentine (90%).
Crocidolite → Amosite (most dangerous).

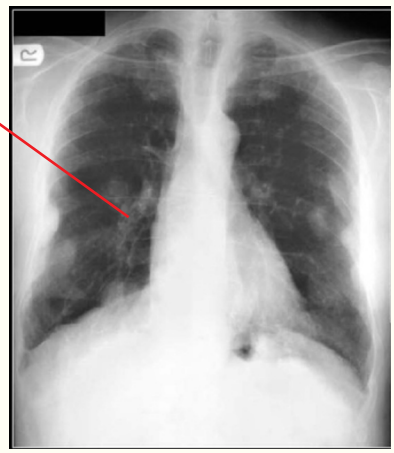
Duration of exposure : 10 years.

Pleural involvement :

- Unrelated to smoking.
- Manifestations :

– Thickening → Parietal pleura (m/c) :
  - Pleural plaques + calcification.
  - Holly leaf sign/Table mountain sign/Candle drip sign.

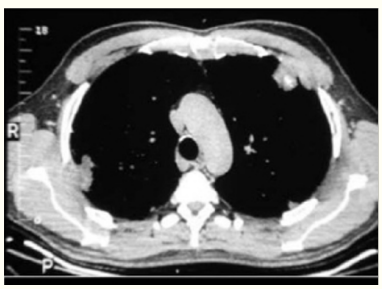
→ Visceral pleura with lung retraction : Crow feet's sign.



CXR : Pleural plaques

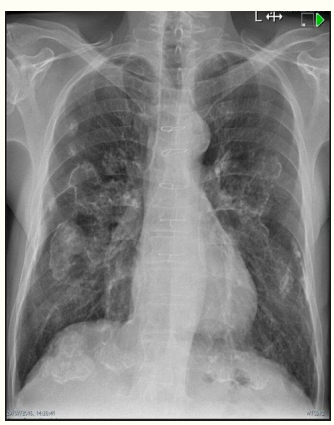
– Benign asbestos related pleural effusion (Earliest).

Exudative. Eosinophilic. Mesothelial cells.


Axial CT scan : Pleural plaques

Parenchymal involvement :

- Lower lobe ILD : Diffuse massive fibrosis.
- Infiltrates → dyspnea.
- No lung signs.
- Spirometry : Restrictive pattern.


CXR : Holly leaf sign

Malignancy :

	Pleural mesothelioma	Ca. lung
Smoking	Unrelated	Related
Duration of exposure	30 years	10–30 years
Type	Epithelioid (m/c)	Adenocarcinoma
Clinical features	• Chest pain • Mass detected	Cough with hemoptysis
Markers	• Pan cytokeratin • Calreticulin	

RS REVISION - 3

----- Active space -----

Airway diseases :

- No parenchymal involvement.
- Type I respiratory failure (Normal $PaCO_2$).

Eosinophilic Lung Disease

00:02:04

Types :

- BAL (Bronchoalveolar lavage) eosinophilia : > 25%.
- Lung tissue eosinophilia.
- Peripheral eosinophilia + lung infiltrates.

Causes :

Known :

- Parasite :
  - Loeffler's syndrome : Hypersensitivity to ascaris.
  - Lung fluke invasion.
- Drugs : Nitrofurantoin.
- Tropical pulmonary eosinophilia (D/t microfilaria).
- Allergic bronchopulmonary aspergillosis (ABPA).

Unknown :

- Eosinophilic granulomatous polyangitis (EGPA).
- Acute eosinophilic pneumonia (AEP) :
  - ARDS like presentation.
  - Quick recovery.
- Chronic eosinophilic pneumonia (CEP) :
  - Reverse batwing appearance.
- Idiopathic hyper eosinophilic syndrome.

Note :

- Conditions not under eosinophilic lung diseases :
  - HSP (Hypersensitivity pneumonitis) in lung.
  - Bronchial asthma (A/w eosinophilia).
  - Pulmonary eosinophilic granuloma diseases.
- BAL eosinophilia with > 40% : CEP & Tropical pulmonary eosinophilia.

Aspergillus in Lung

00:06:56

Organism :

- Aspergillus fumigatus.
- Saprophyte.
- Septate hyphae : Forms mucus plug.

Note :

Aspergillus niger in ear infections.

----- Active space -----

manifestations of aspergillus infection :

1. ABPA.
2. Aspergilloma : Old tuberculosis cavity.
3. Chronic Cavitary Pulmonary Aspergillosis (CCPA) :
   COPD patients : Thick walled cavities + bronchial wall invasion.
4. Invasive aspergillosis :
   - Immunocompromised (Neutropenic patients)/steroid use.
   - CT : Halo sign → Consolidation surrounded by ground glass opacities.

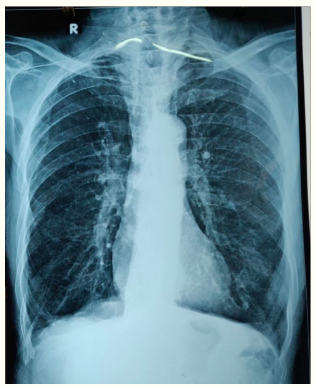
ABPA

Pathophysiology :

Bronchial asthma/ Cystic Fibrosis (CF) patients —A.fumigatus colonization→ Type 1 > Type 3 hypersensitivity.

Clinical Manifestations :

- Fever.
- Cough with brownish thick mucus plugs :
  Bronchiectasis : Proximal B/L symmetrical central type.
- Fleeting infiltrates (Eosinophilic).
- Crackles/clubbing (15% patients).
- Lung findings (20% patients).
  Rare : Converted to ILD (Upper lobe).



CXR : Tram track lines

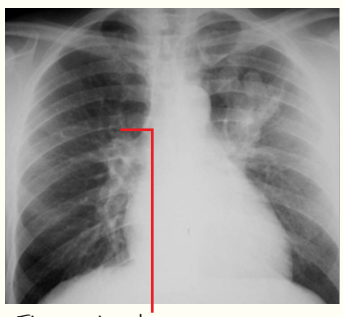
Investigations :

- IgE > 1000 (Obligatory criteria & follow up).
- Precipitin ⊕.
- Eosinophilia > 500 (Supportive criteria).

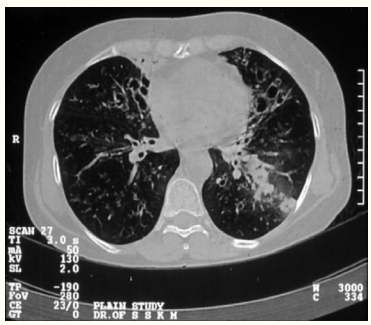
Imaging :

CXR :

- Transient, irregular, parenchymal infiltrates.
- Tram track appearance (Dilated airways).
- Finger in glove appearance :
  D/t mucoid impaction in dilated airways.


Finger in glove appearance

CT : Tree in bud appearance
(Also seen in Sarcoidosis & TB).
Endobronchial involvement.



HRCT : Tree in bud appearance
(Central bronchiectasis)

Treatment :

----- Active space -----

Steroids :
- DOC
- For 12 weeks

Itraconazole :
- In steroid non responders
- For 16 weeks

Omalizumab :
Monoclonal antibody against IgE

HYPERSENSITIVITY PNEUMONITIS (HSP)

AKA Extrinsic allergic alveolitis.

Pathophysiology :

Repeated exposure to organic dust → Type 4 > Type 3 hypersensitivity.

↓

Involvement : Airways > Parenchyma

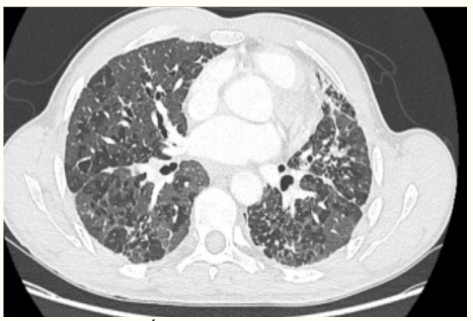
Features :
- IgE/eosinophils absent.
- Precipitin ⊕.
- Non caseating granuloma.
- Non – fleeting interstitial infiltrates (Parenchyma).

Systemic Symptoms : Nil.

Forms :
- Subacute (m/c) : A/w response to steroids.
- Acute & chronic : Rare.

Imaging :

HRCT : Mosaic/head cheese pattern (various densities seen).



Mosaic/head cheese pattern

Organic Dust Exposure :

Disease	Exposure	Antigen
Farmer's lung (m/c)	Moldy hay	Thermophilic actinomycete (m/c) : Thermoactinomyces vulgaris
Bagassosis	Moldy Sugarcane	
Mushroom worker's lung	Moldy compost/mushroom	
Malt worker's lung	Barley	Aspergillus clavatus (2nd m/c)
Tobacco worker's lung	Mold on tobacco	
Compost lung	Compost	
Wood worker's lung	Wood pulp	–

Other causes of organic dust exposure :
- Bird fancier's lung : Droppings of pigeon/parrots/chicken. (Obstructive/emphysematous pattern)
- Chemical worker's lung : Polyurethane foams (Isocyanates).
- Hot tube/humidifier/air conditioner lung : Cladosporium, MAC.
- Wood trimmer's lung : Rhizopus.
- Familial HP/wood workers : Bacillus subtilis.

Note :

HSP & ABA : Unrelated to smoking.

----- Active space -----

Comparison with Differentials :

	Asthma	ABPA	Extrinsic allergic alveolitis/HSP
Pathology	Hypertrophied mucus glands	• Colonization of airways • Viscid mucoid impaction • Tissue eosinophilia	• Interstitial lymphocytic infiltration • Non caseating granuloma
Radiographic features :			
Early	Normal hyperinflation	• Migratory peripheral infiltrates • Atelectasis • Bronchiectasis	Diffuse alveolar interstitial infiltrates
Late	Normal hyperinflation	Fibrosis	Reticulonodular interstitial opacities
Skin test reactions to aspergillus antigens :			
Immediate	⊕	⊕	⊕
Delayed	⊖	⊕	⊕
Other findings :			
Peripheral eosinophilia	⊖	⊕	⊖
IgG aspergillus precipitins	⊕	⊕	⊕
Serum IgE levels	Normal/mildly elevated	Marked elevation	Normal

Note : BAL lymphocytosis.

- Sarcoidosis : CD4/CD8. } > 2 : 1
- HSP : CD8/CD4. }

Bronchiectasis

00:23:50

Obstructive type.

- Exception : Traction bronchiectasis → Restrictive type.

Features :

Demographics : Females > males, 50–70 years.

Areas affected :

- Left lower lobe (m/c).
- Middle lobe : mycobacterium avium complex (MAC).
- Right middle lobe : Brock's syndrome (D/t lymph node in TB).

Pathological Changes :

1. Abnormal irreversible dilatation of bronchi :

   D/t loss of smooth muscles & elastic tissue.

   - Causes :
     - Idiopathic (30%).
     - Tuberculosis (40–50%), measles & pertussis.

- Genetic → Alpha-1 antitrypsin deficiency.
  → Yellow nail syndrome, William Campbell syndrome.

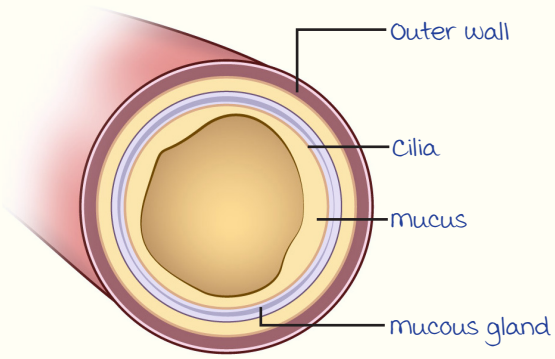
----- Active space -----

- Types of dilatation :

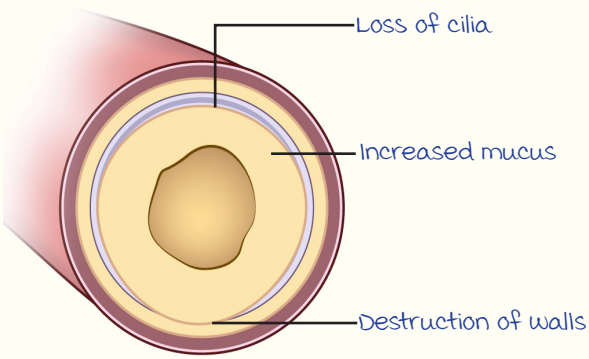
Cylindrical (m/c) | Cystic : | Tubular | Varicose

- Children
- A/w clubbing

2. Obliterative fibrosis of bronchioles :



Normal bronchus



Bronchiectasis

Clinical Features :

- Chronic cough with mucopurulent (Foul smelling) sputum.
- Hemoptysis.
- Early & mid inspiratory coarse crackles, diffuse rhonchi.

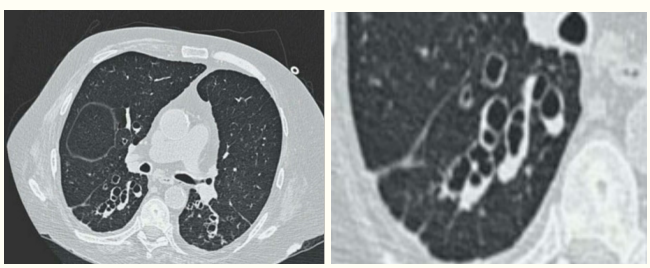
Note : Dry bronchiectasis (Sicca) → TB

Imaging :

IOC : Volumetric multidetector helical CT scan/HRCT.

Findings :

- Airway dilatation : 1 – 1.5 times adjacent vessel diameter → Signet ring sign.
- Tram track sign.
- Tree in bud pattern.


CT : Signet ring

Treatment :

- Airway clearance :
  - Physiotherapy & postural drainage (Best).
  - Nebulized 7% hypertonic saline/steam inhalation.
- Recombinant DNAse : For CF a/w bronchiectasis.
- Resection : Localized bronchiectasis + recurrent + unresponsive to drugs.
- Prophylaxis : Macrolides (Azithromycin) x 6 – 9 months.

Note : m/c organism causing infection in bronchiectasis : Pseudomonas.

----- Active space -----

Chronic Obstructive Pulmonary Disease (COPD)

00:36:00

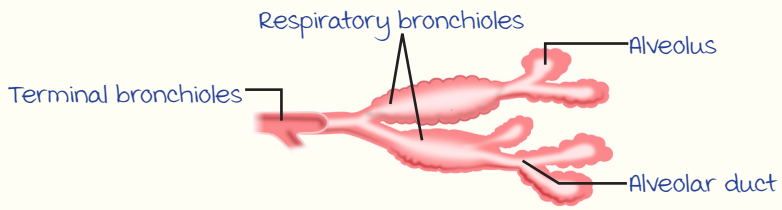
Types :

Chronic bronchitis (Clinical) : Cough with sputum x 3 months for 2 consecutive years.

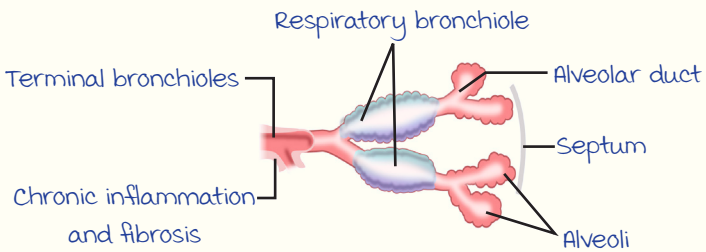
Emphysema (Pathological) :

Airspace dilatation (Distal to terminal bronchiole) —Followed by→ Destruction of walls of airspaces.

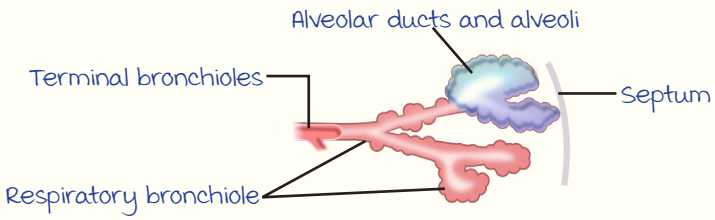
Types of Emphysema :



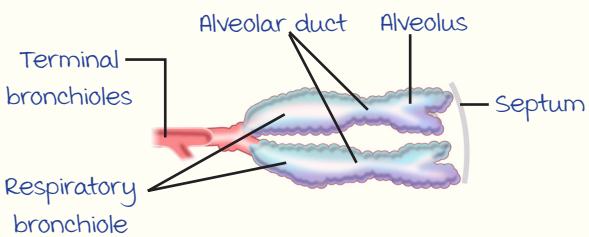
Normal acinus



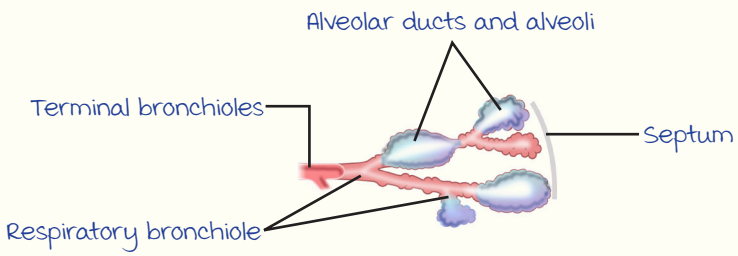
Centriacinar emphysema



Paraseptal emphysema



Panacinar emphysema



Irregular emphysema

	Centriacinar (m/c)	Panacinar	Paraseptal
Demographics	Males	Younger population	Younger males
Smokers	⊕	⊖	⊕
Areas of lung involved	• Respiratory bronchiole • Upper lobe predominant	• Complete involvement • Lower lobe predominant	-
Associations	-	• α-1 antitrypsin deficiency • Liver disease	Spontaneous pneumothorax

Note : α–1 antitrypsin phenotypes → PiMM : Normal.
→ PiZZ : Severe deficiency.

Features of Chronic Bronchitis & Emphysema :

----- Active space -----

	Chronic Bronchitis	Emphysema
Structure involved	• Parenchyma (more) • Vascular changes	Airway
Gaseous changes	• ↓ PaO_a • ↑ $PaCO_a$	• ↓ PaO_a • Normal $PaCO_a$
Type of respiratory failure	Type 2	Type 1
Hypoxia	more	Less severe
Pulmonary hypertension/ Right ventricle failure/ Infections	more common	Less common
Prognosis	more mortality	Better outcomes

Note :

Pulmonary hypertension : D/t ventilation perfusion mismatch $\xrightarrow{\text{Leads to}}$ Cor pulmonale.

Treatment :

Guidelines :

	mMRC 0-1, CAT< 10	mMRC ≥ 2, CAT ≥ 10
0 to 1 moderate exacerbations (Not leading to hospital admission)	Group A : Bronchodilators (Short acting)	Group B : LABA + LAMA
≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization	Group E : • LABA + LAMA • LAMA + LABA ± ICS (if blood eos ≥ 300μL)	

Key :

- LABA : Long acting beta agonist.
- LAMA : Long acting muscarinic antagonists.
- ICS : Inhaled Corticosteroids.
- mMRC : modified medical research council dyspnea questionnaire.
- CAT : COPD assessment test.
- eos : Blood eosinophil count in cells per microliter.

Exacerbation : SABA + Short oral steroid therapy x 5-10 days.

Long Term Oxygen Therapy (LTOT) :

- Given for 14-18 hours/day after exacerbation.
- Indications :
  - PaO_a < 55 mmHg.
  - PaO_a 55-60 mmHg (Pulmonary hypertension/RV failure).

Lobe resection : Localized emphysema (Limited cardiac problem, FEV > 20%).

Lung transplant : Severe cases.

----- Active space -----

Pneumonia Management

00:53:36

CURB 65 Score :

C : Confusion.

U : Urea > 42 mg/dL.

R : Respiratory rate > 30/min.

B : < 90/60 mm Hg.

65 : ≥ 65 years.

Interpretation :

- Score 0, 1 : Outpatient management.
- Score 2 : Inpatient management.
- Score 3 : ICU management.

management :

Inpatient :

- Severe (ICU) :
  - Beta lactam + Macrolide.

    OR
  - Beta lactam + Levofloxacin.
- Non Severe :

  Beta lactam antibiotics

  (Ampicillin-Sulbactam 1.5 - 3 g Q6h)

  +

  Macrolide (Azithral 500mg OD)

  OR

  Levofloxacin

  (750 mg OD)

Outpatient :

- Amoxicillin 1g TDS / Amoxyclav 625mg BD (If risk factors like diabetes ⊕)

  +

  Azithromycin 500mg OD / Doxycycline 100mg BD.

RHEUMATOLOGY REVISION - 1

----- Active space -----

Approach to Rheumatology

00:00:33

1. Intra-articular vs. Extra-articular Involvement :

Features	Intra-articular	Extra-articular
Structures involved	• Synovium • Articular cartilage • Intra-articular joint capsule	• Ligaments • Tendons • Muscles of fascia
Pain	• Diffuse, deep seated pain • Pain on active + passive motion • Swelling/crepitus, deformity	• Localised, superficial pain • Pain on active motion • Localised swelling, away from joint

Synovial involvement :

- Chronic (>6 weeks) inflammatory multi-system autoimmune CTD → RA.
- Progression : Synovitis → Synovial hypertrophy → Pannus → Bone erosion

Articular cartilage :

- Osteoarthritis : Involves the articular cartilage.
  - Loss of joint space.
  - Osteophytes.
  - Subchondral sclerosis.
- Non-inflammatory.

Types of arthritis :

- Synovitis
  - RA
  - SLE
  - SLE like (Sjogren, polymyositis, dermatomyositis)
- Spondyloarthritis (SpA) (Synovitis + Enthesitis+ Dactylitis)
  - Axial SpA: Ankylosing spondylitis (Sacroiliitis)
  - Peripheral predominant SpA
    - Psoriatic arthritis
    - Reactive arthritis
- Crystal arthropathy (Synovitis d/t crystal)
  - Monosodium urate monohydrate (MSUM)/Gout
  - Calcium pyrophosphate dihydrate (CPPD)/Pseudogout

2. Inflammatory vs Non-inflammatory :

a. Inflammatory :

m/c → Rheumatoid arthritis (RA) > Sjogren's syndrome.

b. Non-inflammatory :

Osteoarthritis (OA) : m/c non-inflammatory arthritis (m/c arthritis as a whole).

----- Active space -----

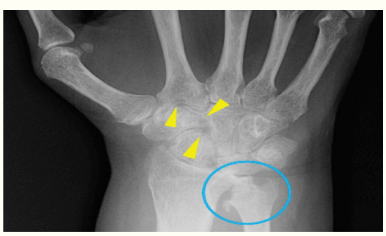
ASSESSMENT PROTOCOL

Parameters	RA findings (Symptoms >6 weeks)
1. Intra-articular v/s extra-articular	Intra-articular (Sometimes has tenosynovitis)
2. Inflammatory v/s non-inflammatory	Inflammatory (Signified by morning stiffness)
3. Unilateral v/s bilateral	Bilateral
4. Symmetrical v/s asymmetrical	Symmetrical
5. U/L vs L/L	Upper limb
6. Mono/oligo/polyarthritis	Polyarthritis
7. Small joint v/s large joint	Small joint
8. Axial vs peripheral	Peripheral

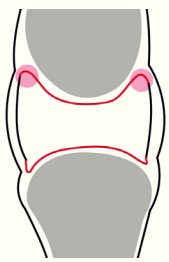
Note : SLE and SLE-like arthritis have a similar clinical picture.

JOINT INVOLVEMENT IN PATTERNS

Erosion :



Erosions in RA



Juxta-articular osteopenia in RA

Causes of erosive arthritis :

1. RA (m/c) —Causes→ Deformity.
2. Psoriatic arthritis.
3. Chronic crystal arthritis (MSUM > CPPD).
4. Multicentric reticulohistiocytosis.

Causes of non-erosive arthritis :

1. SLE/SLE-like arthritis
2. Acute rheumatic fever (Jaccoud's arthropathy)
3. Acute crystal arthropathy
4. Relapsing polychondritis (RPC) → Affects the pinna.

Note :

Erosions in SLE → Rhupus (RA/SLE overlap).

MAGIC syndrome → Mouth And Genital ulcers (Behçet's) + Inflamed Cartilage (RPC).

Jaccoud's arthropathy :

- Non-erosive, deforming arthropathy.
- m/c d/t laxity of ligaments.
- Seen in acute RF, SLE, and SLE-like arthritis.

----- Active space -----

Joints Involved and Spared :

RA :

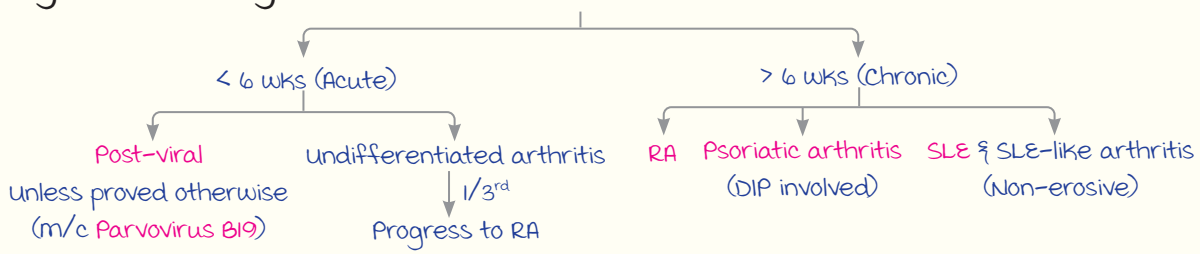
- Involves : MCP + wrist + PIP + cervical spine.
- Spares : DIP (No synovium) + 1st CMC + 1st MTP + axial skeleton (Except C-spine).

Diseases involving DIP :

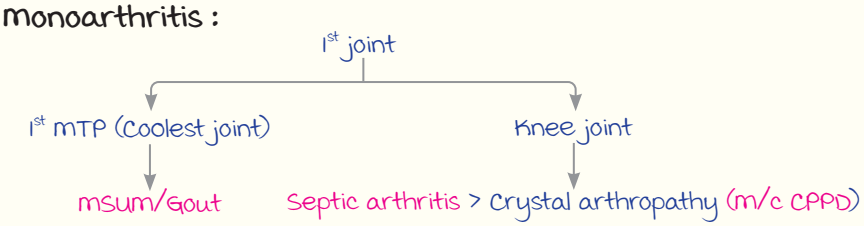
- Psoriatic arthritis (Also involves wrist, MCP, & PIP).
- Multicentric Reticulohistiocytosis (MRH).
- Osteoarthritis (Spares wrist and MCP).
- Juvenile Idiopathic Arthritis (JIA).

CLINICAL PATTERNS

1. Symmetrical Polyarthritis of Small Joints of U/L :

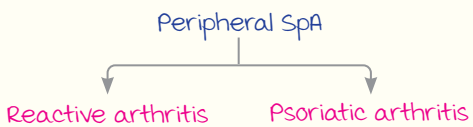


2. Acute Monoarthritis :



3. Asymmetrical Oligoarthritis :

m/c joint involved → Knee



Pathophysiology of RA

00:25:40

m/c multisystem inflammatory autoimmune CTD.

Progression :

1. Very early RA : < 3 months (Must be treated).
2. 3m-1y → Early established RA.
3. 1-2 yrs → Late established RA.
4. Chronic stabilized RA : >2 yrs (Starting Rx → Not useful).

Epidemiology :

- Most common : 40-60 yrs old.
- F : M = 3 : 1.

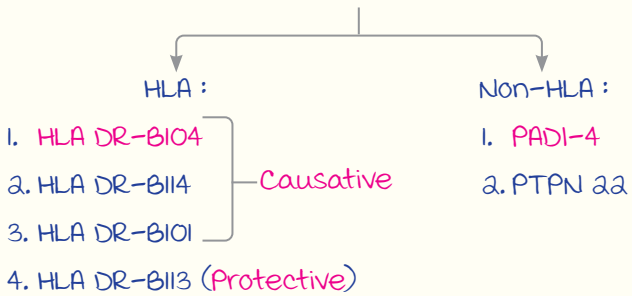
----- Active space -----

Note :

- Rheumatological conditions with F:M = 9:1.
  - Sjögren's syndrome.
  - SLE.
  - Takayasu arteritis.
  - Fibromyalgia.
  - Chronic fatigue syndrome.
  - Primary biliary cirrhosis.
- Mixed connective tissue disease → F:M = 15:1.

Factors :

A. Genetic factors :



- HLA DRB104 :
  - DR β chain hypervariable region → QKRAA motif (Common to HLADRB114).
  - ↑ risk by 5 times.
- PADI-4 :
  - Responsible for post-translational modification (Arginine → Citrulline).
  - Citrulline is an abnormal amino acid.

B. Environmental factors :

1. Smoking :
   - Single most important environmental factor (Bad prognosis).
   - ↑ risk for extra-articular manifestations (↑ ILD).
   - ↑ PADI-4 expression in airway → ↑ abnormal protein modification.
2. Chronic periodontitis → Etiology : Porphyromonas gingivitis.

Note :

- Smoking-associated ILD seen in
  a. Desquamative interstitial pneumonia (DIP).
  b. Langerhan's cell histiocytosis (LCH).
  c. Respiratory bronchiolitis associated ILD (RB-ILD).
  d. ILD-RA.
- Alcohol & OCPs are mild protective factors for RA.
- Pregnancy is a protective factor (↑ IL-10 production → Anti-inflammatory).

Pathology :

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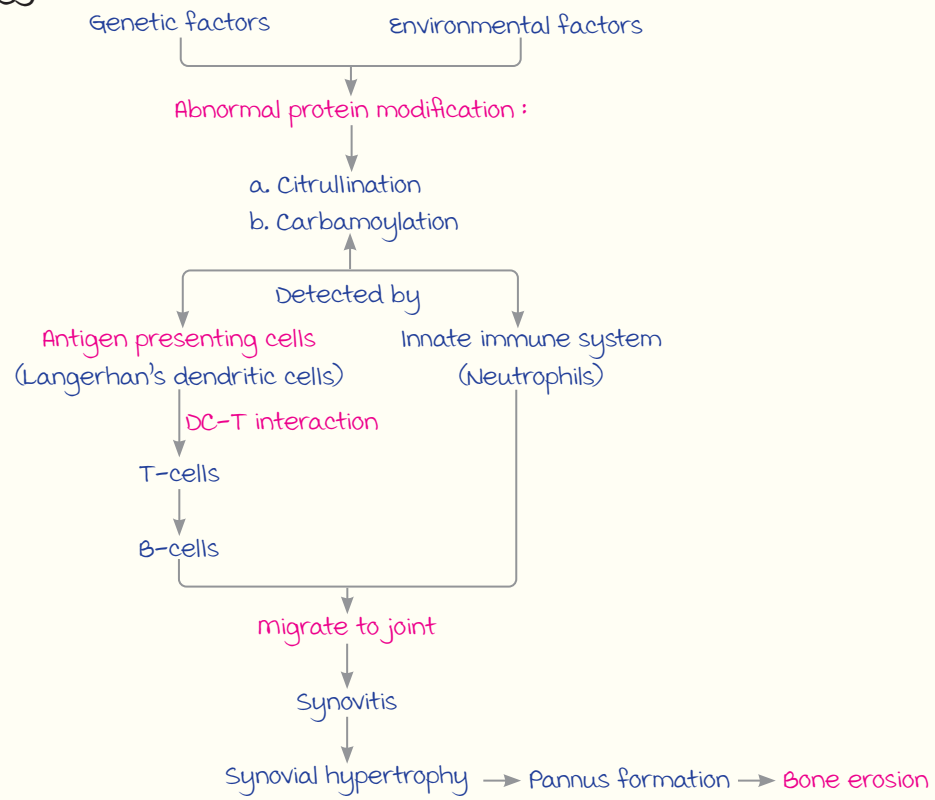


Antibodies in RA

00:44:00

1. Anti-CCP Antibody :

AKA Anti Citrullinated Polypeptide Antibody (ACPA)/mutated Citrullinated Vimentin (MCV) antibody.

- Highly specific, ⊕ in majority cases.
- Best marker for pre-clinical infection.
- High titres → Extra-articular manifestation.

2. Anti-CARP Antibody :

- Anti-carbamoylated peptide antibody.
- A/w palindromic rheumatism.

Note : Anti-PADI-4 antibody is also associated with RA.

3. Rheumatoid Factor :

- Less specific than anti-CCP (75-80%).
  - ⊕ in other rheumatological conditions : Sjögren, cryoglobulinemia (2/3 cases), polyarticular JIA.
  - Also seen IE, leprosy, PBC, parasitic infections, silicosis, sarcoidosis, HBV & HCV.
- High titres → ↑ disease activity.
- IgM antibody against Fc portion of IgG variable heavy chain 3 (IgGVH3).

----- Active space -----

Note :

- Markers for relapse in RA → ESR & CRP.
- Anti-CCP and RF are helpful in prognosis, but are of no use in relapse of RA.

Presentation in RA

00:48:52

CLINICAL PICTURE

A. Articular Manifestations and Progression :

Disease starts at the Distal Radio-Ulnar Joint (DRUJ).

Early changes (Reversible) :

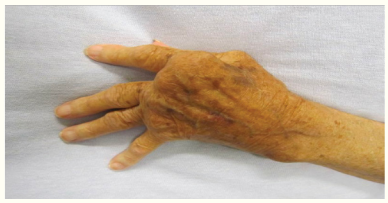
Synovitis
↓
Synovial hypertrophy
(Type A > Type B synoviocytes)
↓
Pannus formation
→ Extra-articular changes :
Flexor tenosynovitis, bursitis

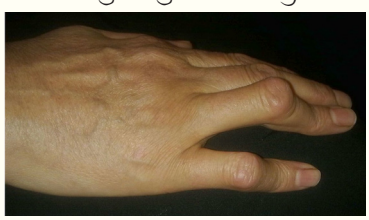
Articular changes : In order of appearance

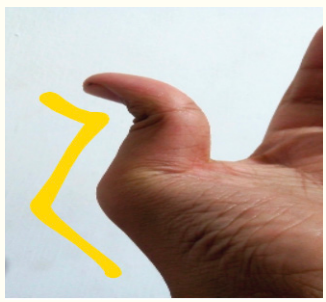
1. Radial deviation of wrist + ulnar deviation of MCP (Zigzag deformity).
2. Subluxation of MCP joint.
3. Rupture of ulnar collateral ligament (Piano Key styloid).
4. Hitchhikers thumb deformity (Abduction + hyperextension).

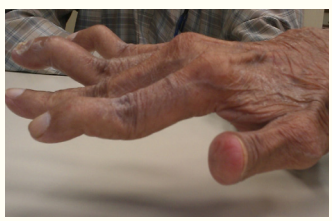
Irreversible changes :

1. Boutonnière's deformity : Flexion of PIP + hyperextension of DIP.
2. Swan neck deformity : Hyperextension of PIP + flexion of DIP.
3. Opera glass hand deformity : Arthritis mutilans. (Complete destruction).


Zig-zag deformity


Boutonniere deformity


Hitchhiker's thumb deformity


Swan neck deformity

Other joints :

Joint affected	Presentation/Deformity
Temporomandibular joint	Mouth opening affected
C1-C2 joint	Odontoid process affected → Acute onset quadriparesis
Cricoarytenoid joint	Change in voice
Lower limb : 5th MTP (m/c)	Pes planus, forefoot varus, ankle valgus

Note : 1st MCP spared, and Knee joint less commonly affected in RA.

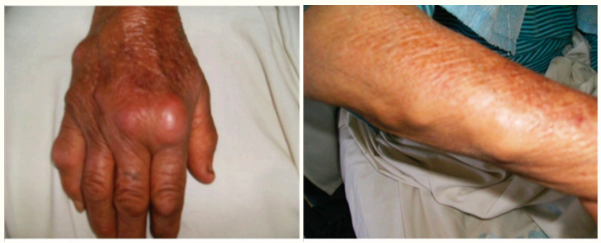
----- Active space -----

B. Extra-articular Manifestations :

m/c extra-articular manifestation → Rheumatoid nodules (40%).

Rheumatoid nodules :

- ↑ risk :
  - Smokers (+++).
  - Anti-CCP/RF positive.
  - Early onset and long duration disease.
- Site : Olecranon.
- Non-tender.
- Granulomatous reaction seen (Type IV hypersensitivity).
- Size ↓ on treatment.



Rheumatoid nodules

PATTERNS OF PRESENTATION

1. Pre-clinical RA :

Presence of risk factors + autoantibodies + symptoms w/o clinical evidence of arthritis.

2. Chronic Symmetrical Polyarthritis :

- m/c presentation (60%).
- > 6 weeks.
- Evidence of pain and inflammation in joints.
- Small joints involved.

Differentials :

- SLE & SLE-like disease → Erosions ⊖.
- Psoriatic arthritis → DIP involvement ⊕.
- CPPD/Pseudo RA → Waxing & waning ⊕, erosion ⊖.

3. Palindromic Rheumatism :

- Intense, brief episodes of monoarticular arthritis.
- Sites : Knee and fingers.
- Attack → Baseline (Intercritical period) → 2nd attack (Similar to gout).
- Antibodies : Anti-CARP positive.

HEAD-TO-FOOT MANIFESTATIONS

1. CNS/Neuro-ocular :

a. C1-C2 myelopathy.
b. Synovial hypertrophy → Entrapment neuropathy.
c. RA related small fibre peripheral neuropathy.
d. Brain parenchyma and thoracic/lumbar/sacral vertebra not involved.

2. Ocular :

a. m/c → Keratoconjunctivitis sicca (Dry eye/2° Sjögren's syndrome).
b. Episcleritis (> scleritis) : Correlates with disease activity.
c. Scleritis : Can cause painful loss of vision and scleromalacia perforans.
d. Uveitis is never seen.

----- Active space -----

3. Hematology :

a. Anemia of chronic disease (m/c anemia).

b. Total lymphocyte count → Normal.

c. Thrombocytosis (2° ITP not seen).

d. Rapidly progressive anemia → Autoimmune hemolytic anemia (Warm Ab, IgG mediated).

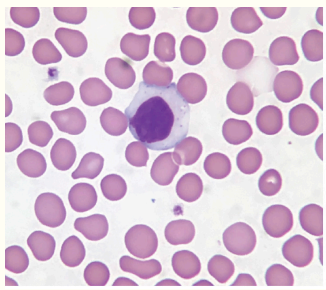
e. ↑ risk of diffuse large B-cell lymphoma (DLBCL).

f. Large granular lymphocytes seen → LGL leukemia (1% progresses to AML).

Felty syndrome : LGL ⟷ (Spectrum) Felty's

RA + neutropenia + splenomegaly.

- Seen late in the course of RA.
- RF and HLADRB1*04 positive.
- Seen in patients with nodules/deformities.
- Antibody against citrullinated histones ⊕.



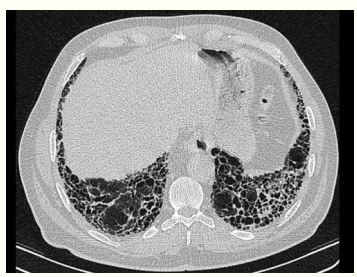
Large granular lymphocytes

4. Lung :

- Pleuritis ± effusion : Exudative, low sugars (<30mg/dL) and low pH effusion.
- ILD (m/c in smokers) → Usual Interstitial Pneumonia (UIP) pattern : Severe manifestation.

Caplan syndrome :

- RA + nodules + Coal workers pneumoconiosis (CWP).
- Seen with active synovitis.
- RF ⊕



UIP pattern

5. Cardiovascular :

a. Vascular :

- Accelerated atherosclerosis → MI (m/c cause of death).
- Immune complex mediated, small vessel lymphocytoclastic vasculitis (CV) with purpura.
- Dangerous vasculitis forms (m/c males) :
  - i. Medium vessel vasculitis : Gangrene, mononeuritis multiplex.
  - ii. GI vasculitis : Intestinal infarcts.

  → Rx : Rituximab

b. Cardiac :

- Pericarditis w/o tamponade (Post-mortem finding).
- Mitral regurgitation (Similar to SLE).

6. Renal :

- 2° renal amyloidosis (m/c).
- Glomerular involvement (membranous) : Very rare.

----- Active space -----

7. Gastrointestinal :

GI vasculitis seen.

Note : Hypoandrogenism, osteoporosis, and pyoderma gangrenosum are also associated with RA.

Treatment of RA

01:11:45

Drug classes :

DMARDS	Biologics	Small molecules
Methotrexate Leflunomide Sulfasalazine Hydroxychloroquine	Anti-TNF α : Etanercept Anti-CD20 : Rituximab Anti-IL-1 : Anakinra Anti-IL-6 : Tocilizumab CTLA-4/IgG : Abatacept	JAK 1/3 ⊖ : Tofacitinib JAK 1/2 ⊖ : Baricitinib

Therapy :

Methotrexate (mtx) :

- 1st line drug.
- 5 mg/week (2.5 mg + 2.5 mg). Dose may be increased to 25 mg/week.
- MOA in RA : ↑ in adenosine.
- Monitoring :
  - CBC (D/t bone marrow suppression).
  - LFT (>4 times ↑ ⟶ Stop MTX).
- Side effects :
  - Mucositis (m/c).
  - Hypersensitivity pneumonitis.
  - ↑ nodule size.
  - Dose dependant bone marrow suppression.

Other drugs :

- In absence of remission with MTX.
- Combination therapy :
  i. Mtx + Sulfasalazine + HCQ (S/E : Bull's eye maculopathy).
  ii. Mtx + TNF-α ⊖ inhibitors (Best).
  iii. Mtx + JAK (may be cardiotoxic).

Remission (Boolean based definition) :

Clinical assessment ≤1 + Tender joint count ≤1 + Swollen joint count ≤1 +CRP ≤1 mg/dL.

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RHEUMATOLOGY REVISION - 2

Features of Systemic Lupus Erythematosus (SLE) 00:00:57

- F >> M.
- Childhood SLE : 100% renal involvement.
- Post menopausal SLE : Milder form (Renal sparing).
- m/c cause of death :
  - 1st 5 yrs → Infection > Lupus nephritis.
  - After 5 – 10 yrs → Accelerated atherosclerosis, MI.
- Male SLE : Severe, poor prognosis.
- Strong family history.

RISK FACTORS

Genetic :

HLA	Non HLA
• C_2, C_4 deficiency • HLA DR2 • HLA DR3	• C_{1q} deficiency (m/c) : Early complement deficiency • TREX gene → Chromosome 3 • Genes on X chromosome : ↑ Risk with Klinefelter's syndrome

Environmental :

- Estrogen (Oral contraceptive pills).
- EBV.
- UV – B rays.

PATHOPHYSIOLOGY

Defective apoptotic/ NETotic debris clearance by neutrophils → Innate immune system activated → (Plasmacytoid dendritic cell → IFN α secreted) → Abundant T cell activation (m/c : Th_2) → (IL4 (Th_2)) → B cell activation : Antibodies formed and immune complex deposited (Type 3 Hypersensitivity)

Sites of Immune complex deposition :

- Vessel (Vasculitis).
- Synovium (Synovitis).
- Glomerulus (Glomerulonephritis).

Anti Nuclear Antibodies (ANA) and ANA profile

00:08:44 ----- Active space -----

ANA :

- Screening test for multisystem connective tissue diseases.
- ANA +ve in :
  - SLE : 97 % cases (3 % ANA -ve → Anti Ro W-52/SS-A).
  - Sjogren's : 85 % cases (Least).

Note :

Conditions where 100 % ANA positive :

- Drug induced lupus erytheomatosus (DILE).
- Type I autoimmune hepatitis.
- Mixed connective tissue disease (MCTD).

Indirect Immunofluorescence (IF) :

- ANA done by IF using Hep 2 cell line.
- ≥ 1 : 80 → Positive titre.

Pattern	Antibodies	Specific diseases
Homogenous	ds - DNA	SLE
	Anti histone	DILE
Dense fine speckled	Rule out CTD	
Fine speckled	• SS - A • SS - B	Sjogren's syndrome
Coarse speckled	anti smith	SLE
	anti U1 RNP	MCTD
Nucleolar	anti PM-SCL-70	Polymyositis - Scleroderma overlap syndrome
Cytoplasm	anti Jo - 1	Polymyositis and Dermatomyositis

Note :

- Overlap syndrome :
  - Features of > 1 CTD.
  - CTD included : SLE, Sjogren (m/c), Polymyositis, Dermatomyositis, Systemic sclerosis, RA.
- MCTD :
  - Specific overlap along with +ve anti U1 RNP + 100 % +ve ANA and F >> M (15 : 1)
  - A/w severe Raynaud's phenomenon.

----- Active space -----

ANA PROFILE (IMMUNOBLOT)

Done for ANA +ve/High suspicion cases.

Antibodies in SLE	Significance
Anti ds – DNA	• Titres measured separately (by ELISA). • A/w ↑ risk Nephritis, vasculitis. • +ve in 75 % of cases. • Assess disease activity in relapses.
Anti Smith	• +ve in 25 % cases. • Most specific.
Anti Ro/La (ANA –ve lupus)	• Indicates 2° Sjogren's. • In pregnancy : A/w Neonatal Lupus + Complete heart block. • Better prognosis in SLE : ↓ Risk in Nephritis, Vasculitis. • A/w Subacute cutaneous lupus. • A/w Shrinking lung syndrome (d/t diaphragmatic palsy).
Antiphospholipid antibody	Seen in 1/3rd SLE patients.
Anti RBC	Indicates warm Ab Autoimmune Hemolytic Anemia (IgG).
Anti platelet	Causes 2° ITP in SLE.
Anti Glutamate/ anti Neuronal	• M/c Antibodies in CNS lupus. • A/w cognitive dysfunction.
Anti – Ribosomal – P	A/w psychosis/depression in lupus.

FACTORS CORRELATING WITH DISEASE ACTIVITY IN SLE

1. anti ds – DNA titres.
2. ↓ C_3, ↓ C_4 levels.
3. ↓ CRP, ↑ ESR.

Symptoms and Manifestations of SLE 00:22:42

Constitutional Symptoms (most striking) :

Fever, fatigue, weight loss.

MANIFESTATIONS

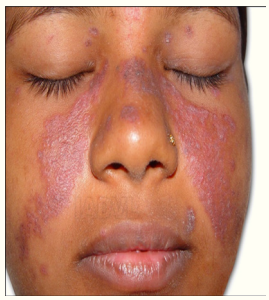
Musculoskeletal :

- Chronic inflammatory polyarthritis, multisystem involvement.
- B/L symmetrical small joints of upper limb affected.
- Non erosive.
- Deformity d/t laxity of ligament : Jaccoud's arthropathy.

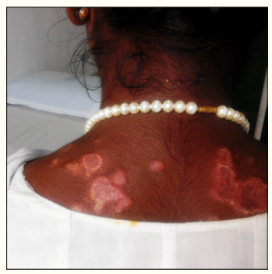
Mucocutaneous :

----- Active space -----

Cutaneous Lupus Erythematosus (CLE)	Description of Rash
Acute (ACLE) 1. Localised Rash (m/c) 2. Generalised Rash – Rare 3. Toxic epidermal necrolysis	Localized Rash (AKA butterfly rash): • Malar, photosensitive, ± scaling • Non scarring, highly erythematous • A/w oral ulcers (Hard palate) • Spares nasolabial folds • Non premalignant
Subacute (SCLE) 1. Annular SCLE (m/c) 2. Psoriasiform SCLE	Rash : • ↑ photosensitivity, Non scarring • A/w anti Ro/La : ↓ Nephritis, vasculitis risk. • Spares mid facial region • A/w HLA DR3
Chronic (CCLE) (or) Disseminated LE (DLE) : • m/c : Discoid Rash • 5/20 rule : – 5 % discoid rash ⟶ SLE – 20 % SLE ⟶ Discoid rash	Discoid Rash : • Site : Face, scalp, neck • Deep circular erythematous • Dermal atrophy + follicular plugs • Premalignant risk for SCC • Scarring alopecia • Carpet track sign on back.



Malar rash



SCLE

Disseminated DLE

CNS involvement :

- Cognitive dysfunction (m/c) : Anti glutamate antibody.
- Psychosis, Depression : Anti ribosomal – P Antibody.
- Axial skeleton spared ; No entrapment neuropathy.
- Small fibre neuropathy can be seen.

Ocular :

2° Sjogren syndrome (m/c), absent uveitis.

Lung :

- Pleuritis ± effusion :
  - Lymphocytic exudate.
  - Normal sugars.
  - Risk of malignancy related effusion.
- Diffuse alveolar haemorrhage : marker of high disease activity.

Hematological :

- Anemia of chronic disease, warm Ab AIHA.
- Leucopenia.
- Thrombocytopenia (2° ITP).
- ↑ Risk of DLBCL.

CVS :

Cardiac manifestations :

- Pericarditis without tamponade (m/c).
- Mitral regurgitation (m/c valvular heart disease).
- Libman sacks endocarditis (Vegetation on undersurface of valve cusps).

----- Active space -----

Vascular manifestations :

- ↑ risk of acute coronary syndrome (After 5-10 years).
- Small vessel vasculitis (Leucocytoclastic Angitis).
- Dangerous forms : GI and CNS vasculitis.

Renal :

Class	Type & features	Treatment
1	Minimal mesangial	No treatment required
2	Mesangioproliferative	
3	Focal (< 50 % Glomeruli involved)	
4	Diffuse (> 50 % Glomeruli involved) - m/c type - Most dangerous type Investigations : 1. Immunofluroscence (IF) : - Full house appearance (IgG, IgM, IgA, C_{1q}, C_3 seen) 2. Electron microscopy : - Hematoxilin bodies of Gross	Aggressive Immunotherapy
5	Lupus membranous Nephropathy (↓ Risk for CKD)	• Rx : MMF + CNI based regimes • Refractory to steroid therapy

DIAGNOSTIC CRITERIA

SLICC : ≥ 4 criteria (At least 1 clinical and 1 laboratory criteria) or biospy proven lupus nephritis with positive ANA/Anti - DNA).

Treatment of SLE

00:36:55

Mild to moderate SLE : Skin + Joint involved only.

Only steroid + Hydroxycholoquine + Methotrexate + Belimumab (B - Lymphocytestimulation inhibitor) (If arthritis +)

Severe SLE (Organ involved/Life threatening) :

- IV methyl prednisolone → Oral prednisolone + IV cyclophosphamide/mycophenolate mofetil (MMF)
- Assess response to Rx X 3 months
  - Good : Maintenance Rx X 3 years (Oral steroids + MMF > Axathioprine).
  - Poor : Change cyclophosphamide to MMF or vice versa → No response after 6 months (Resistant Lupus) → Rx : Rituximab

Indications for plasmapheresis in SLE :

- Diffuse alveolar haemorrhage.
- CNS vasculitis.

Classification of Spondyloarthritis

00:39:46

----- Active space -----

Types :

Axial Predominant	Peripheral predominant
1. Non - radiographic spondyloarthritis 2. Radiographic spondyloarthritis	1. Reactive arthritis 2. Psoriatic arthritis 3. IBD arthritis (Enteropathic arthritis) 4. Juvenile onset spondyloarthritis.

Features :

- Extra - articular manifestation : Asymmetrical, anterior, alternating, anterior uveitis (m/c).
- HLA B27 +ve
- RF -ve
- Axial component : Sacroilitis.
- Age < 40 years.
- Major central pathogenic cytokine : TNF α.
- Males > females.

Axial Predominant Spondyloarthritis

00:42:39

NON-RADIOGRAPHIC SPONDYLOARTHRITIS

- Symptoms: +
- MRI : Sacroiliitis
- HLA B - 27 +
- Normal X-ray
- 5 - 10 % of patients $\xrightarrow{5-10\ yrs}$ Radiographic Spondyloarthritis.

RADIOGRAPHIC SPONDYLOARTHRITIS

- AKA Ankylosing spondylitis.
- M : F = 3 : 1
- Age : Late teens to early twenties.

Disease Progression :

Inflammatory granulation tissue → Erodes annulus fibrosus + Calcification of its peripheral fibers → Syndesmophyte formation (Thin, marginal, symmetrical) → Bony ankylosis → Bamboo spine.

Clinical Features :

- Chronic presentation (> 3 months).
- Inflammatory alternating buttock / Deep lower back pain.
  - Early morning stiffness (> 30 mins) → Improves with activity.
  - Nocturnal awakening due to pain.
  - d/t B/L Symmetrical Sacroiliitis (ascending).
  - m/c complication : Spinal fracture (C_5 - C_6).

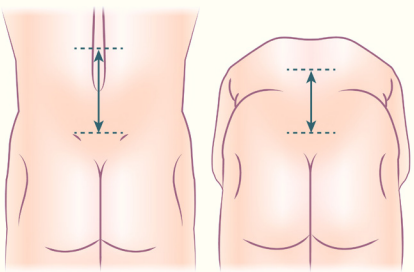
----- Active space -----

- Enthesitis :
  - Achilles tendinitis and plantar fasciitis.
  - Costo/manubriosternal joint : Chest pain.
- Root Joint Involvement : Hip and shoulder joint arthritis.

- Extra-articular manifestations :
  - Uveitis (most common).
  - Lung : B/L upper lobe fibrosis.
  - Cardiac : Aortic regurgitation.
  - Renal : 2° IgA nephropathy.
  - Osteoporosis.

Investigations :

1. X - ray : IOC.
   Findings :
   - Sacroiliitis.
   - Bony ankylosis : Bamboo spine.
   - Square wave vertebrae.
   - Secondary sclerosis : Shiny corner sign.
   - Bony erosions : Romano sign.
   - Interspinous ligament calcification : Dagger sign.
   - Apophyseal joint capsule calcification : Trolley track sign.
2. MRI : STIR (T_2) sequence to detect sacroilitis.



Clinical Test : Modified Schober Test

TREATMENT OF AXIAL PREDOMINANT SPONDYLOARTHRITIS

- First line : NSAIDS (Indomethacin → Reverses disease progression) + Physiotherapy.
- TNF - α inhibitors.
- IL - 17 antagonists : Secukinumab.

Note :

Diffuse idiopathic skeletal hyperostosis (DISH) :

- Flowing candle wax appearance (d/t ligamentous calcification).
- A/w metabolic syndrome.
- Intervertebral disc space preserved : No sacrolitis.

Peripheral Predominant Spondyloarthritis

00:55:43

REACTIVE ARTHRITIS

Causes :

- Post infective (After 2-4 weeks) :

Infection	Organism	m : F ratio
Genitourinary Tract	Chlamydia trachomatis (m/c world wide)	m >> F
Gastrointestinal Tract	Shigella flexneri (m/c : India)	m = F
Upper respiratory tract	• β -hemolytic streptococcus • Chlamydia pneumoniae	-

Note : Neisseria and E. coli do not cause reactive arthritis.

----- Active space -----

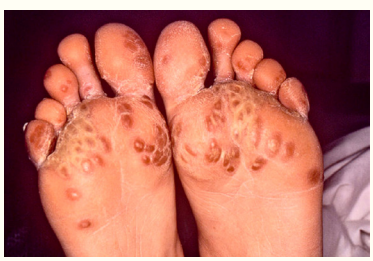
- HLA B27 +ve : ↑ Risk for chronic reactive arthritis.

Features and Manifestations :

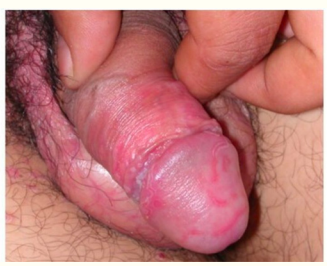
- Peripheral predominant spondyloarthritis :
  - Asymmetrical (LL > UL) oligoarthritis.
  - Additive and painful.
  - Acute onset + Sterile/non-purulent.
- Axial Arthritis :
  - Asymmetrical sacroilitis
  - Syndesmophytes : Thick, non-marginal, coarse, fluffy, asymmetrical.
- Enthesitis.
- Dactylitis : Sausage digits.
- Mucocutaneous features :
  - Keratoderma blenorrhagica.
  - Circinate balanitis.
- Extra - articular manifestations : Aortic regurgitation.

Treatment :

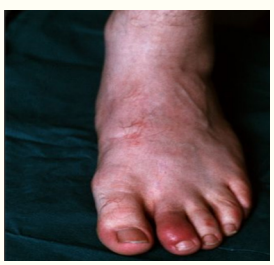
- NSAIDs : Indomethacin.
- Chronic reactive arthritis : Sulfasalazine.



Keratoderma blenorrhagica



Circinate balanitis



Dachylitis

IBD ARTHRITIS

- Crohn's disease > Ulcerative colitis.
- M = F.
- 25 % cases : Peripheral predominant arthritis.
- 10 % cases : Ankylosing Spondylitis like arthritis (HLA B27 +ve).

Types :

Type I : LMAP	Type II : SMAP - U
Large joint predominant (m/c : Knee), Migratory, Asymmetrical, Pauci articular arthritis	Small joint predominant, Migratory, Aggressive, Polyarticular arthritis + Uveitis
Correlates with bowel disease activity	Does not correlate with bowel disease activity
Self limiting	-

Treatment :

DOC : TNF α inhibitors.

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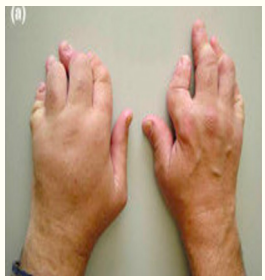
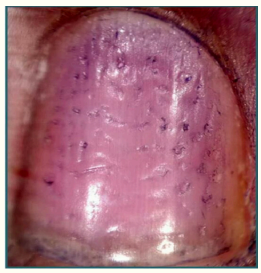
PSORIATIC ARTHRITIS

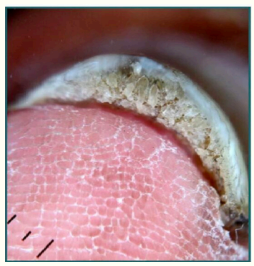
- 60/20/20 rule :
  - 60 % : Psoriasis f/b → Arthritis.
  - 20 % : Psoriasis and Arthritis concurrently.
  - 20%: Arthritis f/b → Psoriasis.
- Male = Female.
- Age: > 40 years.
- HLA CW*0602 +ve.

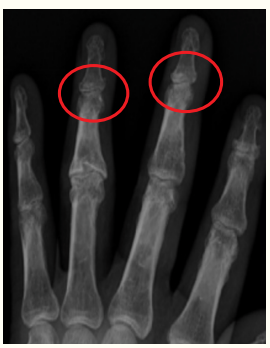

Arthritis mutilans

Clinical features :

- Peripheral predominant arthritis :
  - Plaque psoriasis > Pustular psoriasis (Severe destructive arthritis a/w HIV).
- Enthesitis.
- Dactylitis.
- Nail changes :
  - Pitting (m/c).
  - Onycholysis.
  - Horizontal ridging.
  - Yellowish nail margin.
  - Oil drop sign.
- Extra-articular manifestations :
  - Aortic regurgitation and chronic B/L posterior uveitis.


Nail pitting


Onycholysis


Pencil – in – cup deformity

Patterns of Psoriatic Arthritis :

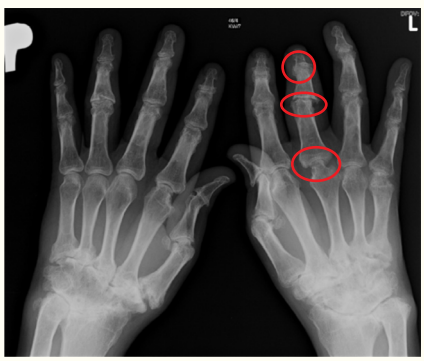
- Symmetric polyarthritis (m/c).
- Asymmetric oligoarthritis.
- Axial arthropathy : Cervical spine involved, thick, asymmetrical, non-marginal, coarse, fluffy syndesmophytes.
- Pure DIP arthritis.
- Arthritis mutilans.

X-ray findings :

- Ray pattern : Involvement of DIP, PIP & MCP joints (Characteristic).
- Pencil – in – cup deformity : metatarsophalangeal joints.
- Arthritis mutilans.
- Whiskering : Marginal erosion with adjacent bony proliferation.
- Ivory phalanx.

Treatment :

- First line : TNF – α inhibitors.
- Second line : Methotrexate.
- Others :
  - IL – 17 inhibitors : Secukinumab.
  - IL – 12/23 inhibitors : Ustekinumab.
  - JAK inhibitors : Tofacitinib, Baricitinib.
  - PDE – 4 inhibitors : Apremilast.


Ray pattern

COMPARING MANIFESTATIONS OF SPONDYLOARTHRITIS

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	Ankylosing Spondylitis	Reactive Arthritis	IBD Arthritis	Psoriatic Arthritis
Laterality/Symmetry	B/L sacroiliitis	Asymmetrical involvement	B/L sacroiliitis	Asymmetrical involvement
Syndesmophytes	Thin marginal symmetrical	Thick non - marginal asymmetrical	Thin marginal symmetrical	Thick, non - marginal asymmetrical
Enthesitis	+	+++	-	+++
Dactylitis	-	+++	-	+++
Skin and Nail changes	-	Mucocutaneous manifestations	-	Nail changes
Ocular	Anterior uveitis	Anterior uveitis	Uveitis a/w SMAP. u	B/L chronic posterior uveitis

Summary of Arthritis

01:15:35

Chronic symmetrical small joint arthritis	Acute asymmetrical oligoarthritis	Monoarthritis
• Rheumatoid arthritis. • SLE/SLE - like arthritis • Psoriatic arthritis (DIP joint +) • Calcium pyrophosphate deposition disease (CPPD)	• Reactive arthritis • Psoriatic arthritis	• Crystal arthritis (MTP joint) • Septic arthritis (Knee +)

Non-inflammatory arthritis	Inflammatory non-erosive arthritis	Erosive arthritis
• Osteoarthritis. • Asymptomatic CPPD. • Calcium oxalate crystal disease. • Calcium hydroxy apatite deposition disease.	• SLE • SLE-like arthritis	• Rheumatoid arthritis • Chronic tophaceous gout • Peripheral spondyloarthritis

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RHEUMATOLOGY REVISION – 3

Classification of Vasculitis

00:00:37

Vasculitis

- Based on size of the predominant vessel involved
  - a. Large vessel :
    - Giant cell arteritis (GCA)
    - Takayasu arteritis
  - b. Medium vessel :
    - Kawasaki
    - Polyarteritis nodosa (PAN)
  - c. Small vessel (m/c : Venules)
  - d. Variable vessel :
    - Bechet's disease
    - Cogan's syndrome
- Single organ vasculitis
- 2° vasculitis

a. Anti Neutrophilic Cytoplasmic Antibody (ANCA) :
- Granulomatosis with Polyangiitis (GPA)
- Microscopic Polyangiitis (MPA)
- Eosinophilic Granulomatosis with Polyangiitis (EGPA).

b. Immune Complex Mediated :
- IgA vasculitis (Henoch-Schonlein purpura)
- Cryoglobulinemic vasculitis (CAV)
- Goodpasture Syndrome (GPS)
- Hypocomplementemic urticarial vasculitis (HUV) : Anti C_{1q} antibodies.

Secondary vasculitis :

Causes :

1. Connective tissue diseases (CTD) :
   - Immune complex (IC) mediated small vessel vasculitis (m/c).
   - Medium vessel involvement :
     - Rheumatoid arthritis : Gangrene, GI vasculitis.
     - SLE : CNS vasculitis, GI vasculitis.

   a. Only CTD causing aortitis : IgG_4 related disease.
2. Lymphoproliferative malignancy.
3. Drug Induced :
   - IC mediated vasculitis.
   - ANCA vasculitis : Hydralazine, PTU, minocycline, levamisole.
4. Infections :
   - HBV : Vasculitis similar to PAN.
   - HCV : Vasculitis similar to Cryoglobulinemia.

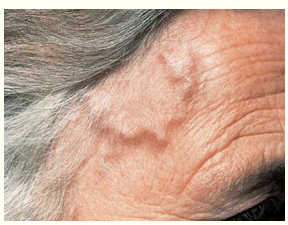
Note : Cogan's Syndrome ⟶ Aortitis + Interstitial Keratitis + vestibulitis (SNHL).

Temporal Arteritis and Takayasu Arteritis

00:08:52

Pathogenesis :
- Transmural inflammation of vessel wall (Granulomatous inflammation).
- a/w HLA DRB_1*04.

Note : Causes of granulomatous vasculitis.
- GPA
- EGPA
- Temporal arteritis
- Takayasu arteritis
- Rheumatoid arthritis
- Cogan's Syndrome
- CNS vasculitis



Temporal arteritis

TEMPORAL ARTERITIS (GIANT CELL ARTERITIS) VS. TAKAYASU ARTERITIS

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	Temporal Arteritis	Takayasu Arteritis
Features	• Age : > 50 years (median : 72 years) • F > M	• Age : <40 years (median : 25 years) • F >> M
Arteries affected	Superficial temporal (M/C) > vertebral > ophthalmic > Posterior ciliary artery (Causes altitudinal hemianopia & is a/w Anterior Ischemic optic neuropathy)	• Left subclavian artery (M/C) • Aorta • Mesenteric, coronary arteries • Renal, pulmonary artery ±
Clinical Symptoms	Typical GCA (M/C) : • New onset headache + ↑ ESR • Jaw claudication • Temporal artery tenderness • Visual symptoms • a/w Polymyalgia Rheumatica (PMR) Atypical GCA : • Pyrexia of unknown origin (PUO)	• Upper limb claudication (M/C) • Asymmetry in pulse & BP • Carotid/Aortic bruit ⊕ • Renovascular hypertension especially in young Indian females • Renal & pulmonary involvement can be seen
Investigations	• IOC : Temporal artery biopsy (Skip lesions) • Doppler ultrasound • PET scan : Rule out aortitis	• IOC : CT angiogram • Best Ix : MR Angiogram • Gold standard : Arteriography
Treatment	• Steroids : Immediately started in suspected GCA (To avoid vision loss) • Relapse : Tocilizumab (IL-6 inhibitor)	Steroids ± surgical revascularization (Especially renal artery involved)

Note : Polymyalgia Rheumatica (PMR).

- A/w GCA with ↑ ESR (> 50).
- Good response to low dose steroids.
- C/F : Pain + Stiffness of hip, shoulder and pelvic girdle.

ANCA Vasculitis

00:20:18

- Antibodies against Proteinase 3 or myeloperoxidase (MPO) in neutrophilic granules.
- ANCA study :
  - Screening test by Indirect Immunofluorescence (IIF)
  - Confirmatory test : ELISA (For p - ANCA).

IIF PATTERNS

	Cytoplasmic	Perinuclear	
	True ⊕ C - ANCA	True ⊕ p - ANCA	False ⊕ p ANCA
Ab against Proteiase-3	⊕	⊖	⊖
Ab against MPO	⊖	⊕	⊖
Causes	• GPA (70 - 75 %) • MPA (40 %) • Renal limited vasculitis • EGPA	• Renal limited vasculitis (M/C) • MPA (50 %) • EGPA, GPA • Drugs (Hydralazine) • Goodpasture syndrome	• Type I autoimmune hepatitis • Primary sclerosing cholangitis • RA, IBD • Infective endocarditis • Cystic fibrosis

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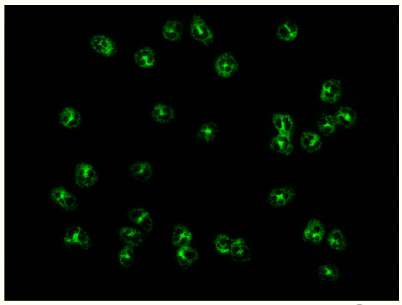
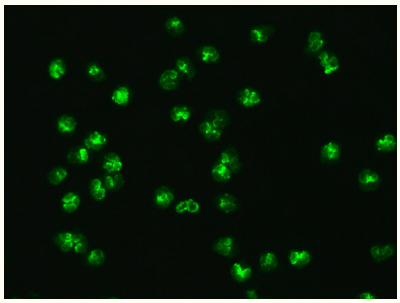


Cytoplasm pattern : C-ANCA ⊕



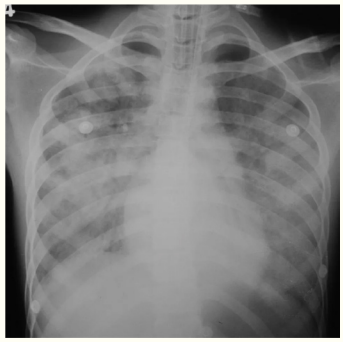
Perinuclear pattern : p-ANCA ⊕

GPA v/s MPA v/s EGPA v/s PAN

	GPA (Wegner's granulomatosis)	MPA	EGPA (Churg strauss syndrome)	PAN
ANCA	C – ANCA > p ANCA (Pauci immune)	p – ANCA > C – ANCA (Pauci – immune)	⊖	⊖
Vasculitis	Necrotising small vessel vasculitis (Neutrophils + Fibrinoid necrosis)		Eosinophils + Fibrinoid necrosis	Focal necrotising inflammation
Granuloma	⊕	⊖	⊕ (Extravascular)	–
Age	> 40 yrs	Elderly	–	–
Vessels affected	Small vessels		Small + Medium vessels	Medium vessels
Constitutional Symptoms	⊖	⊕	⊖	⊕ (Weight loss)
URT Symptoms	• Mainly GPA • Sinusitis (Staph. aureus) • SNHL	• Subglottic stenosis • Serous otitis media • Midline nasal deformities	Asthmatic phase ↓ Vasculitic phase	⊕
LRT Symptoms	• Seen in most cases • Thick walled cavitating nodules • Diffuse alveolar haemorrhagic	Diffuse alveolar haemorrhage	Fleeting lung infiltrates (Asthma like featues)	Lung spared.
Kidney Symptoms	• Rapidly proliferating glomerulonephritis (RPGN) – Type III • Seen in all MPA cases		Rare (Mild in severity if present)	Kidney spared.
Minor Manifestations				
Ocular	Scleritis	⊖	⊖	⊖
Skin	⊕	+ + + (Purpura)	⊕	Nodules, ulcers, gangrene, Livedo reticularis
Neuropathy	+ +	⊕	+ + + (Cranial neuropathy, Mononeuritis multiplex)	Mononeuritis multiplex or polyneuropathy

Other features :

1. EGPA :
   - Eosinophilic gastroenteritis.
   - Eosinophilic myocarditis (m/c cause of death).
2. PAN :
   - a/w Hepatitis B positivity & Hairy cell leukemia.
   - Microaneurysms ⊕ (MR Angio > CT angiography).
   - Involvement of :
     - Bronchial artery : Hemoptysis.
     - Testicular artery : Tender/pain.
     - Renal artery : RVH.
   - Poorest prognosis.



Diffuse alveolar haemorrhage

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TREATMENT OF ANCA VASCULITIS

First line : Steroids + oral/IV Cyclophosphamide (or) Rituximab.

Maintenance : Azathioprine > mycophenolate mofetil.

EGPA : IL – 5 Antagonist (mepolizumab).

Immune Complex Mediated Vasculitis

00:37:21

	IgA vasculitis	Cryoglobulinemia
Age	• Children (< 5 years) : M > F • Adults : More severe renal involvement	Middle aged females
Skin	Non thrombocytopenic palpable purpura in lower limb (IgA) : 100% cases	• Confluent purpura • Medium vessel involved : Ulcers, gangrene
GIT	• Abdominal angina (m/c) : Severe abdominal pain. • Intussusception (Dangerous complication) • Testicular torsion • Scrotal swelling • Blood in stool	Hepatitis C Virus (HCV) a/w Type 2, 3 of cryoglobulinemia
Joints	Mnemonic : KLMNO arthritis • Knee joint predominant • Large joint • Migratory, Non-deforming • Oligoarthritis	SLE like arthritis a/w myalgia
Renal	• IgA nephropathy (Self limiting) • RPGN	Membranoproliferative glomerulonephritis (MPGN)
Types	-	3 types : • Type 1 : Monoclonal IgM a/w Waldenstrom's disease • Type 2 : Monoclonal IgM + Polyclonal IgG (RF ⊕) • Type 3 : Polyclonal IgG (RF ⊕)
Rx	• Joint and GIT manifestations : Rx ⟶ Steroids • Good prognosis in children.	• HCV management • If severe : Rituximab

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RHEUMATOLOGY REVISION - 4

IgG4 Related Disease

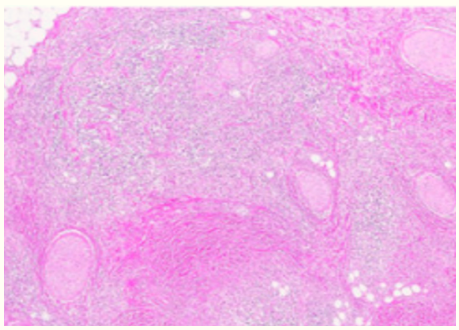
00:01:05

FEATURES

- Age : >60 years; M>F.
- Subacute presentation.
- Constitutional symptoms without fever and arthritis.

PATHOPHYSIOLOGY

Chronic antigenic stimulation (Galectin-3) → ↑↑ IgG4 → Activate myofibroblasts → ↑ collagen formation —TGF-β→ Fibrosis >> Inflammation.



Storiform fibrosis

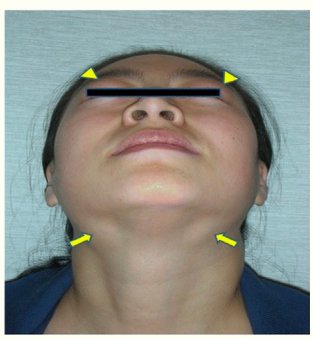
Histology findings :

- Tumefactive lesions/lymphadenopathy.
- Storiform fibrosis (Swirling/cart-wheeling).
- Obliterative phlebitis.
- Mild eosinophilia (H/o atopy ⊕).
- No fibrinoid necrosis/granuloma.

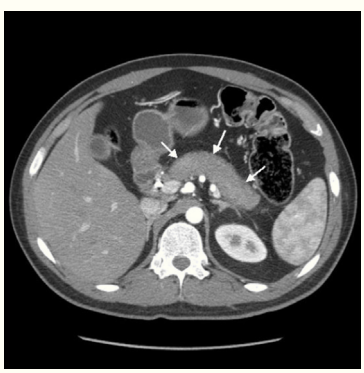
CLINICAL MANIFESTATIONS

Major manifestations :

Type I autoimmune pancreatitis	Submandibular glands swelling	Lacrimal glands swelling	Retroperitoneal fibrosis (RPF)
• m/c manifestation. • Young age group. • Presentation : Obstructive jaundice > acute pancreatitis. • Exocrine + endocrine pancreatic insufficiency (Type 3c DM). • Sausage shaped, large pancreas + irregular borders.	• Painless/asymptomatic B/L symmetrical swelling. • Minor sicca symptoms (Good response to steroids).		Present as : B/L obstructive nephropathy.



Submandibular gland swelling



Sausage-shaped pancreas

Note :

Parotid + submandibular + lacrimal gland swelling → Previously Mikulicz syndrome.

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Minor manifestations :

Organ/system	Manifestations
CNS	• Lymphocytic hypophysitis (Postpartum + headache). • Pachymeningitis (Brain parenchyma spared).
Eye	Orbital pseudotumour (Painful inflammatory mass).
Lungs	• Bronchovascular bundle thickening. • Non-specific interstitial pneumonia (NSIP) : Risk of ILD. • Paravertebral mass.
Vascular	Vasculitis : Proximal aortitis (Only vasculitis affecting aorta)
Biliary tract	IgG4 sclerosing cholangitis (Previously : Primary sclerosing cholangitis).
Thyroid	Reidel's thyroiditis.
Renal	Tubulointerstitial nephritis > Membranous nephropathy (Low complements).
Lymphatic	Lymphadenopathy ±.

INVESTIGATIONS

- Serum IgG4 levels : ↑/Normal.
- Best Ix : Biopsy → ↑ IgG4/IgG ratio in sample.

TREATMENT

- First line : Steroids (Excellent response in 2 weeks).
- Relapse : Rituximab (Steroid sparing).

Sarcoidosis 00:19:00

FEATURES

- Age : >18 years.
- M=F.
- Histology : Non-caseating granulomas >> caseating.
- Immune paradox : ↑ T-lymphocytes in granuloma → Lymphopenia. (↑ infection risk)

BASED ON DISEASE PROGRESSION

Prognosis →
- Spontaneous resolution (m/c).
- Mortality (5%).
- Chronic disease (25%).

Acute Sarcoidosis :

	Lofgren syndrome	Heerfordt-waldenstrom syndrome
Triad	1. Arthritis. 2. Hilar lymphadenopathy. 3. Erythema nodosum. } ± fever, ± uveitis.	1. Uveitis. 2. Parotitis. 3. 7th nerve palsy. } ± fever

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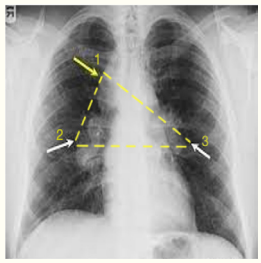
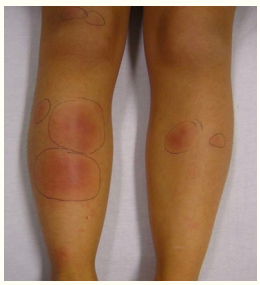
	Lofgren syndrome	Heerfordt-waldenstrom syndrome
Features	• Arthritis (misnomer) : Acute onset painful B/L ankle joint tenosynovitis.  • Garland sign → Lymphadenopathy : 1. Paratracheal. 2. Right hilar. 3. Left hilar.  • Erythema nodosum : Mnemonic → 3P's. Painful. Pre-tibial. Papule without pigmentation. • Prognosis : Good (HLADRB1*03)	m/c manifestations : • Neurological : B/L LMN 7th nerve palsy. • Ocular : Acute B/L symmetrical anterior uveitis.

Note :

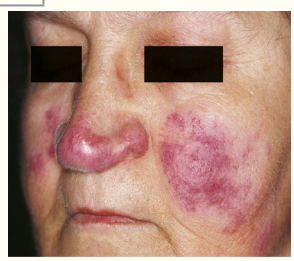
Condition	Uveitis
Spondyloarthritis	Acute anterior alternating asymmetrical uveitis
Behcet's disease	Posterior uveitis

Chronic Sarcoidosis :

Lung > skin > eye.

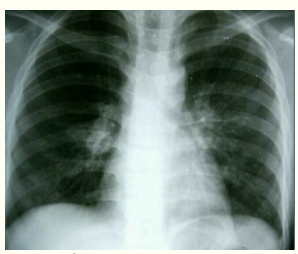
Eyes : Chronic uveitis, panuveitis, retinal vasculitis.

Skin : Lupus pernio (maculopapular/nodular).

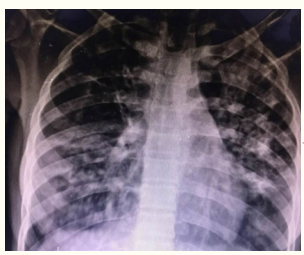

Lupus pernio

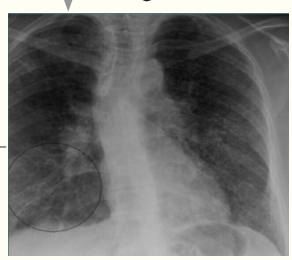
Lung :

- Interstitial lung disease : m/c cause of death.
- Upper lobe ILD : NSIP.
- Bronchovascular bundle thickening.
- No paravertebral mass/aortitis.
- Small airway disease and endobronchial obstruction ⊕.
- Stages : Scadding scoring system (Based on CXR).


Stage 1

Stage 1 : B/L hilar lymphadenopathy.
↓
Stage 2 : • ↓ hilar lymphadenopathy.
• ↑ lung infiltrates.
↓
Stage 3 : ↑↑ Lung infiltrates.
↓
Stage 4 : Fibrosis.


Infiltrates with fibrosis


Stage 2

- Clinical paradox (Lymph node size ↓, disease ↑).

Head to toe manifestation :

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Organ system	Manifestations
CNS	• B/L LMN 7th nerve palsy (m/c) : A/w Heerfordt syndrome. • Acute transverse myelitis. • Central Diabetes Insipidus. • Leptomeningeal enhancement.
Eye	May affect any compartment.
Salivary glands	Parotitis (Heerfordt's) > parotid swelling.
Cardiac	Dilated cardiomyopathy, conduction blocks.
Vascular	Immune complex mediated small vessel vasculitis.
Joint	Arthritis, bone cyst, bone erosions.
Liver	Intrahepatic cholestasis.
Kidney	→ AKI (Prerenal) : Hypercalcemia. (↑ 1 α hydroxylase from granuloma → ↑ vit D3). → CKD : Tubulointerstitial disease.
Bone marrow (Rare)	Pancytopenia, splenomegaly.

Note :

Connective tissue disease causing erosive arthritis : MCTD > sarcoidosis.

MANAGEMENT

Investigations :

- Endobronchial ultrasound (EBUS) + transbronchial biopsy → IOC.
- PET scan (Localization).

Treatment :

- 1st line : Steroids.
- 2nd line : Methotrexate, azathioprine, hydroxychloroquine.
- 3rd line : TNF-α inhibitors.

Sjogren's Syndrome

00:38:37

FEATURES

- Multisystem autoimmune CTD (2nd m/c).
- Middle aged ; F >> M.
- Dry eye + dry mouth (Autoimmune exocrinopathy).
- 50% case : Extraglandular manifestations → Serious (Some cases).
- 2° Sjogren's : m/c cause → Rheumatoid arthritis > SLE.

----- Active space -----

CLINICAL MANIFESTATIONS

Glandular :

Salivary gland swelling :

- IL-18 mediated swelling.
- m/c : Parotid gland.
- Sicca symptoms +++ (Steroid non-responsive).
- Asymmetric painful enlargement → ↑ risk of marginal zone B-cell lymphoma.
- Raynaud's phenomenon → Precede sicca symptoms (Some cases).

Extraglandular :

Organ system	manifestation
Joint	Arthralgia/arthritis (Jaccoud's) : m/c extraglandular manifestation
CNS	Ganglionopathy (Classical)
Ocular	Dry eye
Endocrine	Thyroid disorders
Lung	NSIP : Lymphoid Interstitial pneumonia (LIP) (Ground glass opacities + nodules + cysts)
Vascular	Immune complex mediated small vessel vasculitis
Cardiac	Pericarditis
Liver	• Primary Biliary cirrhosis (PBC) • A/w Hepatitis C virus (HCV)
Kidney	Distal Renal Tubular Acidosis (RTA)

Note :

Other conditions associated with HCV :

- Cryoglobulinemia type 2, 3.
- Porphyria cutanea tarda.
- Cutaneous lichen planus.
- membranoproliferative glomerulonephritis (MPGN).

INVESTIGATIONS :

- Antibodies :
  - a. Anti Ro :
    - A/w early onset, long duration disease.
    - ↑ risk → Extraglandular manifestations.
      → Lymphoma.
    - Bad prognosis.
  - b. Anti La.
- Biopsy : Gold standard for diagnosis.

Systemic Sclerosis

00:49:03 ----- Active space -----

Risk Factors :

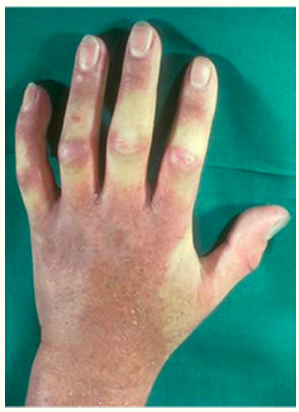
1. Environmental agents and drugs :
   - Silicosis.
   - Bleomycin.
   - Pentazocine.
   - Vinyl chloride.
   - Contaminated L-tryptophan.
2. Genetic factors.

Pathogenesis :

Risk factors → Vasculopathy (Small vessel endothelial injury) → Thrombosis → Capillary hypoxia (myofibroblast activation) —TGF-β (Collagen formation)→ Fibrosis. (No inflammation; ESR, CRP : N/↓)

Types of Systemic Sclerosis (SSc) :

1. Diffuse SSc : Skin lesions anywhere in the body.
2. Limited SSc : Limited to face and distal to elbow.
3. Sine scleroderma : No skin lesions.



Raynaud's phenomenon

Features & Manifestations :

- Raynaud's phenomenon (RP) :
  - Episodic vasoconstriction (D/t cold > stress/vibration).
  - A/w PCR : Pallor → Cyanosis → Redness.
  - 2° RP (most dangerous) :
    a. Critical limb ischemia → Gangrene.
    b. Nail fold capillaroscopy → Dilatation and dropout of capillaries.

Features of Limited SSc vs Diffuse SSc :

	Limited SSc	Diffuse SSc
Pathogenesis	Vasculopathy.	Fibrosis.
2° RP	Severe, long standing (Critical limb ischemia ⊕).	Short-lasting, ↓ severe, ↓ painful.
Skin changes	• ↓ tightening. • ↑↑ telangiectasia.	• Dry skin + tightening. • Hyperpigmentation. • Alopecia. • Loss of body oil. • Salt and pepper skin.
Cardiac	↓ / ⊖	⊕
Renal		
Lung (ILD)		
Tendon friction rub		
Bone/joint	Acral osteolysis → Erosive arthritis.	Joint contractures > arthralgia, myalgia.

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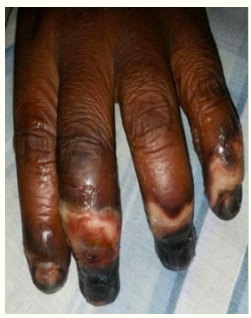
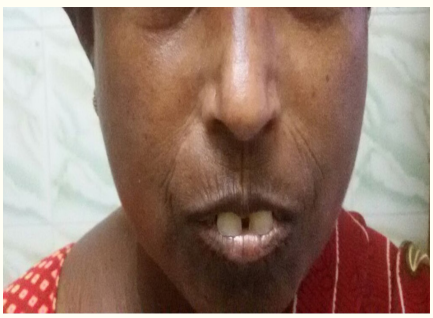
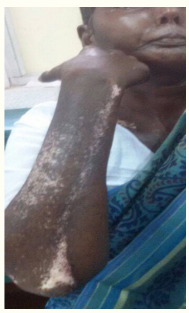
	Limited SSc	Diffuse SSc
Characteristic feature	CREST syndrome : • Calcinosis cutis : Calcium hydroxyapatite deposition (Subcutaneous). • Raynaud's phenomenon. • Esophagitis (m/c GI feature). • Sclerodactyly. • Telangiectasia.	Mask facies : • Microstomia. • Pursed lips. • Puckered mouth.
GI features (D/t ↓ motility)	Gastric Antral Vascular Ectasia (GAVE).	
	• LES tone loss : Recurrent oesophagitis. • Pneumatosis intestinalis. • Small intestinal bacterial overgrowth.	-
m/c cause of death	Pulmonary arterial hypertension (PAH) (A/w ↑ telangiectasia).	ILD.


Critical limb ischemia


Mask facies

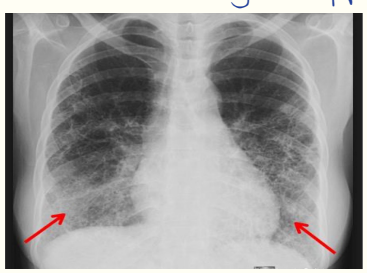

Salt and pepper skin

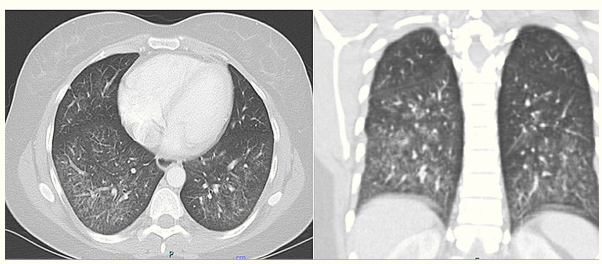
SSc Specific Antibodies :

Autoantibodies	Associated conditions
Anti-topoisomerase-I (Scl-70).	Diffuse SSc.
Anti-centromere.	CREST syndrome (Limited SSc).
Anti-RNA polymerase 3 (Anti-RNAP-3).	• Diffuse SSc. • Scleroderma renal crisis (most specific). • Rapidly progressing skin lesions. • GAVE (Watermelon stomach). • Malignancy. • Tendon friction rub.
PM/Scl-70 (Shows nucleolar pattern).	Overlap syndrome (Polymyositis & scleroderma).

Investigations :

HRCT chest : Ground glass appearance ⟶ NSIP.


CXR : Reticulo-nodular infiltrates


NSIP pattern

Note :

----- Active space -----

- Calcinosis cutis also seen in juvenile dermatomyositis.
- Other conditions a/w 2° RP : MCTD, Sjogren's syndrome, anti-synthetase syndrome.

Scleroderma Renal Crisis :

- Seen in diffuse SSc.
- Antibodies : Anti RNAP-3 > Anti-topoisomerase-I.
- Thrombotic microangiopathy (TMA).
- within 1st 4 years of disease.
- Presentation : 2° hypertension (HTN emergency) + microangiopathic hemolytic anemia + thrombocytopenia.
- Early use of steroids in diffuse SSc ⟶ Development of renal crisis.
- Rx : ACE inhibitors (↓ mortality).

Inflammatory Muscle Disease

01:13:31

Conditions :

a. Polymyositis (PM).
b. Dermatomyositis (DM).
c. Juvenile dermatomyositis.
d. Inclusion body myositis (IBM).
e. Immune mediated necrotising myopathy.
f. Cancer induced myositis.
g. Amyopathic dermatomyositis.

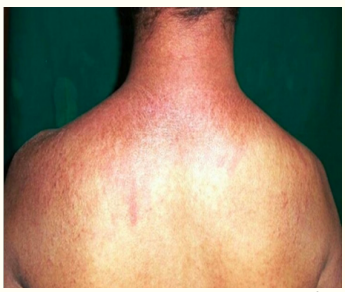
Polymyositis v/s Dermatomyositis :

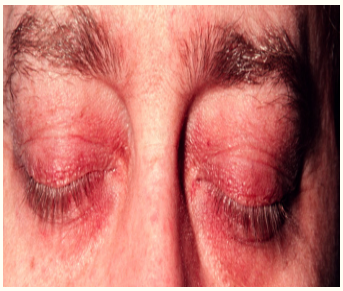
		Polymyositis	Dermatomyositis
Age		Adults	Adults + children
Gender		F > M	
Presentation		Overlap syndrome	Isolated/overlap
Features	Muscle	LMN weakness (m/c) : • B/L Symmetrical, subacute. • LL >> UL. • Proximal weakness. • N : Sensation, reflexes, bowel & bladder function.	
	Skin	⊖	⊕
Muscle biopsy	Necrosis	Not seen	
	Cells seen	CD8 T cells	CD4 T cells + B cells
	Endomysial + perimysial inflammation	⊕	
	Perivascular inflammation	⊖	⊕
	Perifascicular atrophy	⊖	⊕
CPK		Positive	

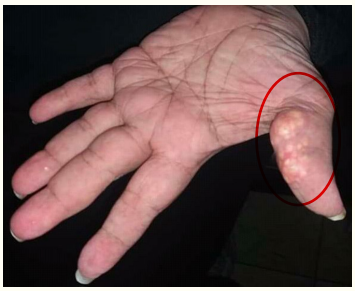
----- Active space -----

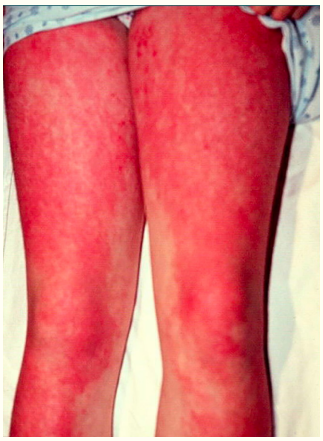
Skin manifestations in dermatomyositis :

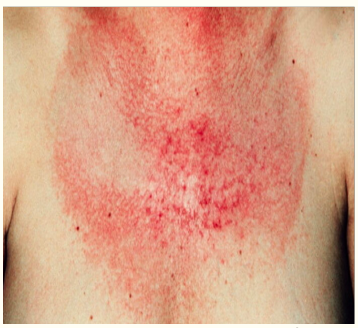
- Gottron's papule :
  - Scaly erythematous, flat topped (Pathognomonic).
  - Pruritis, knuckle involvement (+).

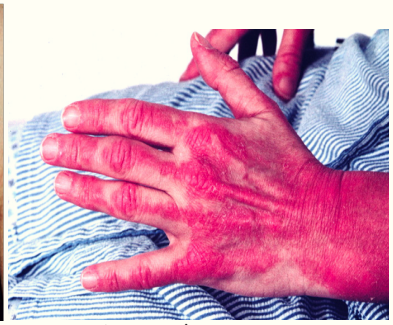

Shawl sign (Photosensitive)

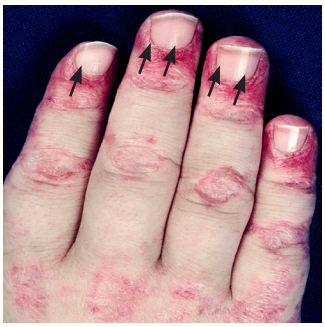

Heliotrope rash

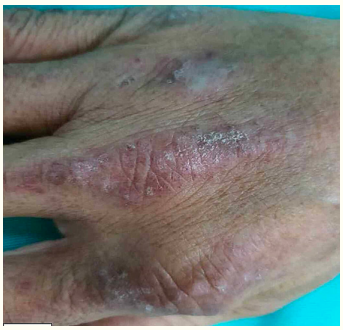

Calcinosis cutis


Holster sign


V sign (Photosensitive)

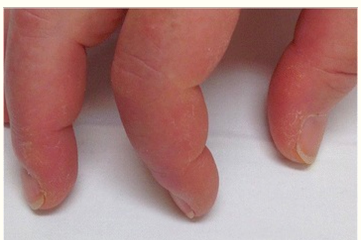

Gottron's sign/Linear erythema


Periungual telangiectasia


Gottron's papules

Anti-synthetase Syndrome :

- Seen in polymyositis and dermatomyositis.
- Antibodies → Anti Jo-1.
- Presents as fever.


Mechanic's hand

Findings :

1. Arthritis : SLE-like.
2. ILD : NSIP (m/c).
3. Mechanic's hand : Crusting & erosion of radial aspect of index + middle fingers.
4. Raynaud's phenomenon.

Cancer Associated Myositis :

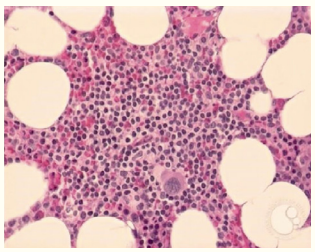
- Dermatomyositis >> Polymyositis > IBM.
- Antibodies : Anti TIF1 gamma, anti NXP 2.

HEMATOLOGY REVISION - 1

----- Active space -----

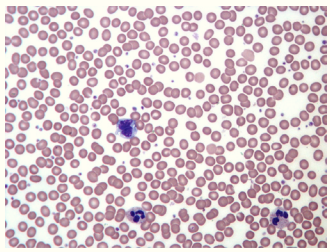
Hematopoiesis

00:01:30



Normal bone marrow

(Cellularity : 100 – age)



Normal peripheral smear

Pluripotent hematopoietic stem cell

- Common myeloid Progenitor (CMP) → RBC, platelet, granulocyte, monocyte (macrophage).
- Common Lymphoid Progenitor (CLP) → B & T lymphocytes, NK cells.

RBC development :

CMP

↓

Blood forming unit (Erythroid)

↓ Erythropoietin first involved (Iron independent)

Colony forming unit (Erythroid)

↓ First iron dependent step

Proerythroblast

↓

Erythroblast/ Normoblast

- → Early (Basophilic).
- → Intermediate (Polychromatic) : Hemoglobin first appears.
- → Late (Orthochromatic) → Reticulocyte → RBC.

Erythropoietin synthesis : Peritubular interstitial fibroblast in cortex & outer medulla of kidney.

Note : Supra-Vital stain for reticulocyte → New methylene blue/Brilliant cresyl blue (For RNA).

----- Active space -----

Evaluation of Anemia

00:06:57

Hemoglobin reference range for evaluation :

- male : <13 g/dL; ≥16.5 g/dL.
- Female : <12 g/dL; ≥16 g/dL.
- Pregnancy : <11 g/dL.
- Chronic kidney disease (CKD) : <10 g/dL.

Laboratory Evaluation :

Retic count : Differentiates underlying cause of ↓ RBC (In %).

- Decreases if ↓ production of RBC.
- Increases if ↑ destruction of RBC.

Corrected retic count (To account for low hemoglobin-induced RBC production).

$$= \text{Retic count} \times \frac{\text{Hb of patient}}{\text{Desired Hb}}$$; where desired Hb → 15 g/dL in males. / 13 g/dL in females.

Reticulocyte Production Index (RPI) : Best parameter.

- Value = $\frac{\text{Corrected retic count}}{2}$ (Accounts for longer reticulocyte half-life in circulation)
- Interpretation → <2.5 : Hypoproliferative. / >2.5 : Hyperproliferative.

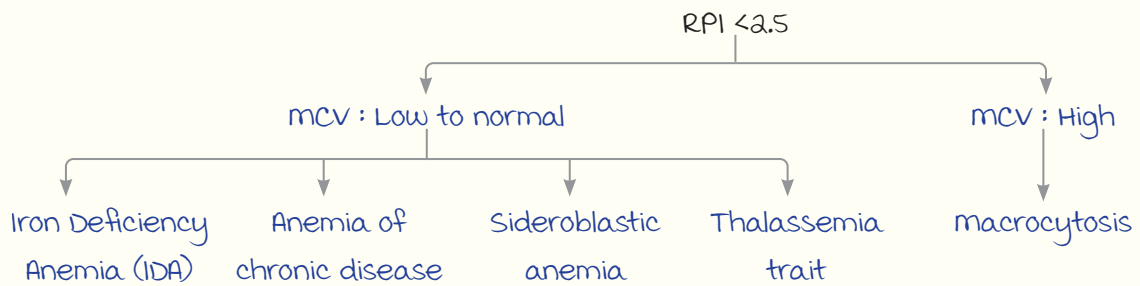
Mean Corpuscular Volume (MCV) : Average volume of RBC.

- Normal range : 80 to 100 fL.
- If MCV >100 : macrocytosis (megaloblastic/Non-megaloblastic).

Hypoproliferative Anemia Classification

00:14:00

Symptom duration : 2 to 3 months.



Differentials :

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	IDA	Anemia of chronic disease	Thalassemia trait (α or β)	Sideroblastic anemia
MCV	↓/(N)	↓/(N)	↓	↓ (Congenital)/ ↑ (Acquired)
S. Iron	↓	↓	(N)	↑
Total Iron Binding Capacity (TIBC)	↑	(N)/↓	(N)	(N)/↓
Transferrin saturation	↓	↓	(N)	↑
S. Ferritin	↓	(N)/↑	(N)	(N)/↑
S. Transferrin	↑	(N)	(N)	(N)/↑
S. Hepcidin	↓	↑	(N)	↓
BM iron stores	↓	(N)/↑	(N)	(N)/↑
Erythroblasts iron	↓	↓	(N)	Ring forms
Peripheral smear	Normocytic normochromic/ microcytic hypochromic	Normocytic normochromic (microcytes in miliary TB, RA)	Microcytes	Dimorphic

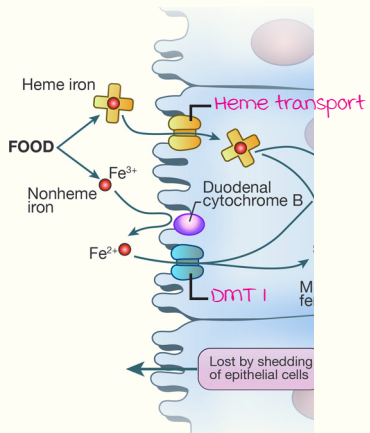
Iron Deficiency Anemia

00:18:18

Iron Metabolism :

Iron absorption : In duodenum.

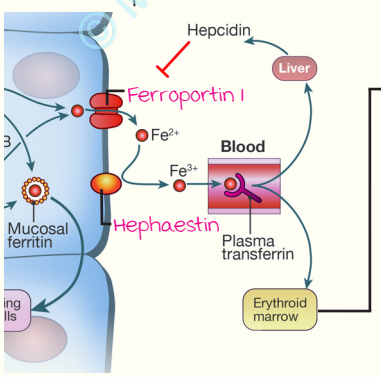
- Dietary iron → 2/3rd heme iron : Absorbed via heme transporter.
  → 1/3rd non-heme iron ($Fe^{3+} \rightarrow Fe^{2+}$) (Absorbed via divalent metal transporter 1).



Iron storage :

- Storage forms → Ferritin (m/c).
  → Hemosiderin (Detected by Prussian blue).
- Sites : Marrow, macrophages, liver, duodenal enterocyte.

Iron transport :



Iron uptake :

Soluble transferrin receptor → Transferrin released into circulation.
→ Fe^{3+} taken up for erythropoiesis.

Note : Ceruloplasmin converts Fe^{2+} to Fe^{3+} in brain.

----- Active space -----

Investigations :

Iron indices :

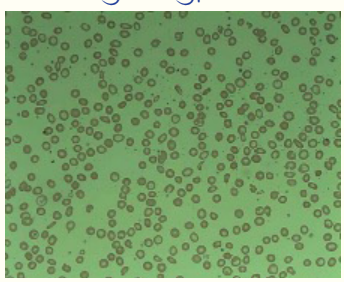
Parameter	Details	Normal values
S. Ferritin	• Measure of iron stores : Earliest marker. • Positive acute phase reactant (↑ value ≠ IDA).	30–300 ng/mL
S. Iron	Transferrin bound iron in circulation.	50–150 mcg/dL
Total Iron Binding Capacity (TIBC)	measure of iron binding capacity of transferrin.	300–360 mcg/dL
Transferrin Saturation (TSAT)	(S. Iron/TIBC) x 100. ↓ in IDA.	~33% or 1/3rd of TIBC
Free erythrocyte protoporphyrin	↑ D/t lack of iron binding.	-
Red cell distribution width (RDW)	Indicates degree of anisopoikilocytosis (Directly proportional).	11.5%–14.5%

Peripheral smear :

Negative iron balance → Iron deficiency erythropoiesis → Iron deficiency anemia

Normocytic normochromic

Microcytic hypochromic



Note :

Most specific & sensitive marker.

(Soluble transferrin receptor assay (STFR)/log ferritin) > STFR ↑ > S Ferritin.

Clinical Features :

General symptoms : Fatigue, pallor, palpitations.

Specific symptoms :

1. Pica symptoms : Pagophagia (Craving for ice).
2. Restless leg syndrome.
3. Epithelial changes :
   - Koilonychia : Nail changes.
   - Plummer-Vinson syndrome : Dysphagia, esophageal webs.
4. Growth retardation.
5. Neuro-psychiatric issues.

(4, 5 : In growing children.)

6. Alopecia.

Etiology :

- m/c etiology :
  - General : blood loss.
  - Female : menstrual loss.
  - Male : GI bleed (Evaluate by colonoscopy + upper GI endoscopy).
- Other etiology :
  - Malabsorption : Rule out celiac disease (Anti-TTG Ab, anti-endomysial Ab).
  - CKD patient with EPO resistance.
  - Nutritional deficiency.

Note : EPO should be started only after iron stores are replenished.

----- Active space -----

Treatment :

- Absorbed Fe = 10% of Fe intake.
- Fe requirement = [2.2 x body weight x (Desired Hb − Patient Hb)] +1000.
- RDA → Adult male : 1 mg.
  → Adult female : 2 mg.
  → Pregnancy : 3 mg.
- IV iron → Ferric carboxymaltose, Iron isomaltose } 1 g/500 mg injections (≥2 doses required).
- Disadvantage of oral iron : Dyspepsia, unpleasant taste.

Response to IV treatment :

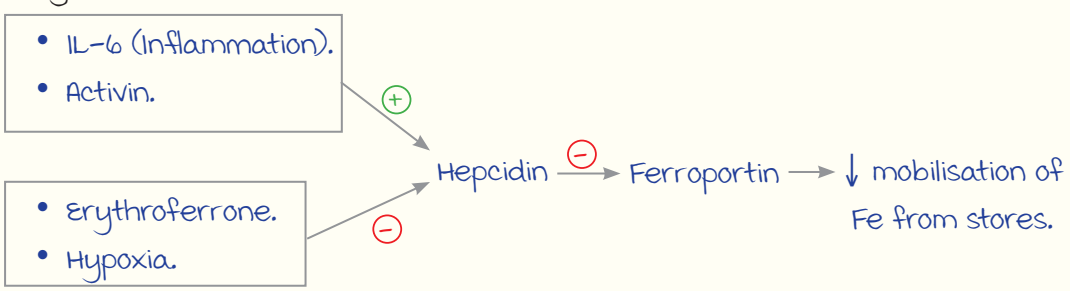
- Retic count : ↑ by 5 to 7 days → Peaks in 2 weeks.
- Hb begins to rise in 2 weeks → ↑ by 2 g/dL in 1 month.

Anemia of Chronic Disease

00:48:00

AKA functional IDA.

Pathogenesis :



Note : Hepcidin regulation → HFE gene on Chr 6.

Sideroblastic Anemia

00:53:30

Disorder of protoporphyrin synthesis.

Heme synthesis :

Succinyl CoA + glycine $\xrightarrow[\text{PLP}]{\text{ALA synthase}}$ ALA $\xrightarrow{\downarrow \text{Protoporphyrin}}$ ↓ Heme.

Causes :

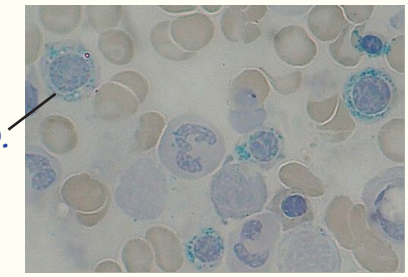
- Congenital : X-linked ALA synthase defect (m/c).
- Acquired :
  1. Myelodysplastic syndrome (m/c).
  2. Lead poisoning.
  3. Copper deficiency.
  4. Chloramphenicol/Pyrazinamide.

Note : Rarely alcohol → Sideroblastic anemia.

----- Active space -----

Investigations :

1. Peripheral smear :
   - Dimorphic blood picture.
   - Ringed sideroblasts (↑ Fe deposited as a ring).
2. Electron microscopy : Pappenheimer bodies.



Prussian blue staining

Thalassemia Trait

00:58:59

Types
- $\beta^0\beta^0$: Thalassemia major.
- $\beta^+\beta^+$: Intermediate.
- $\beta\beta^0$ or $\beta\beta^+$: Thalassemia trait/minor (Asymptomatic).

- Usually asymptomatic.

Investigations :

- Confirmatory test : Serum electrophoresis.
  - HbA_2 : 4–8.5% (Normal : 1.5–3%).
- Mentzer index (MCV/RBC count) :
  - <13 for Thalassemia trait (>13 for IDA).
- RDW : Normal.

HEMATOLOGY REVISION - 2

----- Active space -----

MACROCYTIC ANEMIA

Hypoproliferative anemia with RPI < 2.5 & MCV > 100fL.

Types

Megaloblastic (Lag in nuclear maturation) :

- B_{12} deficiency.
- Folate deficiency.
- DNA synthesis inhibitor drugs : Cytarabine, 5 – FU, 6 – MP.
- Thiamine deficiency.
- Orotic aciduria.

Normoblastic :

- Liver disease (m/c) : Target cells.
- Aplastic anemia.
- COPD.
- Scurvy.
- Hypothyroidism.
- Post hemolysis.
- Alcohol.

Vitamin B_{12} and Folate Deficiency

00:05:26

Vitamin B_{12} :

Metabolism :

- Body store : 2 to 5mg (Deficiency is rare).
- RDA : 3 to 7 µg/day.
- Source : Dietary animal meats.
- Form : Adenosylcobalamine & methylcobalamine.

Absorption :

Site : — Process :

Adenosylcobalamine (Or) methylcobalamine.

↓

Stomach — Combines with R factor (Haptocorrin).

↓

D2 — R factor & B_{12} complex is broken down.

↓

D2/D3 — B_{12} + Intrinsic Factor (IF) complex formation.

↓

Ileum — Complex binds to cubam receptor.

↓

Blood — B_{12} + Transcolabamin II.

↓

B_{12} absorbed into blood.

↓

Tissues — Reaches tissues for various functions.

----- Active space -----

Etiology of B_{12} deficiency :

- Pernicious anemia (Autoimmune disorder) : Ab against parietal cells of stomach/IF.
- Ileal pathologies : Crohn's disease, TB, tropical sprue.
- Small intestinal bacterial overgrowth (SIBO).
- Imerslund Grasbeck Syndrome :
  Congenital deficiency of cubam receptor → ↓ B_{12} + Proteinuria.
- Dietary deficiency.

Folic Acid :

Folate metabolism :

- Polyglutamate —(In intestinal lumen; PPI ⊖)→ monoglutamate (5 methyl THFA/Folate).
  Homocysteine —(B_{12})→ methionine
  THFA (For IC transfer & DNA synthesis).
- Folate independent reaction : methylmalonyl CoA —(B_{12})→ Succinyl CoA.

Etiology of folate deficiency :

1. Nutritional deficiency.
2. ↑ requirement in pregnancy, myeloproliferative neoplasms, hemolysis.
3. Drugs :
   - Methotrexate.
   - Triamterene.
   - Pyrimethamine.
   - PPI.
   - Phenytoin.
   - Anticonvulsants.

Evaluation of Vit B_{12} vs Folate Deficiency :

	B_{12} Deficiency	Folate Deficiency	B_{12} + Folate Deficiency
Methylmalonic acid	↑	Ⓝ	↑
Homocysteine	↑	↑	↑
Folate	↑ (Folate trap : ↑ 5-methyl THFA d/t ↓ conversion to THFA)	↓	↓

Evaluation of B_{12} deficiency :

- Check red cell folate in B_{12} deficiency.
- If B_{12} levels
  - <200 pg/ml : B_{12} deficiency.
  - 200 – 300 pg/ml : Look for methylmalonic acid & homocysteine
    If ↑ B_{12} deficiency.
  - >300 pg/ml : No B_{12} deficiency.

Peripheral smear findings :

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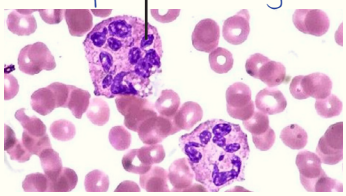
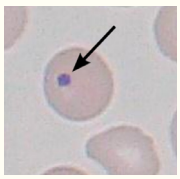
1. Megaloblasts

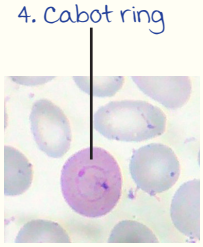
2. Hypersegmented neutrophils (Earliest sign)



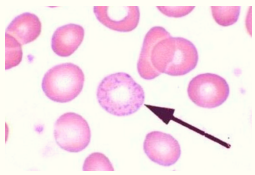
3. Howell – Jolly bodies



4. Cabot ring



5. Basophilic stippling



6. Pancytopenia (In 20% cases)

Pernicious Anemia :

- Autoimmune disorder d/t Ab against → Parietal cell (Sensitive) → Hypergastrinemia/ ↑ risk of Gastrin secreting tumor.
  → Intrinsic factor (Specific)
- Associated with other autoimmune disorders : Type I DM, vitiligo, Addison's disease etc.
- Risk factors : Females > males, age > 60y.

Symptoms :

1. Neurological symptoms :

   Progression of areas affected :

   Nerve (Neuropathy) → Dorsolateral part of spinal cord → Cerebrum.
   1. Dorsal column f/b,
   2. Lat. Spinothalamic tract f/b,
   3. Corticospinal tract.

2. G.I symptoms : Gastritis, gastrin secreting carcinoid (Antral sparing), angular cheilitis & atrophic glossitis.

Note : Tumors associated with pernicious anemia m/c in males.

Treatment :

1000 µg IM of hydroxycobalamine :

Once weekly for 6 weeks f/b Once every 3 months.

Hyperproliferative Anemia Classification

00:23:56

Hemolytic anemias : Hyperproliferation d/t hemolysis → Reticulocytosis/macrocytosis.

Causes :

Inherited causes :
(All intracorpuscular, except HUS)

Hemoglobinopathies :
- Sickle cell anemia
- Thalassemia

Enzyme deficiency :
- G – 6 – PD
- Pyruvate kinase
- 5' nucleotidase

Membrane defects :
- Hereditary spherocytosis
- Elliptocytosis
- ovalocytosis

HUS : Hemolytic uremic syndrome.
PNH : Paroxysmal nocturnal hemoglobinuria.

----- Active space -----

Acquired causes
(All extracorpuscular, except PNH)

Immune :
- Autoimmune
- Alloimmune
  - Hemolytic disease of newborn (HDN)
  - Febrile hemolytic transfusion reactions
- Drugs

Non – immune :
- Drug/toxins
- Infections
- PNH
- Fragmentation hemolysis

Hemolysis Classification Based on Site :

	Intravascular Hemolysis	Extravascular Hemolysis
Site	Within blood vessel	M/C in spleen
Features	• Dark urine : – Hemoglobinuria – Hemosiderinuria • LDH ↑ ↑ ↑ • Haptoglobin ↓ ↓ ↓ • Jaundice (+)	• Moderate splenomegaly • Fe stores ↑ • Jaundice + + + (d/t protoporphyrin breakdown) • Urobilinogen ↑ ↑ & stercobilinogen ↑ • LDH ↑ & haptoglobin ↓
Causes	• PNH (m/c) • Infections : Malaria, sepsis • Paroxysmal cold hemoglobinuria (PCH) • Acute G6PD deficiency • Microangiopathic hemolytic anemia (MAHA) • Transfusion related hemolysis	• Autoimmune hemolytic anemia (AIHA) : Warm • Hereditary spherocytosis • Sickle cell anemia • Thalassemia

Immune Hemolysis

00:35:50

Drug induced immune hemolytic anemia :

1. Membrane modifying drug : Cephalosporin.
2. Autoantibody forming drug : Quinidine, Rifampicin, Isoniazid.
3. Anti – RBC antibody forming drug : Methyldopa.

Autoimmune Hemolytic Anemia (AIHA) :

Site of RBC destruction :

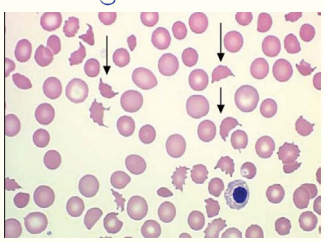
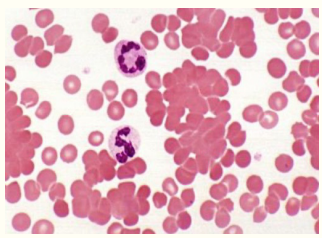
- RBC coated with warm antibodies : Spleen.
- RBC coated with complement only :
  Peripheral circulation ⟶ Acrocyanosis, Raynaud's phenomenon.

Clinical presentation of warm AIHA :

- Progressive fatigue, palpitations.
- Moderate splenomegaly.
- Progressive ↓ in Hb.
- (N) TLC & platelet count.

Differences of types of AIHA :

----- Active space -----

	Warm AIHA	Cold agglutinin disease	PCH
Antibody	IgG (Receptor : Splenic macrophage)	IgM	Polyclonal IgG (Donath-Landsteiner)
Site of hemolysis	Extravascular	Intravascular > Extravascular	Intravascular
Secondary causes	• SLE • PAN • Lymphoma (CLL) • RA • HIV	• IMN • Mycoplasma • IgM secreting tumors (Waldenstrom macroglobulinemia) • Lenalidomide	Syphilis (Rule out)
Treatment	Steroids + Rituximab Splenectomy : Second line	Rituximab	Supportive care
Course of disease	Sub-acute/Acute	Chronic	Acute
Peripheral smear	Polychromasia, spherocytes, fragmented RBC 	RBC aggregation in cooler peripheral circulation 	Combined
Temperature of max activation of Ab	37°C	0 to 4°C	4°C
Mechanism of hemolysis	Opsonization	Complement	Complement
Antigen	Panagglutinin	I antigen	P antigen
Investigations :			
Donath Landsteiner	-	-	⊕
Direct antigen test	⊕ (IgG + , C3 +/-)	⊕ (IgG - , C3 +)	⊕

Note :

- AIHA + thrombocytopenia : Evan's syndrome.
- Direct Coombs test.

Diagnostic Algorithm :

Direct antiglobulin Test
- IgG ⊕, C3 ± → Warm AIHA.
- IgG ⊖, C3 ⊕ → Peripheral smear
  - Agglutinins → Cold agglutinin disease.
  - No agglutinins → Donath-Landsteiner test → If ⊕ : PCH.

----- Active space -----

Paroxysmal Nocturnal Hemoglobinuria

00:50:30

m/c acquired cause of intravascular hemolysis.

Pathogenesis :

✕ PIGA gene (X chromosome) Acquired PIGA mutation → Codes for → GPI anchor proteins → Anchors → ✕ CD55 (Decay accelerating factor). ✕ CD59 (membrane inhibitor of reactive lysis). } Complement regulator proteins

- PIGA gene mutation → RBCs sensitive to lysis (AKA PNH III RBC).

IOC : Flow cytometry (% of PNH III RBC determines disease type).

Clinical presentation :

- High colored urine : D/t intravascular hemolysis.
- Thrombosis :
  D/t defective urokinase plasminogen activator receptor (uPAR) on RBC.
  - Budd-Chiari Syndrome, Cerebral venous thrombosis.
- Pancytopenia : Hypercellular marrow.
- Refractory anemia.
- Aplastic anemia (In 25% cases).

Treatment : Eculizumab.

Note : ↓ Neutrophil Alkaline phosphatase → CML & PNH only.

Fragmentation Hemolysis

00:54:30

Types → Microangiopathic : Hemolytic uremic syndrome (HUS)/TTP.
Types → Macroangiopathic : Cardiac hemolysis (Prosthetic valves).

HUS

Classical Features :

- Microangiopathic hemolytic anemia (MAHA).
- Thrombocytopenia.
- Renal failure.

.Pathogenesis :

D/t traumatic microangiopathy.

Endothelial injury → VWF released → Thrombus formation + Platelet trapping → Passage of RBC → Schistocyte formation.

----- Active space -----

Types :

1. Childhood HUS (D+) :

- Causative organism → Shigella dysenteriae type 1 (Shiga toxin).
  → EHEC O157 : H7 (Shiga – like toxin/Verocytotoxin).
- Clinical presentation :
  - Dysentery.
  - Rapidly progressive renal failure (RPRF) : Over few days to weeks.
- Treatment : Supportive care (Excellent prognosis).

2. Adult HUS (D–) :

- Associated with alternate complement pathway activation → ↓ C3.
  → (N) C4.
- Types :

Familial Type :

D/t defect in alternate complement pathway

- Complement Factor H mutation (m/c)
- Complement Factor B mutation : Poor prognosis
- Membrane co – factor P mutation : Good prognosis

Acquired Type :

- Drugs :
  - Mitomycin.
  - Ticlopidine, clopidogrel (Also cause TTP).
  - Cisplatin.
  - Calcineurin inhibitors.
- Post Hematopoietic stem cell transplant.
- HIV.

- Clinical presentation : Renal failure with hypertensive crisis (Secondary HTN).
- Treatment (Poor prognosis) :
  - Plasmapheresis (If early presentation).
  - Rituximab + Eculizumab : For recurrence post renal transplant.

THROMBOTIC THROMBOCYTOPENIC PURPURA (TTP)

Classical features :

1. MAHA.
2. Thrombocytopenia.
3. CNS features (Stroke, headache).
4. GI features.
5. Fever.

Pathogenesis :

Antibody against VWF metalloproteinase (ADAMTS 13) → Excess VWF → Platelet trap.

Causes :

1. SLE.
2. HIV.
3. Drugs : Ticlopidine, clopidogrel.

Treatment : Plasmapheresis (PLEX) + Rituximab.

----- Active space -----

HEMATOLOGY REVISION - 3

Myeloproliferative Neoplasms (MPN)

00:00:06

Terminal myeloid cell expansion.

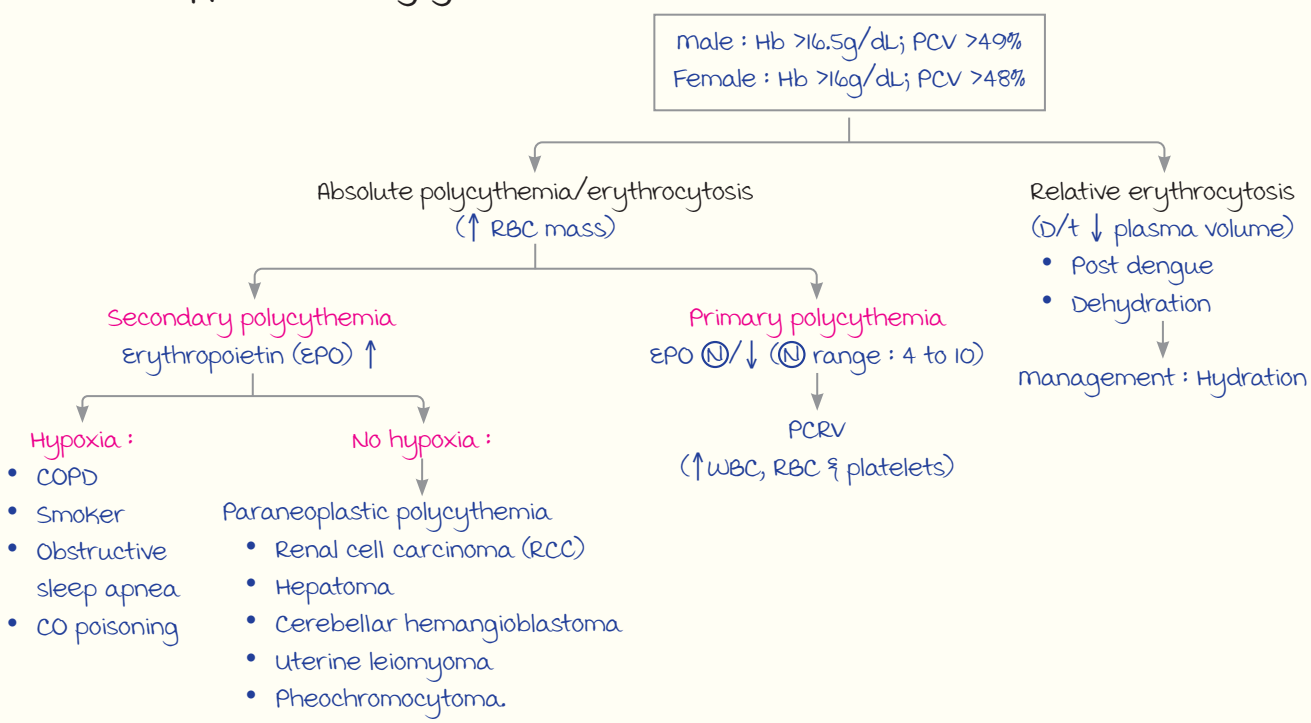
Common Features :

1. No dysplasia : Mature cell expansion.
2. Extramedullary hematopoiesis → Hepato/splenomegaly.
3. Can transform into one another/into Acute Myeloid Leukemia (AML).
4. Hyperviscosity → Thrombosis.
5. Fatigue +/- systemic features.

Classification :

BCR-ABL mutation	JAK-2 mutation
Translocation of (9;22) Chr	Deletion of Chr. 9p
• Chronic Myeloid Leukemia (CML) • Chronic Neutrophilic Leukemia (CNL) • Chronic Eosinophilic Leukemia (CEL)	• Polycythemia rubra vera (m/c) : 100% • Primary Myelofibrosis (PMF) : 50-60% • Essential Thrombocytosis (ET) : 50-60%

Approach to Polycythemia :



Polycythemia Rubra Vera (PCRV)

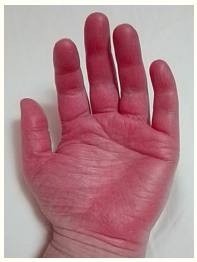
00:04:15 ----- Active space -----

Clinical Presentation :

- Population at risk : >50y; female preponderance.

Symptoms :

	Specificity	Presentation
↑ RBC	Non specific to PCRV	Systemic HTN, vertigo, headache, thrombosis.
↑ WBC	Specific to PCRV	Basophilia → Aquagenic pruritis, hyperuricemia, ↑ Transcobalamin-I → ↑ Vit B_{12} binding capacity, ↑ risk of AML.
↑ Platelet		Acquired Von Willebrand Disease (VWD), microvascular thrombosis → Erythromyalgia (Burning pain in hand & feet).



Erythromyalgia

Laboratory investigations :

1. ↑ Hb.
2. ↑ WBC.
3. ↑ platelets.
4. Microcytic erythrocytosis (MCH compensated by ↓ MCV).
5. ESR ↓↓.

Note : Microcytic erythrocytosis only in thalassemia, PCRV & hypoxia.

WHO diagnostic criteria : (2 major + 1 minor/3 major for diagnosis)

Major criteria	Minor criteria
1. Hb → Male >16.5g/dL; Female >16g/dL	Ⓝ/↓EPO.
2. JAK-2 mutation + → V617F mutation (m/c); Exon 12 mutation	
3. Bone marrow biopsy → Hypercellularity with panmyelosis	

Treatment :

1. <60 yrs → Aspirin + phlebotomy (Target Hb : 12 to 13g/dL).
2. >60 yrs or h/o stroke → Add ruxolitinib (JAK 1/2 inhibitor).

Primary Myelofibrosis (PMF)

00:12:57

Associated mutations :

- JAK2 mutations (m/c) : 50-60%
- Calreticulin mutation
- MPL mutation (Thrombopoietin)

} Triple negative : very poor prognosis.

----- Active space -----

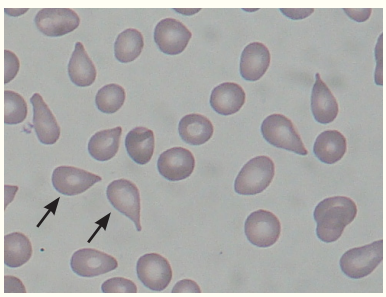
Clinical presentation :

- Population at risk : 60 to 70 y; Male = Female.
- Prognosis : Poor.
- ↑ risk of thrombosis & AML (Risk lower than in PCRV).
- Disease progression :

Hypercellular marrow (Initial phase)
↓
megakaryocyte dysplasia (Cloud megakaryocyte)
↓ Produces
TGF-β
↓
Bone marrow fibrosis

Bone marrow fibrosis :

1. Pancytopenia → Fatigue (m/c symptom).
2. Leucoerythroblastic blood picture :
   - Left shift.
   - Dacrocytes (Teardrop RBCs) ⊕.
3. Hepatomegaly & massive splenomegaly.
4. Bone pain.
5. Sweet syndrome : Extramedullary hematopoiesis in the skin.


Dacrocytes

Note : Splenomegaly → Mild/absent : Essential thrombocytosis.
→ Moderate : PCRV.
→ Massive : PMF, CML.

Treatment :

- Bone marrow transplantation.
- If unfit : Ruxolitinib.

Essential Thrombocytosis (ET) 00:17:26

Clinical Presentation :

- 50 to 60 y; Male = Female.
- Thrombosis +/- splenomegaly.
- Bleeding may be present (D/t Acquired vWD).
- Risk of AML, extra-medullary hematopoiesis : Nil.
- Prognosis : Good.

Laboratory Investigations :

- Platelet count >4,50,000 (Incidental finding) : Rule out reactive thrombocytosis.
- Large mature platelets.
- Staghorn megakaryocytes : Giant cells with hyper-lobulated nucleus & mature cytoplasm.

Note :

----- Active space -----

- Giant megakaryocyte : Idiopathic thrombocytopenic purpura.
- Dwarf megakaryocyte : CML.
- Cloud megakaryocyte : PMF.
- Small platelet : Wiskott-Aldrich syndrome.

Treatment :

Aspirin → If >60 yrs/evidence of thrombosis → Add Hydroxyurea > IFN α.

Note : Anagrelide → ↑ risk of leukemia (Discontinued in Rx of ET).

Pancytopenia

00:20:50

Bone marrow failure syndromes :

- Aplastic anemia.
- Myelodysplastic syndrome (MDS).
- Pure Red Cell Aplasia (PRCA).
- Secondary myelofibrosis (Secondary to drugs & toxin).

Approach to Pancytopenia :

Pancytopenia

On bone marrow biopsy (Cellularity = 100 – Age)

Hypocellular marrow

1. Aplastic anemia : Chronic course
2. MDS (Hypocellular variants)
3. Aleukemic leukemia
4. PNH (Rare)

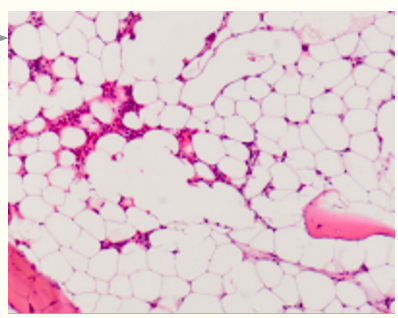
Hypercellular marrow

1. AML/ALL : Acute course
2. MDS
3. Megaloblastic anemia (Rare)
4. PMF
5. Hairy cell leukemia (Good prognosis)
6. PNH
7. Lymphoma with BM involvement
8. TB, SLE, HIV, sarcoidosis

Aplastic Anemia

00:24:56

Pancytopenia + hypocellular marrow. →



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Etiology :

Inherited (Pediatric) :

1. Fanconi's anemia :
   FANCA mutation (A/w polydactyly).
2. Dyskeratosis congenita (DC) :
   Telomerase repair complex defect.
3. Shwamann-Diamond syndrome (Ribosomopathy) :
   Pancreatic malabsorption + BM failure.

Acquired :

1. Idiopathic (m/c).
2. Non A-Non B-Non C hepatitis virus.
3. Drugs → Chloramphenicol.
   → NSAIDs.
   → d-Penicillamine.
4. Eosinophilic fasciitis (Scleroderma mimic).

Clinical Presentation :

- Age at presentation : >60 yrs.
- Very poor prognosis.
- Bleeding (m/c) : (Well-preserved patient).
- Fatigue.
- Profound neutropenia : ↑ risk for invasive aspergillosis.

Treatment :

- TOC : Allogeneic Hematopoietic Stem Cell Transplant (AHSCT).
- If unfit : Equine Anti-thymocyte Globulin (e-ATG) + cyclosporin.

Pure Red Cell Aplasia 00:30:08

Gene mutation : RPS-19.

Associations → Diamond-Blackfan syndrome.
→ Hereditary spherocytosis + Parvo B19 (Giant proerythroblast) → Aplastic crisis.
→ Thymoma/CLL.

Myelodysplastic Syndrome (MDS) 00:31:16

Presentation :

- Worldwide : >60 yrs.
- India : 40-60 yrs (m/c : 5q deletion MDS; Female > Male).
  - Good response to lenalidomide.
- Anemia (m/c) : Macrocytic > Microcytic.

Pathogenesis :

Myeloid cell dysplasia → Ineffective myelopoiesis → Pancytopenia.

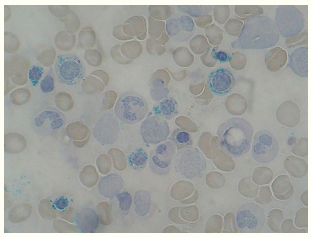
----- Active space -----

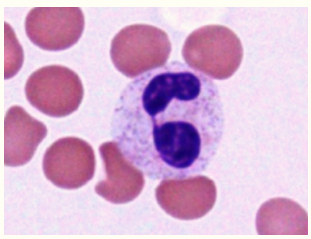
Laboratory Investigations :

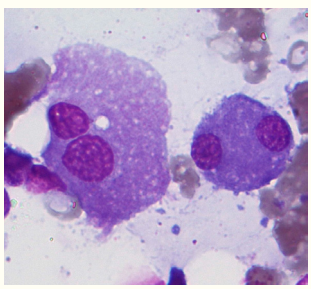
BM biopsy : Hypercellular > hypocellular marrow.

Cells on peripheral smear :

- RBC : Ringed sideroblast.
  Megaloblast.
  Macrocytic normoblast.
- WBC : 5 to 19% blast cells (↑ risk of ALL).
  Pseudo Pelger Huet cells (<2 lobes in nucleus).
  Dohle bodies.
  Toxic granules.
- Platelets : Pawn ball megakaryocytes.


Ringed sideroblast


Pseudo Pelger Huet cells


Pawn ball megakaryocyte

Treatment :

- Trilineage involvement (m/c) :
  - AHSCT.
  - If unfit → Hypomethylating agents :
    Azacitidine, decitabine.
- Single lineage involvement :
  - 5q deletion ⊕ : Lenalidomide.
  - 5q deletion ⊖ : EPO.
- Luspatercept (New drug) : Inhibits SMAD signalling pathway.

Plasma Cell Dyscrasias

00:37:25

Pathogenesis :

Germinal centre B-cell → Marginal zone → Memory B-cell
Germinal centre B-cell → Activated B-cell → Plasma cell (Polyclonal : Different Ab light chains → κ/λ)
if monoclonal
Plasma cell tumor/dyscrasia
- IgG κ/IgG λ (m/c) : M component.

Types :

1. Multiple myeloma.
2. Waldenstrom macroglobulinemia.
3. Amyloid Light chain (AL) amyloidosis.
4. Heavy chain disease.

Types of monoclonal gammopathies :

	Monoclonal Gammopathy of Undetermined Significance (MGUS)	Smoldering myeloma (Asymptomatic myeloma)	Multiple myeloma
M protein concentration	<3 g/dL	≥3 g/dL	≥3 g/dL
BM plasma cells	<10%	≥10%	≥10%
myeloma defining event	Absent	Absent	Present

Note : Risk of transformation of MGUS to myeloma → 1%.

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MULTIPLE MYELOMA

Myeloma defining events : (Any one)

Mnemonic : SLiM CRAB

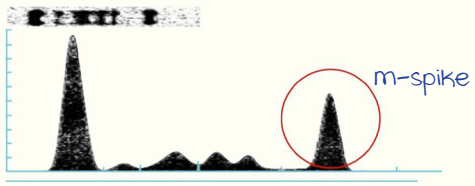
1. Sixty : ≥60% BM plasma cells.
2. Light chain ratio : κ/λ or λ/κ >100.
3. MRI : At least one focal lesion.
4. Hypercalcemia : >11 g/dL.
5. Renal failure : Creatinine >2 mg/dL.
6. Anemia : Hb <10g/dL.
7. Bone lytic lesions ≥1.

Diagnosis of myeloma : 1 out of 7 events + M-protein + BM plasma cells.

Investigations :

- Serum protein electrophoresis (SPEP) + Serum immunoelectrophoresis (SIFE) + Serum Free Light Chain ratio (SFLC) → Followed by → BM biopsy.
- Flow cytometry → ⊕ CD 38; CD 138.
  → ⊖ CD 19.

Note : SPEP alone → Less specificity (67%).



Serum protein electrophoresis

High risk for MM : Very poor prognosis.

1. Deletion 17p.
2. t(14; 16).
3. t(14; 20).
4. t(4; 14).

Clinical presentation :

1. Age >70 yrs.
2. Anemia + ↑ ESR + reversal of A:G ratio.
3. Hypogammaglobulinemia : ↑ risk of infections (Recurrent pneumonia/UTI).
4. Acute Kidney Injury (AKI).
5. Radiculopathy.
6. Bone pain and/or unexplained fracture.

Treatment :

Low/moderate risk :

(Bortezomib + Dexamethasone + Lenalidomide) x 3 cycles
↓ Followed by
Autologous stem cell transplant.
(Non-curative)

High risk MM : Replace bortezomib with carfilzomib.

- New drug : Daratumumab (CD38 monoclonal antibody).

Waldenstrom Macroglobulinemia

00:52:20 ----- Active space -----

- AKA Lymphoplasmacytic lymphoma (misnomer).
- Lymphoplasmacytic cells proliferation in BM : IgM bearing memory B-cell.
- Myd 88 mutation +.

Presentation :

- No lytic or renal lesions.
- IgM related hyperviscosity symptoms → Cryoglobulinemia.
  → Cold agglutinin disease.

Treatment : Plasmapheresis.

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HEMATOLOGY REVISION - 4

B-cell Maturation & Neoplasms

00:01:00

In bone marrow :

Common lymphoid progenitor — CD34, HLA DR

↓

Pro-B cell — CD19, CD34, HLADR

↓

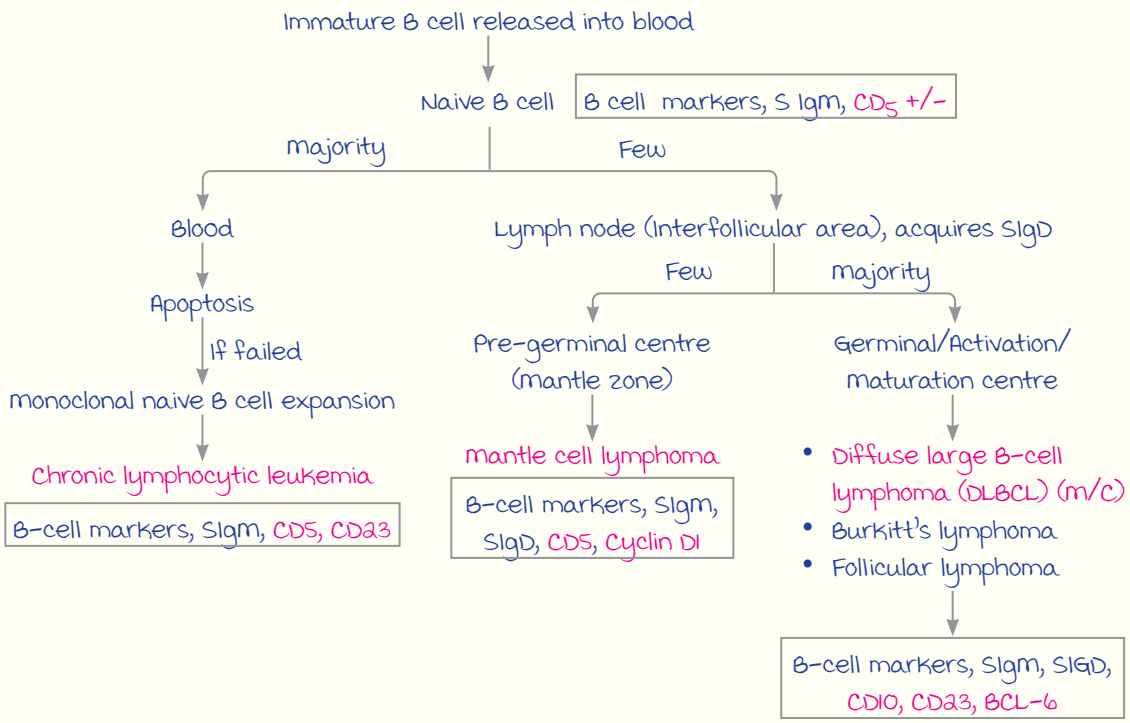
Pre-B cell — CD10 (CALLA antigen), TdT : Specific markers of Pre-B cell. B-cell markers : CD19, CD20, CD21, CD22, CD79a, CD79b

↓

Immature B-cell. — B-cell markers, SIgM (Surface IgM)

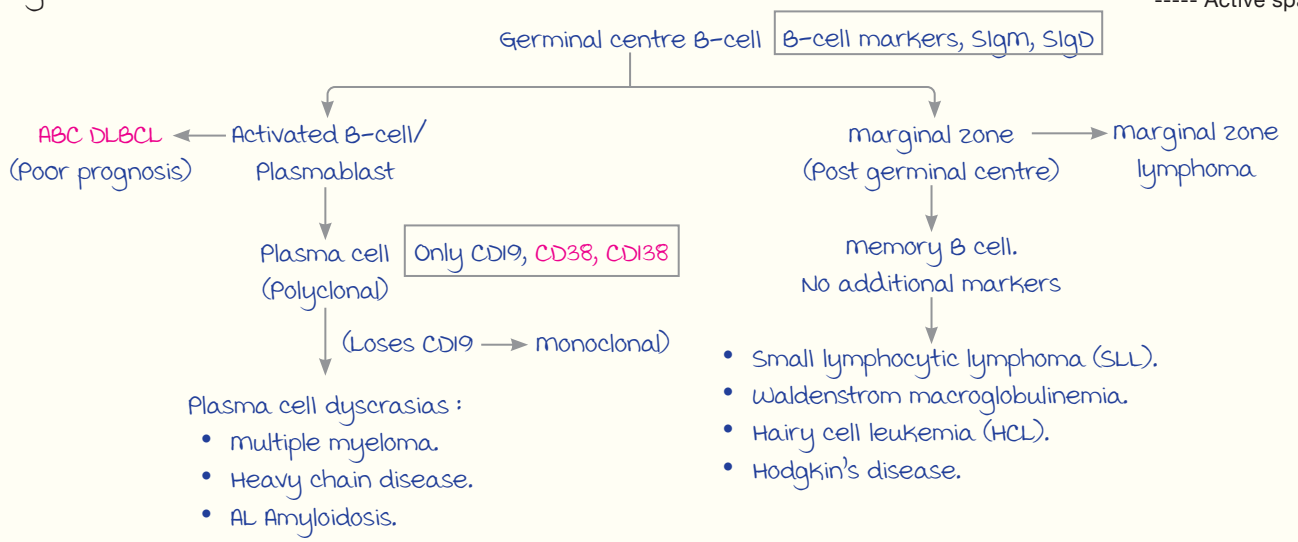
Note : Precursor B-cell ALL →
- Pro-B ALL (Acute lymphoblastic leukemia).
- Pre-B ALL (m/c) :
  - Overall best prognosis in child.
  - Early pre B cell ALL : Best prognosis in child.
- Immature B cell ALL.

In blood & lymph nodes :



In germinal centre :

----- Active space -----



T-cell Neoplasms

00:19:30

Precursor T-cell Leukemia/Lymphoma (T-cell ALL) :

Few cells proliferate in thymus → Mediastinal widening → Respiratory symptoms.
(Hence lymphoma)

Mature T-cell neoplasms :

1. Cutaneous T-cell lymphoma : AKA mycosis fungoides/Sezary syndrome.
2. Anaplastic large cell lymphoma : A/w breast implants, markers → CD30 ⊕ & ALK ⊕.
3. Angio immunoblastic lymphoma : Midline deformities ⊕.
4. Large granular lymphocytic leukemia : A/w rheumatoid arthritis (Usually benign).
5. Enteropathic T-cell lymphoma : A/w celiac disease.
6. Extranodal NK/T-cell lymphoma : Presents as nasal mass.
7. Adult T-cell leukemia/Lymphoma : A/w HTLV I.

Causative Agents of Neoplasms

00:22:40

A. Ebstein-Barr Virus (EBV) :

1. Hodgkin's disease (Classical) :
   100/70/40/20 rule
   - → 100% Lymphocyte depleted.
   - → 70% : Mixed cellularity
   - → 40% : Nodular sclerosis
   - → 20% : Lymphocyte rich.
2. Burkitt's lymphoma
   - → 100% : Child.
   - → ~ 75% : Adult.
3. Primary CNS lymphoma.
4. Post transplant lymphoma.
5. Extranodal NK/T-cell lymphoma.

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B. Human Immunodeficiency Virus (HIV) :

1. Diffuse large B-cell lymphoma (DLBCL).
2. Burkitt's lymphoma.

C. H. pylori MALToma :

m/c extronodal marginal zone lymphoma.

D. HHV 8 :

1. Primary effusion lymphoma.
2. Castleman's disease.

E. HTLV I : Adult T-cell leukemia/Lymphoma.

F. HCV :

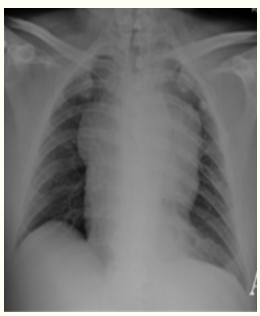
1. Waldenstrom macroglobulinemia.
2. Splenic marginal zone lymphoma.

Note : Non-classical Hodgkin's : No EBV association.

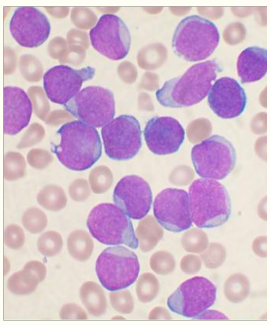
Acute Lymphoblastic Leukemia (ALL)

00:26:30

	B-cell ALL (m/c)	T-cell ALL
Significant types	• Pro B-cell ALL • Pre B-cell ALL • Immature B-cell ALL	Precursor T-cell ALL (Leukemia/lymphoma)
Age group	• Children <10 yrs (Excellent prognosis) • Adolescents (Good prognosis) • Adults > 60 yrs (Poor prognosis)	Mostly adolescent (Poor prognosis)
Presentation	Bone marrow involvement	Mediastinal widening



Mediastinal widening



Blasts in bone marrow

Diagnosis :

Clinical presentation of B-cell ALL :

- Bone pain
- pancytopenia

D/t ↑ proliferation in bone marrow (BM).

- Involvement of CNS, testes
- Hyperviscosity of blood

D/t ↑ blast cell dissemination (High count phase).

Morphology : ≥20% blasts in marrow.

Cytology : PAS, Acid phosphatase ⊕.

Immunophenotyping : CD10; tdt.

Note :

----- Active space -----

- Myeloblasts have → Nucleolus.
  → Larger cell size.
  → Auer rods.
  → MPO & Sudan black staining ⊕.

Prognostic Factors :

		Good prognosis	Bad prognosis.
Race		White	Black
Age		2-9y	<1 or >10 yrs
Sex		Female	Male
CNS involvement		-	+
Hepatosplenomegaly, Lymphadenopathy		-	+
Mediastinal mass		-	+
Testicular involvement		-	+
Type		L1	L2, L3
Cytogenetics		Hyperdiploidy	Hypodiploidy
Immunophenotype		B-cell early Pre-B-cell	T-cell
Cytogenetics	Translocation	t(12;21)	t(9;22) ; t(4;11) ; t(1;19)
	Genes	Notch 1 gene	

Treatment :

1. Induction phase : (main phase)
   - To achieve minimal residiual disease (MRD) negative (<0.01% blasts in BM).
   - Drugs used :
     - Steroids (DOC).
     - L. asparginase : Used in children, minimal use in adult d/t S/E.
     - Vincristine : In hyper CVAD regimen for adults (+ Cyclophosphamide, Adriamycin, Dexamethasone).
     - Daunorubicin.
     - High dose methotrexate (MTX) : In adult & child ALL.

Note : High dose MTX is also used in osteosarcoma.

   - If remission not achieved at the end of cycle : Blinatumomab (CD19 & CD23 antagonist).

2. Consolidation : 2 cycles given once MRD negative.
3. Maintenance : Oral MTX & 6-mercaptopurine (6-MP) for 2 years.

----- Active space -----

Chronic Lymphocytic Leukemia

00:38:50

Pathogenesis :

Failure of apoptosis of naive B-cell $\xrightarrow{\oplus\ CD5\ \&\ CD23}$ Monoclonal expansion of naive B-cell (>5000 cells/μL).

Note : If monoclonal expansion in lymph node → SLL.

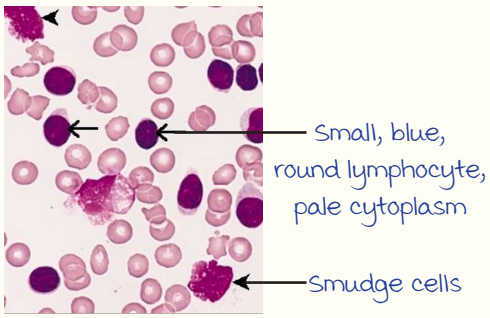
Diagnosis :

Diagnosed incidentally on routine check-up.

Population at risk : 65 to 85y ; Male > Female.

Blood picture :

- TLC : 70,000 to 80,000 cells/μL.
- Absolute lymphocyte count : ↑↑↑.
- Hb & platelet count : Normal.



Peripheral smear : Lymphocytosis

Rai & Binet staging :

- Stage 0 : Only lymphocytosis.
- Stage I : Lymphocytosis + lymphadenopathy.

Prognosis :

Good prognosis : Deletion 13q, hyperdiploidy & mutated Ig heavy chain.

Poor prognosis : Zap70 expression, β_2 microglobulin & unmutated Ig heavy chain.

Treatment :

Most cases do not require treatment.

Indications for treatment :

1. Development of B-symptoms : Fever, night sweats, weight loss.
2. Lymphadenopathy, hepatosplenomegaly.
3. BM involvement.
4. Richter's syndrome : Low grade tumor (CLL/SLL) → High grade tumor (DLBCL).
5. Autoimmune hemolytic anemia (Warm AIHA).

Drugs used :

- FCR regimen (Fludarabine, Cyclophosphamide, Rituximab) : Not fit for elderly.
- BR regimen (Bendamustine, Rituximab) : Preferred regimen.
- If relapse occurs/unfit for above regimen :
  - Ibrutinib : Tyrosine kinase inhibitor.
  - Venetoclax : BCL2 inhibitor.
  - Idelalisib : PI3K inhibitor.

Lymphomas

00:46:43 ----- Active space -----

Grade of tumor :

Low grade	High grade
• Follicular lymphoma • Marginal Zone Lymphoma (MZL) • Hairy cell leukemia • SLL • Waldenstrom macroglobulinemia	• DLBCL (m/c) • Burkitt's lymphoma • Mantle cell lymphoma (MCL)

Common clinical presentation :

1. Age : >60y (Except Burkitt's lymphoma : In children).
2. Sex : Male > Female (Except MZL).
3. B-symptoms less common.
4. Non-contiguous involvement.
5. Asymptomatic lymphadenopathy.
6. Extranodal involvement :
   - GIT (m/c).
   - Waldeyer's ring.
   - Oropharynx.

Mantle Cell Lymphoma :

Extranodal involvement :

- Aggressive tumor (most aggresive : Non-nodal subtype) :
  - BM involvement.
  - GIT involvement.
  - Waldeyer's ring involvement.
  - Lymphomatoid polyposis.

Immunophenotyping :

- CD5 ⊕, Cyclin D1 ⊕.
- CD10 ⊖, CD23 ⊖.

Translocation : t(11; 14).

Prognosis : SOX11 upregulation (Good prognosis).

Note : R-CHOP regimen (used in Non-Hodgkin's lymphoma) inadequate for MCL.

Follicular Lymphoma :

Low grade : May undergo spontaneous remission.

Immunophenotyping : CD10, CD23, BCL-6 & aberrant BCL-2.

Translocation : t(14;18) (Ig heavy chain gene → Chr 14 & BCL → Chr 18).

Treatment :

- Low grade : Rituximab (DOC).
- Advanced : R-CHOP regimen

Marginal Zone Lymphoma :

Prevalence : Females > Males d/t autoimmune association.

Extranodal involvement :

- GIT : MALToma (A/w non-atrophic pangastritis of H. pylori).
- Spleen : A/w HCV.
- Salivary gland : A/w Sjogren's syndrome.

----- Active space -----

Immunophenotyping :

- Positive : B cell markers, S. IgM, S. IgD.
- Negative : CD5, CD10, CD23.

Translocation : t(11;18).

Treatment : Responds to H. pylori therapy.

DLBCL :

Clinical presentation :

- Rapid enlargement of lymphnodes → B-symptoms & compression symptoms.
- BM involvement +/-.
- Extranodal involvement : Primary CNS lymphoma, effusion lymphoma, body cavity lymphoma.

Immunophenotyping :

Germinal centre DLBCL (Good prognosis) > ABC-DLBCL (Poor prognosis)

↓ CD10, CD23, BCL-6, aberrant BCL-2

↓ MUM 1 antigen ⊕

Prognosis : Poor prognosis seen in :

- Double hit lymphoma : BCL-2 or BCL-6
- Triple hit lymphoma : BCL-2 and BCL-6

} + high grade lymphoma & rearrangement of c-myc.

Treatment : R-CHOP regimen.

Burkitt's lymphoma :

- Ki 67 +++ : High proliferation index.
- Chemosensitive.

Varieties :

	Age	A/w EBV	Presentation
Endemic	Child	100%	Jaw/axillary mass
Sporadic	Adult	70%	Abdominal mass

Translocation :

- t(2;8), t(8;14), t(8;22).
- C-myc is on chromosome 8.

HPE : Starry sky appearance (Star : Macrophages, Sky : Tumor cells).

Hairy Cell Leukemia :

Memory B-cells —BRAF-1 mutation→ Hairy cells → Bone marrow. / Spleen.

Presentation : Pancytopenia + Massive splenomegaly.

Immunophenotyping : CD11C, CD25, CD103, CD123, TRAP ⊕, Annexin ⊕.

Bone marrow biopsy : Fried egg appearance + fibrosis.

Complications : Increased risk of infection d/t neutropenia + monocytopenia.

- Atypical mycobacterial infection.
- Aspergillus infection.

Treatment : Cladribine (or) Pentostatin.

----- Active space -----

Hodgkin's Disease

01:03:40

Pathogenesis :

Memory cells $\xrightarrow{\text{Aberration of PDL1 gene}}$ Reed sternberg cell (RS cell) in appropriate inflammatory background.

Hodgkin's disease v/s Non-Hodgkin's lymphoma :

	Hodgkin's disease	Non-Hodgkin's lymphoma
Age	15-34y (Bimodal peak)	Elderly
Contiguous	Contiguous	Non-contiguous
Disease node	Nodal disease : Posterior cervical > supraclavicular > axillary	Mostly extranodal
B-symptoms	More common	Less common
A/w EBV	More	Less

Classification :

Types	RS cell	EBV ⊕	Other features
Classical Hodgkin's disease : CD15 ⊕, CD30 ⊕			
Lymphocyte rich	Scanty	20%	Good prognosis
Nodular sclerosis	Lacunar	40%	• m/c type in the world • m/c in females • Mediastinal involvement ⊕
Mixed cellularity	Classical	70%	• A/w HIV • m/c in India • Seen in children & elderly
Lymphocyte depleted	Absent	100%	A/w HIV
Non-classical Hodgkin's disease : CD20 ⊕			
Lymphocyte predominant	Popcorn	EBV ⊖	C/F : Enlarged node in axilla

Treatment :

Classical Hodgkin's disease :

- ABVD regimen (Adriamycin, Bleomycin, Vincristine, Dacarbazine).
- If no response in first phase : Brentuximab (Anti-CD30).

Non-classical Hodgkin's disease : Radiotherapy is sufficient.

----- Active space -----

ENDOCRINOLOGY REVISION - 1

Classification of Hormones

00:05:04

BASED ON STRUCTURE

	Hormones	Features
Amino acid derivatives		
Tyrosine	T_3, T_4	–
	Catecholamines : Adrenaline (major), Noradrenaline, Dopamine	Produced by : Adrenal medulla
Tryptophan (Neurotransmitter action)	Serotonin	Produced by : • Enterochromaffin cells of GIT (main). • Raphe nuclei of brainstem.
	Melatonin	Produced by : Pineal gland
Vitamin derivatives		
	• Vitamin A • Vitamin D	–
Peptide hormones		
Small	• Posterior pituitary hormones • Hypothalamic hormones • ACTH	<50 amino acids
Large (>50 aa)	GH	191 aa
	Prolactin	199 aa
	Insulin, Parathormone, Renin	–
Glycoproteins	FSH, LH, TSH	–
Steroid hormones		
Adrenal cortex hormones	1. Aldosterone	Produced by : 1. Zona glomerulosa
	2. Cortisol	2. Zona fasciculata
	3. Adrenal androgens : • DHEAS (m/c). • Androstenedione (2nd m/c)	3. Zona reticularis
Sex steroids	Testosterone, estrogen, progesterone	–

DHEAS : Dihydroepiandrosterone sulphate.

BASED ON MECHANISM OF ACTION

----- Active space -----

	Receptor	Examples	Property
Group 1 (Intracellular receptors)	1. Type 1 : Cytoplasmic (Homodimeric receptor)	• Adrenal cortical hormones • Sex steroids	• Signals mediated by : Receptor hormone complex • Effector action : Gene transcription • Hormone features : – Lipophilic (Require transport protein) – Longer $t_{1/2}$
	2. Type 2 : Nuclear (Heterodimeric receptor)	• Vitamin A • Vitamin D • Thyroid hormones	
	Orphan receptors	• SF 1 • DAX 1 } Gonadotrophs • HNF4α : MODY type 1	Constitutive action without a ligand.
Group 2 (Cell membrane receptors)	GPCR		• Signal mediated by : Second messenger • Effector action : Protein translocation or protein channels • Hormone features : – Hydrophobic (Transport protein not required) – Shorter $t_{1/2}$
	TKR (Tyrosine Kinase receptor)	Insulin, growth factors (Eg : TGF-α)	
	JAK (Janus Kinase aka cytokine receptors)	Twin hormones (GH, PRL), EPO	
	Serine threonine Kinase receptors	Inhibin, activin, BMP-7, TGF-β	

G-Protein Coupled Receptors & their Secondary Messengers :

	cGMP	IP_3/DAG	cAMP
Receptor type	G_t	G_q	G_s/G_i
Action	Vasodilation	Vasoconstriction via Ca^{2+}-calmodulin pathway & PKC	Protein phosphorylation via cAMP-PKA pathway
Hormones	NO, ANP	• Angiotensin II • Substance P • Hypothalamic : TRH, GnRH • Posterior pituitary : V_1 & V_3 receptors, oxytocin • GIT : CCK, gastrin • ANS : α_1, Ach receptor	• Hypothalamic : CRH • Anterior pituitary : FSH, LH, TSH, ACTH • Posterior pituitary : V_2 receptor • GIT : Secretin, glucagon, somatostatin, PTH, calcitonin • ANS : α_2, all β receptors

Note :

- Only α_2 and somatostatin act via G_i (↓cAMP).
- NO and ANP vasodilation occurs d/t cGMP.

----- Active space -----

Pituitary Gland

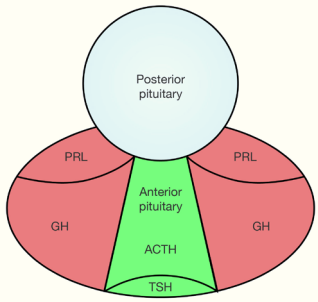
00:24:38

Anatomy :

Anterior pituitary : Oral ectoderm (Rathke's pouch).

Posterior pituitary : Neuroectoderm (Floor of 3rd ventricle).

Note : Pituitary insufficiency rarely causes hypothyroidism (20% TSH release in extra pituitary)



Prone to vascular injury

Prone to mass effect

Transcription Factors :

Transcription Factors	Cells	Hormones Produced
1. Prop-1 > pit-1 (m/c cause for congenital hypopituitarism)	Somatotrophs (most abundant)	GH
	Mammotroph/Lactotroph (Last cell to appear)	PRL
	Thyrotrophs (Least abundant)	TSH
2. T-pit	Corticotrophs (1st cell to appear)	POMC (Proopiomelanocortin) derivatives : • ACTH • MSH • β-lipotropins → Endorphins (Natural painkillers)
3. GATA-3 (SF-1, DAX-1)	Gonadotrophs (Produced throughout gland)	FSH, LH

Acidophilic cells Basophilic cells

Note :

- ↑ACTH is a/w ↑MSH → Hyperpigmentation.
- Hormones of happiness (DOSE) : Dopamine, Oxytocin, Serotonin, Endorphin.

Hypothalamo-hypophyseal Relation :

Hypothalamus acts on :

- Anterior pituitary : Via hypothalamo-hypophyseal portal system & superior hypophyseal A.
- Posterior pituitary : Via axonal-neuronal connection through the stalk.
  - Blood supply : Inferior hypophyseal A.
  - Storage of hormones : ADH (Supraoptic & paraventricular nucleus) Oxytocin (Periventricular nucleus).

Note :

CA breast mets (m/c) reach post. pituitary via inferior hypophyseal A. —leads to→ DI.

----- Active space -----

PITUITARY TUMORS

m/c tumors : Prolactinoma > GH-secreting adenoma > ACTH-secreting adenoma.

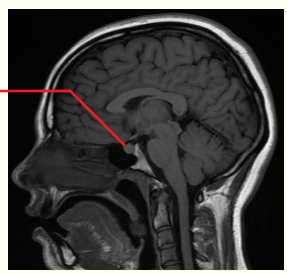
Effects :

1. ↑Hormone release : Functional tumors (Prolactinoma).
2. Stalk effect :
   Loss of hypothalamo-hypophyseal connection → Hypopituitarism, Hyperprolactinemia, Central DI
3. Mass effect :
   - ↑ICT.
   - Optic chiasm compression → Heteronymous/bitemporal hemianopia.
   - Cavernous sinus thrombosis, VIth nerve palsy.

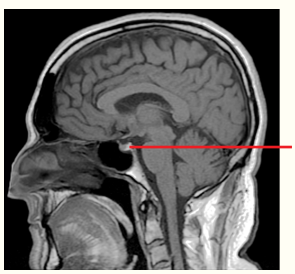
Ix :

T_1-weighted MRI :

Tumor displacing stalk



Sagittal section



MRI: Normal pituitary

Prolactinoma

00:45:35

Serological Interpretation :

PRL values (µg/L or ng/ml)	Inference	Etiology
<25	Normal value	-
25–40	Physiological ↑	REM sleep/stress/chest wall stimulation/pregnancy (upto 180 mcg/L).
40–100	Drugs	• Typical antipsychotics, Risperidone, TCA, SSRI, metoclopramide. • Opiates, verapamil, H_a blockers, α-methyldopa.
	Hormones	Estrogen, TRH, VIP, oxytocin.
	Systemic conditions	CKD, CLD, PCOS.
>100	Suspect tumor	-
	Macroprolactin (Inactive prolactin)	No tumor
	Hook effect (↑PRL seen only on serial dilution)	Tumor present
>200	Tumor confirmed	-

----- Active space -----

Types of Tumors :

	microadenoma	macroadenoma
Size	<1 cm	> 1 cm > 4 cm : Giant adenoma
Incidence	m/c	Less common
F : m	F > m	F = m

Clinical Presentation :

Based on age :

- >25 yrs (m/c)
- <25 years (Genetic cause)
  - MEN I
  - Carney's complex
  - McCune-Albright
    - Cafe-au-lait spots
    - Polyostotic fibrous dysplasia
    - Precocious puberty
    - Tumors

Note : Acromegaly in <20 years, suspect the same causes.

Based on sex :

In females :

Galactorrhea-amenorrhea complex :

↑PRL → Inhibits hypothalamopituitary gonadal axis → Hypogonadism → 2° amenorrhea, infertility, hot flushes

In males :

Late presentation d/t giant adenoma (>4 cm).

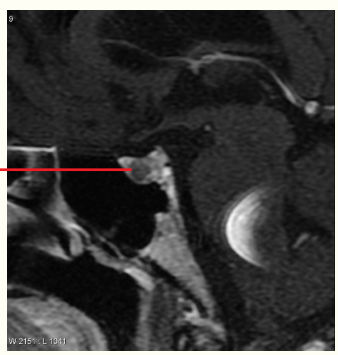
- Stalk effect, mass effect.
- Loss of libido, erectile dysfunction (Rare).

Investigations :

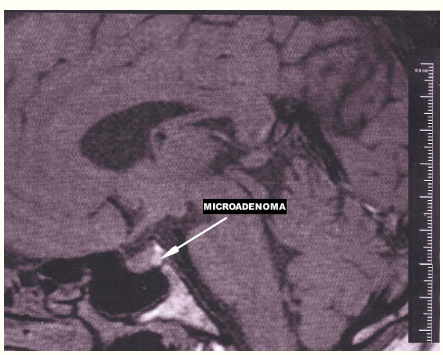
Screening test : Fasting PRL.

IOC : Gadolinium-enhanced MRI.

- Microadenoma : Hypointense (No contrast).
- Surrounding pituitary gland : Hyperintense (Contrast uptake).



Gd enhanced MRI



MRI

----- Active space -----

Treatment :

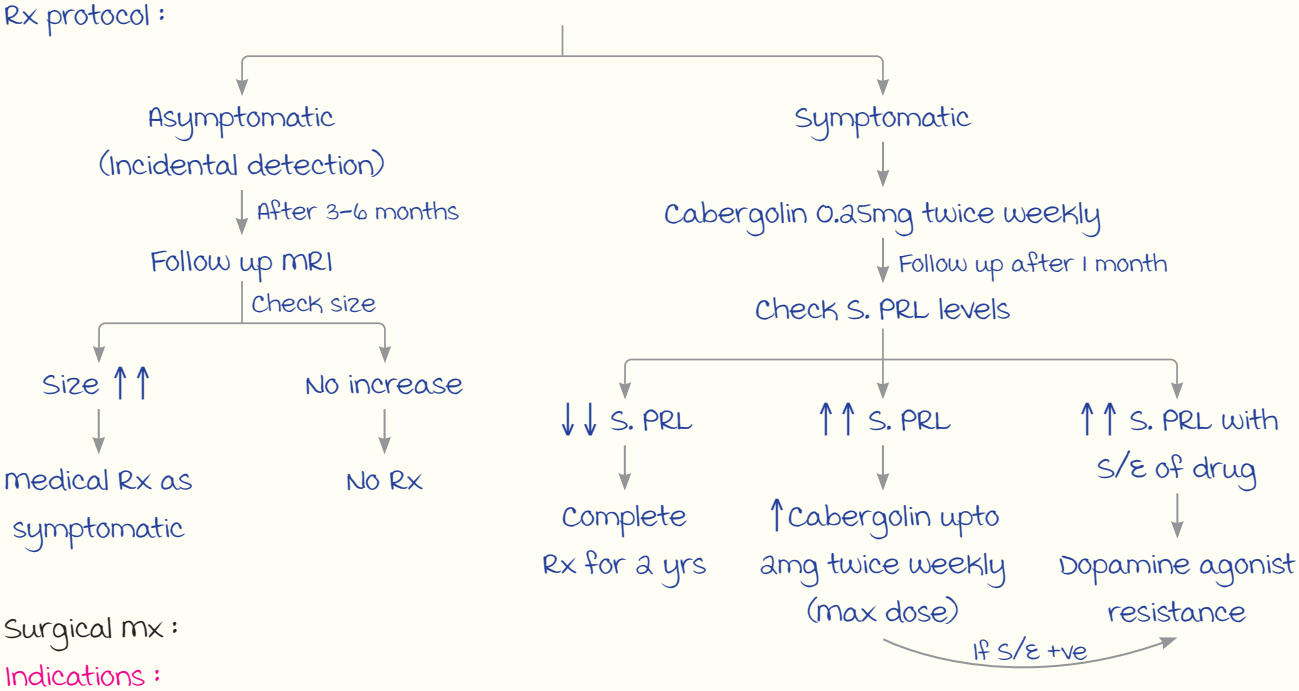
Medical Mx : 1st line.

Drugs :

Dopaminergic agonist :

- Cabergoline (DOC)
  - S/E : TR, ILD seen at dose >2mg.
- Bromocriptine (Pregnancy DOC).

Rx protocol :



Surgical Mx :

Indications :

1. Dopamine agonist resistance (20%).
2. Pituitary apoplexy.
3. Pregnancy (Refractory to 4 weeks bromocriptine).
4. Persistence of compression symptoms.

Surgery : Trans-sphenoidal tumor resection/hypophysectomy.

Growth Hormone

01:02:41

PHYSIOLOGY

Comparative Features with PRL :

	GH	PRL
Stimulators		
Sleep stage	N_2, N_3 of NREM	REM
Others	Hypoglycemia, ghrelin, GHRH	Estrogen, TRH, oxytocin
Inhibitors	Somatostatin, obesity, malnutrition (GH resistance)	Dopamine

----- Active space -----

Screening Test :

- IGF + IGFBP-3 levels ($t_{1/2}$ 12-15 hrs).
  - GH levels not used (D/t short $t_{1/2}$ & pulsatile release).

Effects :

Mechanism :

1. Direct.
2. Indirect : Via somatomedin-C/IGF-1 (Produced in liver)

↓

Peripheral actions.

Site of action :

	GH	IGF-1
Epiphyseal growth (Bone)	⊕	⊕
Adipose tissue	Lipolysis	Anti-lipolytic
Muscle protein synthesis	⊕	⊕
Salt and H_2O retention	⊕	⊖
Carbohydrates	Diabetogenic	Anti-diabetogenic

GH actions independent of IGF-1 : Mnemonic BEAMS

Note : Thyroid hormone & testosterone produce IGF-1 independent of GH.

ACROMEGALY

Etiology :

GH secreting → Pituitary adenoma (98%) :
- Macroadenoma (m/c).
- 20% a/w ↑PRL : Somatomammotrophic adenoma.
- Densely granulated & sparsely granulated types (Poor prognosis).

→ Ectopic : Pancreatic islet cell tumor.

GHRH secreting → Hypothalamic tumor : Hypothalamic hamartoma.

→ Ectopic : Bronchial carcinoid.

Clinical Presentation :

Sex : M > F.

Age : >40 years (m/c).

On examination :

1. Coarse facies : Thickening of lips, tongue, & face + Frontal bossing + Prominent supraorbital ridge
2. Acral enlargement.

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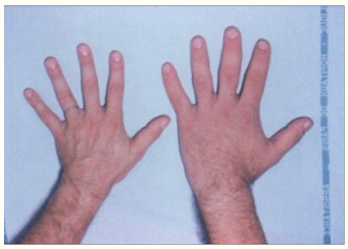
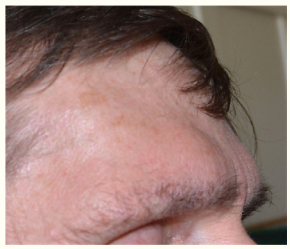

Acral enlargement


Frontal bossing


Coarse facies

Complications :

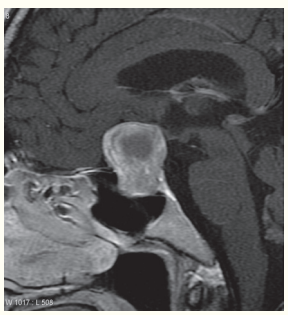
System/structure	Complication
Nerve	Entrapment neuropathy
Muscle	Myopathy
Metabolic	• Hypertriglyceridemia. • Hypercalcemia (D/t 1-α-hydroxylase) → Hypercalciuria → Stones. • Hyperphosphatemia. • Diabetes (Uncontrolled, short duration).
Ophthalmic	Angle closure glaucoma
Respiratory	OSAS, PAH
CVS	• M/C cause of death. • Asymmetrical LVH → Heart failure with preserved EF. • ↑ incidence of CAD. • HTN.
Thyroid	Goiter
GIT	Colonic polyps (Non-malignant)
Renal	Salt & H_2O retention
Menstrual	Menstrual abnormality (M/C : Oligomenorrhea)
Joints	Arthralgia
Skin	Seborrhea

Indicators of high activity mnemonic : DOSA

Management :

Investigations :

1. Screening : IGF-1 levels.
2. Confirmatory :
   Glucose-induced GH suppression test.
   - GH <1 ng/mL : Normal.
   - GH >40 ng/mL : Poor prognosis.
3. IOC : Gd enhanced MRI
   (Heterogeneous enhancement d/t macroadenoma).


Heterogenous enhancement of macroadenoma

----- Active space -----

Surgical Mx :

Transsphenoidal surgery (TOC) followed by immediate post-op GH :

- Undetectable : Good prognosis.
- Detectable → Risk of relapse → medical Mx initiated → Repeat imaging after 12 weeks.

Medical Mx :

Drugs :

1. Somatostatin receptor ligands : DOC
   - Octreotide.
   - Lanreotide.
   - Pasireotide.
2. Bromocriptine.
3. Cabergoline.
4. GH receptor antagonist : Pegvisomant.

Relapse after medical management :

- Fit for surgery : 2nd surgery done.
- Unfit for surgery : Gamma knife stereotactic RT.

ENDOCRINOLOGY REVISION - 2

----- Active space -----

Acquired Hypopituitarism

00:00:06

Etiology :

1. Stalk effect : Hypopituitarism + ↑ PRL + Central DI.

Cause	m/c examples
Tumor	• Functional : GH secreting. • Non-functional : Rathke cleft cyst, Craniopharyngioma.
Infiltration	Langerhans cell histiocytosis, Sarcoidosis, Hemochromatosis
Trauma/surgery	-
Infection	TB, HIV, Histoplasmosis, Toxoplasmosis

2. Lymphocytic hypophysitis.
3. Sheehan's syndrome.
4. Empty sella syndrome : 1°, 2°.
5. Viper bite.

Clinical Features :

Hormone deficiency	Effect
Central pituitary hormones :	
ACTH	• Asthenia, weight loss, loss of appetite. • Repeated episodes of hypoglycemia/hypotension. • Euvolemic hyponatremia. • Eosinophilia. Note : Cushings syndrome → Eosinopenia.
TSH (Rare)	Cold intolerance, constipation, bradycardia.
Lateral pituitary hormones :	
PRL	Only significant in lactating mothers.
GH	Centripetal obesity, hypertriglyceridemia, endothelial dysfunction.
Gonadotropins (All over the gland) :	
FSH, LH	Hypogonadism features : • muscle wasting, disproportionate fracture. • In males : Loss of libido. • In females : Irregular cycles, hot flushes, 2° amenorrhea.

----- Active space -----

Investigations :

Direct measurement : FSH, LH, TSH, PRL.

Indirect measurement :

- IGF-1.
- GH provocation test with Glucagon, L-dopa, Arginine, Clonidine.

(GH provocation test ... — GH assessment.)

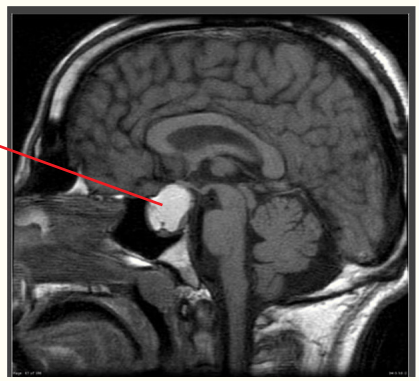
- Insulin tolerance test : Gold standard method.

Pituitary Apoplexy & Differentials

00:10:08

Pituitary Apoplexy :

Acute intrapituitary hemorrhage.



NCCT : Pituitary apoplexy

Etiology :

1. Tumor (Adenoma).
2. Necrosis (Sheehan syndrome).
3. Normal gland :
   - Risk factors : DM, HTN, sickle cell anemia.

Clinical features :

- Progressively worsening headache ± meningeal signs ± ophthalmoplegia.
- Severe hypotension, hypoglycemia.

Management :

Pulse steroid therapy : 1st dose → methylprednisolone 500 mg.

↓ F/b

Surgical decompression.

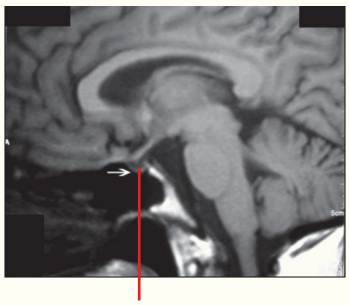
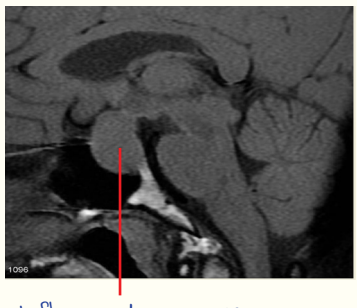
Differentials :

1. Sheehan's syndrome.
2. Lymphocytic hypophysitis.
3. Empty sella syndrome.

Sheehan's syndrome vs Lymphocytic hypophysitis :

	Sheehan's syndrome	Lymphocytic hypophysitis
Etiology	Postpartum ischemic necrosis of the pituitary gland (D/t PPH, shock, DIC).	Postpartum inflammatory mass : IgG4 containing lymphoplasmacytic cells.
Effects	• Hypogonadism. • ACTH failure.	• Stalk effect. • Mass effect.
Hormonal profile	• Anterior pituitary hormones : ↓. • ADH : Normal.	• PRL ↑. • ADH ↓.

----- Active space -----

	Sheehan's syndrome	Lymphocytic hypophysitis
Clinical features	• Immediately post-delivery : Lactational failure. • 3-6 months post delivery : – Lactational failure. – 2° amenorrhea, breast atrophy, ↓ libido, genital & axillary hair loss. – Signs of premature aging. – Asthenia & weakness.	• Pituitary enlargement. • Headache, visual disturbances. • Hypopituitarism. • Hyperprolactinemia. • Associated autoimmune disease. • Diabetes insipidus.
Imaging	 Necrosed gland	 Inflammatory mass
Rx	Complete hormone replacement.	Responds to steroids.

Empty sella syndrome :

	Primary	Secondary
Etiology	Tear in dura ⟶ CSF collects in sella.	As a part of necrosis/tumor ⟶ Empty sella.
Associated with	Benign intracranial hypertension.	Sheehan's syndrome.
Clinical features	• Hypopituitarism absent. • Features of ↑ ICT.	• Hypopituitarism present.

Anti - Diuretic Hormone (ADH)

00:19:50

Stimuli for ADH Release :

1. Osmotic stimuli (main) : ↑ Serum osmolality ⟶ Thirst, ADH release.
2. Non - osmotic stimuli : ↓ Effective circulatory volume.

Note :

- Serum osmolality = 2 x Na^+ + (Blood glucose/18) + (BUN/2.8).
  - ↓ S. osmolality ⟶ Hyponatremia.
- ↑ S. osmolality only in head injury & intubated patients ⟶ Hypernatremia.

----- Active space -----

Action of ADH on Vasopressin Receptors :

	Location	Effect
V_1 (Via IP3/DAG pathway)	Blood	Vasoconstriction, platelet aggregation
	Heart	Myocardial thickening
	Liver	Glycogenolysis
V_2 (Via cAMP protein Kinase A pathway)	Endothelium	VWF release
	Cortical collecting duct (Via AQP2 on luminal side)	Free H_2O reabsorption
V_3 (Via IP3/DAG pathway)	Pituitary	↑ ACTH

Note : AQP_3 & AQP_4 ⟶ Present on basolateral membrane.

Hyponatremia

00:26:02

Disorder of water metabolism : ↑ water ⟶ ↓ S. osmolality (D/t ↓ Na^+).

Causes :

1. Excess ADH release.
2. Psychogenic polydipsia (Water consumption >15L/day).
3. Impaired solute reabsorption in thick ascending limb & DCT :
   - M/c cause of CNS symptoms.
   - D/t diuretics (Thiazides > Furosemide).

Grades of hyponatremia :

	S. Na^+ (mEq/L)	C/F
Very severe	<100	↑ ICT symptoms
Severe	100–119	CNS : Ataxia, confusion
Moderate	120–129	GIT symptoms, lethargy
Mild	130–134	Only GIT symptoms

Pseudohyponatremia :

Normal (285–290 mOsmol/kg) or ↑ S. osmolality with ↓ Na^+.

Causes :

1. Translocational : D/t effective solutes (Glucose, mannitol, glycine, maltose).
2. Paraproteinemia.
3. Hypertriglyceridemia.

Approach to hyponatremia :

1. Rule out pseudohyponatremia.
2. Evaluate true hyponatremia (↓ S. osmolality) :
   a. Rule out psychogenic polydipsia & diuretic overuse.
   b. Evaluate causes for excess ADH.

----- Active space -----

	Causes for excess ADH		
	Appropriate		Inappropriate
Hyponatremia	Hypovolemic hyponatremia	Hypervolemic hyponatremia	Euvolemic hyponatremia
Etiology	Low ECF volume : • GIT loss : ↓ Urine Na^+. • Renal loss : ↓aldosterone, CSW, tubular injury. • 3rd space loss.	↓ effective volume : D/t CCF, cirrhosis.	• SIADH. • Thyroid & cortisol insufficiency. Note : ↑ tonicity & ↓ volume ⟶ Normal ADH release.

SIADH (Syndrome of Inappropriate ADH) :

Causes :

1. Trauma (Head injury).
2. Drugs :
   - Vincristine, oxytocin, NSAIDs.
   - SSRIs, TCAs.
   - 5 Cs (Cyclophosphamide, Carbamazepine, Chlorpromazine, Clofibrate, Chlorpropamide).
3. Paraneoplastic syndrome (Small cell lung cancer, duodenal, thymic tumors).
4. Acute intermittent porphyria.
5. Necrotizing pneumonia.
6. Meningoencephalitis.

Diagnostic criteria :

- ↓ S. osmolality.
- ↑ Urine osmolality.
- Euvolemia.
- ↑ Urine Na^+ (>20 mEq/L, d/t ↑ natriuretic peptides & RAAS inhibition).
- Absence of hypothyroidism, hypocortisolism (Adrenal), pituitary, liver & renal disease.

D/d : Cerebral Salt Wasting Syndrome (CSW).

	CSW	SIADH
Hyponatremia	Hypovolemic	Euvolemic
Cause	Head injury Loss of adrenergic tone ⟶ RAAS suppression	Head injury, drugs
S. uric acid	↓	↓↓↓<2 mg/dL
S. K^+	↑↑	N or ↑
Urine Na+ (Natriuresis)	↑	

----- Active space -----

Diabetes Insipidus (DI)

00:42:32

Updated names (February 2023) :

- Central DI → AVP-d (Arginine vasopressin deficiency).
- Nephrogenic DI → AVP-r (Arginine vasopressin resistance).

POLYURIA :

Diagnostic criteria : >3L/24h or >40 mL/kg/day.

	Water diuresis (m/c)	Solute diuresis
Presentation	Urine output : >7 L/24h	H/o DM, mannitol therapy, diuretic use, relieved urinary obstruction
U. osmolality (mOsmol/kg)	<300	>600
Urine dipstick	⊖	⊕
Nocturnal craving for cold water	⊕	⊖
Urine specific gravity	1.010	-

Hypotonic Polyuria :

3 L/24h + Urine osmolality <600 mOsmol/kg.

Causes : AVP-d, AVP-r, Psychogenic polydipsia.

	AVP-d	AVP-r
Pathophysiology	Deficiency of AVP.	Resistance to action of AVP.
Causes	• Stalk effect. • Genetic causes (AD > AR > XLR). • Pregnancy. Note : Wolfram syndrome/DIDMOAD syndrome : • AR. • Diabetes Insipidus, Diabetes Mellitus, Optic atrophy, Deafness.	• Fibrosed receptors d/t IgG4, Sjogren's, Sarcoidosis. • Drugs : Lithium, Demeclocyline Cisplatin, Foscarnet. • Hypercalcemia, hyperuricemia, hypokalemia, hyperoxaluria. • Sickle cell anemia (Occlusion of vasa recta). • Pregnancy.

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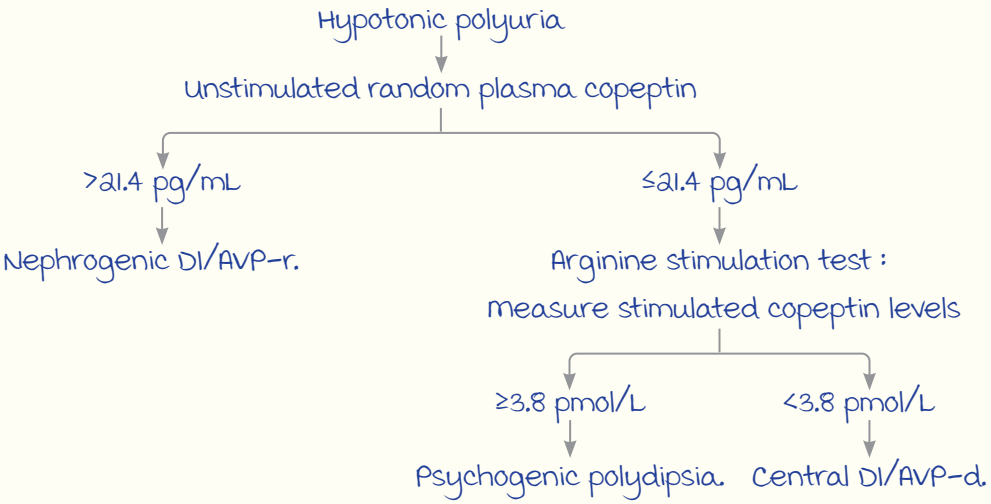
Investigations :

Plasma copeptin assay : Has replaced water deprivation test.



Treatment :

1. Central DI :
   - Desmopressin 10-20 mcg intranasally.
   - Desmopressin 0.1-0.8 mg orally OD.
2. Peripheral DI : Thiazides (DOC)
3. Lithium induced DI : Amiloride/Triamterene.

SIADH v/s DI :

	SIADH	DI
Presentation	Hyponatremia	Polyuria
S. Osmolality	Hypotonia	Hypertonia
S. Na^+	↓	↑
Urine volume	↓	↑↑
Urine osmolality	Relatively ↑	Relatively ↓
Urine Na^+	↑ (>30 mEq/L)	Normal
Plasma volume	Euvolemic	
Treatment	• Acute : 3% saline • Chronic : Fluid restriction, vaptans	Based on type of DI

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ENDOCRINOLOGY REVISION - 3

Primary Hyperaldosteronism (PHA)

00:01:12

Pathophysiology :

Hyporeninemic hyperaldosteronism :

Aldosterone ↑↑ ⟶ Renin ↓ ⟶ 1° hyperaldosteronism.
(Adrenal gland)

Note :

Hyperreninemic aldosteronism is seen in 2° hyperaldosteronism :

↓ renal perfusion ⟶ RAAS activation ⟶ ↑aldosterone.

Causes :

Acquired :

- micronodular B/L adrenal hyperplasia (m/c).
- Adenomas (mostly U/L) ⟶ Conn's syndrome.

Inherited :

Familial hyperaldosteronism (Autosomal dominant) : Type I aka GRA (Glucocorticoid remediable aldosteronism).

Presentation :

Age : 20-60 years.

Sex : M=F.

Triad of PHA :

1. Hypertension :
   - Disproportionate target end organ damage.
   - m/c endocrine cause for 2° hypertension.
2. Hypokalemia : Weakness, ↑ Urine K^+.
3. metabolic alkalosis.

Note :

Hypokalemia + HTN + metabolic alkalosis ⟶ DDx
- PHA (Acquired/GRA).
- Cushing syndrome.
- Apparent Mineralocorticoid Excess (AME).
- Liddle syndrome.

Management :

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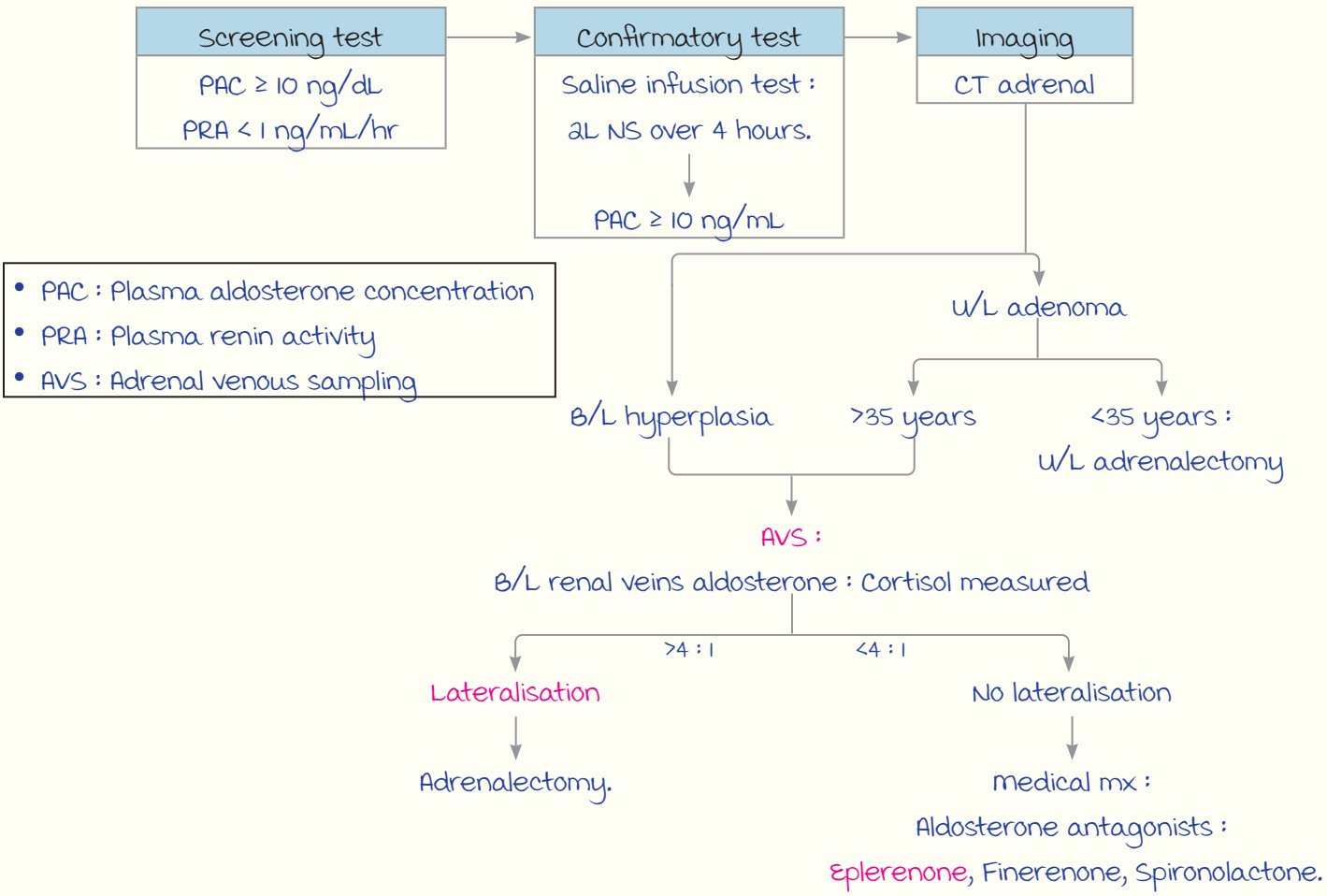

Adrenal Insufficiency/Addison's Disease

00:12:03

Primary V/S Secondary Addison's Disease :

	1°	2°
Etiology	Adrenal cortical cause Autoimmune >TB	Pituitary insufficiency : D/t abrupt steroid withdrawal (m/c)
ACTH	↑	↓
Aldosterone	↓↓	Normal
S. K^+	↑	Normal
S. Na^+	Low	Low
Mineralocorticoid deficiency	⊕	⊖
Salt craving, Postural hypotension	⊕	⊖
Hyperpigmentation	⊕	⊖
Vitiligo	⊕	⊖

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1° ADDISON'S DISEASE

Causes :

Acquired :

1. Autoimmune :
   - m/c worldwide.
   - Autoimmune polyendocrine syndromes (APS)/Polyglandular autoimmune syndromes (PGA).
2. TB : m/c in India.
3. Waterhouse-Friderichsen syndrome.

Inherited :

1. AAA syndrome (D/t aladin gene mutation) :
   - Alacrimia.
   - Achalasia cardia.
   - Addison's.

   4A syndrome : AAA + ANS dysfunction.
2. X-linked adrenoleukodystrophy (D/t ↑ very long chain fatty acids).

Clinical Features :

Hormone insufficiency	manifestation
Cortisol	• Asthenia, weight loss. • Hypoglycemia & hypertension : Repeated episodes. • Euvolemic hyponatremia. • Eosinophilia.
Aldosterone	Dehydration, salt wasting, hyperkalemia, postural hypotension.
Sex steroids	Dry skin.
ACTH	Hyperpigmentation.

Other feature : Extra adrenal calcification (Eg : Auricular).

Note :

2° Addison's : Clinical features a/w ACTH and aldosterone insufficiency is not seen.

Investigations :

CT adrenals : Normal/Small/Asymmetrical.

Serological work-up :

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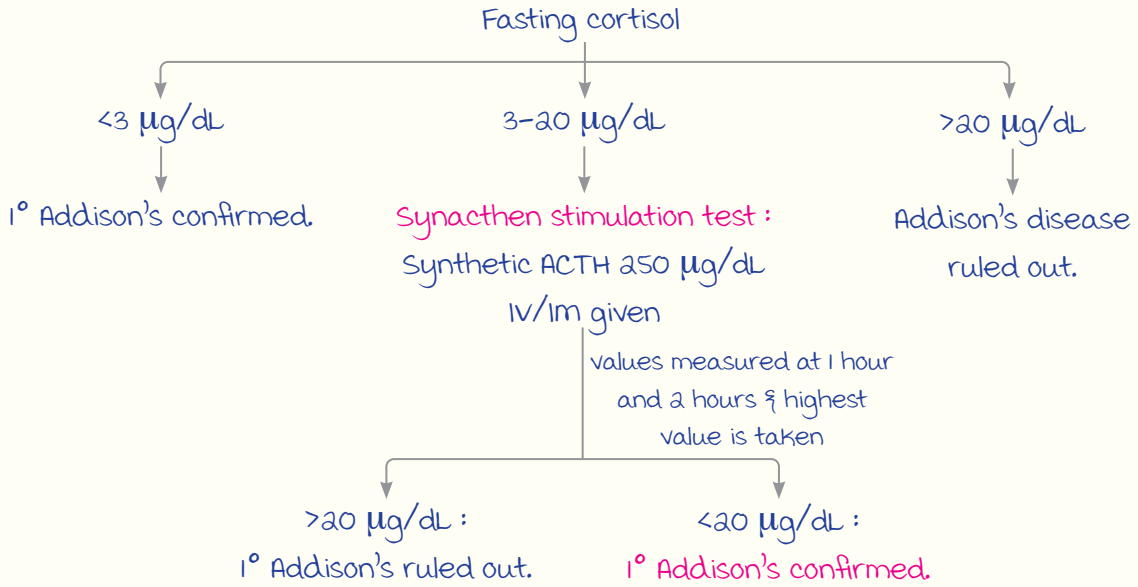

ADDISONIAN CRISIS

Emergency condition.

Clinical features : Acute abdominal pain + hypotension + shock.

Management :

1. 3-4L of NS over 8-12 hours.
2. 100 mg IV hydrocortisone STAT
3. 50 mg IV hydrocortisone 6 hours apart

→ 1st day, total dose : 300 mg.

4. Taper the dose from day 2 to day 4 → Switch to oral hydrocortisone.

Cushing's Syndrome

00:23:27

Pathophysiology :

Cortisol (Glucocorticoid + mineralocorticoid activity) $\xrightarrow{11\text{-}\beta HSD\text{-}2}$ Cortisone (Only glucocorticoid activity).

Defect in enzyme : 11-β-hydroxysteroid dehydrogenase type 2 (11-βHSD-2)

↓

Hypercortisolism

Can be

Inherited :

Apparent mineralocorticoid excess (AME).

Acquired :

- ↑ Licorice consumption.
- Cushing's syndrome.

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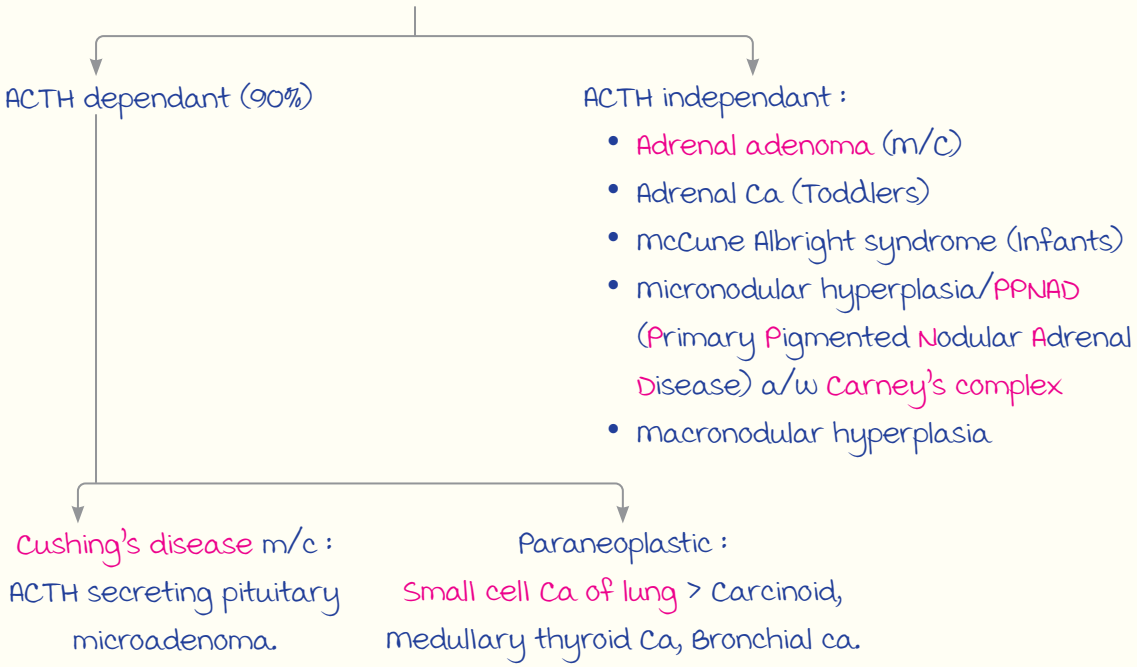
Causes of Hypercortisolism :

1. Endogenous :



2. Exogenous : ↑ steroid intake.

Clinical Presentation :

	Action	Clinical features
Protein	Catabolism ↓ • Most tissues : ↓ Amino acid uptake. • Liver : ↑ Aa uptake	In ↓ order of discriminatory value : 1. Proximal myopathy. 2. Facial plethora. 3. Violaceous purplish striae. 4. Bruising (D/t platelet dysfunction). 5. Young onset osteoporosis/short stature. 6. Disproportionate HTN & DM (Not d/t protein catabolism).
Carbohydrate	↑ Alanine ↓ ↑ Gluconeogenesis ↓ ↑ hepatic glucose output	Diabetes mellitus
Fat	Redistribution of fat ± minimal lipolysis	Buffalo hump, moon face, centripetal obesity
Mineralocorticoid	↑	1. Salt & H_2O retention 2. Hypokalemia 3. Metabolic alkalosis
Sex steroids	↑	Acne, Hirsutism
CNS	-	Steroid induced psychosis, depression, anxiety

Other features :

- Eosinopenia.
- Prone for infection.
- DVT.
- Menstrual irregularity (Oligomenorrhea, Amenorrhea).

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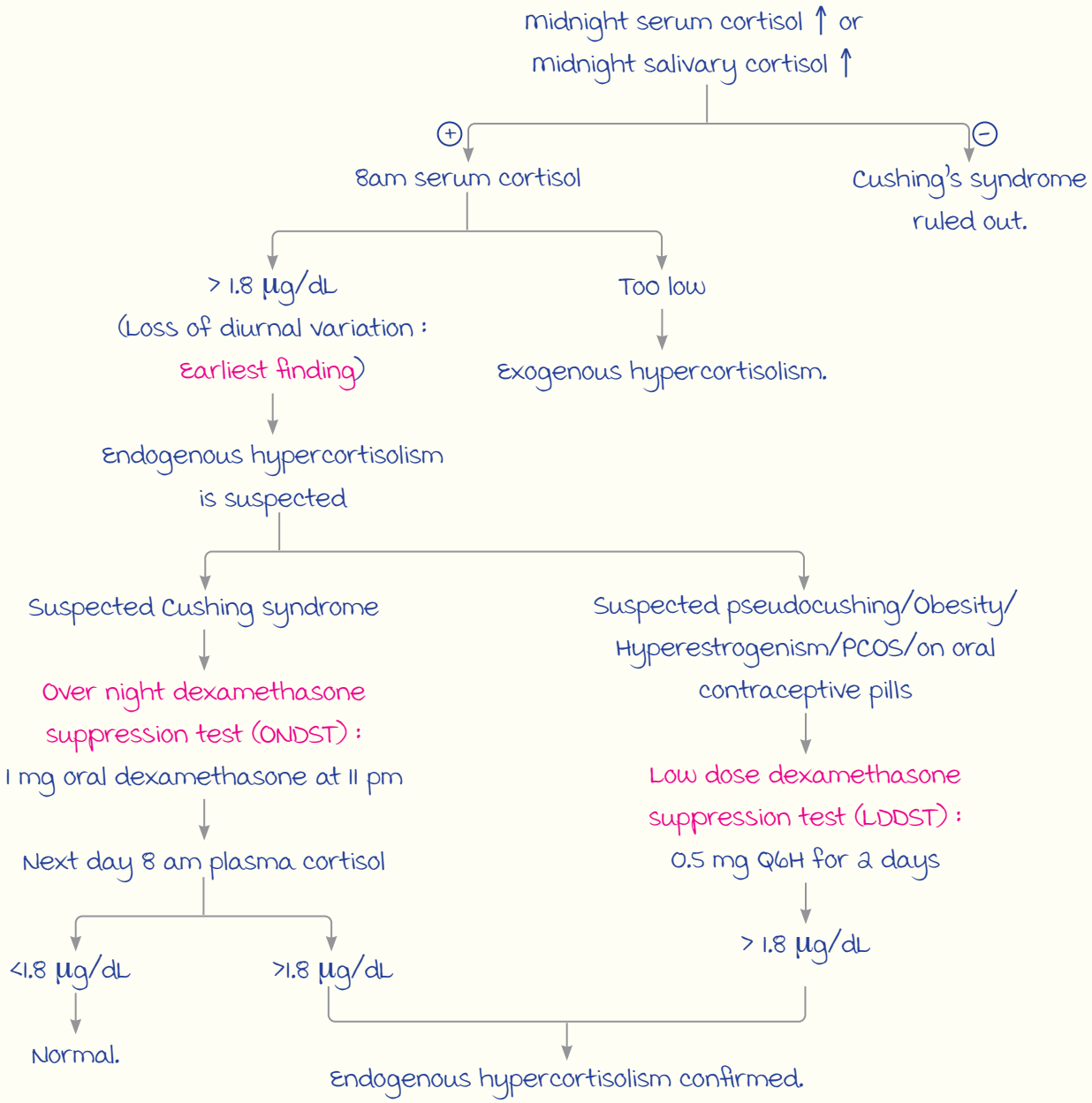
Management :

Diagnostic criteria for endogenous hypercortisolism :

1. Midnight Serum cortisol : >1.8 µg/dL
2. Midnight salivary cortisol : >5.5 nmol/L
3. ONDST or LDDST (Specific) : >1.8 µg/dL

→ If 2 out of 3 ⊕ : Endogenous hypercortisolism confirmed

Work up & treatment :



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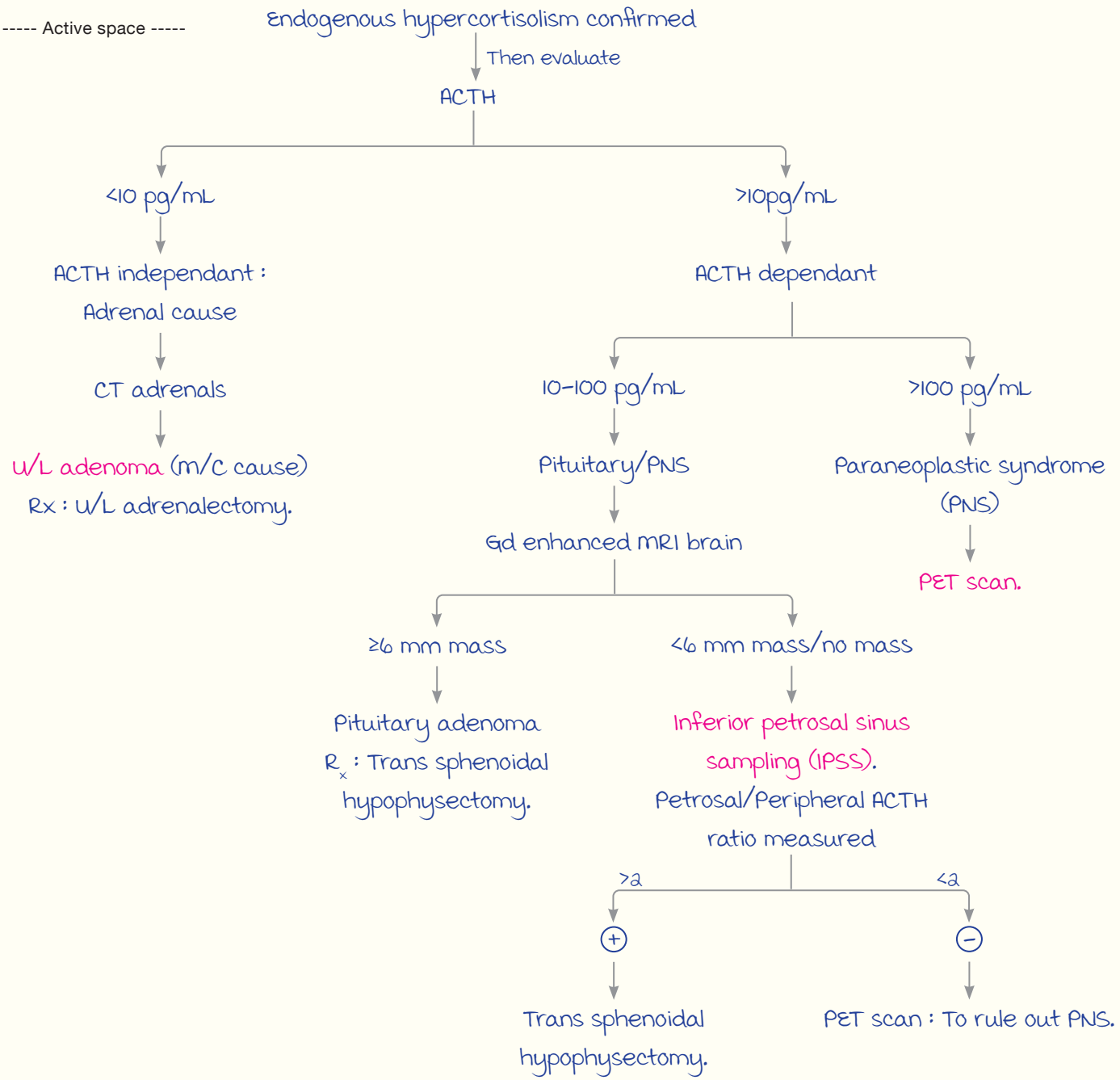

medical mx (Limited role) : Ketoconazole.

Pheochromocytoma

00:47:57

Pathophysiology :

- Neural crest cell tumor ⟶ ↑ production of catecholamines & its metabolites.
- Adrenal medulla hormones :

Catecholamines	Adrenaline (80%)	Noradrenaline (NA) (20%)	Dopamine
metabolites	• metanephrine • VMA (Vanillylmandelic acid)	Normetanephrine	HVA (Homovanillic acid)

- NA $\xrightarrow{PNMT}$ Adrenaline.

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Causes :

Adrenal (75%) : Adrenaline > NA.

Extra-adrenal (25%)

- Sympathetic (20%) :
  - Functional.
  - Organ of Zuckerland (m/c site).
- Parasympathetic (5%) :
  - Mostly non-functional.
  - Sites : Carotid body > Jugular bulb.

- AKA Paraganglioma.
- Produces only NA (PNMT is absent outside the adrenal gland).

Association :

- 40% Hereditary :
  - MEN-2, VHL, NF-1.
  - All hereditary tumors are b/l except NF-1.
- 50% Malignant :
  - Surest sign : Metastasis.
  - A/w succinate dehydrogenase B mutation.

Note : Rule of 10 is outdated.

Clinical Presentation :

m/c sign : Episodic hypertension.

6 Ps and 1W :

- Palpitations
- Perspiration

(+) severe episodic headache (m/c) → Triad of pheochromocytoma.

- Pain (Abdominal pain d/t hypercalcemia).
- Pallor (Suggestive of malignancy).
- Panic attack (2nd m/c).
- Postural hypotension.
- Weight loss.

Investigations :

Lab investigations :

1. 24 hour urine fractionated metanephrine (98% sensitivity & specificity) : Screening test.
2. Plasma fractionated metanephrine (100% sensitivity, But low specificity) : Done if 24 hr urine fractionated metanephrine test is (−) but clinical suspicion for pheochromocytoma is very high.

----- Active space -----

IOC :

- Adrenal pheochromocytoma : MRI abdomen.
- Extra-adrenal pheochromocytoma : Gallium DOTATATE PET scan.

Treatment :

Surgery : Laparoscopic retroperitoneal adrenalectomy.

Pre-operative mx :

Days before surgery	Drug	
10	Liberal IV fluid therapy	
7–10	α-blockers	Phenoxybenzamine (m/c) Prazosin
2–3	β-blockers	Atenolol

HTN crisis during surgery : Sodium nitroprusside or nicardipine.

Multiple Endocrine Neoplasia (MEN)

00:59:16

- Autosomal dominant.
- M=F.

MEN-I

Etiology :

- Mutation of menin gene on chromsome 11 q (Tumor suppressor gene).
- Intron inversion (m/c mutation).

Clinical Presentation :

Major manifestation :

- Parathyroid : Primary hyperparathyroidism (100%).

	1° hyperparathyroidism in MEN-I	1° hyperparathyroidism
Age	<40 years	>50–60 years
Sex	M = F	F >> M
Symptoms	Painful bones, Renal stones, Abdominal groans, Psychotic moans & fatigue overtones	Asymptomatic
Etiology	Asymmetrical hyperplasia of all 4 glands	Adenoma (m/c cause)

----- Active space -----

- Pancreas : Enteropancreatic neuroendocrine tumors (50–70%)
  - m/c cause of death in MEN-1.
  - m/c type : Gastrinoma.
  - m/c site for MEN-1 related gastrinoma → Duodenum (D_1, D_2).

  Note : m/c site for sporadic gastrinoma → Passaro triangle.
- Pituitary : Prolactinoma (Aggressive macroprolactinoma).

Minor manifestation :

- Skin : Angiofibroma (m/c), Collagenoma, Lipoma.
- Neurogenic tumor meningioma (m/c).
- Overall m/c tumor : Adrenocortical tumors (30%).
- Pheochromocytoma in MEN-1 : <1%.
- PNET (Primitive neuroectodermal tumors) : Thymic & foregut carcinoid.

MEN 2A

Etiology :

Point mutation of RET proto-oncogene on chromosome 10q.

Types :

1. Classical MEN 2A :
   - Medullary thyroid Ca (100%).
   - Pheochromocytoma (50%) : Inherited, B/L.
   - Parathyroid hyperplasia (25%).
2. MEN 2A with cutaneous lichen amyloidosis.
3. MEN 2A with Hirschsprung's disease.
4. FMTC (Familial medullary thyroid cancer).

MEN 2B :

Manifestations :

Medullary thyroid Ca + Pheochromocytoma + 3 Ms ± megacolon.

3 M's :

- Marfanoid habitus.
- Mucosal ganglioneuromas.
- Myelinated corneal nerve fibres.

MEN 4

Etiology :

CDKIB mutation (CDK : Cyclin dependant Kinase).

Manifestations :

- Parathyroid involvement.
- Pituitary tumors.
- Gonadal tumors : Ovarian/testicular.
- Renal/Adrenal tumors.

----- Active space -----

MEON

01:08:46

MEON : Multiple Endocrine & Other Organ Neoplasia Syndromes

	Inheritance/Defect	Genes	Endocrine manifestation	Neoplasia
Hyperparathyroidism – Jaw tumor (HPT-JT)	Autosomal dominant	Parafibromin/ CDC 73	Hyperparathyroidism d/t parathyroid carcinoma	Ossifying fibroma of jaw
Carney complex		PPKARIA	• PPNAD/Lean cushing • Acromegaly • Prolactinoma (Rare)	Atrial myxoma
VHL (Von Hippel Lindau disease)		VHL gene on chr 3	Pheochromocytoma	• Renal cell Ca • Cerebellar hemangioblastoma
NF-1 (Neurofibromatosis type 1)		Neurofibromin on chr 17	Pheochromocytoma	Optic nerve sheath tumors
Cowden's syndrome (CWD)		PTEN mutation	Autoimmune hypothyroidism	• Hamartomatous polyps of GIT • Ca breast
McCune Albright syndrome	Post zygotic GS α subunit defect	Post zygotic mutation of GNAS-1 gene	• Adrenal cushing • Acromegaly • Prolactinoma (Rare)	Polyostotic fibrous dysplasia

PPNAD : Primary pigmented nodular adrenocortical disease.

Note : Carney's triad : Pulmonary chondroma + GIST + Paraganglionoma.

PGA (Polyglandular Autoimmune Syndrome)

01:13:37

AKA APS : Autoimmune polyendocrine syndromes.

	APS-I	APS-II
Age of onset	Childhood	Adult
Gender association	M=F	F>M
Skin & nail changes, candidiasis	⊕	⊖
Associated gene	APECED gene mutation	HLA-DR3 and DR4 association
Inheritance pattern	Autosomal recessive	Polygenic
Antibody	Anti 21-OH antibody (m/c cause for addison's disease)	⊖
Major manifestations	1. 1° hypoparathyroidism. 2. Graves > Hashimoto's thyroiditis.	1. Addison's disease. 2. Hashimoto's thyroiditis > Grave's (Rare).
Minor manifestations	• Addison's disease. • Type 1 DM. • Hypogonadism.	• Type 1 DM. • Hypogonadism.

APECED : Autosomal polyendocrinopathy candidiasis & ectodermal dystrophy.

ENDOCRINOLOGY REVISION - 4

----- Active space -----

Hypercalcemia

00:01:15

Adjusted total calcium/Normal S. Ca^{2+} : Measured Ca^{2+} + 0.8 x (4 – S. albumin).

- Includes albumin bound Ca^{2+}.
- Normal range : 8.6 – 10.3 mg/dl.

Pathophysiology :

↑ S. Ca^{2+} (Ionised) ⊖→ Ca^{2+} sensing receptor (CaSR) → Parathyroid gland.
→ Thick ascending limb of loop of Henle.
↓ ⊖ Ca^{2+} reabsorption
↑ Calcum excretion
↓
Stone formation

Causes :

1. PTH related : m/c.
   - 1° and 3° hyperparathyroidism (HyperPTH).

Hyperparathyroidism	Etiology		S. Ca^{2+}	S. PO_4^{3-} (Normal = 2.5–4.5 mg/dl)	PTH (Normal = 50–100 pg/mL)
1° (m/c PTH related cause)	Adenoma : • 60 – 80y • F > M	Hyperplasia : • Young • F = M • A/w MEN 1, 2	↑	↓	↑ (500 pg/ml)
3°	Long standing 2° hyperPTH (Advanced CKD)		↑	↑	↑↑↑ (> 1000 pg/ml)

- Lithium induced 1° hyperparathyroidism.
- Familial hypercalcemic hypocalciuria (FHH) :
  Loss of function mutation of CaSR
  ↓
  ↑ Ca^{2+} reabsorption
  ↓
  Hypercalcemia + Hypocalciuria

Note :
Lithium can also cause :
- Nephrogenic DI.
- Chronic tubulointerstitial disease.
- Hypothyroidism (D/t gland destruction).

----- Active space -----

- Paraneoplastic hypercalcemia / humoral hypercalcemia of malignancy (HHM) :
  - ↑ PTH-rp (related peptide) $\xrightarrow{\ominus}$ PTH → PTH < 50pg/ml, ↑ Ca^{2+}.
  - Seen with squamous cell carcinoma (SCC).

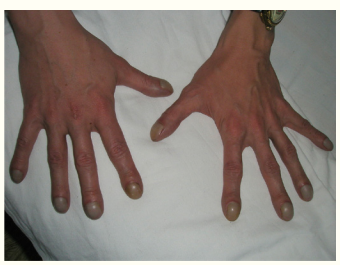
2. Vitamin D related :
   - Active form : 1,25 $(OH)_2$ D_3 / Calcitriol → ↑ Ca^{2+} absorption. ; (–) PTH

	Form of Vitamin D	
	1, 25 $(OH)_2$ D_3	25 $(OH)_2$ D_3
t 1/2	6–8 hours	2–3 weeks
Hypervitaminosis D	↑	↑
Sarcoidosis, acromegaly, lymphomas	↑	Normal

3. Osteolytic hypercalcemia : Multiple myeloma, CA breast.
4. Endocrine : Pheochromocytoma, addisonian crisis, thyrotoxicosis, acromegaly.
5. Drugs : Thiazides, lithium.
6. Milk alkali syndrome : ↑ Ca^{2+} consumption (>4g/day)

Clinical Features :

- Painful bones : D/t osteolysis.
- Renal stones.
- Abdominal groans : In sarcoidosis & addisonian crisis.
- Psychotic moans.
- Fatigue overtones (m/c).
- Pseudoclubbing : Normal lovibond angle.

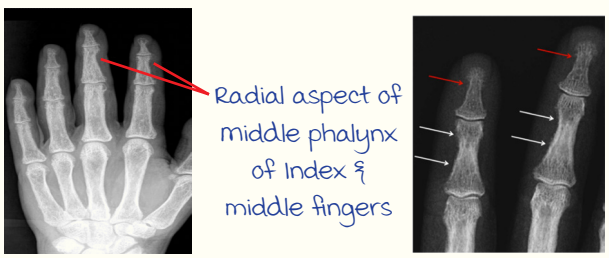


Pseudoclubbing

Investigations :

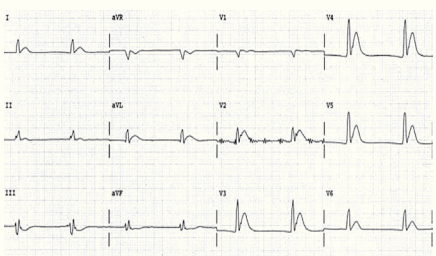
X-ray :

- Subperiosteal bone resorption.
- Rugger jersey spine.
- Acral osteolysis.
- Osteitis fibrosa cystica.
- Salt & pepper skull.
- Diffuse bone resorption.



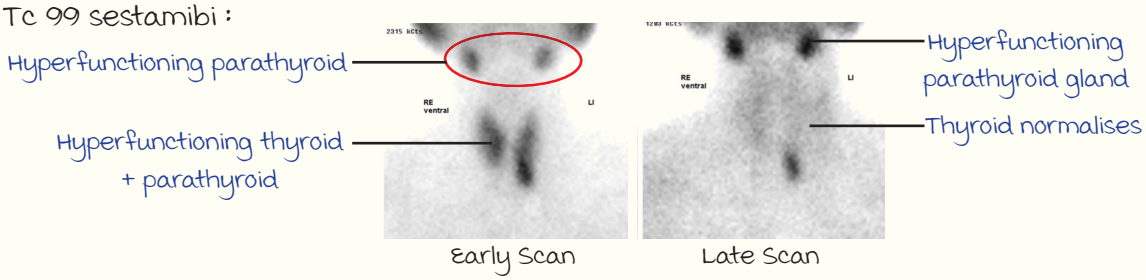
Subperiosteal resorption

ECG : Short QT interval.



Short QT interval

Tc 99 sestamibi :



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Treatment :

Acute :

- Hydration : To prevent nephrogenic DI.
- Bisphosphonates.
- Calcitonin.

Definitive : Surgery.

- Adenoma : Removal of adenoma.
- Hyperplasia : Removal of 3½ glands.

Hypocalcemia

00:21:10

Etiopathogenesis :

2° hyper PTH :

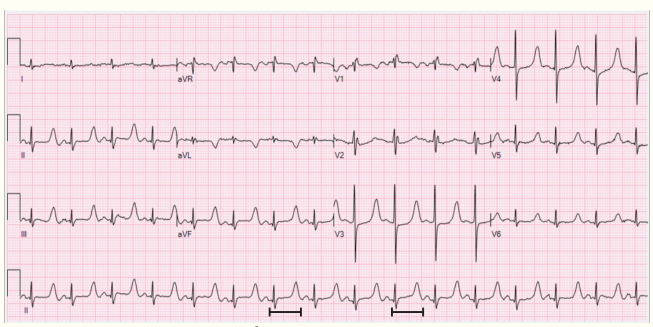
- CKD → Inhibition of 1α hydroxylase, ↓ calcitriol → Hypocalcemia → (+) Parathyroid → ↑↑ PTH, ↓ S. Ca^{2+}, ↑ S PO_4^{3-}

Clinical Presentation :

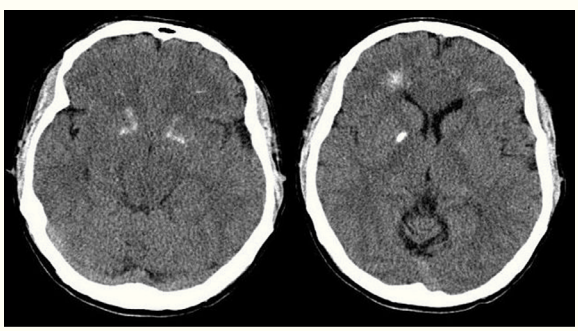
- Arrhythmia : Prolonged QT interval.
- Pseudotumour cerebri : Seizures & papilledema (D/t ↑ ICT) or calcification.
- Neuromuscular irritability : Circumoral tingling, numbness, parasthesia, latent tetany (Chvostek's sign & Trousseau's sign).

Investigations :

- ECG : ↑ QT interval.
- CT brain : Basal ganglia calcification.



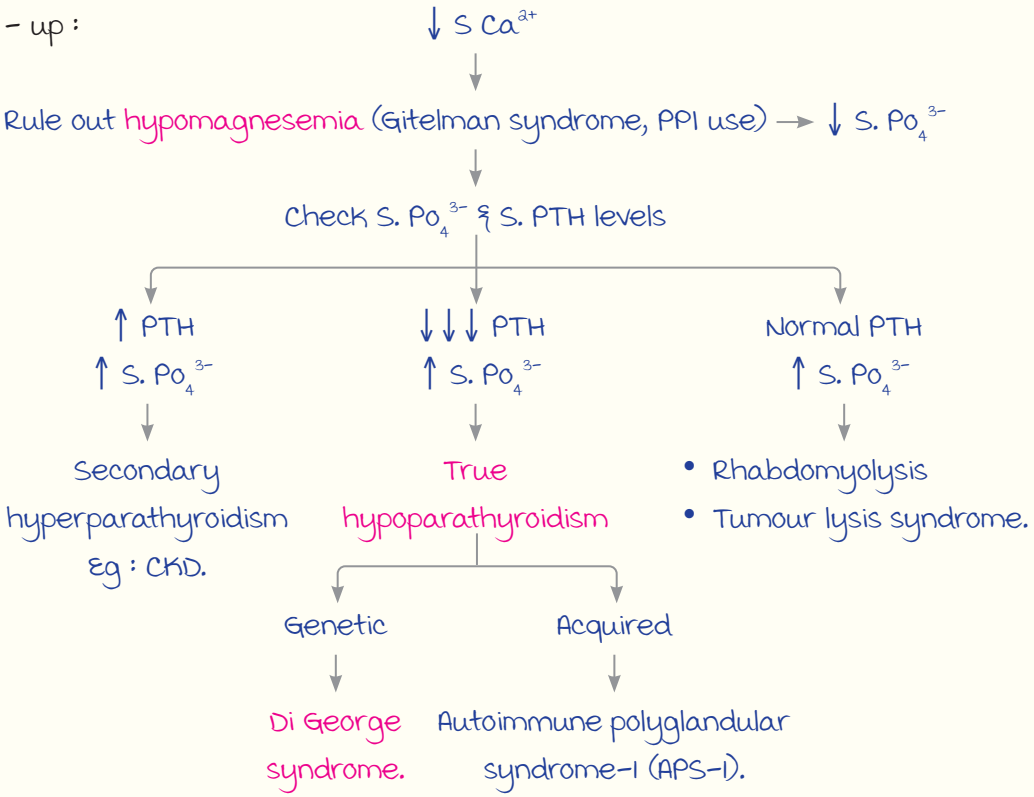
↑ QT interval



Basal ganglia calcification

----- Active space -----

Work – up :



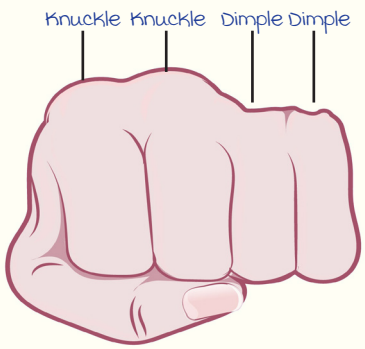
Pseudo Hypoparathyroidism :

Resistance to PTH action (↑ PTH) → ↓ S. Ca^{2+}, ↑ S. PO_4^{3-}.

Types	Etiopathogenesis	Bone mineral changes	Biochemistry
Ia	• Gsα defect d/t GNAS gene mutation. • Complete resistance.	⊕	↓ Ca, ↑ PTH, ↑ P
Pseudo pseudo hypoparathyroidism		⊕	Normal
Ib	No Gsα defect	⊖	-
2	Partial resistance	⊖	↑ cAMP in urine (If PTH is given)

Bone mineral density changes :

- Short stature, round facies, mental retardation.
- Albright hereditary osteodystrophy : Short 4th metacarpal/metatarsal.



Knuckle knuckle dimple dimple sign

Treatment :

Acute : 10% Calcium gluconate 10 ml over 10 mins.

Chronic : Long term Ca^{2+} supplementation.

↑ Ca^{2+} supplementation → Milk alkali syndrome.

Thyroid Disorders

00:32:08 ----- Active space -----

Development :

	Thyroid	Parafollicular C-cells
Derivative	• 3-4 weeks (1st endocrine organ) • Endodermal origin	Ultimobranchial body (Neural crest)
Synthesis	$T_3 < T_4$ (10x times)	Calcitonin

THYROID HORMONES :

Steps of Synthesis :

1. Sodium iodine symport (Basolateral membrane) : Used in Tc^{99} / I^{133} scintigraphy.
2. Iodide - chloride antiport (Pendrin) : Pendred syndrome.
3. Organification : $I^- \rightarrow I_2$,
   mediated by thyroid peroxide (TPO)/dual oxidase (DUOX).
4. Iodination of thyroid residues → MIT, DIT (Enzyme independent).
5. Coupling : MIT + DIT → T_3, DIT + DIT → T_4.
6. Reuptake into epithelial cells.
7. Proteolysis and release of hormone.

Peripheral Conversion :

- $T_4 \xrightarrow{\text{Deiodinase - 2}} T_3$
- $T_4 \xrightarrow{\text{Deiodinase - 3}} rT_3$ (Reverse T_3)

Deiodinase - 2 inhibitors :

- PTU.
- Steroids.
- Amiodarone.
- Propranolol.

Properties :

- Thyroid hormones binds to :
  Thyroid binding globulin (60 - 70 %), albumin (20%), transthyretin (10%).

Sick Euthyroid Syndrome /Low T_3 Syndrome :

- Seen in sick patients, systemic illness fasting.
- $T_4 \rightarrow rT_3$ d/t impaired conversion of $T_4 \rightarrow T_3$.

	Early stages	Advanced stages
T_3	↓↓	↓
T_4	Normal / ↑	↓
rT_3	↑↑	↑
TSH	Normal	↓

----- Active space -----

Investigations :

Hyperthyroxinemia work-up :

	↑↑ TSH (> 5mIU/L)	Normal TSH (0.5–5 mIU/L)	↓ TSH (< 0.5 mIU/L)
fT_3 & fT_4 ↓↓	1° Hypothyroidism (Autoimmune) : Hashimoto's thyroiditis.	Hypopituitarism (Inappropriately normal)	1. Symptomatic : Pituitary cause. 2. Asymptomatic : Last stage of sick euthyroid.
fT_3 & fT_4 Normal	Subclinical hypothyroidism	–	–
fT_3 & fT_4 ↑↑	• Toxic : TSH secreting pituitary adenoma. • Resistance to thyroid hormone (RTH) : – D/t unresponsive receptors. – Euthyroid presentation.	–	Thyrotoxicosis : 1. D/t overworking gland : Hyperthyroidism. 2. D/t ↑ stored hormone release : Thyroiditis (Subacute). 3. Drug induced : Amiodarone.

Euthyroid Hyperthyroxinemia :

- Asymptomatic.
- D/t ↑ TBG : Pregnancy, OCP, chronic active hepatitis, tamoxifen.
- Investigations :
  - fT_3 & fT_4 : Normal.
  - Total T_3, T_4 : ↑

Functions of Thyroid Hormone :

	Functions
CVS	↑ CO, ↑ BP (In hypothyroidism : ↑Peripheral resistance → ↑BP)
Bone	↑↑ Secretion → Osteoporosis
CNS	myelination of CNS.
RBCs	Stimulates erythropoiesis.
Protein	↑ Proteolysis → Osteopenia, hypercalcemia, stones formation, muscle wasting.
Carbohydrate	↑ Gluconeogenesis & ↑uptake of glucose.
Cholesterol	Cholesterol clearance (↓T3 → hypercholesterolemia)
Others	• ↑ Basal metabolic rate. • Thermiogenesis by uncouplers. • ↑ O_2 consumption except brain & gonads. • Beta carotene → Vit A. • ↑ Sensitivity to catecholamines (Indirect effect)

Hypothyroidism

00:52:31 ----- Active space -----

Types :

1. 1° : m/c.
2. 2° : Acquired hypopituitarism.
3. Congenital : Seen in pediatric population.
4. Consumptive : Due to hemangiomas.

PRIMARY HYPOTHYROIDISM :

Causes :

1. Autoimmune (m/c) : Hashimoto's, APS-1 < APS-2.
   - Hashimoto thyroiditis.
     - HLA DR3/DR4.
     - Pre-malignant → Marginal zone lymphoma > Papillary thyroid CA. (MALToma)
     - Thyroid auto antibodies (ab) : Thyroid peroxidase (TPO) ab (90-100%), thyroglobulin-ab (80-90%) & TSH receptor ab (20%).
2. Surgical removal.
3. Iodine deficiency.
4. IFN - α
5. Amiodarone.

Histology :

- Destruction of thyroid gland architecture.
- Oxyphil metaplasia.
- Follicular atrophy.
- Germinal centre formation.
- Lymphocytic infiltration.

Clinical Presentation :

- Females, 45-65 yrs.

↓metabolic processes	Accumulation of matrix GAGS (Traps water in interstitum)	Others
• Fatigue • Weight gain • Constipation • Dryness of mouth • Bradycardia • Cold intolerance • Hoarseness of voice	• Puffiness • Macroglossia • Non-pitting edema • Periorbital edema • Myxedema	• ↓Attention/Concentration • Hair loss • Menorrhagia • Infertility • Oligomenorrhea • Delayed DTR • Dry Skin

O/E : Thyroid swelling.

- Heterogenous, irregular, firm.
- Nodules absent.

----- Active space -----

Investigation :

- fT_3, fT_4 : ↓↓ / N, TSH ↑↑, Antibodies + → Hashimoto's thyroiditis.

Treatment :

- Levothyroxine 1.6–1.8 µg/kg/day.

Note :

False +ve hypothyroidism : Addison's disease.

Rx :

1. Cortisol management.
2. Thyroid correction.

Myxedema Coma :

Cause : Infection + untreated hypothyroidism.

Presentation : Impaired consciousness + seizures.

O/E : Profound bradycardia, hypothermia, hypoventilation, hypoglycemia, hyponatremia.

Investigations : ECHO → Pericardial effusion, ECG → Low voltage complexes.

Rx : IV Levothyroxine (Orphan drug), IV steriods.

Hyperthyroidism

01:02:42

Types :

Hyperthyroidism
- 1° → Diffuse enlargement : Graves disease (Autoimmune).
- 1° → Nodular enlargement : Toxic nodule, toxic MNG.
- 2° → TSH adenoma (Rare).

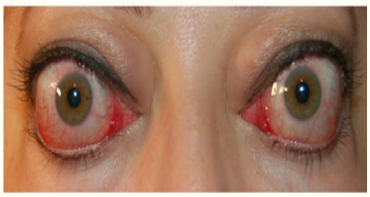
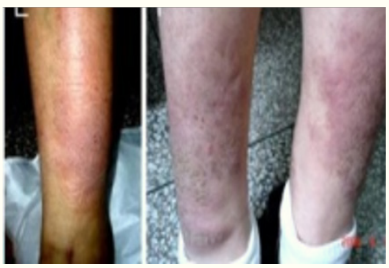
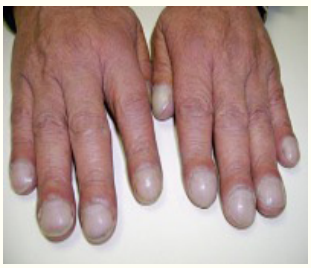
Graves Disease :

Clinical Presentation :

- Age : 20–40yrs.
- Sex : F > M.
- Associations : H/o Smoking, HAART (Highly active antiretroviral therapy).
- Apathetic thyrotoxicosis (elderly) : Asymptomatic, fatigue.

Pathogenesis	Manifestation
↑ fT_3 & fT_4	• Restless/anxiety/tremor. • Arrhythmia : Atrial fibrillation. • Hypokalemic periodic paralysis. • Proximal myopathy. • Diarrhoea. • ↓ Bone mineral density → fracture.

----- Active space -----

Pathogenesis	Manifestation
TSH receptor antibodies ↓ Stimulates fibroblasts ↓ GAGs activation	 Ophthalmopathy  Dermopathy  Acropachy

Antibodies : TSH receptor ab (80%) > TPO ab (50-80%) > Thyroglobulin ab (50-70%).

Investigation : Thyroid scintigraphy (I^{123} or Tc^{99}) : Diffuse ↑ uptake.

Treatment :

- 1st line : Thionamide (Carbimazole) 5mg TDS + Propranalol 40mg Q6H.
- Relapse (50%) : Radioiodine ablation —If C/I (Pregnancy, children)→ Surgery.

Subacute/de Quervains/Viral/Granulomatous thyroiditis :

C/F : Fever, sore throat, painful thyroid.

Investigations :

- ESR ↑.
- Scintigraphy : Low uptake.
- TSH, T4 :
  - Initial (Thyrotoxicosis) : TSH ↓, T_4 ↑.
  - Later (Hypothyroid) : TSH ↑, T_4 ↓.

Rx : Aspirin (DOC), NSAIDS, Steroids.

Postpartum/Painless/Silent Thyroiditis :

Autoimmune illness (+) : m/c a/w type 1 DM.

Investigations : ESR : Normal, Anti TPO ab (+).

Rx : Supportive, no role of steroids.

Chronic/Riedel's Thyroiditis :

- IgG_4 related disease.
- TFT : Normal.
- Dense, hard thyroid mass.

----- Active space -----

Diabetes Mellitus

01:13:00

CLASSIFICATION :

Types	Characteristics
1	• Autoimmune pancreatic destruction (Tcell + B cell mediated). • Fasting C peptide / C-peptide in response to glucagon : ↓↓ • Rx : Insulin.
2	• Insulin resistance, ↑ lipolysis. • Microvascular complications : Ophthalmopathy neuropathy, nephropathy. – Dependant on blood sugar control in initial 5 years. • Macrovascular : Cardiac complications (m/c). – Independent of blood sugar control.
1.5 KPD	• Ketosis prone diabetes. • Type 2 Dm, manifesting as type 1 DM.
1.5 LADA	• Latent autoimmune diabeles in adult. • Type 1 DM manifesting as type 2 DM. • Antibodies ⊕
3	• Brain diabetes/double diabetes/Alzheimer's disease : Insulin resistance in brain.
3c	• Pancreatic diabetes. • Cause : Tropical chronic calcific pancreatitis, hemochromatosis, IgG_4 related disease, cystic fibrosis.
3d	Drug induced diabetes : L-asparginase, growth hormone, tacrolimus.
4	• Elderly • Minimal symptoms & complications. • ↑ T – regulatory cells.
MODY	• Maturity onset diabetes of the young. • MODY – 3 (m/c) d/t HNF-1 α defect. • No symptoms, no complication, no resistance, good prognosis. • Slightly ↑ blood sugar.

MANAGEMENT OF TYPE 2 DM :

Evaluation :

1. Continuous blood sugar monitoring.
2. HbAlc
3. Urine routine.
4. Ophthalmic evaluation.
5. Nerve conduction study.
6. Treadmill test ⊕ → Angiography.

Insulin Therapy :

----- Active space -----

Indications :

- HbAIc ≥ 9.5 at presentation.
- Microvascular complication +.
- H/o macrovascular complication.
- Diabetic Ketoacidosis.
- T_1 DM / LADA.

Types :

Duration of action	Names
Ultra short	Lispro
Short	Regular
Intermediate	NPH
Long	Glargine
Ultra long	Degludec

Target HbAIc : 7%.

Regimen :

- Total insulin to be given : 40 units.
- 24U of regulin insulin (8U x 3 times/day) + 16 U glargine (daily)/ degludec (alternate days).

Note : Artificial pancreas → Best Rx.

OHA :

Metformin : 500 mg BD.

- MOA : ↑ AMP Kinase → ↑ glucose uptake & ↓ gluconeogenesis → Acts against insulin resistance.
- C/I : GFR < 240 ml/min → Risk of lactic acidosis.
- Advantages :
  - Good potency : ↓HbAIc by 1.5%.
  - No risk of hypoglycemia.
  - Weight loss.
  - No effect on CVS.
- Add-on to metformin : For comorbidity control, given in
  - Atherosclerotic vascular disease (CAD, LVH) : GLP-1 analogue /SGLT2 inhibitors.
  - Heart failure with reduced ejection fraction : SGLT2 inhibitors.
  - CKD : SGLT2 inhibitors.

SGLT2 inhibitor :

- Dapagliflozin 10mg (Or) Empagliflozin 25 mg.
- Advantages :
  - Promotes diuresis, natriuresis.
  - No tachycardia.
  - Inhibit RAAS.
  - Prevents proteinuria.
- Disadvantages : ↑ UTI risk, ↑ Ketosis.

----- Active space -----

GLP-1 Analogue > DPP4 Inhibitors :

Actions :

	GLP-1 analogue	DPP4 (-)
Drugs	Liraglutide (S/c) Semaglutide (Oral)	Gliptin
CVS	Cardiac neutral	Neutral
Weight	Loss	
Glucagon	↓	
Potency	1.25% ↓	0.75% ↓
Gastric emptying	Delay	No action

Standard prescription :

- First line : metformin 500 BD (max dose : 1g TDS).
- Add on : SGLT2 inhibitor (Dapagliflozin) 5mg OD + Liraglutide 0.6 - 1.8 mg S/c.

Sulfonylureas :

- High CVS mortality risk.
- Gliclazide can be tried.

CNS REVISION - 1

----- Active space -----

Types of headache :

Primary (90–95%)
- Benign; recurrent.
- No structural cause.
- Causes :
  1. Tension type headache.
  2. Migraine.
  3. Trigeminal autonomic cephalalgia (Cluster headache).
  4. Trigeminal neuralgia.

Secondary (5–10%)
- Infections (mainly).
- Brain tumors.

Note : Intracranial pain insensitive structures → Choroid plexus and ependyma.

Dangerous Headache

00:03:26

1. Age of onset >55 yrs : Could be d/t Giant cell arteritis (GCA) —leading to→ Blindness.
2. ↑sing severity over weeks.
3. Early morning headache (Disturbing sleep) : A/w vomiting f/b relief of headache.
4. Headache a/w blurring of vision.

(2, 3, 4) → D/t ↑ICT.

5. Pain ↑ on bending, lifting, or coughing : D/t meningeal irritation or ↑ICT.

All these patients must be examined for papilledema (↑ICT).

Approach to ↑ICT Headaches :

1st Headache
↓
MRI + MRA/MRV (Imaging of choice)

MRI findings ⊕

Space occupying lesions (m/c)
- Neurocysticercosis
- Tuberculoma
- Brain tumors
- Lesions compressing the stalk :
  1. Tumors
  2. Infiltrative lesions :
     - Sarcoidosis
     - Langerhan's cell histiocytosis (LCH)
     - Hemochromatosis
     - Lymphocytic hypophysitis (IgG_4; Post-partum).

MRI findings ⊖

MR Venogram —Normal MRV→ Benign intracranial hypertension

Findings ⊕ ↓

Cerebral venous thrombosis (2nd m/c)
- Inherited : Factor V Leiden mutation
- Acquired :
  - Post-partum
  - APLA.

----- Active space -----

Benign Intracranial Hypertension :

- Middle aged obese females.
- Slowly increasing ICT (Over 3–6 months).
- CN VI palsy may be seen (False localizing sign) → All other CNS findings normal.
- High CSF opening pressure.
- Rx : Repeated guarded LP ; Topiramate/Acetazolamide.

Tension Type Headache (TTH) 00:12:21

m/c 1° headache.

Patient profile :

- F >>> M : 30–50 yrs.
- Headache : Band of tightness/fullness.
- A/w depression in 1/3rd cases $\xrightarrow{\text{Hence}}$ most effective in prevention : TCAs (Amytriptiline).

Negative history :

- No ↑ICT signs.
- Does not affect activities of daily living.
- No vomiting, photophobia, phonophobia.

Migraine 00:14:09

2nd m/c 1° headache (Intracerebral vasoconstriction $\xrightarrow{\text{f/b}}$ Vasodilatation).

Patient profile :

- Females >> Males : Starts at teenage → Increases in intensity with age.
- Extreme periodic nature.
- Trigger : Sleep deprivation.

Types :

1. Classical (20%) : With visual aura.
2. Common (80%) : Not a/w aura.

Natural history :

1–2 days before episode : Low mood & irritability

Duration : 4–72 hrs — Episode :

Post-headache phase (1–2 days) : Lethargy

a. Aura :
- 15 mins – 1 hr before headache.
- Bright, zig-zag lines in peripheral vision (Fortification spectra).

b. Headache :
- Throbbing/pounding/pulsatile : Frontotemporal/temporal.
- U/L → B/L, as the disease progresses.
- A/w photophobia & phonophobia : Sits in a quiet, dark room.
- Vomiting +/–.

Note : Migraine must be ruled out before diagnosing sinus headache.

Pathology :

Initial intracerebral vasoconstriction → Vasodilatation.

----- Active space -----

Mx :

↑ Prevention

Prophylaxis :

- Mandatory if attacks are recurrent.
- Class I drugs (First line agents) : Propranolol, valproate, topiramate.

Treatment : Vasoconstrictors

- Mild to moderate : NSAIDs.
- Moderate to severe : 5-$HT_{1b/1d}$ agonists (Risatriptan, Eletriptan) → Use with caution if IHD+/elderly.
- Severe to very severe : 6 mg s/c Sumatriptan (Intranasal can also be used).

Trigeminal Autonomic Cephalalgia (TAC) 00:21:00

Types :

1. Cluster headache.
2. Paroxysmal hemicrania (PHC).
3. SUNCT (Short lasting Unilateral Neuralgic headache with Conjunctival injection & Tearing).
4. Hemicrania continua (HC).

General clinical features :

- Unilateral, very severe.
- Stabbing or boring.
- Short lasting/periodic.

⊕ Ipsilateral ANS symptoms →
- Conjunctival congestion.
- Eyelid edema.
- Nasal congestion.
- Rhinorrhea, lacrimation.

CLUSTER HEADACHE

Features :

- Young males with periodic headaches.
- 1-8 attacks/day (Each attack → 15 mins - 3 hrs).
- Alcohol is a trigger.
- Restless d/t pain.
- Headache : U/L, severe, stabbing/boring type in the peri-orbital region. Nocturnal headache ⊕.
- Migrainous features +/-.

Treatment :

1. 100% O_2 : 12-15 mL/min for 15-20 minutes (Best).
2. 6 mg s/c Sumatriptan OD.

Prophylaxis :

1. Short term : Steroids (Or verapamil).
2. Long term : Verapamil.

OTHER TAC

----- Active space -----

Paroxysmal hemicrania	SUNCT	Hemicrania continua
• Female = Male • Less severe attacks • Less periodicity • Nocturnal headache ⊖ • Alcohol is not a trigger • 1–20 attacks/day (2–30 min) • Responds to Indomethacin	• Male > Female • Cutaneous trigger • Extremely short lasting • No refractory period • Prevention : Lamotrigine	• Female > Male • Elderly • U/L continuous headache • ANS symptoms ⊕ • Responds to Indomethacin

Trigeminal Neuralgia

00:28:55

Clinical features :

- Middle aged to elderly.
- Episodic neuralgic pain along CN V_2 and V_3.
- Tic douloureux : Characteristic wincing with pain.
- No sensory signs.
- Pain follows a cutaneous trigger (Refractory period +).
- Etiology according to distribution :
  - U/L → Compression of superior cerebellar artery (m/c).
  - B/L → Demyelination (E.g. : MS).

Treatment :

- Medical : Carbamazepine (CBZ) > Lamotrigine (Check for HLA-B1502 before administering CBZ).
- If not responsive → Decompressive surgery.

CNS REVISION - 2

----- Active space -----

Lower Motor Neuron Lesions

00:00:30

LMN Component	Associated conditions/Affected by
Anterior horn cell (α and γ motor neurons in spinal cord gray matter)	• Degenerative motor neuron disease : Amyotrophic lateral sclerosis (Anterior horn cell + Corticospinal tract = UMN + LMN disease) • Pure LMN : Spinal muscular atrophy (SMA) • Central canal syndrome ⟶ Syringomyelia
Dorsal root ganglion	• Sjogren's syndrome : Asymmetrical truncal + U/L severe sensory ataxia • Paraneoplastic syndrome Anti – Hu antibody +ve • Cisplatin, Taxanes.
Spinal nerve root/Radicle	• Disc compression (i.e., IVDP) • B/L polyradiculoneuropathy (Eg : Guillain – Barré Syndrome)
Plexus	Plexopathies : D/t tumors
Nerve	• Mononeuropathy : Carpal tunnel syndrome (AL amyloidosis, Demyelinating) • Mononeuritis multiplex : Leprosy > Polyarteritis nodosa; Cryoglobulinemia • Polyneuropathy : a. Acquired : – Small fibre neuropathy (Spinothalamic tracts) : Diabetes – Large fibre neuropathy (Dorsal column) : B12/Vit. E/copper deficiencies b. Inherited : Charcot – Marie – Tooth disease
Neuromuscular junction	• Myasthenia gravis • Lambert – Eaton myasthenic syndrome (LEMS)
Muscle	• Intermittent weakness : Channelopathies; mitochondrial myopathies • Persistent weakness : c. Inherited : Dystrophies d. Acquired : Polymyositis/dermatomyositis, drugs/toxins, endocrine causes (Thyrotoxicosis, cushings)

Pure motor Pure sensory Sensory > Motor

Pure Motor Presentation

00:20:10

Muscle – Polymyositis/Dermatomyositis :

- B/L, lower limb predominant proximal muscle weakness : Persistent.
- No ANS/Sensory/Cerebellar symptoms (Pure motor).
- CNS IX, X LMN involvement.
- Diagnosis ⟶ Muscle biopsy.

----- Active space -----

Anterior Horn Cell :

- Degenerative UMN + LMN involvement.
- Asymmetrical wasting of muscles.
- Fasciculations + .
- Deep tendon reflexes +++.

Neuromuscular Junction :

- Fatigability.
- Diurnal variation.

Sensory > Motor Presentation : Asymmetrical 00:28:44

RADICULOPATHIES & PLEXOPATHIES

Symptoms of radiculopathies :

- Root pain : Brief, electric shock – like sensation, worsening with cough.
- Motor weakness : Along the distribution of the root (myotomal distribution).
- Loss of reflexes : Along the distribution of the root.

Radiculopathy Vs Plexopathy :

	Radiculopathy	Plexopathy
Presentation	Asymmetrical sensory/sensori-motor involvement	
m/c Etiology	Compression d/t IVDP (Unilateral)	Compression d/t tumor
Pain	Short, electric shock like	Dull aching, deep, long standing
Distribution	Dermatomal/Myotomal	Proximal + Distal weakness (Complete limb)
Sensory/motor	Sensory > Motor	Sensory + Motor (Complete limb)
Paraspinal NCS	Abnormal	Normal

NCS : Nerve conduction studies

Sensory > Motor Presentation : Symmetrical 00:37:16

NEUROPATHIES

Axonal Vs demyelinating :

		Axonal	Demyelinating
Cause		DM	GBS (B/L polyradiculoneuropathy)
Chronicity	Most commonly	Chronic	Acute
	Exceptions	• AIP • Hereditary coproporphyria } Acute • Variegate porphyria	CIDP → Chronic.
Sensory/motor		Sensory >> Motor	Sensory + Motor
Evolution		Distal → Proximal	Distal + Proximal together
Weakness		Nil	Prominent
Reflexes		Only ankle jerk lost	Reflexes lost
NCS		Amplitude maximally affected	Conduction velocity maximally affected

AIP : Acute intermittent porphyria ; CIDP : Chronic inflammatory demyelinating polyneuropathy.

Large fibre vs Small fibre :

----- Active space -----

	Large fibre neuropathy	Small fibre neuropathy
Positive symptoms	• Tingling • Cotton – wool/Sensations • Paraesthesia/Dysesthesia	Burning pain
Negative symptoms	• Sensory ataxia • Numbness	L/o pain/temperature/crude touch/pressure : • Non-healing ulcers • Charcot joints • Burns
Associated ANS Symptoms	Not seen	• Postural HTN • Tachy/Bradycardia • Nocturnal diarrhea • Gustatory sweating • Erectile dysfunction Seen in : • DM • Amyloid • Porphyrias
Nerve fibres	A α fibres Proprioception + Motor + Reflexes	A δ + C fibres Pain + Temperature + ANS
Course/Evolution	Acute, demyelinating	• Chronic, axonal (Distal → Proximal) • Sensory >>> Motor • Stocking and glove pattern
Causes	• GBS • B_{12}/E/Copper deficiency • Pyridoxine toxicity • Taxanes • Friedrich's Ataxia	• Acquired : DM > Leprosy> Amyloid > Vasculitis > Uremia, drugs, HIV. • Inherited : Fabry's and Tangier's disease.
	Combined small + Large fibre neuropathy : Vincristine and Carcinomatosis.	

Guillain-Barré Syndrome

00:53:29

M > F (mean age : 40).

Types :

1. Acute inflammatory demyelinating polyradiculopathy (AIDP) : m/c
2. Acute motor axonal neuropathy (AMAN) : Anti – GD1a
3. Acute motor sensory axonal neuropathy (AMSAN)

} Poor prognosis

4. Miller Fischer Syndrome (MFS) :
   - Triad of MFS → Ophthalmoplegia + Areflexia + Ataxia.
   - Anti GQ1b.
   - Demyelinating disease.

AIDP :

Pathophysiology :

- Acute demyelinating neuropathy : < 4 week duration.
- Inflammatory autoimmune condition → Triggered by infection (m/c : C.jejuni).
- Anti GM_1 antibody ⊕
- Fibres involved → Aα (Large fibres) and B (Preganglionic ANS fibres).

----- Active space -----

Clinical features :

- Ascending polyradiculoneuropathy LL → UL → Brainstem (B/L LMN CN III/ CN VII palsy).
- Initial phase (1 – 2 d)
  Rubbery legs + Tingling/paraesthesias/cotton-wool sensations.
  (± Transient bladder dysfunction)
  ↓
  Rapidly progressive proximal + distal lower limb weakness
  ↓
  B/L areflexic flaccid paraparesis.
- ANS Symptoms (Tachy/bradycardia, hypo/hypertension) may also be seen.
- Sensory symptoms/signs : Mild.

Investigations :

- NCS → Abnormal .
- CSF → ↑Protein+Albuminocytological dissociation.

Treatment :

- IVIG : 0.4g/kg x 5 days (Best).
- Plasma exchange therapy (PLEX).

Note : CIDP

1. Relapsing neuropathy > 8 wks.
2. Less precise onset.
3. Preceding event in only 30 % cases.
4. A/w HIV/myeloma/POEMS syndrome.

C/F :

- Motor > Sensory presentations.
- Proximal + distal lower limb predominant weakness .
- Prominent sensory symptoms & signs.
- ANS symtoms ⊖
- Cranial nerve involvement ⊖

Rx : Steroids, PLEX.

LMN Lesions : Cheat Sheet

01:03:49

C/F	most likely diagnosis
Pure motor	Polymyositis/Dermatomyositis
Acute motor	Hypokalemic periodic paralysis
Pure sensory	Ganglionopathy (Asymmetrical truncal/U/L ataxia)
Asymmetric sensory + motor	Brachial plexopathy Vs. Radiculopathy
Chronic neuropathy	DM/Leprosy/Uremia/Vasculitis
Acute neuropathy	GBS

CNS REVISION - 3

----- Active space -----

Myasthenia Gravis

00:00:15

Clinical Profile :

- 20-40 years.
- A/w : Type I DM, Addison's disease, vitiligo, pernicious anemia.
- Autoimmune.
- Females > males (males have more severe phenotype).

Cardinal Features and Progression :

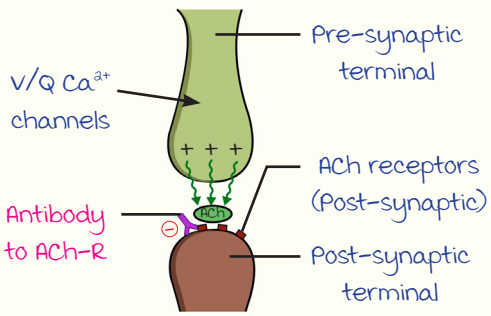
Ocular myasthenia (15-20%)
1. Fatigability
2. Diurnal variation (80-85%)
3. Ophthalmoplegia + Ptosis

Good prognosis

→ Pharyngeal muscle involvement → Proximal muscles of LL → Generalised myasthenia (80-85%)

Pathogenesis :

- Involves the post-synaptic junction of the NMJ.
- Anti-ACh-Receptor antibodies block action of ACh.



Pathophysiology at NMJ

Antibodies in MG

- Anti-ACh-Receptor (80%)
  - Alw :
    - Thymic hyperplasia (70%).
    - Thymoma (10%).
- ACh-R -ve (20%)
  - Anti-Musk Ab (50%)
    - Females w/o thymus involvement.
    - Absent in ocular myasthenia.
    - Tongue fasciculations.
    - Unresponsive to pyridostigmine.
  - Double negative → Anti-LRP-4 +ve

Clinical Features :

1. Ocular symptoms :
   - First symptom in 2/3rds of cases.
   - Asymmetric ptosis with B/L pupil sparing diplopia.
   - m/c muscle → medial rectus.
   - Differential : Chronic progressive external ophthalmoplegia (CPEO) → B/L symmetrical progressive ophthalmoplegia.

----- Active space -----

2. Limb symptoms : First symptom in 10% of cases.
3. Pharyngeal muscle involvement :
   - First symptom in the remainder of the cases.
   - Nasal twang.
   - Dysarthria/dysphonia.
   - Dysphagia.

Evaluation :

1. Ice-pack test.
2. Edrophonium test.
3. Neostigmine test.

} Improvement of symptoms

4. Repetitive Nerve Stimulation Test (RNST) :
   - Step 1 : Baseline compound muscle action potential (CMAP) → Normal.
   - Step 2 : Low frequency (3Hz) repetitive stimulation → Decremental response.
   - Step 3 : High frequency repetitive stimulation → Incremental response (Back to normal).
5. Single nerve fibre electromyography : Most sensitive test.
6. ACh-R antibody : Most specific test.

Lambert-Eaton Myasthenic Syndrome (LEMS) Vs Myasthenia Gravis :

- Paraneoplastic (A/w small cell carcinoma of lung) : Ab against V/Q Ca^{2+} channels.
- ANS Symptoms : +++
- Proximal lower limb weakness +++.
- Diplopia + Ptosis (Mild to absent).

RNST findings :

- Baseline CMAP ↓↓.
- Low frequency : Variable response.
- High frequency : ↑↑ incremental response (Supranormal).

Rx : 3,4-Diaminopyridine.

Treatment of Myasthenia Gravis :

- Initial Rx : Pyridostigmine 30-60mg/QID.
- Myasthenic crisis : I/V steroids + IVIG.
- Relapse prevention : Add on steroids and azathioprine.

Motor Neuron Disease

00:11:40

Types :

1. Pure UMN : Primary lateral sclerosis.
2. LMN + UMN : Amyotrophic lateral sclerosis (ALS).
3. Pure LMN : Spinal muscular atrophy.

AMYOTROPHIC LATERAL SCLEROSIS (ALS)

Pathophysiology :

- Age : >60 yrs (Uncommon <40 yrs).
- Degenerative disease.
- 90% sporadic, 10% Cu-Zn superoxide dismutase.

Structures affected :

- Anterior horn cells.
- Cranial nerve nuclei.
- Corticospinal fibres (upto AHC).
- Corticobulbar fibres (upto cranial nerve nuclei).

Clinical Features :

- Asymmetric U/L involvement, later $\xrightarrow{\text{progresses}}$ L/L.
  Wasting & atrophy → Fasciculations & cramps → Exaggerated DTRs.
- Distal > Proximal involvement (Both seen).
- Weakness; Loss of dexterity (Last symptom).

Functions preserved :

Higher mental functions ; Sensory system ; ANS ; Cerebellar functions.

BULBAR VS. PSEUDOBULBAR PALSY

Either bulbar/pseudobulbar palsy is seen in motor neuron disease.

Bulbar palsy (40%)	Pseudobulbar palsy (25%)
LMN involvement of CN nuclei in brainstem (CN IX, X, XI, XII) : • Nasal twang • Nasal regurgitation/aspiration • Flaccid tongue • Flaccid dysarthria (Bulbar dysarthria)	UMN involvement (Corticobulbar fibres) : • Gag reflex +++; Jaw jerk +++. • Dysphonia • Small & spastic tongue • Spastic dysarthria (Pseudobulbar dysarthria) • Emotional incontinence (Inappropriate, unregulated emotions)

Spinal Cord

00:18:40

Clinical Anatomy :

- 45cm long → Extends up to L_1-L_2.
- 31 segments (8 cervical + 12 thoracic + 5 lumbar + 5 sacral + 1 coccyx).

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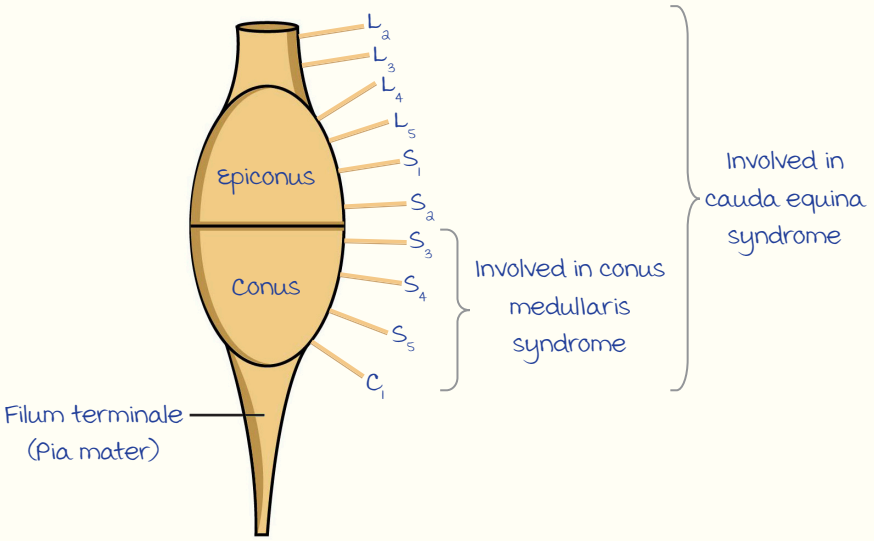
Conus & Epiconus :

Terminal portion of spinal cord.



Localisation of spinal cord segments :

Spinal segment	Vertebral level
Lower cervical	+1
Upper thoracic (T_1–T_6)	+2
T_7–T_9	+3
T_{10}	L_1–L_2
T_{11}	L_3–L_4
T_{12}	L_5

Note : Arrangement of fibres in the spinal cord medial to lateral.

- All tracts : Cervical → Thoracic → Lumbar → Sacral.
- Posterior column alone : Sacral → Lumbar → Thoracic → Cervical.

COMPRESSIVE MYELOPATHY

Stages of extramedullary compression :

Stage I : Root compression → Radiculopathy-like features.

Stage II : Hemisection of the cord → Brown-Sequard syndrome

- I/L pyramidal tract
- I/L posterior column
- C/L spinothalamic tract

Stage III : Complete involvement.

	Intramedullary	Extramedullary
Causes	• Ependymoma • Syringomyelia	Intradural : Neurofibromatosis; Meningioma Extradural (m/c) : Vertebral causes (Fracture, mets, TB), rarely aneurysm
Pain	Funicular, dull aching	Root pain (Tightness/band like in posterior compression)
Sensory symptoms	Dissociated sensory loss : • Spinothalamic tract ⊕ • Posterior column spared	m/c : Posterior column involved (Radiculopathy → Brown-Sequard → Complete)
Bowel & bladder	Involved	Spared
Motor	Minimal symptoms (Sacral sparing)	Predominant (LL > UL)
LMN features (AHC involvement)	⊕	⊖

Note : Glove and stocking neuropathy.

U/L sensory involvement + L/L motor involvement (In extramedullary pathologies).

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Cauda equina vs Conus medullaris :

	Conus medullaris	Cauda equina
Roots involved	S_3-C_1	L_2-C_1
Extent/symmetry	B/L symmetrical involvement	Asymmetrical involvement (Root pain)
Motor symptoms	⊖	Variable (Depends on roots involved)
Reflexes	Anal/bulbocavernosus reflexes lost	Variable loss of reflexes
Bladder	LMN bladder	No bladder involvement
Anaesthesia	Saddle anaesthesia	Variable patterns of anaesthesia

NON COMPRESSIVE MYELOPATHY

Causes : VITAMIN

Vascular : Anterior spinal A. infarction.

Inherited : Friedreich's ataxia.

Toxins : Arsenic.

Autoimmune : Sarcoidosis.

Metabolic : B_{12}/Vit E/Cu^{2+} deficiencies.

Infectious : TB, HIV.

Neoplasia.

Acute Transverse Myelitis (ATM) :

Bilateral lower limb areflexic atonic paraparesis (Similar to GBS).

Rx : Steroids.

ATM vs GBS :

1. Infectious trigger : Clear history (Compared to GBS).
2. Clear level of symptoms :
   - Band like sensation perceived.
   - Hyperaesthesia at the level; UMN findings below the level. (Power/Sensations ⊖ ; Reflexes ++).
3. Bowel/bladder symptoms +++ (Not seen in GBS).

Vitamin B_{12}/E/copper deficiency :

Posterolateral cord + Nerve ± Cerebrum (Rare) involvement.

Clinical features & progression :

Posterior column → Lateral spinothalamic tract → Corticospinal tract

↓

Large fibre neuropathy (Last) ← Reflexes lost later in the disease

- Ankle and knee jerk absent.
- Extensor plantar reflex ⊕ (D/t spinal cord involvement).

----- Active space -----

CNS REVISION - 4

DEMENTIA

Major cognitive impairment → Affects basic/instrumental activities of daily living.

Diagnostic Criteria :

≥1 of the following 6 impaired :

1. Memory : Medial temporal lobe/ hippocampus.
2. Language :
   - Broca's (Inferior frontal).
   - Wernicke's (Superior temporal).
3. Executive function : Dorsolateral prefrontal cortex.
4. Social cognition : Orbital prefrontal cortex.
5. Perceptual motor : Praxicon : Superior parietal lobule.
6. Complex attention : Orbital prefrontal cortex.

Prefrontal Cortex (PFC) :

- Medial → Energisation and motivation : Disorder → Apathy
- Orbital → Associated with :
  - J : Judgement
  - I : Insight
  - P : Personality, Problem solving
  - F : Fluency
  - A : Abstract thinking, Attention
- Dorsolateral → Executive function

Causes :

1. Alzheimer's dementia (m/c).
2. Diffuse Lewy body (DLB) dementia (2nd m/c) : Part of Parkinson's plus syndrome.
3. Vascular dementia (3rd m/c).
4. Frontotemporal dementia.
5. Normal pressure hydrocephalus (NPH).
6. Prion disease.

Note :

10% causes, reversible : Drugs, Vit B_{12} ↓, chronic meningitis, autoimmune, normal pressure hydrocephalus.

Rapidly progressive dementia causes :

- Frontotemporal dementia.
- Prion disease.
- DLB dementia.
- HIV.
- Whipple's disease.

Young onset dementia causes :

- Frontotemporal dementia.
- Prion disease.
- DLB dementia.
- Autoimmune conditions.
- Chronic meningitis.

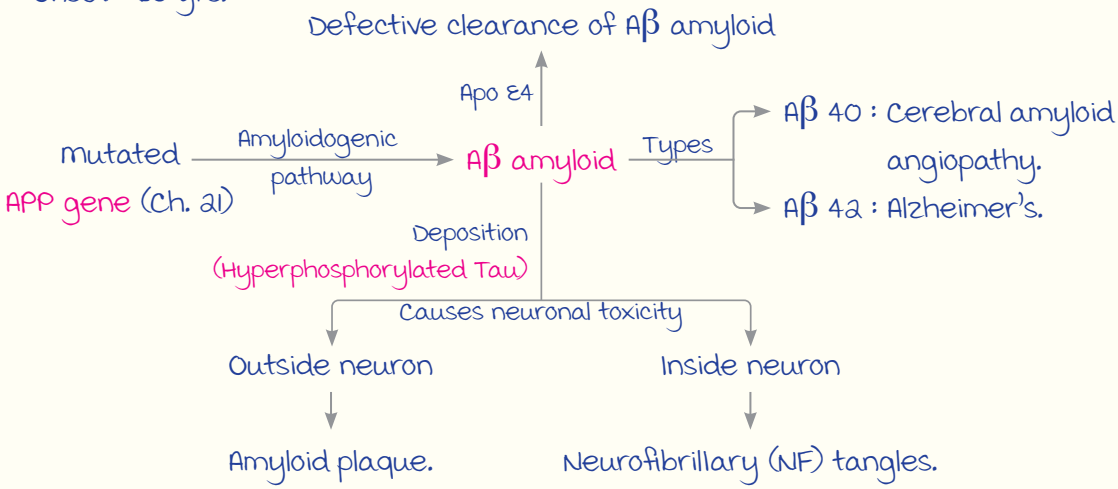
Alzheimer's Dementia (AD) & Frontotemporal Dementia (FTD) 00:08:23 ----- Active space -----

AD is a Tauopathy.

Etiopathology :

1. Sporadic disease :

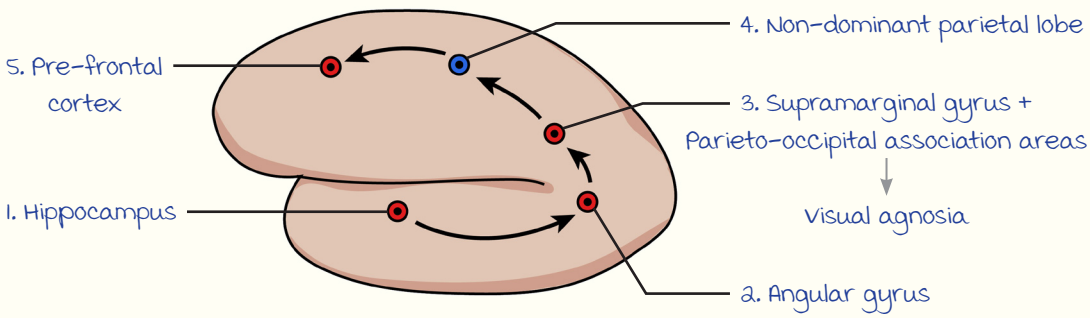
Onset >60 yrs.



2. Hereditary disease :
   - Onset <45 yrs (Rare).
   - Presenilin 1 (Chr. 14) and Presenilin 2 (Chr. 1).

Note : No proven risk factors exist for Alzheimer's.

Disease Progression :



Stages :

Stage of	Area affected	Clinical features
Amnesia	Hippocampus	Episodic memory loss
Anomia	Angular gyrus	Gerstmann syndrome : • Acalculia • Finger anomia • Rt. to Lt. disorientation • Alexia with agraphia
Visuo spatial disorientation	Non-dominant parietal lobe	Visuo spatial disorientation
Executive dysfunction	Pre-frontal cortex	Executive dysfunction

----- Active space -----

Note :

- Non-dominant parietal lobe dysfunction also leads to constructional apraxia, dressing apraxia & hemispatial neglect → But, these are not seen with Alzheimer's.
- Alexia without agraphia → Involvement of splenium of corpus callosum.

Treatment :

Cholinesterase inhibitors : Rivastigmine, donepezil & tacrine.

NMDA antagonist : Memantine.

Frontotemporal Dementia (FTD) vs Alzheimer's :

FTD is also a tauopathy.

	Frontotemporal dementia	Alzheimer's disease
Pathogenesis	Loss of function of Tau	Deposition of hyperphosphorylated Tau
Genetic basis	MAPT (Chr. 17)	APP (Chr. 21) & Apo E4; (Elderly) Presenilin 1 & 2 (Chr. 1 & 14) (Young)
Age of onset	Young onset m/c	Elderly onset (>60 yrs)
Genetic predisposition	30% genetic	5% genetic
Progression	Rapidly progressive	Slow progression
PFC involvement	Prefrontal cortex first	Prefrontal cortex involved at end stage

Diffuse Lewy Body Dementia (DLB)

00:19:49

Pathology : α-synuclein —Deposition→ Lewy bodies in the neuronal cytoplasm.

α-synucleinopathies : Parkinson's, DLB dementia and multisystem atrophy

Clinical Features :

- Years before disease onset :
  REM sleep disorders +
  ANS dysfunction (Orthostatic hypotension, erectile dysfunction).
- Dementia predominates over rigidity and tremors
  (DLB is a Parkinson's plus disease).
- Visual hallucinations.
- Fluctuating alertness/consciousness.
- Antipsychotics worsen illness.
- No response to L-DOPA.

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Cortical vs Subcortical Dementia :

	Cortical dementia	Subcortical dementia
Examples	Alzheimer's, FTD	DLB dementia, NPH, Progressive supranuclear palsy.
Severity	Severe	Less severe
Apraxia/Agnosia/Aphasia	⊕	⊖
Extrapyramidal symptoms	⊖	+++
Corticobulbar involvement	⊖	++
Emotional incontinence	Less	more

Prion Disease

00:27:00

General characteristics :

- Long incubation period.
- No immunity/inflammation.
- β-pleated sheet of prion → PrPsc protein involved.
- Young onset dementia.
- Rapidly progressive.

Creutzfeldt-Jakob Disease :

- Dementia + Myoclonus.
- Cortex → Ribboning/spongiform changes.
- EEG : High voltage sharp waves with a low slow background.

Vascular Dementia

00:28:34

Types :

1. Post-stroke vascular dementia (Multi-infarct state) → Stepwise decline in cognition.
2. Small vessel stroke (Lacunar stroke) : AKA Binswanger's disease.
   - Pathogenesis : HTN → Lipohyalinosis → Sub-cortical areas involvement (White matter disease).
   - No step-wise decline of function.
   - C/F : Emotional instability + Corticobulbar symptoms + Gait issues + Urinary incontinence.

Normal Pressure Hydrocephalus (NPH)

00:31:20

Pathogenesis : D/t defective CSF absorption → Ventriculomegaly.

C/F : GUD (In order of occurrence).

- Gait disturbance : Apraxia ("Ignition foot" → Unable to start walking).
- Urinary incontinence.
- Dementia : Subcortical.

----- Active space -----

Movement Disorders

00:34:28

Types → Hyperkinetic : Chorea, athetosis, hemiballismus, dystonia.
Hypokinetic : Parkinson's and Atypical Parkinson's syndromes.

HYPOKINETIC MOVEMENT DISORDERS

Hypokinesia → Slowness/paucity of movement with no evidence of weakness/spasticity.

Parkinson's Disease :

- >60 yrs (Usually).
- Young onset Parkinson's :
  - PARK 1 (Autosomal Dominant) on Chr. 4.
  - PARK 2 (Autosomal Recessive) on Chr. 6.

Clinical picture : Tremor predominant (80%) vs Akinetic rigid (20%, poor prognosis).

- Cardinal features :
  a. Tremor.
  b. Akinesia.
  c. Rigidity.
  d. Postural instability (5–10 yrs after disease onset).
- Tremor characteristics :
  a. Asymmetric distal : Pill rolling tremor.
  b. 4–6 Hz.
  c. Micrographia.
  d. ↑ses on concentration.
- Gait :
  a. Flexion hypertonia (Stooped posture).
  b. Short steps/festinating gait.
  c. Reduced arm-swing.
- Other features :
  a. Glabellar tap sign ⊕.
  b. Lead pipe/cog-wheel rigidity.
  c. Hypomimia & hypophonia.

Atypical Parkinsonism :

Conditions included :

1. DLB dementia.
2. MSA.

} α-Synucleinopathies

3. Progressive Supranuclear Palsy (PSP).
4. Corticobasal Degeneration.

} Tauopathies

Symptoms : (In contrast to Parkinson's)

1. Rapid progression.
2. No response to L-DOPA.
3. Absence of tremors.

} Common

4. Visual hallucinations (DLB).
5. Dementia : <1 yr of disease onset (DLB).

----- Active space -----

6. ANS + REM behavioral disorders (DLB & MSA).
7. B/L symmetrical axial rigidity (MSA & PSP).
8. Early postural instability → Falls (PSP).
9. Gaze palsy (PSP).
10. Myoclonus (Corticobasal degeneration).

Multisystem Atrophy (MSA) :

Types of MSA →
1. MSA-P : Parkinson type.
2. MSA-A : Shydrager syndrome (ANS +++).
3. MSA-C : Cerebellar features.

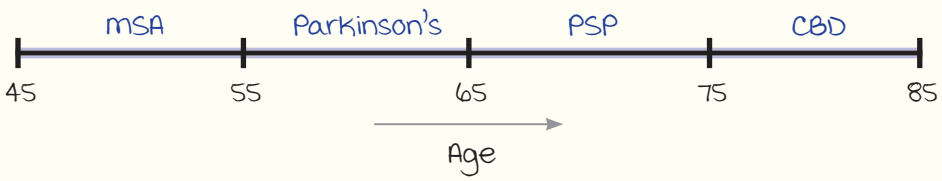
MSA Vs. PSP :

	MSA	PSP
Pathogenesis	α-synucleinopathy	Tauopathy
Clinical features	• Predominant ANS symptoms. • REM sleep disorders. • B/L symmetrical akinetic rigidity (Axial). • Cranio cervical dystonia. • Stridor ⊕.	• B/L symmetrical akinetic rigidity (Classical). • Extensor hypertonia. • Wide based gait. } Frequent falls • Postural instability. } • Supranuclear gaze palsy (Downgaze). • Procerus sign : Wrinkling/furrowing of forehead. • Applause sign : Continuous clapping.
MRI	Hot cross bun sign	Hummingbird sign; Morning glory sign

Corticobasal degeneration : Tauopathy, disease of elderly.

- Asymmetrical involvement.
- Triad : Myoclonus + Cortical dementia + Apraxia (D/t superior parietal lobule involvement).
- Hemiballismus and Parkinson's-like features (D/t basal ganglia involvement).
- Alien limb phenomenon : Disuse of limb d/t motor symptoms.

Agewise Distribution of Movement Disorders :



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CNS REVISION - 5

Upper Motor Neurons :

Descending motor pathways.

Components :

1. Corticospinal tract
2. Extrapyramidal tracts

} Cortex → Anterior horn cell (AHC).

3. Corticobulbar tracts : Cortex → Cranial nerve nuclei (Brainstem).

Hence, UMN lesions include lesions of the cortex, subcortex, and the brainstem.

Note : Brainstem lesions → Crossed hemiplegia : I/L LMN cranial nerve palsy + C/L UMN hemiplegia.

Approach to Cortical and Subcortical Lesions

00:04:50

CORTEX

Origin of cortical motor fibres →
- Motor cortex (Area 4) : 30%
- Premotor cortex : 30%

} Frontal lobe.

- Sensory cortex (Areas 3, 1, 2 parietal lobe) : 40%.

- Frontal and parietal lobe lesions → C/L hemiplegia seen.
- Temporal lobe (Supplied by M_2 inferior division) lesions → Wernicke's aphasia.
- Occipital lobe (Supplied by posterior cerebral A.) lesions → Incongruent C/L homonymous hemianopia with macular sparing.

Blood Vessel Involvement :

- M_1 Artery (Sylvian fissure)
- Superior division of M_2
- Anterior cerebral artery (ACA)

} Produce maximum motor weakness.

Features of ACA occlusion :

- LL >> UL weakness.
- Gait issues.
- Bowel/bladder involvement.
- B/L occlusion (Rare) : Severe apathy, akinetic rigidity, abulia.

Cortical Lobe Lesions :

1. Frontal lobe :
   a. Pre-frontal cortex (Orbital, medial, and dorsal PFC) involvement.
   b. Frontal eye field → Helps in looking at the opposite side (Pts. look towards the side of the lesion).
   c. Broca's area.
   d. Motor & pre-motor cortex involvement.
   e. Affected in ACA involvement.

2. Parietal lobe :

----- Active space -----

Dominant	Non – Dominant
CLAP : Calculation, Language, Apraxia, Proprioception. • Angular gyrus : a. Acalculia, anomia b. Left to right disorientation } Gerstmann Syndrome. c. Alexia with agraphia • Superior parietal lobule : Apraxia. • Supramarginal gyrus + Association areas : Visual agnosia.	• Visuospatial disorientation. • Constructional apraxia. • Dressing apraxia. • Hemispatial neglect (Severe → Anosognosia).

Note : Inferior quadrantanopia ⊕ in parietal lobe lesions.

3. Temporal Lobe :

Medial	Lateral	Limbic cortex
• Responsible for memory (Hippocampus) • Epileptogenic area	• Auditory cortex • Auditory association areas → Auditory agnosia • Wernicke's area	Lesion : Kluver-Bucy Syndrome

Note : Superior quadrantanopia ⊕ in temporal lobe lesions.

Aphasias :

Indicates dominant hemisphere involvement.

Fluency

Present Absent

	Sensory aphasia				Motor aphasia			
Comprehension	Preserved		Lost		Preserved		Lost	
Repitition	Preserved	Lost	Preserved	Lost	Preserved	Lost	Preserved	Lost
Type of aphasia	Nominal aphasia	Conduction aphasia	Transcortical sensory aphasia	Wernicke aphasia	Transcortical motor aphasia	Broca's aphasia	Isolation aphasia (Echolalia)	Global aphasia

Note : Naming is affected in all aphasias.

SUBCORTEX

White matter (Internal capsule & corona radiata) with islands of gray matter (Basal ganglia nuclei).

Internal Capsule (IC) :

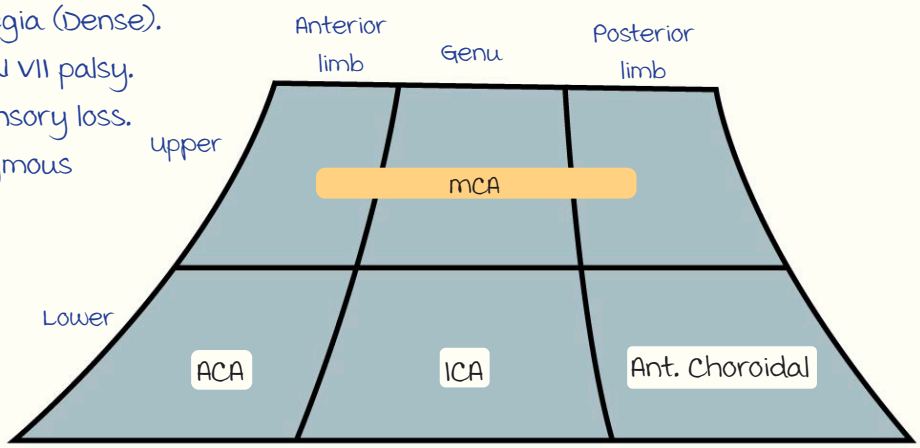
- Corticospinal tract passes through posterior limb (Anterior 2/3rd).
- Closely a/w corticobulbar fibers.
- Dense fibers.

----- Active space -----

C/F of IC lesions :

- C/L hemiplegia (Dense).
- C/L UMN CN VII palsy.
- +/- hemisensory loss.
- +/- homonymous hemianopia.

Blood supply of IC :



Approach to Brainstem Lesions : Crossed Hemiplegia

00:20:30

Midbrain Syndromes :

m/c vessel involved : P2 segment of Posterior Cerebral Artery (PCA)

1. Ventral midbrain syndromes :

	Weber	Claude	Benedict
Site	Base of midbrain	Tegmentum	Extensive (Weber + Claude)
C/f	• I/L LMN CN III palsy • C/L UMN hemiplegia	• I/L LMN CN III palsy • C/L ataxia/tremor (D/t Dentato-rubro-thalamo-cortical fibers)	• C/f of Weber + Claude • C/L hemiballismus

2. Dorsal midbrain syndromes :

Cause : Pinealoma.

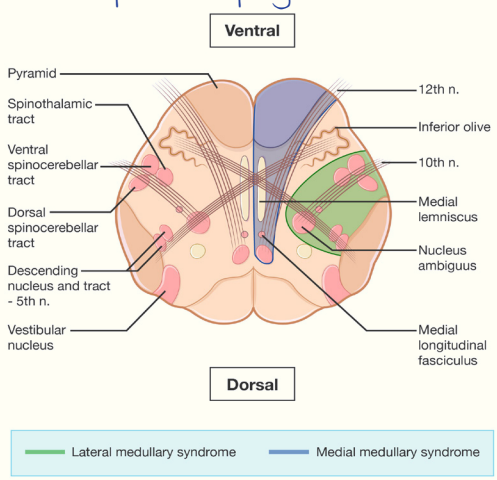
Parinaud Syndrome	Nothnagel Syndrome
• Lesion : Tectum. • C/F : – Vertical upgaze palsy (Sunsetting sign). – Overactive LPS → Lid retraction (Collier's sign). – Accommodation reflex present + Pupillary reflex absent (Pretectal nucleus involvement). – Convergence retraction nystagmus. – Skew deviation of eyes.	• Lesion : Ventral/anterior to Parinaud. • C/f : – I/L LMN CN III palsy. – Gaze palsy. – C/L ataxia (d/t Superior cerebellar peduncle inv).

Pontine Syndromes :

----- Active space -----

Ventral pontine syndrome	Dorsal pontine syndrome	Lateral pontine syndrome
AKA : Millard Gubler Syndrome	AKA : Foville Syndrome	AKA : Marie Fox Syndrome
F : I/L Facial palsy S : I/L Sixth nerve palsy H : C/L Hemiplegia	F : I/L Facial palsy G : Gaze palsy H : C/L Hemiplegia	A : I/L Ataxia S : C/L Spinothalamic involvement (L/o pain & temperature) H : C/L Hemiplegia

Medullary Syndromes :

Lateral medullary syndrome	Medial medullary syndrome
• Vessel : Vertebral A. (V_4) > PICA. • Cranial nerves : – CN V : Spinal nucleus (I/L facial sensations). – CN VII : Nucleus tractus solitarius (Taste, anterior 2/3rd). – CN VIII : Vestibulocerebellar fibers (Ataxia, vertigo). – CN IX/X : Nucleus ambiguus (Dysarthria, dysphagia). – CN X : Dorsal nucleus of vagus (ANS feature). – CN XIII : AKA Horner's Syndrome. • Motor : No motor weakness. • Sensory : Spinothalamic tract (Loss of C/L pain & temp). • Cerebellar : Spinocerebellar fibres (I/L ataxia).	• Motor nucleus of CN XII (I/L LMN CN XII palsy). • Motor fibers of pyramidal tract (C/L Hemiplegia). • Medial lemniscus (C/L posterior column findings). • Medial longitudinal fasciculus (Internuclear ophthalmoplegia). 

Stroke

00:34:50

Brain perfusion :

- Normal : > 22 mL/100gm/min.
- Penumbra : 10–22 mL/100gm/min.
- Infarct : < 10mL/100 gm/min.

Transient ischemic attack (TIA) :

- Neurologic symptoms $\xrightarrow{\text{Return to normal}}$ < 24hrs (usually < 1hr).
- Rx : Dual antiplatelets x 21 days.

----- Active space -----

MANAGEMENT OF STROKE

Suspected case → ABCD2 score (Assess risk of stroke) → Admit

↓

CT Brain Plain (Rule out bleed) + CT Angio (Localise large vessel occlusion)

↓

MR Angio (Site of lesion)

↓

Thrombectomy possible at institute?

- Yes → Thrombectomy :
  - Only if M_1/PCA involved.
  - Can be done < 24hrs post stroke onset.
- No ↓

Thrombolysis : Alteplase 0.9mg/kg (10% bolus, rest infusion)

Ideal candidate :
- > 18 yrs.
- < 4.5 hrs from onset of disease.
- No bleed.
- Edema < $1/3^{rd}$ of brain territory.

Contraindications :
- Bleeding episode.
- Intracranial Hemorrhage.
- Surgery in the last 14 days.
- GI bleed in the last 21 days.
- BP > 185/110 mmHg despite Rx.

Ideal Imaging Protocol :

Diffusion weighted MRI (DWI) + CT brain :

- DWI : Ischemia detected early (30min – 6 hrs) → Hyperintense → Perform ADC (Apparent diffusion coefficient).
  Hyperintense DWI + hypointense ADC : Stroke.
- CT Brain : Best to rule out bleed.

DWI Flair :
- Shows hyperintensity > 6hrs (DWI : 30min–6 hrs).
- Time of stroke can be inferred. (Useful in early morning stroke).

Perfusion MRI : Defines the penumbra (Differentiates ischemic & infarcted area).

MR Angio : Done before thrombolysis/thrombectomy to detect site of occlusion.

Medical Management :

1. Aspirin :
   - Given within 48hrs → Continued lifelong.
   - Low dose : 75mg.
2. Anticoagulants :
   - Only indicated in cardioembolic stroke.
   - Valvular heart disease, A-fib, mechanical valve → Warfarin.
   - Rest : Dabigatran.
3. Antihypertensives : Only if BP >220/110 mmHg.

Carotid Endarterectomy : Indicated if carotid atherosclerosis >70% (OR 50–70% with symptoms).

Note : Role of statins is debatable.

NEPHROLOGY REVISION - 1

----- Active space -----

Renal anatomy :

3 compartments

- Tubulointerstitial (85%).
- Glomerular (10%).
- Vascular (5%).

Syndromes in nephrology :

- CKD.
- Renovascular hypertension.
- Hematuria related diseases.
- Nephritic syndrome.

Chronic Kidney Disease

00:01:46

Definition :

Mnemonic : IF TA GS.

- Interstitial Fibrosis.
- Tubular Atrophy.
- Glomerular Sclerosis.

Pathophysiology :

- GFR = Single nephron GFR (snGFR) x No. of functional nephrons.

CKD : ↓ no. of functional nephrons → Compensatory ↑ in snGFR → Hyperfiltration injury → Intraglomerular hypertension → Alters capillary pore diameter → Proteinuria → Interstitial inflammation (Protein : Tubulotoxic) → Interstitial fibrosis (D/t TGF-β). / Tubular atrophy. / Glomerular sclerosis.

Assessment of GFR :

1. eGFR calculation :

- Factors :
  - Age.
  - Race.
  - Sex.
  - S. Creatinine.

- Staging :

Stage	G1	G2	G3	G4	G5
GFR (mL/min)	≥90	60–89	30–59	15–29	<15

  - G1 : Normal GFR + histological/biochemical/radiological evidence of kidney disease.
  - G5 : End stage renal disease (ESRD).

----- Active space -----

2. USG :

- Kidney size → <8 cm.
  → 8–10 cm + loss in CMD.
- CKD with normal/↑ Kidney size :
  - Diabetes.
  - HIV.
  - Amyloidosis.

PRESENTATION

Diabetic Nephropathy :

Presence of CKD with :

- Hypertension.
- Extravascular edema (Progressive).
- Nephrotic range proteinuria: (>3.5g/day).
- H/o diabetes for 5–10 years.
- Frothy urine (Long standing).
- Diabetic retinopathy :
  - 100% T_1DM.
  - 65% T_2DM.

  } Develop retinopathy by the time of developing nephropathy.

Note :

1. Pancreatic diabetes (3c) : Renal impairment present at diagnosis of DM.
2. Nephrotic syndrome : Proteinuria + edema + hypoalbuminemia + hypercholesterolemia.

Chronic Glomerulonephritis (CGN) :

End stage complication of glomerular disease (m/c d/t IgA nephropathy).

Presentation :

- Edema.
- Uremia (Vomiting).
- Proteinuria.
- Frothy urine.
- Hypertension.
- Fatigue.

Ischemic/Vascular Nephropathy :

CKD as a complication of renal artery stenosis.

History of : Hypertension + smoking, CAD, PVD.

Investigation : Proteinuria (Trace to 1+), no RBCs in urine.

Chronic Tubulo-Interstitial Disease (CTID) :

- Slow, B/L fibrosis.
- Cause is mostly unknown → AKA CKD-U (CKD of unknown cause).

Known causes :

- Drugs : Lithium, calcineurin inhibitors, PPI.
- Autoimmune diseases : IgG4, sarcoidosis, Sjögren's syndrome.
- Inherited diseases : ADPKD, Medullary Cystic Disease of Kidney (MCDK).
- Reflux nephropathy.
- Obstruction.
- Metabolic disorders : ↑ Ca^{2+}, ↓ K^+, hyperuricemia, hyperoxaluria.

Features :

----- Active space -----

- Slow onset.
- Mostly asymptomatic.
- ± Polyuria & nocturia d/t poor concentrating capacity (Similar to peripheral diabetes insipidus).
- ↓ Erythropoietin synthesis → Disproportionate anemia → Fatigue.
- Metabolic acidosis : Renal tubular acidosis type IV → Disproportionate ↑ K^+.
- Proteinuria ⊖ (Bland).
- No edema.

Renovascular Hypertension

00:30:18

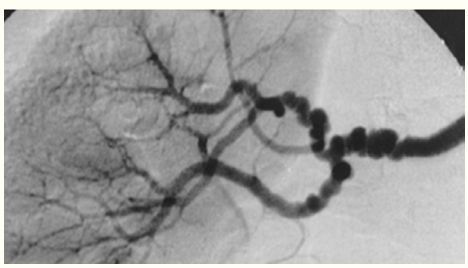
Vascular Kidney disease :

- Large vessel related :
  - Renal artery stenosis.
- Small vessel related :
  - AKA Thrombotic microangiopathy (TMA).
  - Eg : HUS → Presents as
    - Thrombocytopenia.
    - Microangiopathic hemolytic anemia (MAHA).
    - Renal failure.

Renal Artery Stenosis :

Causes :

- Atherosclerosis (m/c overall).
- Fibromuscular dysplasia (FMD) (m/c in young worldwide).
- Takayasu arteritis (F : M ratio → 9 : 1) (m/c in young in India).
- Polyarteritis nodosa (m/c in young male).



String of beads appearance in FMD

Presentation :

- Significant hypertension (Emergency presentation) + complications (Panic attacks, dyspnea, PRES).
- Significant vascular disease with comorbidities.
- No edema/significant proteinuria.

Investigations :

- CT renal angiography/MR angiography (Definitive).
- USG : Normal sized kidney.

Treatment : Angioplasty & stenting.

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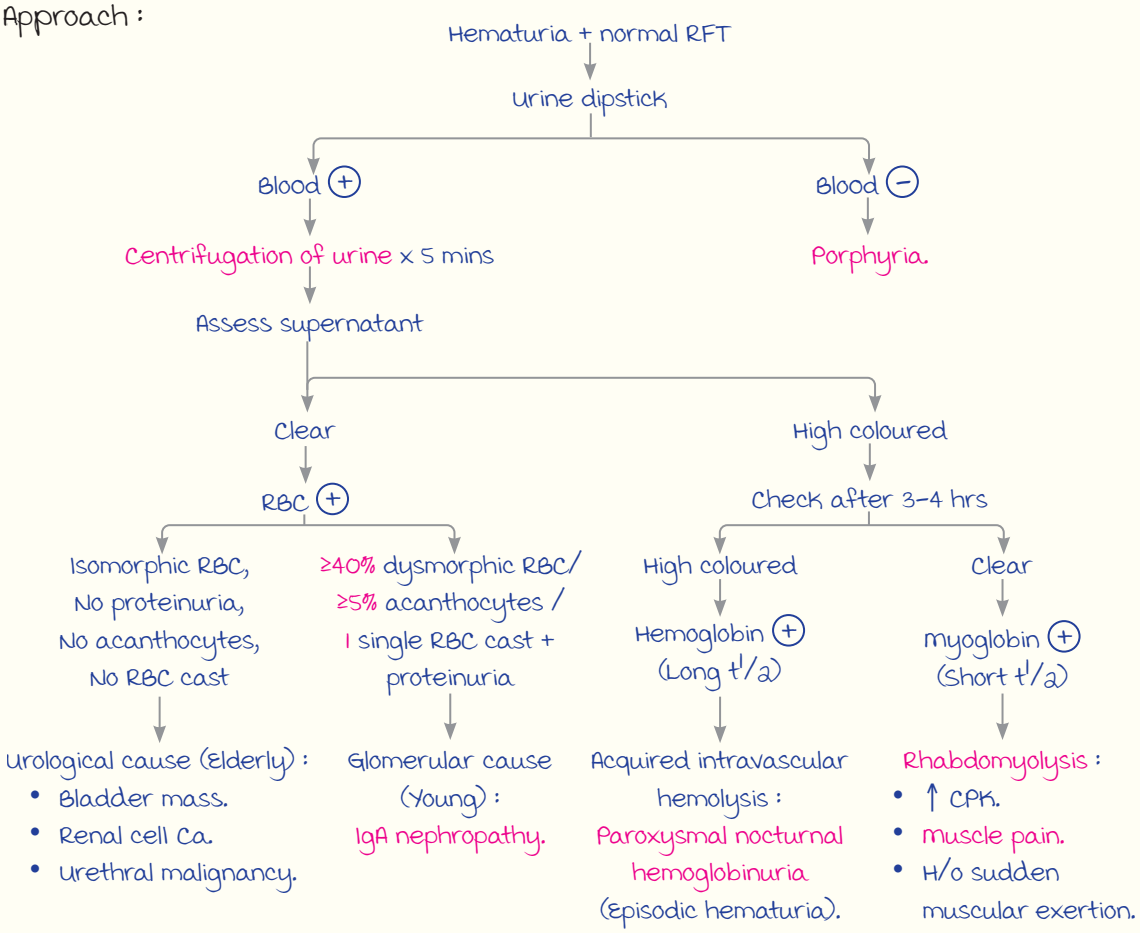
Hematuria Related Diseases

00:40:25

Hematuria → Urological cause (90%).
→ Nephrological cause (9%).
→ Hematological cause (1%).

Approach :



Nephritic Syndrome

00:48:51

AKA acute glomerulonephritis/nephritis.

	Post Streptococcal Glomerulonephritis (PSGN)	Infection Related Glomerulonephritis (IRGN)/Post infectious Glomerulonephritis
Affected group	Pediatrics (2-7 yrs)	Adult
Immune status	Immunocompetent	Immunocompromised (Eg : Diabetic foot)
Incubation period	3-5 weeks	Nil
Prognosis	Excellent	Poor
Causative organism	Group A β hemolytic streptococci	MRSA
Renal failure	Mildly altered RFT	Profound (Requires dialysis)
Immunofluorescence	Starry sky pattern : IgG, C_3 deposits along capillary wall	Rope/garland pattern : IgA, C_3 deposits

	Post Streptococcal Glomerulonephritis (PSGN)	Infection Related Glomerulonephritis (IRGN)/Post infectious Glomerulonephritis
Electron microscopy	Subepithelial camel hump deposits	-
Light microscopy	Diffuse proliferative glomerulonephritis (DPGN) : Endocapillary > mesangial proliferation of neutrophils + no crescent	Rapidly proliferating glomerulonephritis (RPGN) : DPGN + crescent

----- Active space -----

PSGN :

- Acute onset.
- High coloured urine.
- H/O infection (Skin > throat).
- Hypertension ⊕.
- RBC casts ⊕.
- Mild edema.
- Proteinuria 1+.
- Normal S. albumin.

} Common to PSGN and IRGN

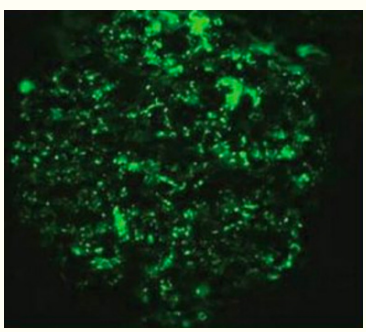
Complications of PSGN :

- Hyperkalemia (D/t renal failure).
- Hypertensive crisis.
- Sudden pulmonary edema (↑ ENaC activation ⟶ Intravascular volume overload).

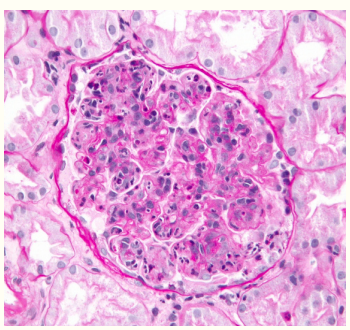
Biopsy in PSGN :

Indications :

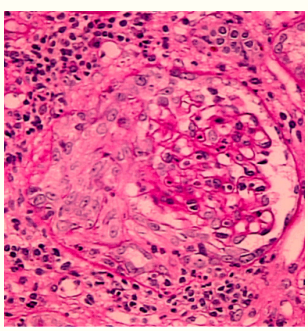
- Failure of C_3 normalisation in 8 weeks ⟶ C_3 glomerulonephritis.
- Recurrence.



Granular deposits in PSGN



DPGN : Absence of crescent



Crescentic glomerulonephritis

Nephrotic syndrome vs. Nephritic syndrome :

	Nephrotic syndrome	Nephritic syndrome
Onset	Insidious	Acute
Proteinuria	Nephrotic range	Mild
Edema	Extravascular	Intravascular
RFT	Normal	Deranged (Hyperkalemia)
Albumin	↓	Normal
Lipid	↑	Normal

----- Active space -----

NEPHROLOGY REVISION - 2

Acute renal failure — Presents as:
- Days to weeks : Rapidly Progressive Renal Failure (RPRF).
- Hours to days : Acute Kidney Injury (AKI).

Classification of non-CKD renal disease :

Vascular :
a. Reno vascular hypertension (HTN crisis).
b. Thrombotic microangiopathy (TMA).

Glomerulus :
a. Asymptomatic.
b. Nephritic syndrome.
c. Macrohematuria.
d. Nephrotic syndrome.
e. Rapidly progressive glomerulonephritis (RPGN).

Tubulo-interstitial :
a. Acute Tubular Necrosis (ATN).
   - Presents as AKI.
b. Acute Interstitial Nephritis (AIN)
   - AKI/RPRF.

Rapidly Progressive Renal Failure

00:00:10

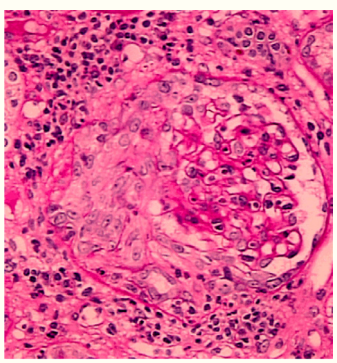
Compartment	Causes
Vascular	TMA : • Adult hemolytic uremic syndrome. • Antiphospholipid syndrome. • Scleroderma, HELLP syndrome.
Glomerulus	RPGN (Clinicopathological disease) : RPRF + crescents on biopsy.
Tubulo-interstitium	Severe AIN (2° to drug/infection).

RPGN :

Types :

Type 1
- Linear IgG + C3 deposits along GBM : Goodpasture disease.
- Type 4 : Double positive (ANCA ⊕ & Anti-GBM ⊕).
- Type 5 : Double negative.

Type 2 (Immune complex deposits)
- Full house effect : SLE.
- IgA + C_3 : IgA dominant infection Related Glomerulonephritis (IRGN).
- Adult Henoch Schonlein purpura (HSP).
- Membranoproliferative glomerulonephritis.


Crescentic glomerulonephritis

Type 3 → Pauci-immune RPGN (m/c) : ANCA vasculitis (Microscopic polyangiitis).

In age <20 years : Type 2 > Type 3.

Features and management :

----- Active space -----

- Volume overload (Facial puffiness + edema ↑↑), high coloured urine (↓ urine output).
- Ix : RFT (Deranged : Urea ↑, creatinine ↑), ECG, ABG, volume status.
- Mx : Hemodialysis (Uremia) $\xrightarrow[F/b]{}$ Biopsy (Diagnostic : Crescents +).

Nephrotic Syndrome

00:12:50

Definition :

- Nephrotic range proteinuria + (>3.5g/24 hours. / Urine PCR ≥2000 mg/g. / >50 mg/kg/day (Children).)
- Edema + hypoalbuminemia + hyperlipidemia (Lipiduria).

NEPHROTIC SYNDROME IN CHILDREN

Causes :

- Minimal change disease (MCD) : m/c podocytopathy in children.
- Focal sclerosing glomerulosclerosis (FSGS) : Genetic, podocin mutations ⊕.

Features :

- Onset : 3–4 weeks (Subacute).
- ↓ S. Albumin : Severe extravascular edema + facial puffiness.
- Ⓝ BP, Ⓝ RFT, hematuria ⊖ : MCD.
- Hypertension/mild RFT ↑/microhematuria : Likely FSGS.

Management :

Steroids $\xrightarrow{\text{After 4 weeks}}$ Monitor response.

(2 mg/kg/day or 60 mg/m^2/day)

Based on response to steroids :

	Outcome	Further Rx
Good response : U. albumin : Nil x 3 days	Complete recovery (25%)	-
	Infrequent relapses (25%)	Steroids (Good recovery)
	FRNS (50%) ↓ (Few) SDNS	Cyclophosphamide/ mycophenolate mofetil } Oral → No response → Rituximab
No response/ resistance (Few cases)	SRNS	Biopsy → Genetic FSGS → Rx : Transplant; Biopsy → Ⓝ → Steroid Resistant MCD : DOC : Calcineurin inhibitors (Tacrolimus > cyclosporin)

----- Active space -----

- SRNS (Steroid resistant nephrotic syndrome) :
  Persistent proteinuria despite steroids x 4 weeks.
- FRNS (Frequently relapsing nephrotic syndrome) :
  ≥2 relapses in 6 months or ≥4 relapses in 1 year.
- SDNS (Steroid dependent nephrotic syndrome) :
  ≥2 relapses while on tapering dose/within 14 days of stopping steroids.

ADULT ONSET NEPHROTIC SYNDROME

Features :

- Present over 3-4 weeks : Frothy urine + oedema (m/c → Pedal).
- Ⓝ RFT, U. albumin : 3+, no RBCs in urine.

Conditions :

- MCD.
- FSGS : m/c worldwide.
- Membranous Nephropathy (MN) :
  m/c in >60 years.
- Membranoproliferative Glomerulonephritis (MPGN).
- IgA nephropathy.
- Amyloidosis.

Secondary causes :

MCD	FSGS		MN	MPGN
• Hodgkin's disease • NSAIDs • Allergy/ Immunisations	• HIV • Heroin • Obesity • Sickle cell anemia • Hyperfiltration injury	• EBV, CMV • Parvovirus B19 • IFN-α • Pamidronate • Reflux nephropathy	• Adenocarcinoma (m/c : Colorectal) • Hepatitis B virus • SLE • d-Penicillamine	• Infective endocarditis • Plasma cell disorders • Hepatitis C virus

Management :

- Biopsy : Mandatory in adults.
  Indication : Confirm the diagnosis + rule out 2° causes.

	1° MCD	1° FSGS	MN	MPGN
Light microscopy	Normal	Focal segmental sclerosis	Thickened GBM (Spike pattern)	• Thickened GBM • Mesangial proliferation • Lobular structure • Double contour/ Tram track sign
Immuno – fluorescence microscopy	Normal	Focal IgM ± C3 deposits	Granular IgG ± C_3 deposits	
			Along capillary wall	Capillary wall & mesangium
Rx	Steroids (1 mg/kg) : • Full dose x 6 weeks • Taper x next 6 weeks	Steroids (most cases resistant to Rx)	Ponticelli regime (Steroid + cyclophosphamide alternatively x 6 months)	Treat 2° causes
Prognosis	Good	2/3rd → CKD	1/3rd → CKD	Poor

- Electron microscopy findings in 1° MCD and 1° FSGS : Effacement of podocytes.

Acute Kidney Injury (AKI)

00:28:04 ----- Active space -----

Causes :

1. Pre-renal : m/c cause of AKI.
2. Renal :
   - ATN.
   - AIN : Asymptomatic presentation/rash + eosinophilia (Type 4 hypersensitivity).
3. Post-renal : Mostly urological causes.

Pre-renal	ATN	AIN
• True volume depletion : Eg : Fluid loss from GI. • Third space loss : Eg : Burns. • Hypoalbuminemia . • Leads to ischemic ATN.	• Ischemic (m/c) : 2° to sepsis. • Drugs : Mnemonic → ACES. Aminoglycosides, Amphotericin B, Cisplatin, Cyclophosphamide, Ethylene glycol, Salicylates, Vancomycin. • Contrast. • Tumour lysis syndrome (Uric acid nephropathy). • Rhabdomyolysis. • Myeloma cast nephropathy.	• Drugs (m/c) : Type IV hypersensitivity Mnemonic : BRAND. Beta lactams, Rifampicin, Anti-convulsants, Allopurinol, NSAIDs, Diuretics • Infections. • Infiltration injury.

Pre-renal AKI vs ATN assessment :

	Pre-renal AKI	ATN
Urinalysis	Normal	• Albumin : Trace/ 1+. • Muddy brown epithelial cast.
U. Na^+	↓	↑
U. Creatinine	↑	↓
Fe Na	<1%	>2%
Urine osmolality	Normal	300 mOsm/kg
Urine pH		Alkaline
Urine specific gravity		1.010
BUN : Creatinine	> 20 : 1	≤ 10 : 1

Fractional excretion of Na^+ :

$$\text{Fe Na} = \frac{\text{U. } Na^+}{\text{U. Creatinine}} \times \frac{\text{Plasma creatinine}}{\text{Plasma } Na^+}$$ } Normal = 1–2%.

Hypokalemia

00:37:22

↓ S K^+
- → Non – renal loss (Intracellular shift of K^+; levels : 2.5–3.5 mEq/L).
- → Renal loss (S. K^+ < 2.5 mEq/L)
  - – Urine K^+ ↑.
  - – Urine K^+ : Creatinine ↑.
  - → Acidosis.
  - → Alkalosis.

----- Active space -----

Acidosis :

	Renal Tubular Acidosis (RTA)	
	Type 1	Type 2
Anion gap	Normal Anion Gap Metabolic Acidosis (NAGMA)	
Acidosis	Severe	Mild
Site affected	α-intercalated cells of collecting duct	Proximal convoluted tubule
Urine pH	>5.5	<5.5
Urine calcium	↑↑ (Urinary stone formation)	Absent
Rickets	+	++
Acquired causes	Sjogren's syndrome	• Wilson's disease (In young) • Myeloma (In elderly) • Fanconi's syndrome : – In children – Cystinosis seen

Alkalosis :

Causes :

a. With hypertension :

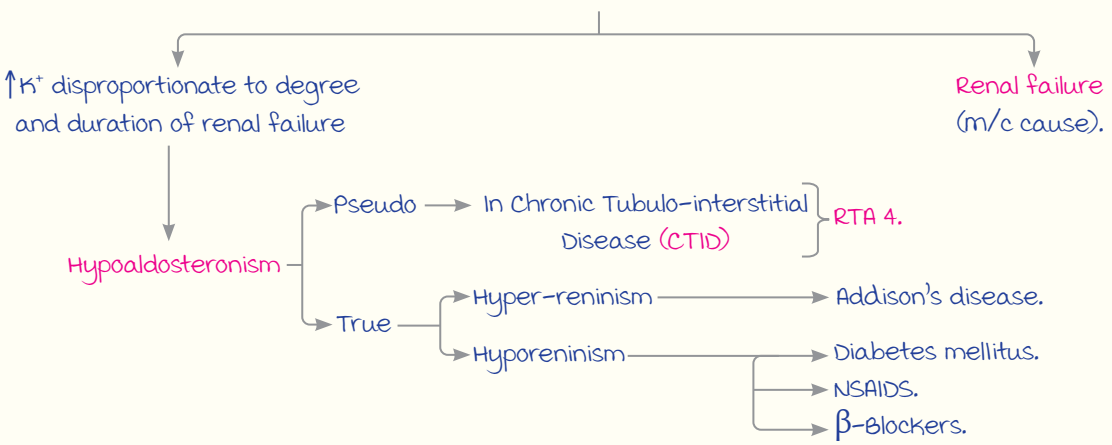
- Conn's syndrome.
- Liddle syndrome.
- Cushing's syndrome.
- Glucocorticoid Remediable Aldosteronism (GRA).
- Syndrome of Apparent Mineralocorticoid Excess (AME).

b. Normal/Low BP :

	Bartter syndrome	Gitelman syndrome
Affected site	Thick ascending limb of LOH	Distal convoluted tubule
Urinary calcium	↑↑ (Stone formation)	↓↓
Hypomagnesemia	20% cases	100% cases
Prognosis	Cannot survive (Seen in children only, except Type 3 Bartter)	Can survive

Hyperkalemia

00:43:38



GIT REVISION

----- Active space -----

Malabsorption

00:00:31

Site: Small intestine → Proximal : Duodenum, jejunum
→ Distal : Ileum

STEATORRHEA

- Hallmark of malabsorption.
- Pale, fatty, voluminous, bulky, greasy, malodorous stools.

Investigation :

Quantitative :

72-hour fecal fat estimation : Gold standard.

- 100g fat diet (x 5 days) → Stool fat estimation On D3-D5 → >7g/day : Steatorrhea.

Qualitative : Sudan III/Sudan black.

DIARRHOEA

Most consistent symptom.

Classification Based on Type :

	Osmotic	Secretory	Factitious diarrhea
Etiopathogenesis	↑Unabsorbed fats into colon → ↑osmolality → water influx from epithelial cells → Osmotic diarrhea	• Toxin-mediated : ETEC, V. cholerae • Tumor induced : VIPoma AKA WDAS/ Pancreatic diarrhoea	Very low stool osmolality. Sample collected under supervision shows normal values.
Effect of fasting	Improves	No change	
Stool osmotic gap	> 100 mOsm/kg water	25 – 50 mOsm/kg water	

WDAS : Watery diarrhea achlorhydria syndrome.

- Calculated stool osmolality : 2x stool ($Na^+ + K^+$).
- Stool osmotic gap :
  - measured osmolality (measure with osmometer) – Calculated osmolality.
  - Ⓝ : 50-100 mOsm/kg.

Classification Based on Site :

	Small intestinal	Large intestinal
Causes	• Osmotic (Chronic)/secretory (Acute) • Ileal cause : Crohn's disease/TB	• Invasive organism : Shigella, salmonella, Campylobacter, Yersinia • Inflammatory : Ulcerative colitis (UC)
Volume of stool	Large volume, watery	Small volume

----- Active space -----

	Small intestinal	Large intestinal
Blood/pus/mucus	⊖	⊕
Frequency/urgency/tenesmus	⊖	↑Frequency
Other presentations	Ileitis : Pain ⊕	Proctitis/proctocolitis

Classification Based on Duration :

- Acute : < 14 days
- Persistent : > 14 days.
- Chronic : > 30 days.

CLINICAL PRESENTATION

GI symptoms :

1. Diarrhea : Small intestinal type.
2. Gaseous abdominal distention : D/t bacterial fermentation.
3. Foul smelling stools.
4. Ascites (mild) : D/t hypoproteinemia/ hypoalbuminemia.
5. Unexplained weight loss.

Features	Causes
Musculoskeletal symptoms :	
Bone pain, osteopenia, fracture	↓Vit. D, Ca^{3+}
Cutaneous symptoms :	
Hyperpigmentation	Vit B12, niacin deficiency
Perifollicular hemorrhage	Vit C deficiency
Acrodermatitis enteropathica	Zinc deficiency
Miscellaneous	
Anemia	Iron deficiency (Proximal SI) B12 deficiency (Distal SI)
• Ataxia : Posterior lateral cord syndrome : Sensory ataxia • Peripheral neuropathy	Vit B12, E, deficiency
Renal stones	Unbound oxalates d/t unavailability of long chain FA
Weight loss	Occult malabsorption : SIBO (Small intestinal bacterial overgrowth)

Note : Posterior lateral cord syndrome is also seen in copper deficiency.

Celiac disease, Whipple, & Tropical Sprue 00:18:16

CELIAC DISEASE

All age groups, M = F.

Etiopathogenesis :

Gliadin + IgA dimers (MALT) → (Tissue transglutaminase) → Lamina propria (SI) → (Deamination) → Taken up by antigen presenting cells

----- Active space -----

Presentation :

- Classical (50%) : GI symptoms.
- Atypical : Only non GI symptoms.
- Silent : Serology +ve, no symptoms.
- Latent :HLA DQ_2, or DQ_8 +ve, serology & symptoms -ve.

Atypical Celiac :

- Iron deficiency anemia (Absorption in proximal SI).
- Ataxia : A, D, E, K deficiency
- ↑ALT & AST : leads to cirrhosis (Cryptogenic).
- Bone fracture
- Short stature / failure to thrive.

Association :

- Dermatitis herpetiformis.
- Type I DM.
- Thyroid disorders (Hypo/hyper).
- microscopic colitis.
- IgA deficiency & nephropathy.
- Bird fancier lung.

Investigations :

Serology :

- Anti TTG antibody (IgA) by ELISA : ↑Sensitive, ↑specificity.
- Anti deaminated glutamine dipeptide (IgG) : Done in IgA deficiency.

Biopsy : Non-specific

- Villous atrophy (Total).
- Crypt hyperplasia.
- Lymphocytes in lamina propria.
- Total mucosal thickness remains same.

Biopsy	Serology	
	⊕	⊖
⊕	Celiac disease	No celiac disease
⊖	+ High suspicion → Repeat biopsy	

Treatment :

Gluten-free diet (Barley, rye, oats, wheat) → Reverts to Ⓝ biopsy within 6 months.

Refractory celiac : Irreversible after Rx of 6 months.

- Rx → Steroids.
- Complications : Enteropathy associated T-cell lymphoma, small cell adeno Ca, esophageal sq. cell Ca.

WHIPPLE DISEASE

- 50-60 yrs, M > F.
- Site : Proximal SI > distal SI.
- Dx : Biopsy.

Note : Conditions diagnosed with biopsy alone.

- Agammaglobulinemia
- Abetalipoproteinemia.
- Whipple's disease.

Causative organism :

Tropheryma whipplei (Gram +ve, Acinetobacter, not cultured).

- PAS +ve in macrophage.

----- Active space -----

Clinical Features :

CNS (40%) :

- Poor prognosis, relapse ⊕.
- Rapidly progressive dementia (Progressive supranuclear palsy + oculomasticatory nystagmus).

Joints : Large joint (knee m/c), migratory, intermittent, oligoarthritis.

CVS : Culture negative endocarditis (Followed by HACEK organisms).

GIT : Features of malabsorption + lymphadenopathy, abdominal pain (D/t ileitis).

Treatment :

- Ceftriaxone/meropenem : For 14 days.
- Cotrimoxazole : Crosses BBB & prevents relapse.

TROPICAL SPRUE

m/c cause of malabsorption in Asia.

Etiology :

Coliform infection → Toxins & fermentation products released → Triggers tropical sprue
(E. coli, Klebsiella)

Clinical Features :

- Pan-intestinal : Ileal involvement mainly.
- Hyperpigmentation d/t B12 deficiency.
  Neurological features : Rare.
- Spares other systems.

Management :

Biopsy : Similar to celiac disease with partial villous atrophy.

Rx : Folic acid + Tetracycline.

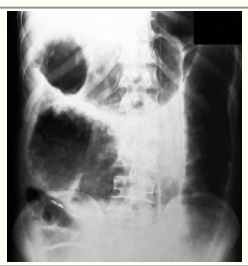
Inflammatory Bowel Disease

00:32:36

- Bimodal peak : 15–30 yrs, 70–90 yrs. • M > F, CD > UC • Ethnicity : Jewish (m/c).

		Crohn's disease (CD)	Ulcerative colitis (UC)
Associations	OCP	⊕ (F > M)	⊖
	Smoking	Causative	Protective
	Appendicectomy	Unrelated	
Familial		CD > UC	
Antibiotics use < 1 yr of life		Strong associations	
Syndromes associated		• Turner syndrome (m/c) • IL-10 receptor defect : Childhood IBD (Refractory/drug resistant)	
		• Hermansky Pudlak • Von-Gierke (GSD-I)	• Wiscott Aldrich syndrome – Recurrent sinopulmonary infection – Thrombocytopenia : Microplatelets • IPEX : Immune polyendocrinopathy X-linked syndrome – D/t FOX-P_3 mutation (T-regulatory cells defect) – Dematitis, UC, endocrine (Type I DM)

----- Active space -----

	Crohn's disease	Ulcerative colitis
Etiopathogenesis	• NOD_2/CARD 15 gene ⟶ Defective innate immunity • Retention of M. paratuberculosis • Th_1/Th_{17} cells involved	Th_2 cells involved
Site involved	• Mouth to anal • Ileocolitis (m/c)	• Rectum (m/c) • Proctitis/Proctosigmoiditis • Pan-colitis • Backwash ileitis (Rare)
Constitutional features	⊕	⊖
Clinical features	• Diarrhea • Abdominal pain (D/t ileitis) • P/A : Inflammatory mass • Malabsorption features (In jejunal involvement)	• Large intestinal diarrhoea • Fresh bleeding PR • Blood streaks on hard stool surface
Lower GI endoscopy	• Transmural, segmental • Asymmetrical • Aphthoid ulcers (Deep) • Rose thorn ulcer • Cobblestone pattern • String sign (Circumpressure fibrosis)	• Superficial, continuous • Symmetrical • Erythematous mucosal surface (Early) ⟶ ↓Vascularity ⟶ Friable ulcer • Pseudo polyp (Inflammatory masses) • Lead pipe appearance • Deep collar button ulcer
Radiological features	• Colonic thickening in CT • Creeping mesenteric fat • Fat halo sign	• Fine mucosal granularity (Earliest) • Serrations
Marker	⊖	Calprotectin
Biopsy	Granuloma	⊖
Complications	• Bowel obstruction • Stricture (Jejunoileitis) • Fissure • Fistula : Enterovesical • Fibrosis	Toxic megalcolon 
Response to antibiotics	⊕	⊖
Recurrence after Sx	⊕	⊖
Extraintestinal manifestations	• Ankylosing spondylitis • Uveitis • Cholelithiasis, nephrolithiasis • Thromboembolism	Primary sclerosing cholangitis (PSC)
	Pyoderma gangrenosum	

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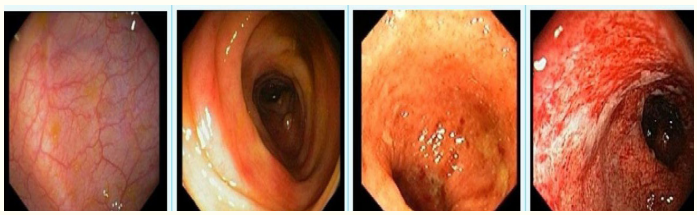
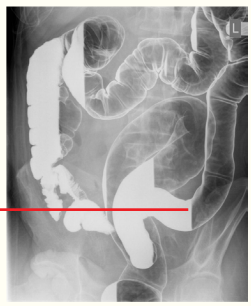
	Crohn's disease	Ulcerative colitis
Features associated with relapse	• Erythema nodosum • Episcleritis • Large joint migratory, asymmetrical pauciarthritis (Knee : m/c)	
Serology	• ASCA : A/w complication • OMP-C (Outer membrane protein- citrullinated) • APB (Anti-pancreatic antibody) • Anti-flagellin • Anti-I_2 : ↑Risk of indications for surgery.	• Anti-goblet cell antibody • p-ANCA (Seen in PSC) : ↑Risk of cholangiocarcinoma

Features of Ulcerative Colitis :



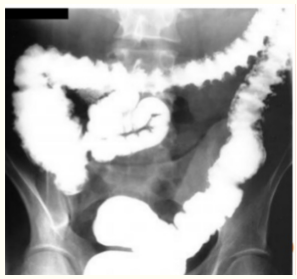
Endoscopy (mayo criteria)



Lead pipe colon

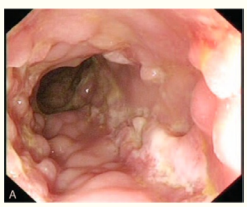
Absent haustral markings

Pseudopolyps

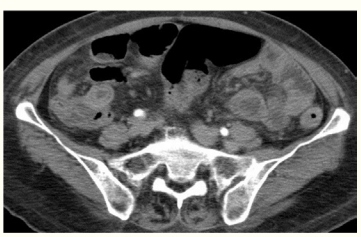


Collar stud appearance

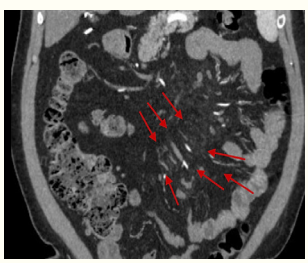
Features of Crohn's Disease :



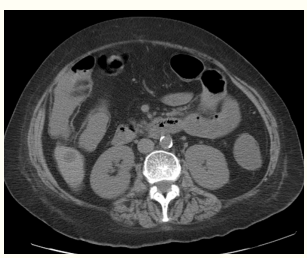
Cobble stoning



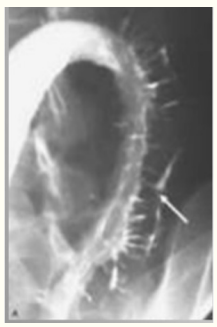
Colonic thickening



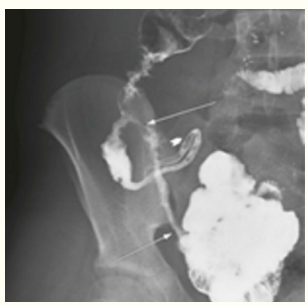
Creeping mesenteric fat



Fat halo sign



Rose thorn ulcer



String sign

Irritable Bowel Syndrome (IBS)

00:47:17 ----- Active space -----

- Functional disorder.
- < 45 yrs, F > M.

Clinical Presentation :

- Recurrent abdominal pain A/w
  1. Defecation.
  2. Change of frequency of stools :
     Alternating diarrhoea with constipation.
  3. Change in appearance of stools.

  Lower GI cramping type.
- Nausea/vomiting.
- Mucus in stools.

Exclude IBS if :

- > 45 yrs at first presentation.
- Anemia.
- Fever, ↑ESR.
- Nocturnal diarrhea, steatorrhea, bloody stools.
- Small bowel pathology.
- Weight loss.

Management :

- Low FODMAP diet.

IBS-C (Conspitation predominant)	IBS-D (Diarrhea predominant)
• Chloride channel activator : Lubiprostone. • Guanylyl cyclase agonist : Linaclotide. • Na-H exchanger : Tenapanor.	• Loperamide. • μ receptor agonist : Eluxadoline.

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HEPATOLOGY REVISION

Acute Hepatitis

00:00:27

Viral prodrome : 1-2 days → Disease :
- Malaise.
- Vomiting.
- Hypoglycemia.
- Jaundice.
- ALT, AST : >1000 IU/L (ALT > AST).

→ Recovery.
→ Hepatic failure → Fulminant.
→ Acute.

Etiology :

- Virus : Hep A (m/c in children), Hep E (m/c), Hep B.
- Drug Induced Liver Injury (DILI) :
  - Dose dependent : Paracetamol.
  - Dose independent : Idiosyncracy (Rifampicin), hypersensitivity (Carbamazepine, phenytoin, azathioprine, propylthiouracil, valproate, INH).
- Toxin : Alcohol (Poor prognosis), rat killer poison (Zinc oxide).
- Ischemic.
- Wilson disease/autoimmune hepatitis/Budd-Chiari syndrome.
- Acute fatty liver in pregnancy.

Hep A v/s Hep E :

	Hep A	Hep E
Incubation	30 days	40 days
Route of transmission	Feco-oral	
	Never vertical	Never parenteral/sexual
Pathophysiology	Cytotoxic effect	Immune-mediated (Cholestatic phase ⊕)
Risk of liver failure	1 in 2,00,000	0.5-2%, 20% in pregnancy
Rx	Supportive	
Chronicity	-	

Note : HBV + HDV → 5-20% risk of hepatitis.

Liver Failure (Complication) :

- Based on time of presentation since jaundice :
  - Fulminant failure : <7 days.
  - Acute failure : 7-21 days.
- Coagulopathy (INR ≥ 1.5) + encephalopathy (Acute ↑ NH_3 → ↑ ICT).
- Other features :
  - Lactic acidosis.
  - Sepsis/MODS.
  - Acute Tubular Necrosis (ATN).
  - Hypoglycemia/hyponatremia.

----- Active space -----

Treatment :

- Supportive.
- Glucose supplementation : 150 g using 10% dextrose.
- Transplant : In liver failure.

PARACETAMOL POISONING

Toxic dose : >7.5 g.

Time since dose	Features	Treatment
24 hrs	Nausea, vomiting.	• Charcoal hemoperfusion : within first 4 hrs. • N-acetyl cysteine (100 mg/kg) : within first 16 hrs.
24–72 hrs	• Enzyme ↑, PT ↑. • Abdominal pain.	
72–96 hrs	Fulminant hepatic failure.	

Chronic Hepatitis

00:08:20

Etiology :

- Non-alcoholic steatohepatitis (NASH).
- Chronic viral hepatitis : HBV, HCV.
- Autoimmune : SLE.
- Hemochromatosis (Bronze pigmentation, small joint arthritis, pancreatic DM, dilated cardiomyopathy, hypogonadotropic hypogonadism).
- Wilson's disease : Age <20 yrs.

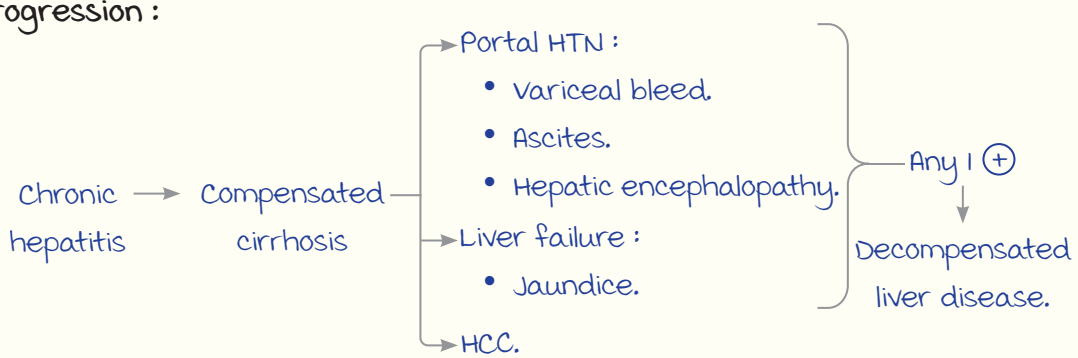
Investigations :

- ALT, AST : ↑ (<150 U/L).
  - ALT > AST : Chronic hepatitis.
  - AST > ALT : Cirrhosis.
- Fibroscan (Transient elastography) : For cirrhosis.
- MR elastography.

Clinical features :

- Asymptomatic usually.
- Wasting of muscle, fatigue.
- Altered sleep pattern.
- ↓ libido.

Progression :



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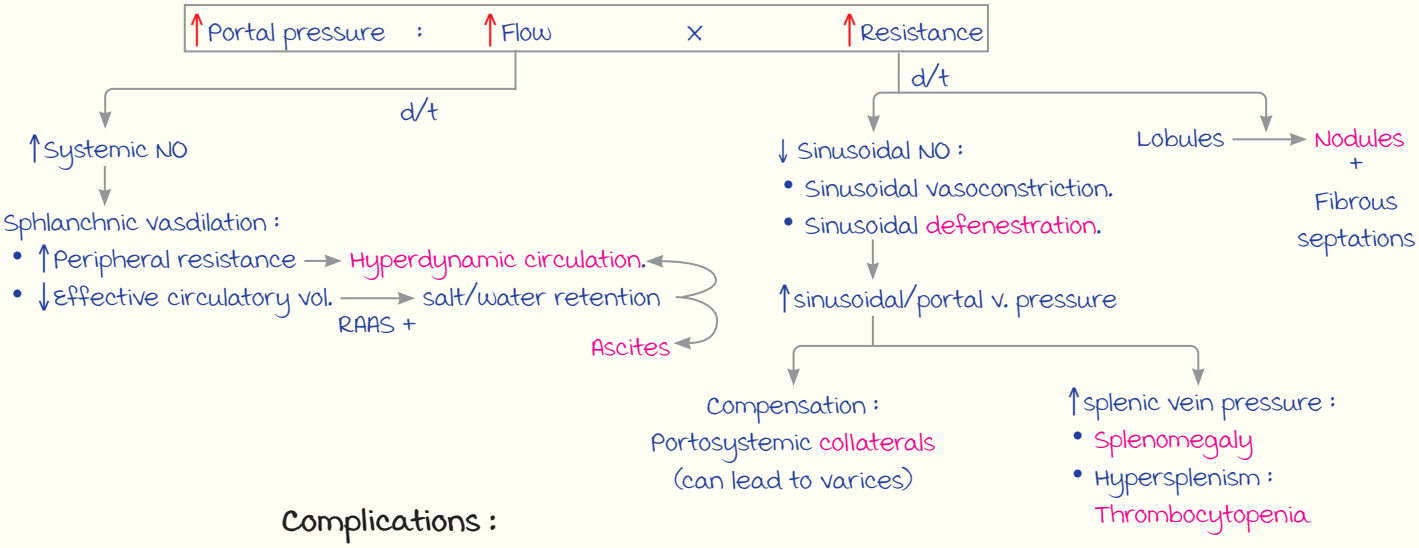
Pathophysiology of Portal HTN :



Complications :

Portal HTN :

- Thrombocytopenia : Earliest lab finding.
- Splenomegaly : Earliest clinical finding.
- Varices (Endoscopy) : D/t portosystemic collaterals.
- Ascites : SBP, Hepatorenal syndrome (HRS).
- Hepatic encephalopathy.

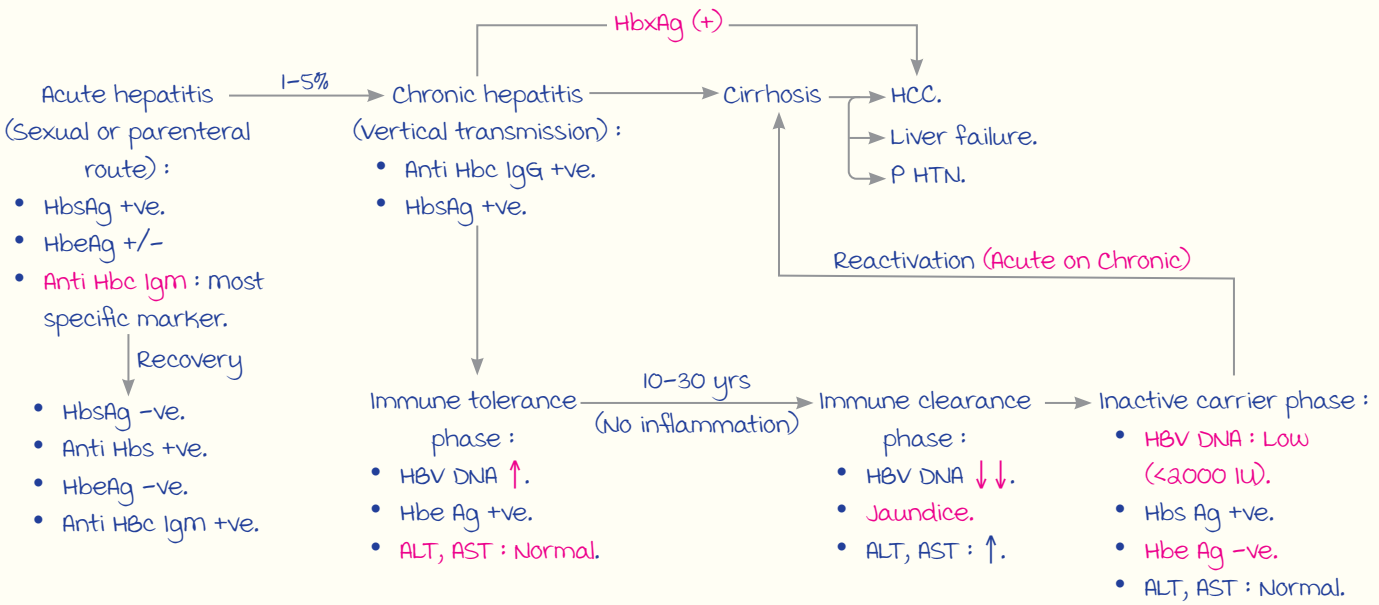
Liver failure :

- Jaundice.
- Alopecia.
- Dupuytren's contracture. } Alcohol induced.
- Parotid swelling.
- Palmar erythema, hyperpigmentation.
- Gynecomastia.
- Testicular atrophy. } D/t ↓ estrogen & defective 5α reductase.
- Caput medusae.

Hepatitis B & C

00:22:20

HEPATITIS B



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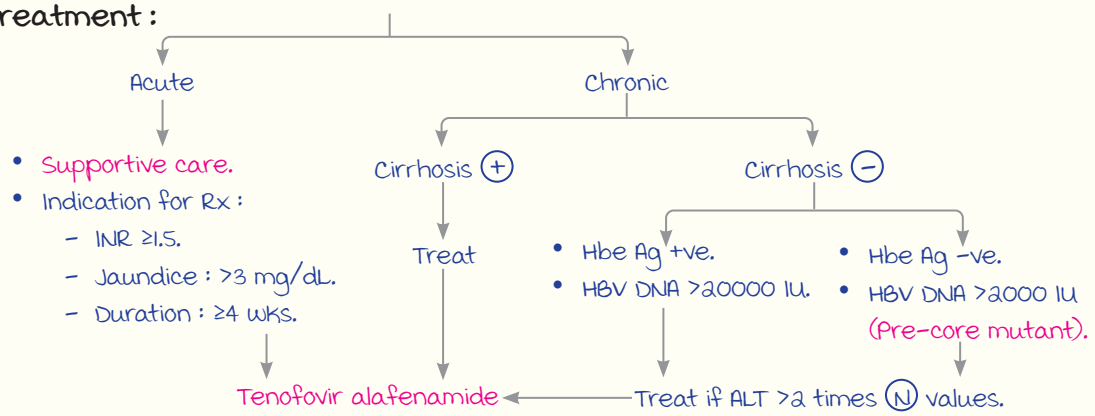
Acute v/s Acute On Chronic Hepatitis :

		Acute hepatitis B	Acute on chronic hepatitis B
Etiology		Needle prick	Reactivation of carrier
Serology	HbsAg	+ve	+ve
	HbeAg	+/-	+ve
	HBV DNA	<2000 IU	↑↑↑
	Anti Hbc IgM	+ve	+ve
	q HbsAg		+ve
Symptoms			Severe
Progression to cirrhosis		<5%	High risk

Treatment :

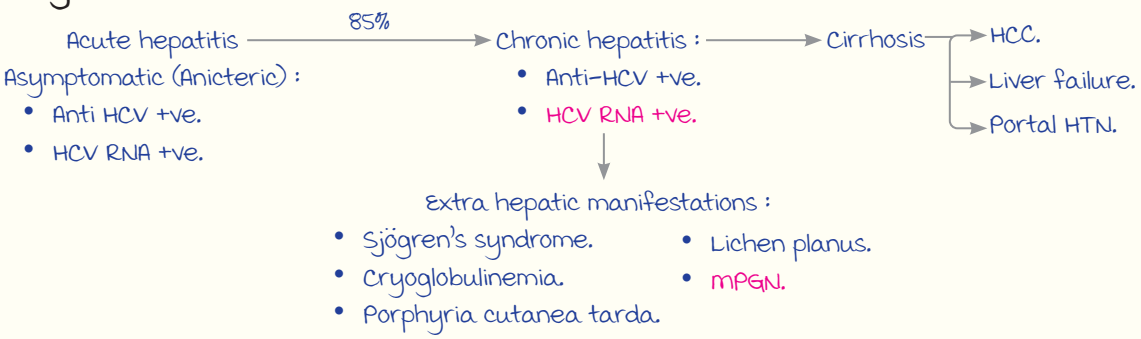


Serological Patterns :

HBsAg	Anti HBs	Anti HBc	HBeAg	Interpretation
+	–	IgM	+	Acute hepatitis, high infectivity
+	–	IgG	+	Chronic hepatitis, high infectivity
+	–	IgM	–	Acute hepatitis with high infectivity : Pre-core mutant (Does not produce HBeAg)
–	–	IgM	–	Acute hepatitis
–	–	IgG	–	Remote infection
–	+	IgG	–	Recovered from acute hepatitis
–	+	–	–	Vaccinated

HEPATITIS C

Progression :



----- Active space -----

Treatment :

- NS5A Inhibitors (Velpatasvir) + NS5B Inhibitors (Sofosbuvir) × 12 weeks.
- Add Ribavirin : If cirrhosis ⊕.

Autoimmune Disorders

00:35:49

AUTOIMMUNE HEPATITIS

Type 1 : Lupoid hepatitis.

- m/c in females.
- 2nd & 3rd decade.
- A/w SLE.

Pathogenesis :

- Lymphoplasmacytic infiltrate.
- Interface hepatitis : B/w portal tract & hepatocyte.
- Emperipolesis.
- Rosette formation.

} Histologic features.

Clinical Presentation :

- Acute hepatitis + waxing & waning jaundice.
  - Polyclonal hypergamma globulinemia.
- Chronic hepatitis.

Antibodies :

Type 1 :

- ANA.
- SMA (Smooth muscle Ab).
- AAA (Anti-actin Ab) : Poor prognosis.
- Anti SLA (Soluble liver Ag) : most specific.
- Atypical p-ANCA.

Type 2 :

- LKM-1 (Also in Hep C).
- ALC-1.

Note :

LKM-2 : Drug induced.

LKM-3 : Hep D infection.

PBC v/s PSC :

	PBC (1° biliary cirrhosis)	PSC (1° sclerosing cholangitis)
Host	Middle aged female.	Young male.
Pathology	Autoimmune inflammatory destruction of intrahepatic bile duct.	Fibrosing destruction of intra & extrahepatic bile ducts.
Association	• Sjogrens syndrome. • Distal RTA. • Xanthoma/xanthelasma.	Ulcerative colitis.
Antibodies	AMA (Antimitochondrial Ab).	Atypical p-ANCA.
Intrahepatic cholestasis	+	+
Symptoms	Fatigue, pruritis.	
Investigation	ALP↑↑.	MRCP (IOC), ERCP.
Rx	Ursodeoxycholic acid.	Transplant.

Wilson's Disease

00:41:24 ----- Active space -----

Gene : ATP 7b (Wilson's ATPase) of chromosome 13q.

Age : 3 – 20 yrs.

Pathogenesis :

- Failure of Cu^{2+} to incorporate into ceruloplasmin → Degrades ceruloplasmin → ↓ ceruloplasmin in serum : <10 mg/dL.
- Defective biliary excretion of Cu.
- Copper levels :
  - Total S. Cu ↓↓.
  - Non-ceruloplasmin bound Cu : Urinary & free Cu ↑↑ → Hepatic & neurological symptoms.
  - Ceruloplasmin bound Cu ↓↓↓.

Investigation :

- ↓ S ceruloplasmin : Marker.
- Liver biopsy.
- Quantitative Cu estimation.

} Gold standard.

Clinical Presentation :

Hepatic :

- Acute hepatitis : ALP ↓ + Coomb's –ve hemolytic anemia.
- Chronic hepatitis :
  - <20 yrs + non-specific symptoms.
  - Fatty liver.
  - Asymptomatic ALT/AST ↑.
- Cirrhosis.
- Decompensated liver failure.
- Jaundice.

CNS :

- Dysarthria (m/c).
- KF ring in descemet's membrane : Non-specific.
  - 95% in neuro Wilson.
  - 60% in hepatic Wilson.
- Psychiatric symptoms.
- Parkinson's symptoms.
- Dystonia & posturing : Risus sardonicus.
- Wing beating tremor.

Note : KF rings → Also seen in cholestasis.

Others :

- Hypoparathyroidism.
- Pancreatitis.
- Amenorrhoea.
- Hemolysis.
- Infertility/recurrent abortion.
- Type 2 RTA.

----- Active space -----

Treatment :

d-penicillamine : DOC.

- Started at 250 mg $\xrightarrow{\text{Dose} \uparrow}$ 1.5 g : Prevents worsening of neurological symptoms.
- S/E : myasthenia, membranous nephropathy, drug induced lupus erythematosus, aplastic crisis.

- Trientere.
- Zinc : Release ↑ metallothionein → ↑ Cu sequestration.

Hemochromatosis 00:48:00

- Age : >40 yrs.
- HFE gene of Chromosome 6p.
- Pathogenesis d/t unregulated iron absorption.

Clinical Presentations :

- Chronic hepatitis :
  - Cirrhosis.
  - Hepatomegaly : Alcohol ↑ risk.
- Hypogonadotropic hypogonadism.
- Non-inflammatory arthritis of 2nd & 3rd MCP joints.

} Irreversible.

- Hook-like osteophytes.
- Bronze grey pigmentation.
- Type 3c DM : Pancreatic diabetes.
- Dilated cardiomyopathy.

Management :

- Investigation :
  - Serum ferritin + transferrin saturation ratio : ↑↑.
  - C282Y mutation : Gold standard.
- Rx : Phlebotomy.

Decompensated Liver Disease 00:54:34

Decompensation :

- Variceal bleed.
- Ascites : Earliest sign.

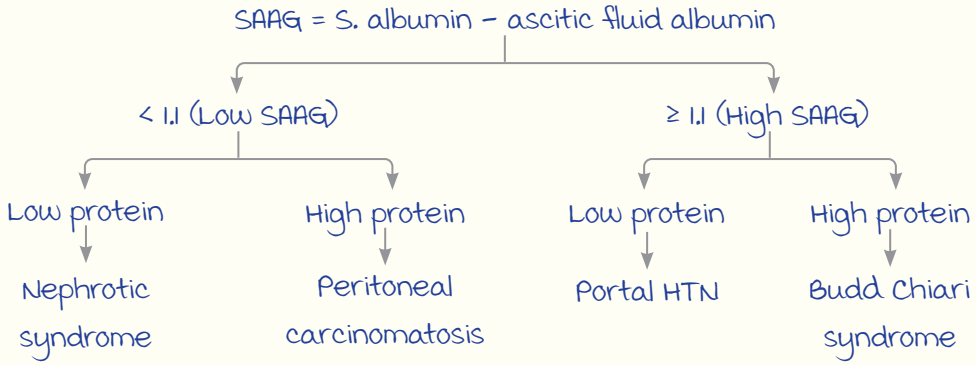
} D/t portal HTN.

- Jaundice d/t liver failure.
- Hepatic encephalopathy.

ASCITES

----- Active space -----

Serum Ascitic Albumin Gradient :



Treatment of Ascites :

Grade	Mx
Grade 1	Salt restriction <2g/day.
Grade 2	Spironolactone 100 mg/dL (max : 400 mg/dL) + Furosemide 40 mg/dL (max : 160 mg/dL) → No response → Diuretic resistant ascites → TIPSS.
Grade 3	Large volume paracentesis → No response → TIPSS.

TIPSS : Transjugular intrahepatic portosystemic shunt.

Refractory ascites :

- Diuretic resistant ascites :
  - No response after max dose.
  - Rx : TIPSS.
- Diuretic intolerant/ Intractable ascites : Not tolerating drug.

Spontaneous Bacterial Peritonitis (SBP) :

- Ascitic fluid WBC : >500 cells/μL or PMN >250 cells/μL in absence of surgically treatable source of infection.
  + Culture +ve : E. coli (M/C).
- Danger signs : Abdominal pain, fever with chills, sepsis.

Variants :

- Monobacterial non-neutrocytic ascites (MNNA) : Gram +ve.
- Culture negative neutrocytic ascites (CNNA).

} mild.

Treatment :

- Inj. Ceftriaxone 2g IV TDS x 5 days.
- Prophylaxis : Norfloxacin 400mg.

----- Active space -----

Hepatorenal Syndrome (HRS) :

- Functional kidney disease : Pre-renal failure + unresponsive to fluids.
- No structural kidney disease (KFT : Ⓝ, except creatinine).
- D/t splanchnic vasodilation ⟶ Intrarenal vasoconstriction.

Treatment :

- Transplant.
- Terlipressin OR
- Norepinephrine OR
- Subcutaneous octreotide + Oral midodrine.

} Vasoconstrictors : If planned for transplant.

Hepatopulmonary Syndrome (HPS) :

Clinical features :

- Cirrhosis with portal HTN.
- Dyspnea.
- Clubbing.
- Platypnea (Dyspnea on standing)/ Orthodeoxia (↓ in O_2 saturation).

Pathophysiology : Splanchnic vasodilation ⟶ Intrapulmonary vasodilation, A-V connections ⟶ V/Q mismatch ⟶ Hypoxia.

Investigations : Bubble ECHO.

Rx : Transplantation.

HEPATIC ENCEPHALOPATHY

Reversible portosystemic encephalopathy (Type C).

Note :

- Type A : Encephalopathy d/t fulminant hepatitis.
- Type B : TIPSS.

Pathophysiology :

Undetoxified ammonia + Other ammonia related products : Mercaptans, phenol, manganese, aromatic amino acids.

↓

Astrocytes ⟵ Toxic

NH_3 + Glutamate ⟶ Glutamine ⟶ 2° neuronal injury.

- High in CSF.
- Bind to NMDA receptors.

Precipitating Factors :

- Alkalosis :
  - Hypovolemia, vomiting, dehydration.
  - Hypokalemia.
- Renal failure.
- Benzodiazepines.
- ↑ NH_3 production :
  - Sepsis.
  - UGI bleed.
  - ↑ protein intake.
  - Constipation.

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West Haven Criteria :

	Grade	Characteristics
Covert HE	Minimal	
	1	• Short attention span. • Sleep disturbance. } Evaluation : Psychometric test
Overt HE	2	• Personality & behavioral change, asterixis.
	3	• Disorientation, clonus, rigidity, hyperreflexia. • Responsive to pain.
	4	• Comatose. • Triphasic wave on EEG.

Treatment :

- Lactulose bowel wash : ↓ pH of lumen → ↑ NH_4^+.
- Rifaximine.
- LOLA.

HEPATIC VENOUS PRESSURE GRADIENT (HVPG)

- HVPG = Wedged HVP − free HVP.
- Sinusoidal pressure : >6 mmHg → Pathology ⊕.

	Cause	WHVP	FHVP	HVPG
Pre-hepatic	EHPVO	N	N	N
Intrahepatic	Cirrhosis	↑	N	↑↑↑
Post-hepatic	Budd Chiari	↑	↑	N

EHPVO : Extrahepatic portal vein obstruction.

Important Formulae

00:49:58

Anion Gap :

- Serum anion gap : $Na^+ - (Cl^- + HCO_3^-)$.
- Urine anion gap (UAG) = Unmeasured anions − unmeasured cations.

NAGMA : Normal anion gap metabolic acidosis.

- Loss of HCO_3^- is compensated by Cl^-.
- Seen in RTA, VIPoma.
  - RTA : H^+ not excreted → ↓ NH_4^+ in urine → UAG +ve.

HAGMA : High anion gap metabolic acidosis.

- ↑ in unmeasured anions (Keto acids, lactic acid, uremic toxins, alcohol).
- Anion gap ∝ Unmeasured anions.

Stool Osmotic Gap :

- Measured stool osmolarity − 2 $(Na^+ + K^+)$.
- ↑osmotic gap = osmotic diarrhea.