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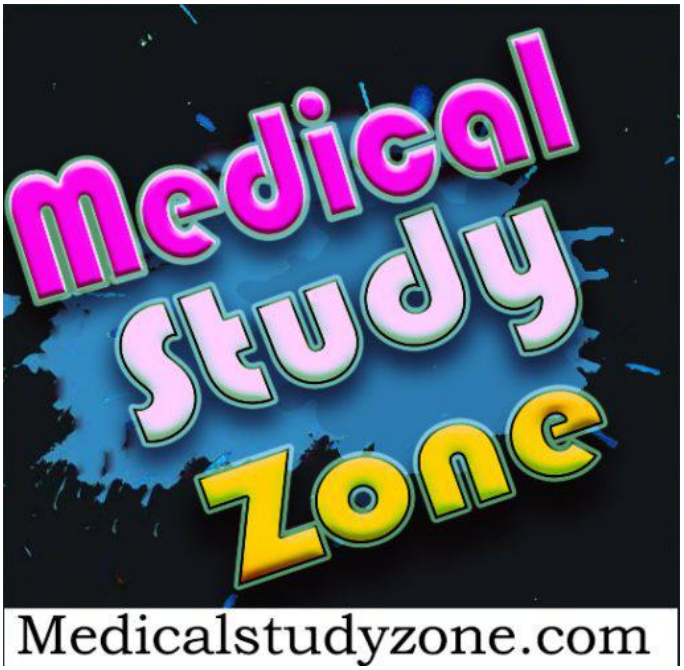

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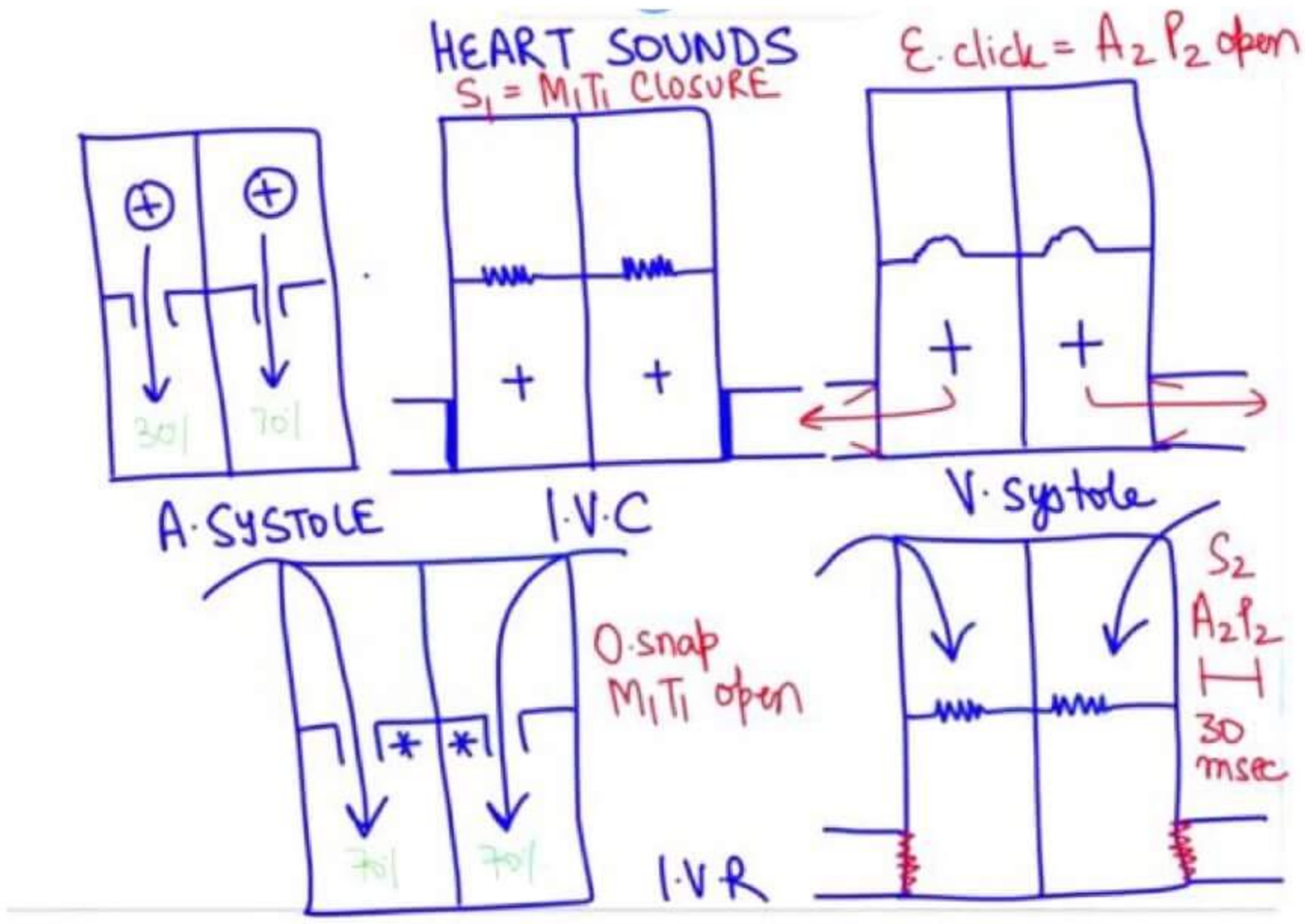
HEART SOUNDS 1



S1 d/t closure of mitral and tricuspid valve

Approximately 30% filling of ventricle occurs in atrial systole and 70% occurs in rapid filling phase

Iso Volumetric Contraction (IVC): stage where no blood is entering or leaving the heart.

Q. Which heart sound is present after S1: Ejection click (d/t aortic and pul. valve opening)

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Amount of blood pumped by left and right ventricle is equal and is pumped at same time

S2 is d/t closure of aortic and pulmonary valve

S2 is always written as **A2P2** because aortic valve closes before the pulmonary valve

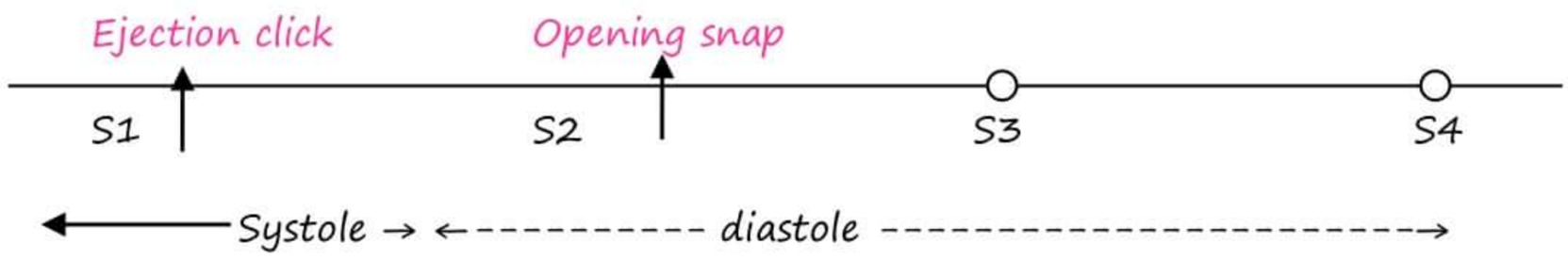
Time lag between aortic and pulmonary can also be heard physiologically which is called as splitting of 2nd heart sound and time lag is **30 msec**

Iso Volumetric Relaxation (IVR): Is a period between S2 and O. snap. blood is trying to come back into ventricles but not allowed to enter the ventricles

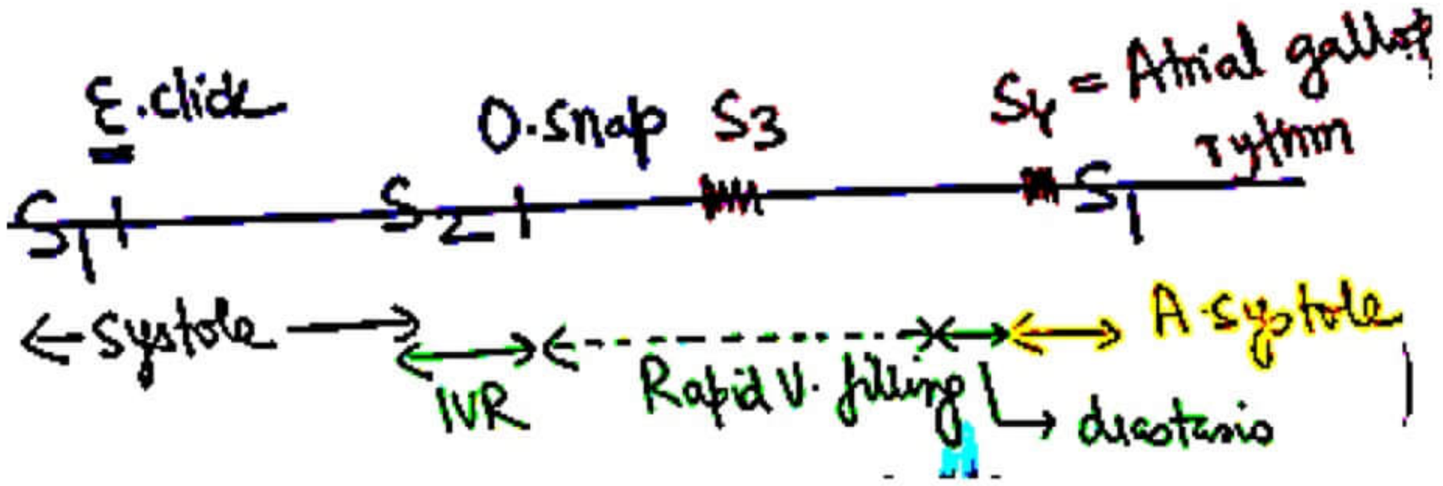
Q. Heart sound present after S2 is: Opening snap

Opening snap: Due to opening of mitral and tricuspid valve

Loud opening snap: Mitral Stenosis (MS)



PrepLadder



* **High pitch heart sounds heard (S1, S2, E. Click & O. Snap)** by diaphragm of Stethoscope
* **Low pitch heart sounds (S3 & S4)** heard by bell of stethoscope
* S4 is present just before S1
* Pre-systolic Heart sound = S4
* Diastasis is period when the heart will have least motor activity.

• S4 - Atrial Gallop rhythm/ Atrial kick- excessive force generated by left atria→ heard in the phase atrial systole.

• S3 - ventricular Gallop rhythm→ heard in rapid ventricular phase esp. during turbulence. Eg. In CHF pts

*** Atrial Myxoma-**

- M/C benign tumor of Heart
- Commonest tumor of heart is metastasis
- Pedunculated tumor

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It is freely floating in the lumen of left atrium. So in a way blocking the blood flow towards mitral valve

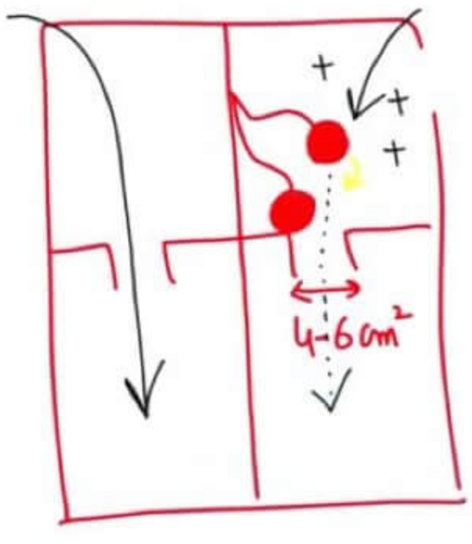
- **Auscultatory finding = Tumor plop sound (low pitched)** → when the blood entering LA hits tumor→ Tx moves like a pendulum and strikes against mitral valve

- If the size of tumor increases it limits the blood flow through mitral valve and behaves like mitral stenosis

- Tumor hits on already open Mitral Valve so the sound will be heard after opening snap

- Symptoms of breathlessness are increased in sitting position→ due to gravity Tumor falls on mitral valve and physically obstruct the blood flow

Q. Young female came with complaints of effort intolerance, she gets tired very soon. She was prescribed iron supplements, but her symptoms were not relieved. When she came back after 1-2 months her breathlessness was increased (even on going to washroom) and she also developed platypnea.



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Clinical Features: -

1. Young female
2. Effort intolerance
3. Dyspnea on Exertion
4. Platypnea (Breathlessness Increase in sitting position)

On Examination: -

1. Tumor plop Sound
   - Low pitch sound (Heard with bell of Stethoscope)
2. Mid to late diastolic murmur
3. Lungs Crepitations → B/L, fine

> Extra mile- Low pitch heart sounds are S3, S4, Tumor plop sound except these 3 all other sound are high pitched.

- IOC = Trans Esophageal Echocardiography
- Treatment → Surgical Resection

Prognosis: Good if tumor is resected early.

Tumor cells might embolize and give TIA like symptoms or tumor can also cause clot formation that can cause embolization.

- Differential diagnosis-

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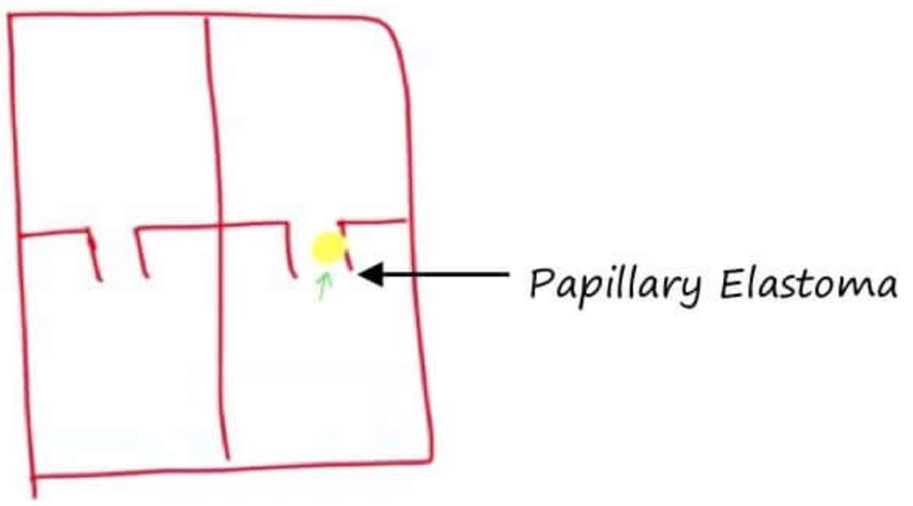
→ Papillary elastoma-
   - Tumor originates from valve leaflets
   - **Rx**: Prosthetic heart valves



* M/c tumor of heart = Metastasis [From • Oat cell carcinoma of lung
• Breast Carcinoma
• Malignant Melanoma

* M/C primary Malignant tumor = Angiosarcoma
* M/C benign tumor = Atrial Myxoma

* Tubercular Pericarditis-

• M/C extrapulmonary TB = Cervical Lymph Node

↓

Gohn's focus = Tonsils

PrepLadder

Clinical features:-

1 Chest pain at rest

2 Night Sweats

3 Low grade fever (Evening rise of temp.)

4 Involuntary weight loss = Decrease in 5% weight over 6 months

On Examination:-

Auscultatory findings- Pericardial friction Rub (Inflammation btw the outermost layers of heart and there is sero-fibrinous exudate present)

↓

It persists on holding breaths

* Pleural Rub is heard best on deep Inspiration
* Breath holding is the best method to differentiate btw these two

Investigation:

ECG Findings:

- **ST segment elevation Concave upwards**

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In Myocardial infarction

↓

ST Elevation convex upwards [Pardee Sign / Tombstone pattern]

It is also associated with **T wave inversion**

* In acute pericarditis → 11 out of 12 leads are having ST elevation except in aVR, which shows reciprocal change of ST depression.
* In a normal person P wave and T wave are always upside down so we will get a reciprocal change of ST segment depression in aVR

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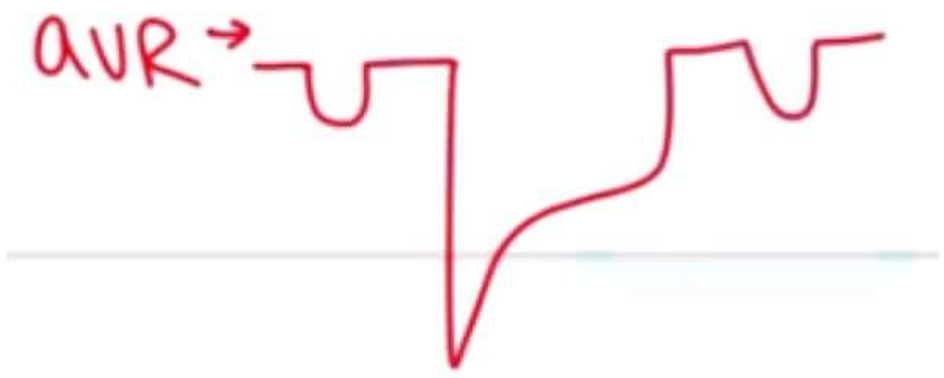

2. Echocardiography: minimal pericardial effusion may be seen
3. CB NAAT/gene expert: On pericardial fluid

Treatment

Antitubercular treatment (ATT) x 6 months

Complications/Sequalae:

* **Constrictive pericarditis-**

-Sequalae of treated case of tubercular pericarditis

-Calcification like eggshell develop around the heart of a person which will limit the filling of heart from outside

-Turbulence is created in diastole when the blood strikes the calcified ventricle

Auscultatory finding = Pericardial shudder/Pericardial shock/Pericardial knock

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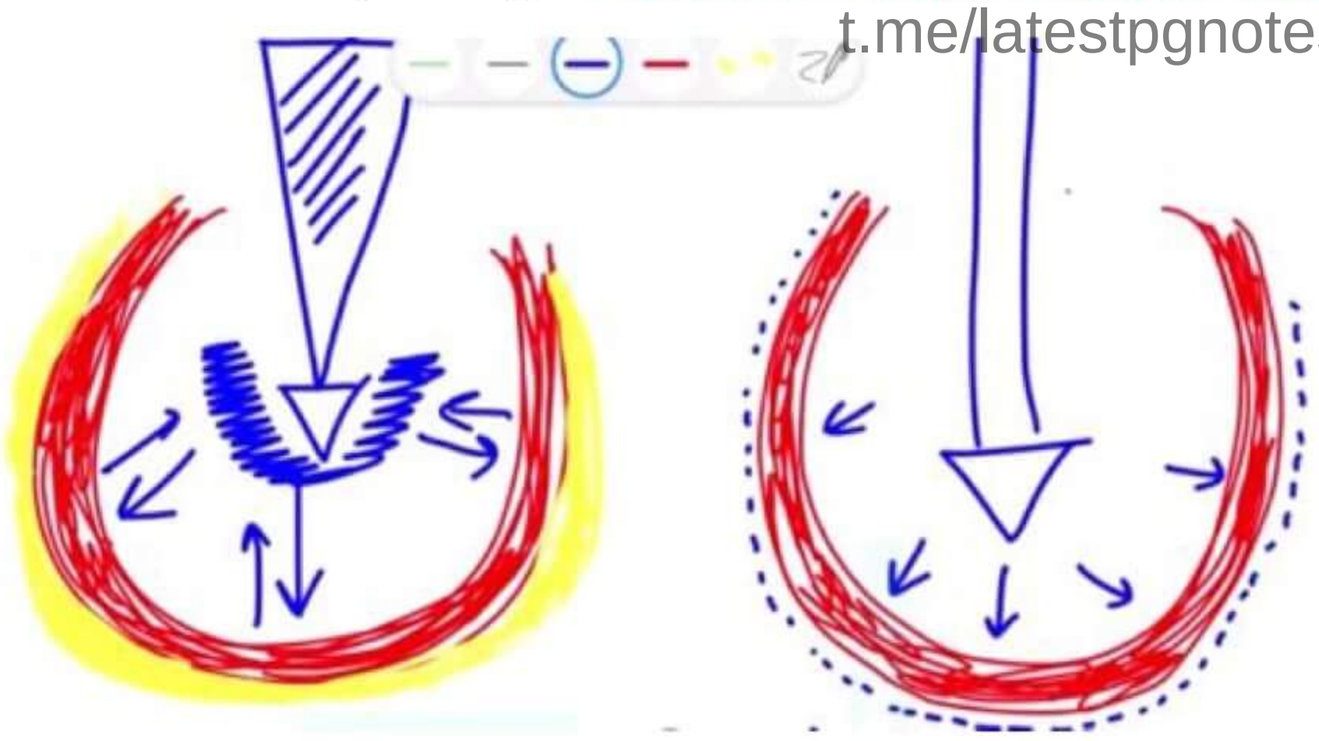
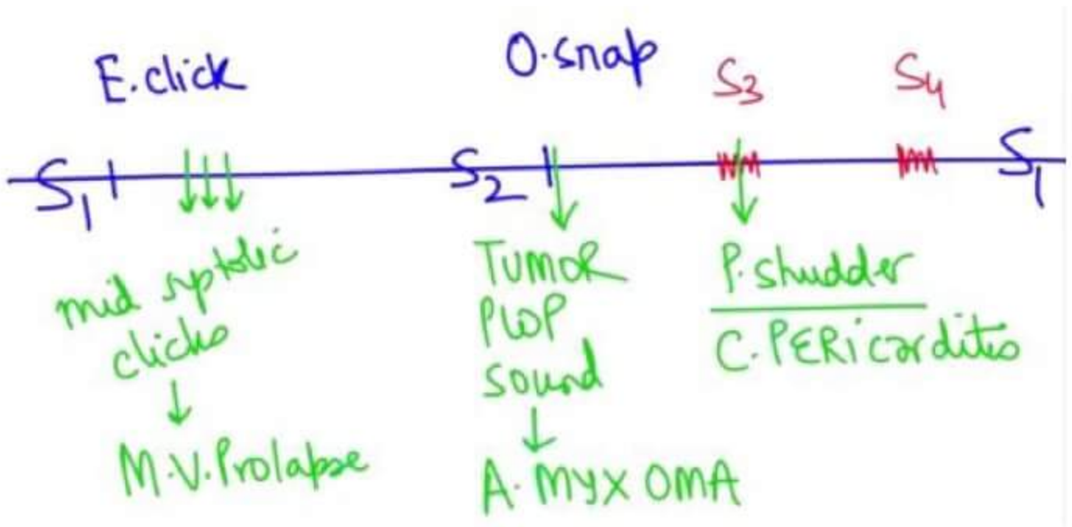


Pericardial shudder is always heard after opening snap

* Pericardial Shudder **mimic 3rd Heart sound**
* Pericardial Shudder = **High pitch Heart Sound**
  (Heard with diaphragm of stethoscope)

Note- Mid systolic clicks are heard in Mitral Valve Prolapse **(MVP)**



PrepLadder

HEART SOUNDS 2

Second HEART Sounds (S_2)

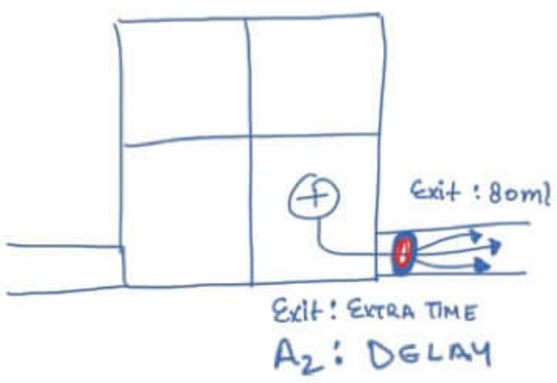
- Characterized by aortic and pulmonic valve closure
- Time LAG: 30 millisec
- K/A physiologic splitting and is best appreciated in phase of inspiration
- Place stethoscope at **Erb's point** (Left side of chest, 3rd intercostal space, parasternal line)

$$S_2 = A_2 \xrightarrow{30\ msec} P_2$$

- Split < 30 m sec: Narrow Split
- Split > 30 m sec: Wide Split

CLINICAL Conditions

1 AORTIC STENOSIS



1 Turbulence or murmur when left ventricle ejects blood into AORTA **280 ml of blood exits (NORMAL)**

3 In AORTic stenosis it will take extra time

4 Aortic VALVE does not close on time thus delayed closure

5 Narrow Split S2 (A2 approaches P2)

6 Mx of calcified stenosed aortic valve – AORTIC VALVE REPLACEMENT

If the condition is not managed surgically, the condition continues to progress. So A2 will close even more later, leading to aortic and pulmonic valves to close at the same time. This is called as **single S2.**

If treatment is still not done, A2 might close after P2, leading to P_2A_2 which is called as **Reverse split S2 / paradoxical Split S2**

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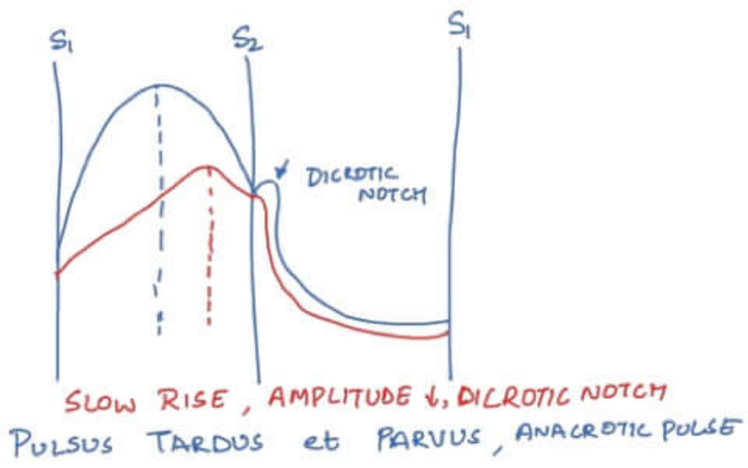
Causes of valvular AS-

1. Bicuspid aortic valve (Infantile presentation)
2. In child, caused is Rheumatic heart disease
3. In adult, > 65 years cause is Senile calcification
4. Bimodal distribution of age of presentation

C/F → (SAD)

1. Syncope on exertion (↓ cardiac output)
2. Angina (obstruction → left Ventricular hypertrophy → oxygen demand ↑)
   - Mismatch btw demand and supply (Demand ↑, supply is normal)
   - Subendocardial ischemia
3. Dyspnea (↑ left ventricular filling pressure, pulmonary edema due to diastolic malfunction)

O/E:



- Pulsus Tardus et Parvus, Anacrotic Pulse
- In carotid ARtery,
- Pulse tends to PEAK in the middle of systole then pressure tends to EASE off

PrepLadder

- **Dicrotic notch**, then A FALL
- Dicrotic notch present right AFTER the S_2
- PEAK of pressure generated in the middle of systole (normAL)
- In valvular aortic stenosis, outlet obstruction pressure TAKES time to rise
- Peak of pulse is delayed, smaller dicrotic notch
- Slow rising pulse (**PULSUS TARDUS et PARVUS**)
- Amplitude is ↓, dicrotic notch MAY be ABSENT (**ANACROTIC pulse**)

- Double apical impulse, heart negatively bigger apex beat: 5^{th}, 6^{th} intercostal space
- Heaving apex beat (forceful)
- S_2: NARrow split / single / paradoxical split
- S_4 is heard. Left ventricular hypertrophy leads to left atrial hypertrophy (LAH). The extra force generated by left atria is responsible for S_4
- On auscultation, murmur is heard

Increase and decrease of spike, intensity not CONSTANT (↑ /↓): Ejection Systolic Murmur

- **AKA CRESCENDO-DECRESCENDO Murmur**

IOC: Transthoracic Echo(TTE)

(Atherosclerotic changes)

+

Coronary Angiography

(Co-existent ATherosclerotic lesions, triple vessel disease is seen in geriatric population)

Treatment:

For SYMPTOMATIC severe AS → transcatheter aortic valve replacement plus coronary artery bypass grafting

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For ASYMPTOMATIC severe AS → wait and watch as intra operative mortality approaches > 1%

PEDIATRIC AS → Balloon valvotomy

IMPORTANT TERMS

- CAROTID THRILL = AS
- DANCING CAROTID = AR

SEVERE AORTIC STENOSIS

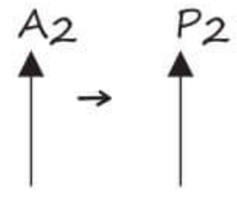
- NARrowing of aortic valve orifice < 1 cm^2
- Transvalvular gradient (L.V-Aorta) > 40 mm Hg
- Ejection velocity ↑ > 4 cm / sec
- NORMAL ejection velocity = 1 m / sec

SUPER SEVERE AS

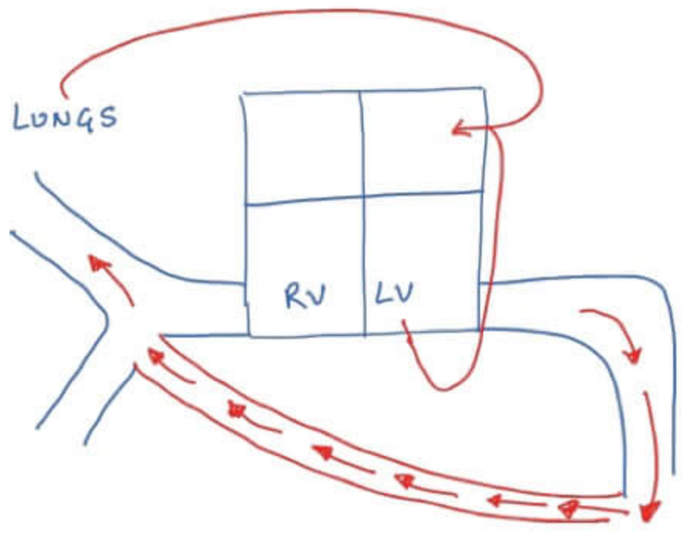
- Trans-vascular gradient: > 55 mm Hg
- Ejection velocity > 5.5 m / sec

PATENT DUCTUS ARTERIOSUS

- Left to right shunt
- Left ventricular failure (LVF)
- Exit of blood: Extra Time
- A_2: close later



- NARrow split S_2



PrepLadder

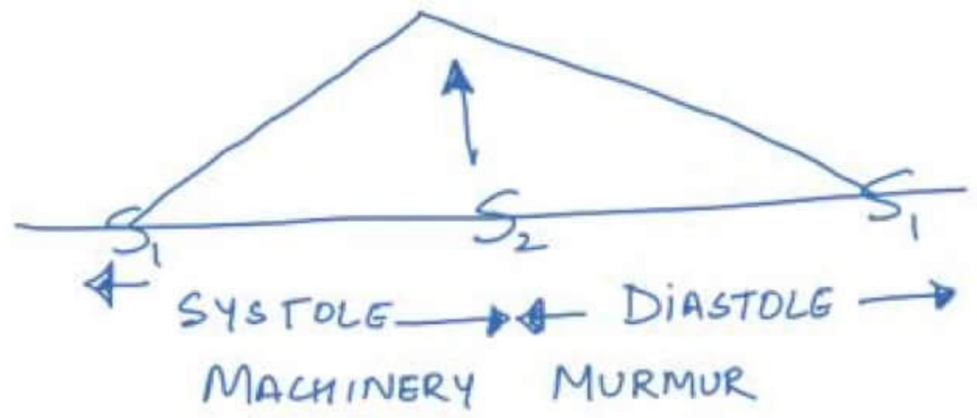
Presentation

- Preterm children @ birth
- Term children @ 6 weeks
- Child becomes breathless on breastfeeding along with excessive sweating / diarrhea
  → hence infant gets irritable due to poor oral intake

PDA

O/E

- NARrow split S_2
- Murmur: **Continuous, machinery murmur*****
  : Heard both in Systole and diastole
  : Peak of murmur @ S_2



IOC: TTE

Treatment

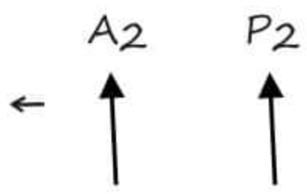
Preterm child:
INDOMETHACIN Term child:
Surgical ligation
1 yr old child: Surgical ligation

Causes of narrow split S_2 →

Aortic Stenosis (Sub-valvular AS) / hypertrophic obstructive cardiomyopathy
LVF / Anterior wall MI / PDA / Coxsackie B myocarditis / wet-beriberi / severe anemia

WIDE SPLIT S2

1, Mitral regurgitation
Blood exit: less time
A2: Closes EARly



2. VSD
- M/C congenital heart disease
- LV to LA shunting
- Less time
- A2 closes early

3. ATRIAL SEPTAL defect (ASD)
- LA to RA
- More blood
- Exit: more time
- P2 closes late

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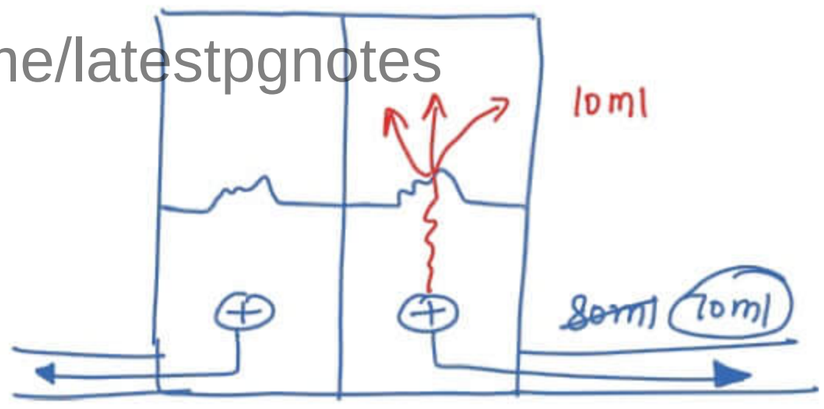
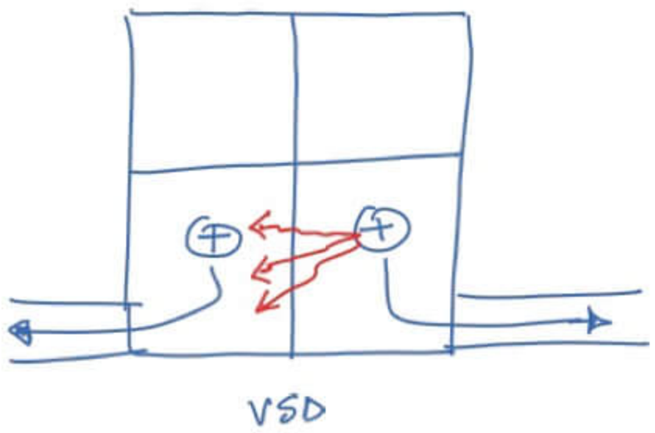
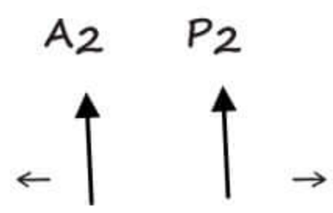




Left side of heart

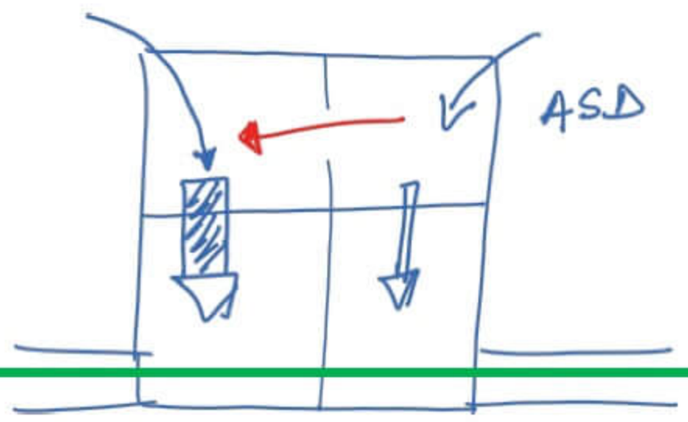
a. Less blood
b. Exit: less time
c. A2: closes EARly

- Wild Split S_2



During Inspiration and Expiration

↓ More (blood) ↓ less



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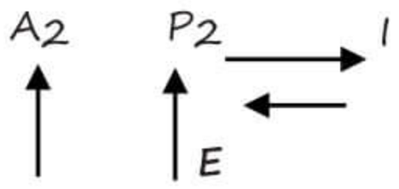
CAUSES in comes
in (more time)
(less time)

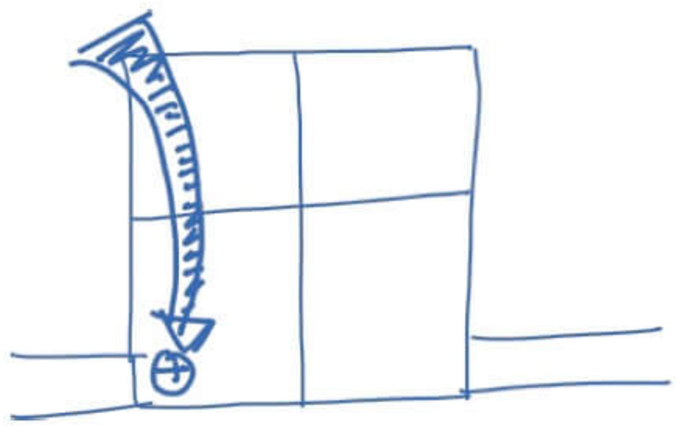


30 m sec

A2 does not depend on respiration

P2 keeps oscillating with respiration

Why is S_2 fixed split in ASD?



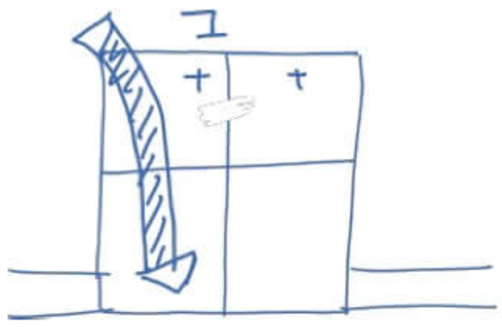
- Shunt not operational in the phase of inspiration as more blood causes equilibration
- Shunt operates only in expiration phase
- Hence Equal amount of blood present in Right ventricle in I and E
- Hence P2 does not vary with respiration

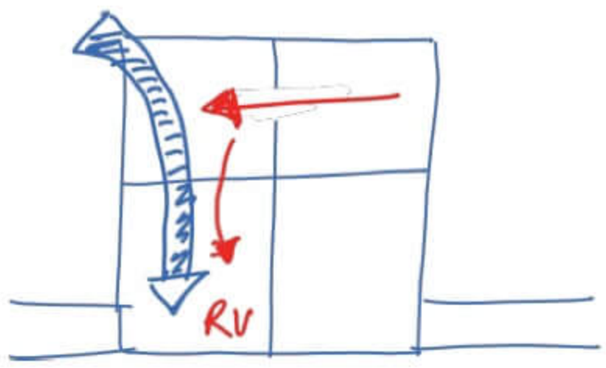
SHUNT MURMUR = Absent

FLOW MURMUR = Mid diastolic

murmur TTE = goose neck defect

Treatment - occlusion device





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S_2

NARROW split

1 AS
2 HOCM
3 LVF
4 LBBB

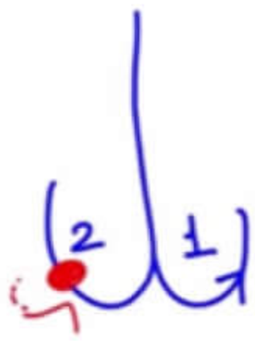
Wide split

VARIABLE
VSD
MR

Fixed
- ASD

1. HOLT ORAM SYNDROME
= ASD + absent Radius bone
2. Lutembacher syndrome = ASD + MS
3. DOWN SYNDROME
4. T A PVC
Total Anomalous Pulmonary venous Connection

PrepLadder

RBBB	LBBB
 - Delayed information provided to right sided valves - Leads to delayed closure of P2 and T1 - Hence wide split S2 and S1	 - Delayed information provided to left sided valves - Leads to delayed closure of M1 and A2 - Hence narrow split S2 and S1

Refractory period of right fascicle is always higher than left fascicle, so the current goes first to left side then to right

$S_1 = M_1\ T_1$ (It is always written so because the current first goes to left side then to right side)

$S_2 = A_2\ P_2$

Right bundle branch block (RBBB):

$S_1 = M_1$ (Will be normal) T_1 (Will be delayed)

Wide Split S1

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$S_2 = A_2$ (Normal) P_2 (Delayed)

Variable Wide Split S_2 (Variability is with respect to inspiration and expiration) heard in **RBBS AND VSD**

Left Bundle Branch Block (LBBB)

$S_1 = M_1$ (Delayed) T_1 (Normal)

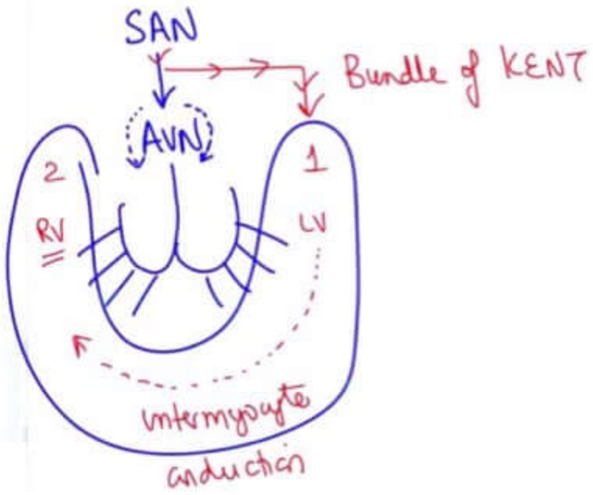
Narrow Split S_1 / Single S_1

$S_2 = A_2$ (Delayed) P_2 (Normal)

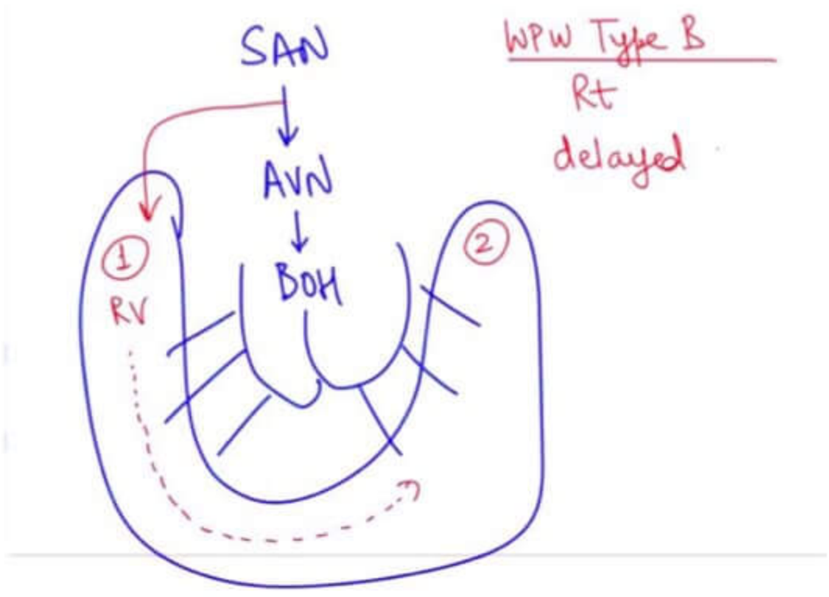
Narrow split S2

PrepLadder

- **WPW (Wolff Parkinson white syndrome) type A:-**
  - **Bundle of Kent is left sided.** (It has no decremental property hence, conduct very fast unlike AV node which is slow conducting. So impulses will reach left side through this pathway and will be delayed to right side because current is not using purkinje network but using inter myocyte conduction)
  - Delayed Information provided to Right Ventricle hence it behaves like RBBB.
  - **Wide Variable Split S_2**



- **WPW type B-**
  - **Bundle of Kent is right sided (Right ventricle is stimulated first)**
  - Delayed Information provided to left ventricle hence it behaves like LBBB.
  - **Narrow Split S_2**



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Quick Revision Summary

- **Causes of Narrow Split S_2:-**
  1. Aortic Stenosis
  2. Hypertrophic obstructive Cardiopathy (HOCM)
  3. LVF
     - Anterior wall myocardial infarction
     - Wet Beri-Beri
     - Patent Ductus Arteriosus (PDA)
  4. LBBB
  5. WPW type B

Wide Split S_2:-

Variable Split	Fixed Split
• VSD • Mitral Regurgitation • RBBB	• ASD – Holt Oram Syndrome – TAPVC (Total Anomalous Pulmonary Venous Connection) – Lutembacher syndrome (ASD+MS)

HEART SOUND 3 & JVP

- First heart sound S_1 = Mitral ant tricuspid valve closure
- **Intensity is directly proportional to speed of closure**
- **Loud S_1** denotes Tachycardia
- **PR** $\propto$ 1/HR ↓

  * Short P-R interval
  * CHF
  * Pheochromocytoma
  * Thyrotoxicosis

2. Physiological: **children / pregnancy**
3. In mitral stenosis there is a physical obstruction that leads to increase in left atrial pressure MS. This leads to

Transvalvular Gradient ↑) — **Faster opening mitral valve**; **Faster elastic recoil mitral valve**

Calcified MS: Elastic recoil decreases: Soft S_1

* Soft S_1 denotes bradycardia

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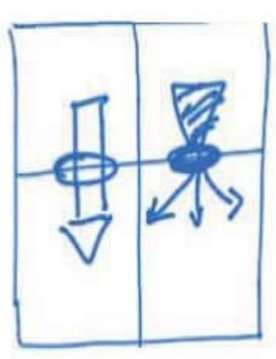
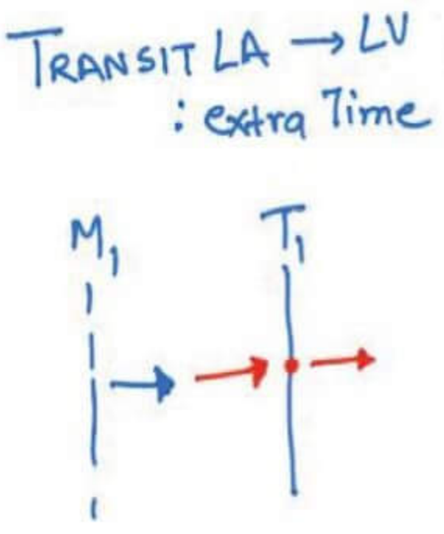
↓

* Prolonged P-R interval
* Hypothyroidism
* SAN #: Sick sinus syndrome
* AVN #: 3rd degree H. block
* BOH #: Mobitz II H. block (Inf. Wall MI)
* Morbid obesity (Fat in chest wall) / emphysema (Air trapping)
* Calcified MS / TS (Due to reduced elastic recoil)
* MR / TR

Remember Variations in S1 asked in case of Mitral Stenosis-

1. Narrow split S1
2. Single S1
3. Paradoxical Split S1
4. Loud S1
5. Soft S1 (due to calcification of valve)





PrepLadder

S_3 Ventricular Gallop Rhythm	S_4 Atrial Gallop Rhythm
Early diastolic	Late diastolic
Rapid V. filling in dilated ventricles 1. CHF 2. DCM 3.**COPD**: Cor pulmonale 4. **PE** - Acute cor pulmonale Cor pulmonale means RVF due to Non-Cardiogenic causes.	Outflow tract obstruction LVH / LAH 1. AORTIC STENOSIS 2. HOCM 3. HTN (Long standing) 4. Pulmonic stenosis 5. PAH **Left Sided S_4** **Right Sided S_4**
	Extra Mile: S_4 Absent in A. fibrillation

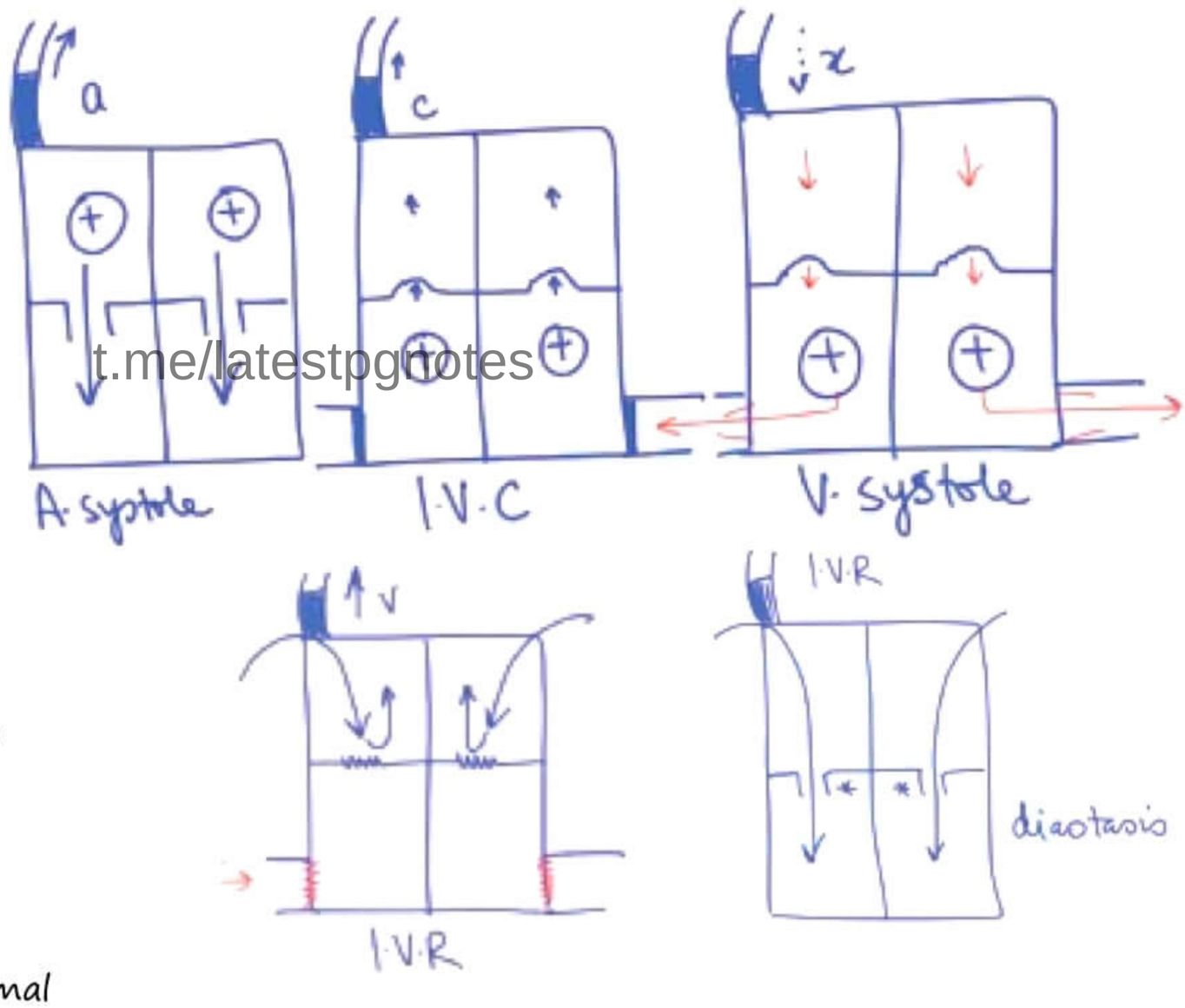
A = A. systole

C = IVC, Bulge

X = V. systole

V = IVR, rebound

Y = Diastasis



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JVP = Internal jugular vein

5-8 cm H_2O @ angle of louis

Pulsations seen, never felt

↳ **2x carotid frequency**

Deep Inspiration→ **JVP falls** → normal

C. pericarditis + deep inspiration → JVP rises

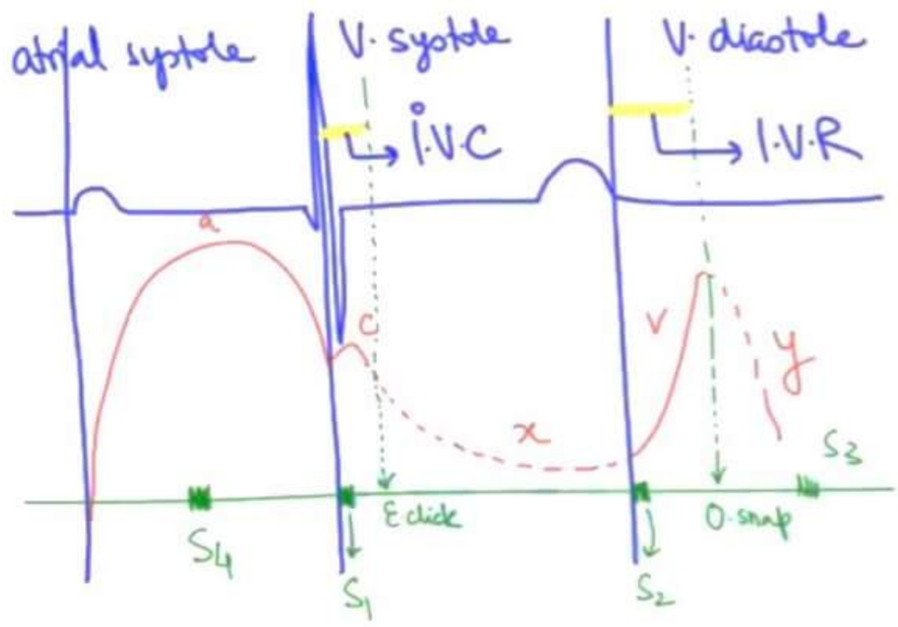
(Compliance ↓)

Causes of Kussmaul sign (CRR)
1. Constructive Pericarditis (Calcification)
2. Restrictive Cardiomyopathy (Fibrosis)
3. Right CHF (Inf. Wall MI / PE / COPD)

PrepLadder

- Non pulsatile elevated JVP seen in cardiac tamponade and SVC thrombosis

  (Only 2 medical conditions where You find "non pulsatile elevated JVP")



Large a wave in JVP

1 TS

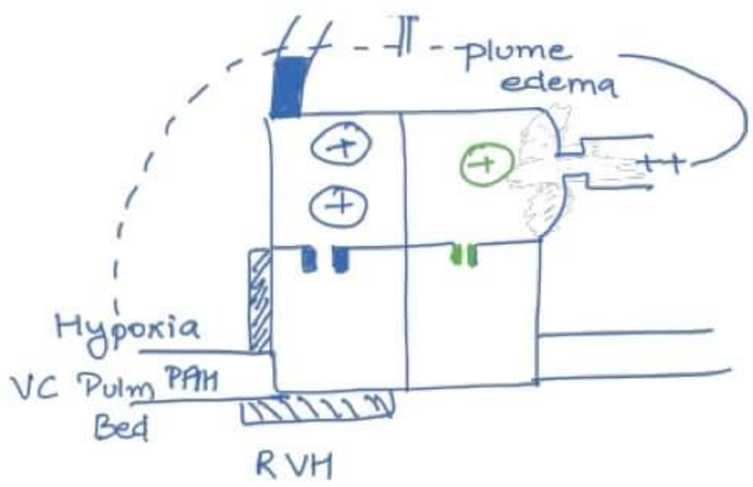
2 PS

3 MS (Long standing)

4 PAH → Fenfluramines

→ Eisenmenger syndrome/ complex

5. T.O.F (Subpulmonic stenosis)



Absent a → Atrial fibrillation **(Twitching)**

Extra mile

* Atrial fibrillation is the most common sustained arrythmia in clinical practice.
* P wave is absent in Atrial fibrillation
* A wave is absent in Atrial fibrillation
* S_4 is absent in a fibrillation

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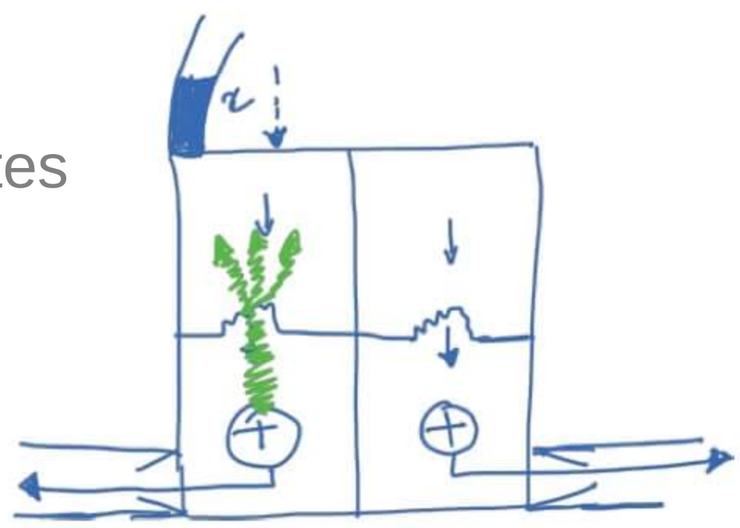


Giant A / Canon A Wave

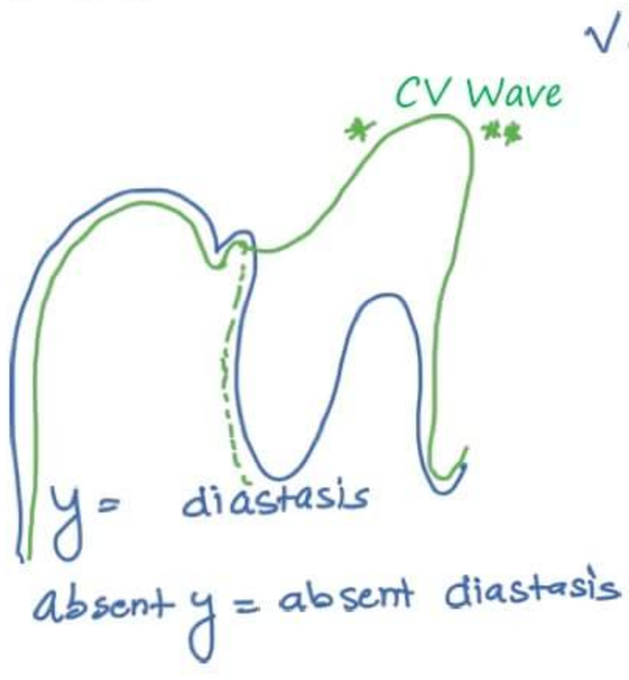
↳ A:V Dissociation

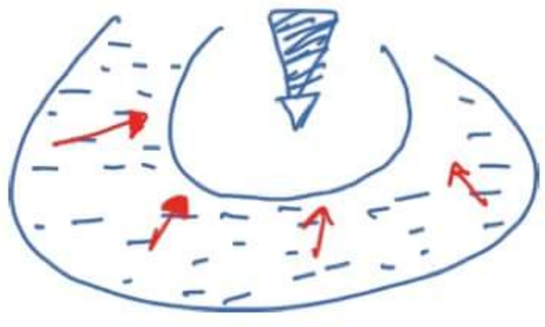
1.V. tachycardia — Complete / 3rd

2.Junctional Tachycardia — degree H. block

Absent X Descent → Tricuspid regurgitation

Absent Y descent → Absent diastole





Filling ↓↓

SV ↓↓

CO ↓↓

BP ↓↓ : Obstructive shock

PrepLadder

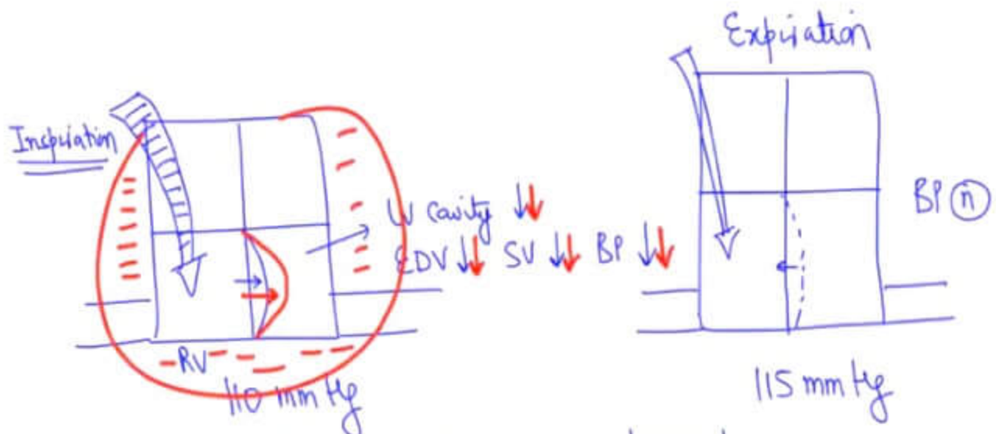
Cardiac tamponade:

P = Pulsus paradoxus

BP = ↓↓

S_1S_2 = muffled

JVP = y descent Θ



Reverse bernheim effect

- Normal difference in SBP is <10mm hg between inspiration and expiration.
- Difference > 12 mm Hg in SBP during Inspiration called as Pulsus Paradoxsus

JVP: Quick Summary

* a
  - **Large** = PAH
  - **Absent** = A. fib
  - **Super large A wave / Canon** = Ventricular /Junctional Tachycardia / 3rd degree H. Block

* **Absent x** = TR
* **CV, steep y** = TR
* **Absent y** = C. tamponade
* **Steep x, absent y** = C. Tamponade
* **Kussmaul sign** → CP, RCM, RVF
* **Steep x, Steep y** = C. Pericarditis

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PrepLadder

MITRAL VALVE PROLAPSE / FLOPPY VALVE SYNDROME / BARLOW SYNDROME

Ballooning of the mitral valve leaflets → pushed higher than its normal position during the phase of systole.

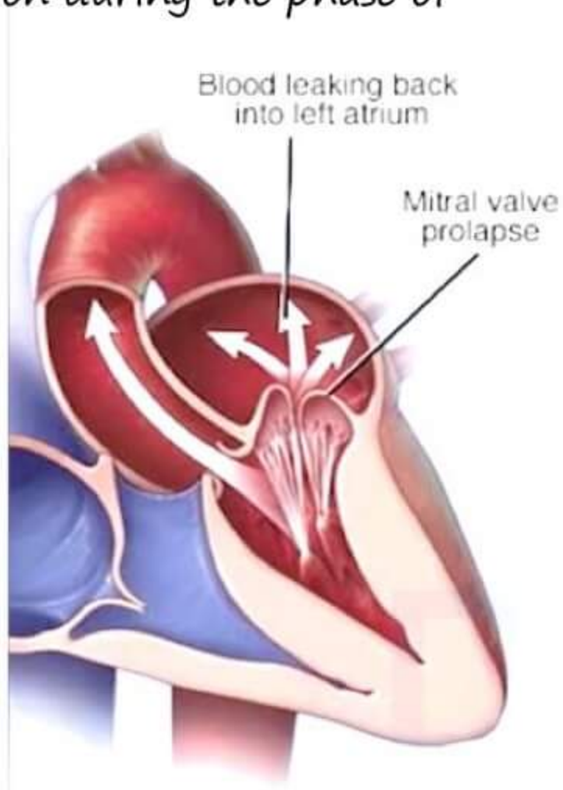
↓

Extra stress on chordae tendinae & papillary muscles

↓

Resulting in subendocardial ischemia due to stress at the subjacent myocardium and the repeated stress causes→ hypoxia → ischemia

Causes development of ventricular arrhythmias



Causes

1. **Myxomatous degeneration of mitral valve tissue**
   - Defect in **type III** collagen arrangement.
   - There occur broken myofibrils in valve tissue due to myxomatous degeneration of tissue.
   - End result is valve bulges up much higher causing development of murmur

   Complication: 1° mitral regurgitation

2. **Connective tissue disorder**
   a. **Marfan's syndrome**
      - Chr 15 defect
      - Defect in Fibrillin– 1
      - Characterized by arachnodactyly
        Thumb sign⊕
      - Mortality is mostly d/t Aortic dissection

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   b. **Rubberman syndrome/Ehler Danlos syndrome**

   c. **Osteogenesis imperfecta**

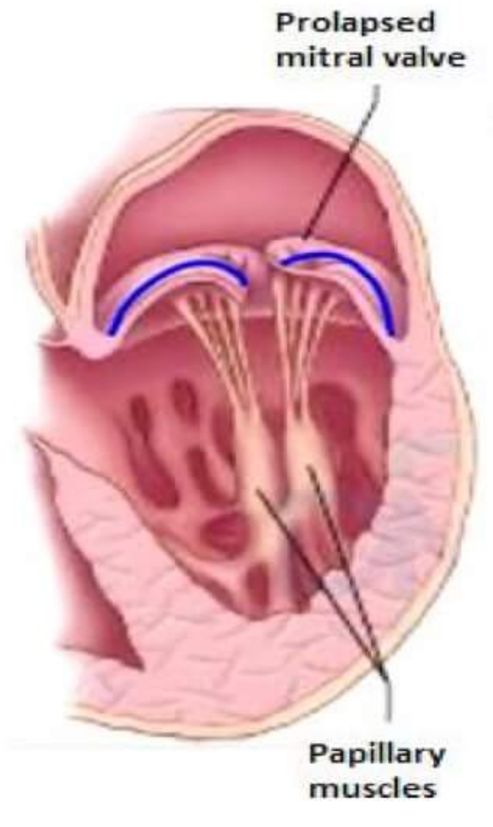
3. **Straight Back Syndrome**

- In this condition there is loss of thoracic kyphosis –antero- posterior diameter of chest is relatively lesser, so place available for heart is also less.
- Heart is sandwiched btw thoracic vertebrae, sternum and rib cage.

4. **Rheumatic fever (Aschoff body), SABE (vegetation), dilated cardiomyopathy, ASD**

Pathophysiology:

- Excessive stretching of chordae tendinae which are connected to papillary muscle, which will contribute to 2 things.



PrepLadder

i Auscultatory finding – **Mid Systolic click**

↓

Due to extra tension of chordae tendinae because of extra stretching and the max pressure develops in middle of systole so mid-systolic click is present.

ii Ischemic damage in subendocardial area causing further ventricular arrhythmias and patient complains of chest pain

Clinical features:

Mostly affects ♀: 15-30 years

1. **M/C symptom/ presentation** – asymptomatic, because it takes some time to develop
2. **C/O** - chest pain: substernal (d/t ischemia)
3. **Palpitations**: due to Premature ventricular contraction, V.T, PSVT, A. fib ++ because of structural dilatation of LA due to blood move from LV to LA.
4. **Infective endocarditis**
5. **Transient ischemic attack** (Due to platelet plugs/fibrin deposits can embolize to brain)
6. **Sudden cardiac death** => d/t MR/LVF

O/E:

On Auscultation, after **(S_1)** → f/b **Ejection click** → f/b **Mid Systolic clicks**

- D/T development of sudden tension in middle of systole in the slack chordae tendinae D/T myxomatous degeneration of them. Subsequently period these slack chordate tendinae may be damaged to such an extent that the frank MR will be developing in this patient of MVP and the blood leaks from LV → LA which causes LVF later on in these patients.

-The sound of this blood leaking will be heard after the mid systolic clicks- **Late systolic crescendo-decrescendo murmur.**

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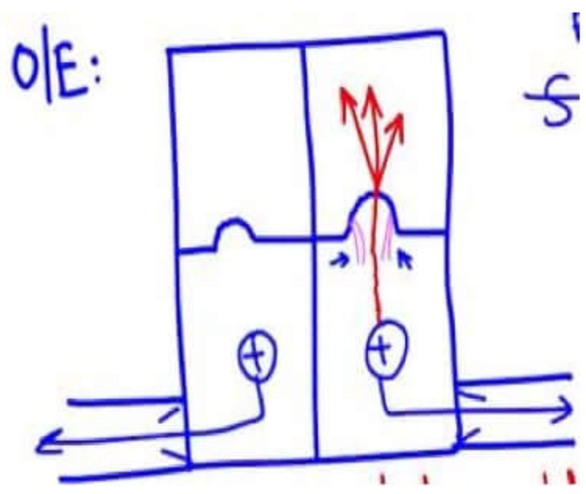
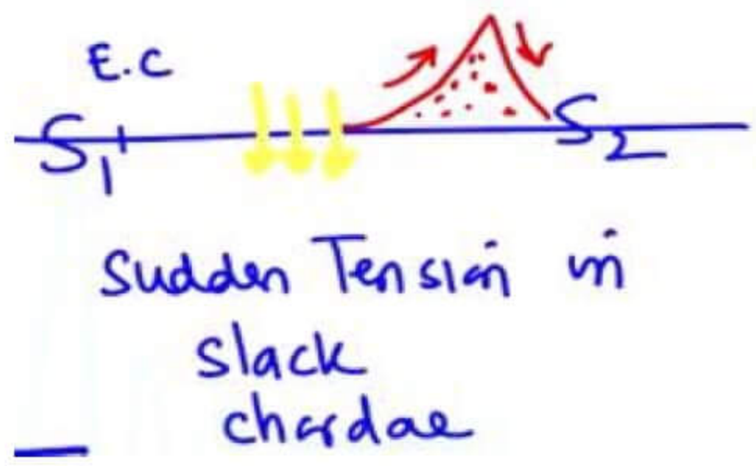
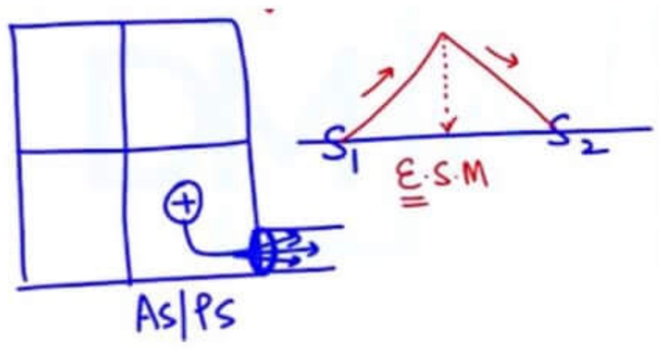




DDX of **MVP murmur** is **AS/PS murmur**, but the murmur is **Ejection systolic murmur** (Crescendo decrescendo), it starts right from S1 and peak intensity is coming back in the middle of systole.



PrepLadder

Note:

Mostly the Posterior leaflet is involved in mitral valve prolapse

↓

Regurgitation of blood is anteriorly (Vice versa in anterior leaflet damage)

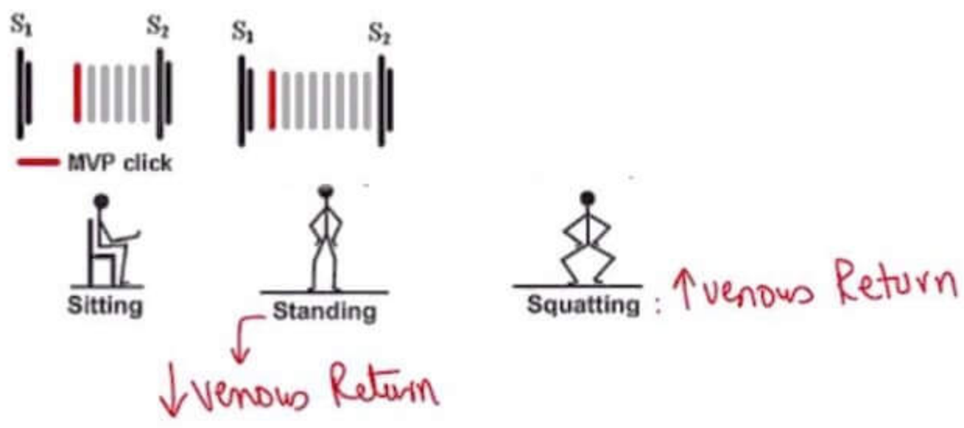
↓

Murmur radiation to base of heart

- However, if anterior leaflet is damaged then jet of blood will be directed posteriorly and radiation of murmur is towards- Axilla/ back (**Murmur of MR also radiates to axilla/back but it is pansystolic**)

Effect of posture on MVP Murmur.

$$\text{Prolapse } \alpha \frac{1}{\text{Size of Cavity of LV}}$$



On standing: ↓ venous return

Cavity size ↓:

MVP ↑: Mid systolic click (Earlier)

On squatting: ↑ venous return

Cavity size ↑:

MVP ↓: Mid systolic click (Later)

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Conclusion:

- Duration of murmur changes with position
- All murmur decreases in intensity with Valsalva, standing, amyl nitrate inhalation except HOCM (Louder) & mitral valve prolapse (Longer)

Work up of patient of MVP:

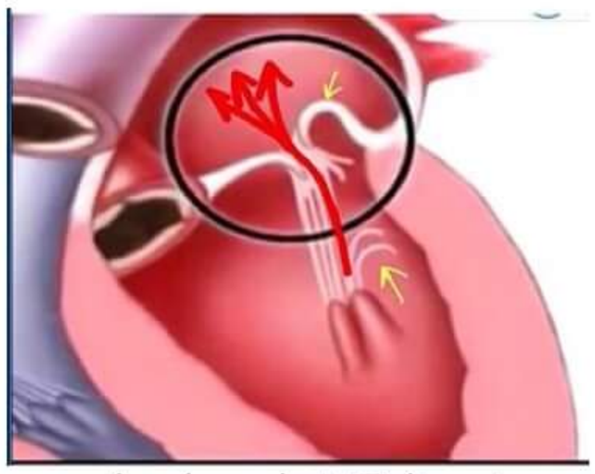
1. **ECG**: Premature ventricular contraction
2. **ECHO**: To demonstrate bulge of valve, if bulge ≥ 2 mm (Compared to tricuspid valve), late systolic murmur

Treatment:

1. 1° prophylaxis for Infective endocarditis
2. β-blocker (For palpitations)
3. If A. Fib occurs: Anticoagulants are required
4. In case of MR – MV repair is needed

PrepLadder

MITRAL REGURGITATION (MR)



- MR is due to damage of chordae tendinae
- Mitral valve prolapse is mostly associated with MR
- Defective coaptation of valves causes regurgitation of blood to L atria and cause LA enlargement
  -Murmurs of acute and chronic MR are diff.
  -Acute MR causes sudden exposure of large amount of blood to LA leading to left sided heart failure and requires Sx repair whereas in chronic MR it gets adjusted to it, so presentation of both may vary
  - whereas the MS causes right ventricular hypertrophy as a sequalae
- Characteristic - systolic murmur

Causes of Acute Mitral Regurgitation:

1. Infective endocarditis
2. Papillary muscle damage due to MI
3. M/C involved posteromedial leaflet (>>anterolateral leaflet) because of single blood supply
4. MVP / Flail leaflet (Myxomatous degeneration)
5. Blunt trauma to chest - Commotio cordis (Due to V. fibrillation) causing "sudden cardiac death".

Causes of Chronic Mitral Regurgitation:

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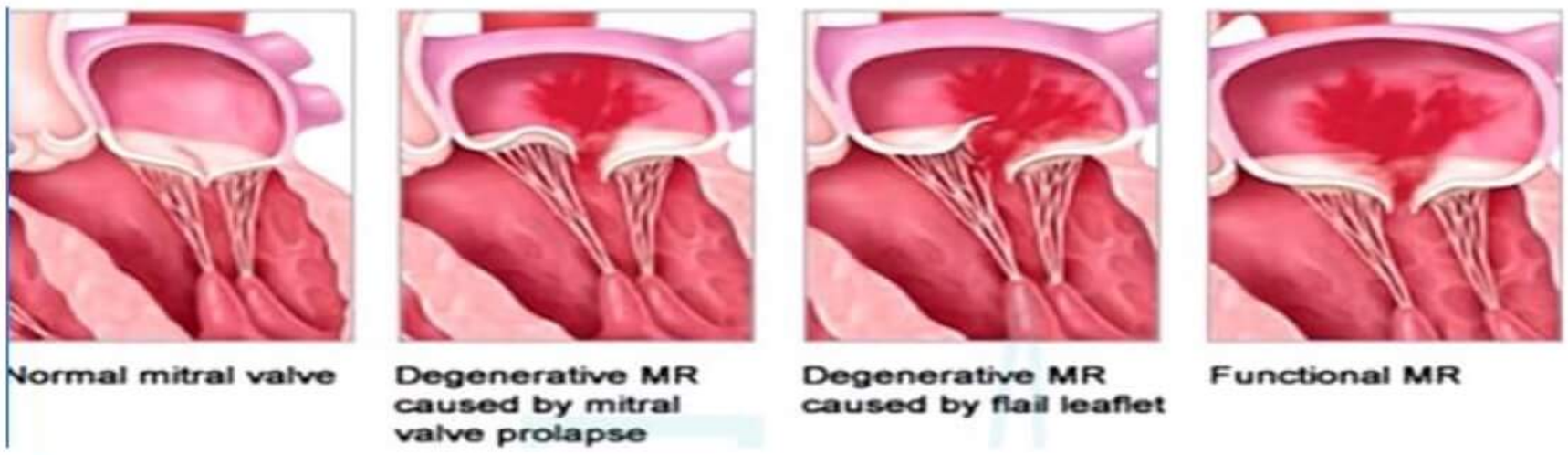
1. MVP
2. Rheumatic: Scarring of leaflets valves
3. SABE
4. Congenital cause: Cleft mitral valve – d/t ostium primum ASD

Chronic MR:



Primary– Intrinsic damage to valve- IE, MVP, radiation, o. primum

Secondary– DCM, ischemic cardiomyopathy, HOCM (Systolic anterior displacement of mitral valve

- In chronic cases atrial fibrillation and left atrial enlargement are seen

M/C characteristic finding occurring in secondary varieties –Mitral annular dilatation

Extra Mile:

→ Mitral annulus calcification can result in both (MS & MR)

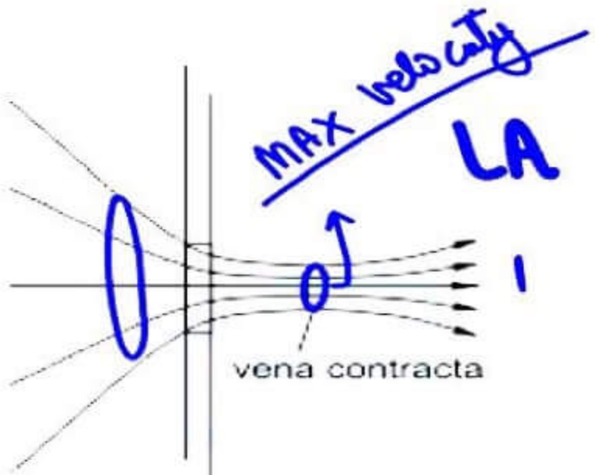
→ SLE & RA associated with mitral stenosis

→ Ankylosing spondylitis (HLA B27), syphilis – Aortic regurgitation

PrepLadder

Note:-

- MR severity is directly proportional to vena contracta.
- Vena contracta – narrowest part with highest velocity of regurgitant jet of blood from LV to LA

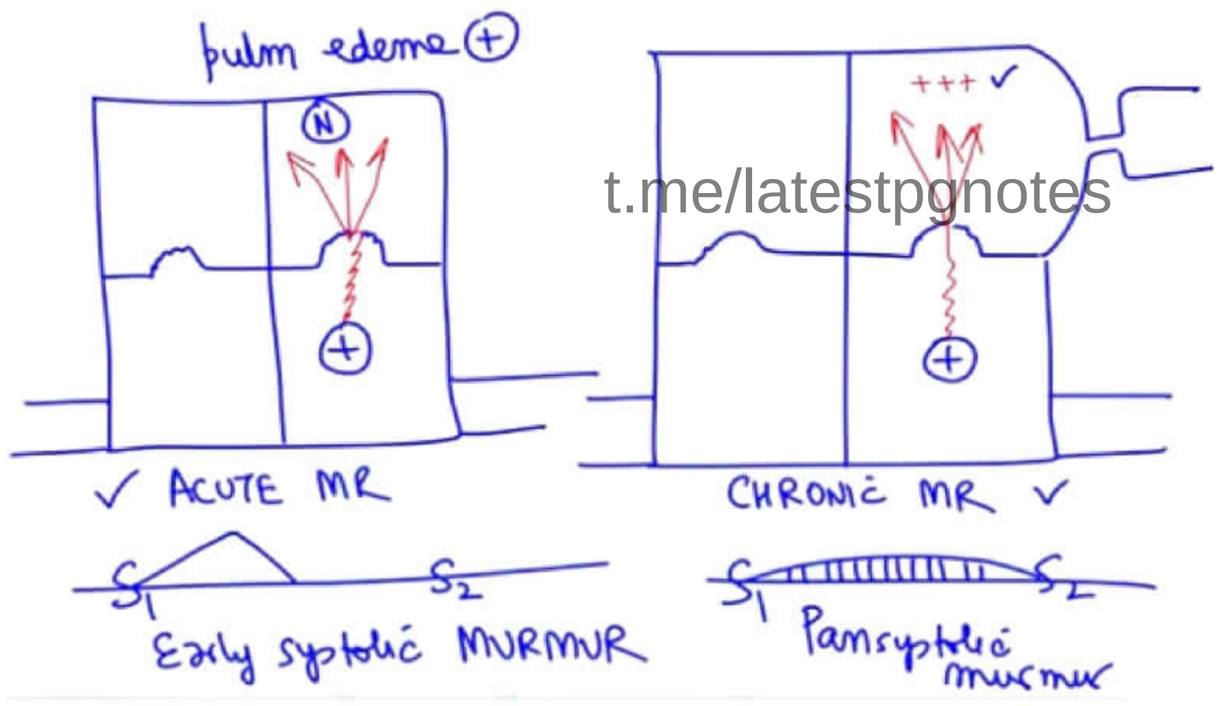


Criteria for severe MR:

1. Vena contracta: >0.7 cm2
2. Regurgitation volume: >60 ml / beat
3. Regurgitation fraction: >50%
4. Regurgitation orifice:->0.4 cm^2

Severe MR is treated by - Mitral valve repair – mostly preferred & superior over mitral valve replacement

Acute MR	Chronic MR
Heart size Normal	Large
LA-Normal	Enlarged
Pulmonary Edema +	Pulmonary edema ±
Early systolic murmur	Pansystolic murmur



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Imp one liners:

- Late Systolic Murmur – MVP
- Ejection systolic murmur – Aortic stenosis

(**Crescendo-decrescendo Murmur**)

C/F:

1. Mild – moderate MR is well tolerated
2. Fatigue, PND (Paroxysmal nocturnal dyspnoea), orthopnoea, hepatomegaly, ankle edema, ↑↑ JVP, TR
3. Palpitation – is caused due to AF, and longstanding AF results in formation of clots/Emboli (If clots/emboli goes to brain → can lead to stroke and may prove to be fatal)

PrepLadder

O/E:

1. BP- Normal
2. Thrill + at apex on palpation
3. Hyperdynamic character at apex
4. Displacement of apex

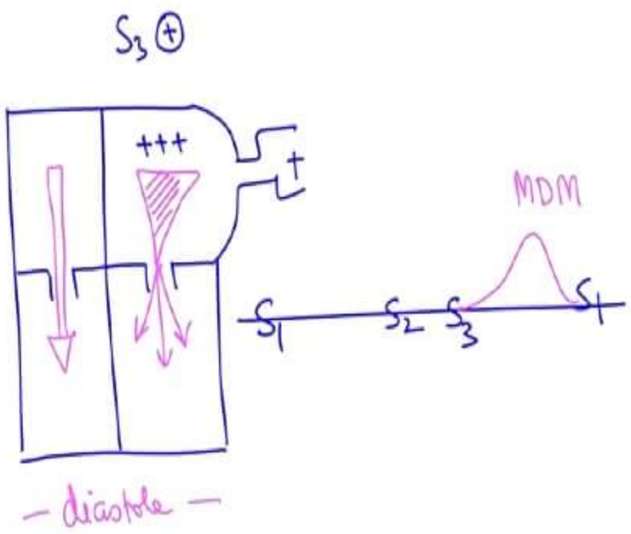
Auscultation:

- S1 – Soft
- S2 – A2 P2 (A2 appears early)

↓

Wide variable split S_2

- S3 – present, diastolic murmur heard – MDM



WORK UP-

1. ECG –

   P- Mitrale:>120 msec

   - Left axis deviation

Extra points:

→ P- Pulmonale – vertical height is > 2.5 mm – RA enlargement

→ Variable amplitude of p wave – multifocal atrial tachyarrhythmias

2. CXR

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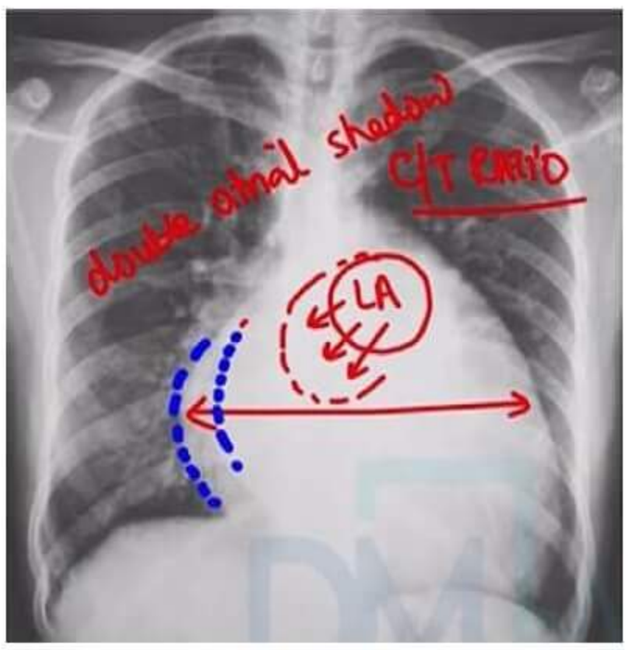
- Cardiothoracic ratio increased – cardiomegaly

  (>0.5- adults, >0.6- children)

- LA enlargement leads to pushing of rt. atria leading to double atrial shadow
- Mild pulmonary congestion with perihilar shadow
- Pulmonary edema – **Kerley B line**
- Walking man sign on lateral view

  (Enlarged lt. atria causing enlargement of carinal angle)



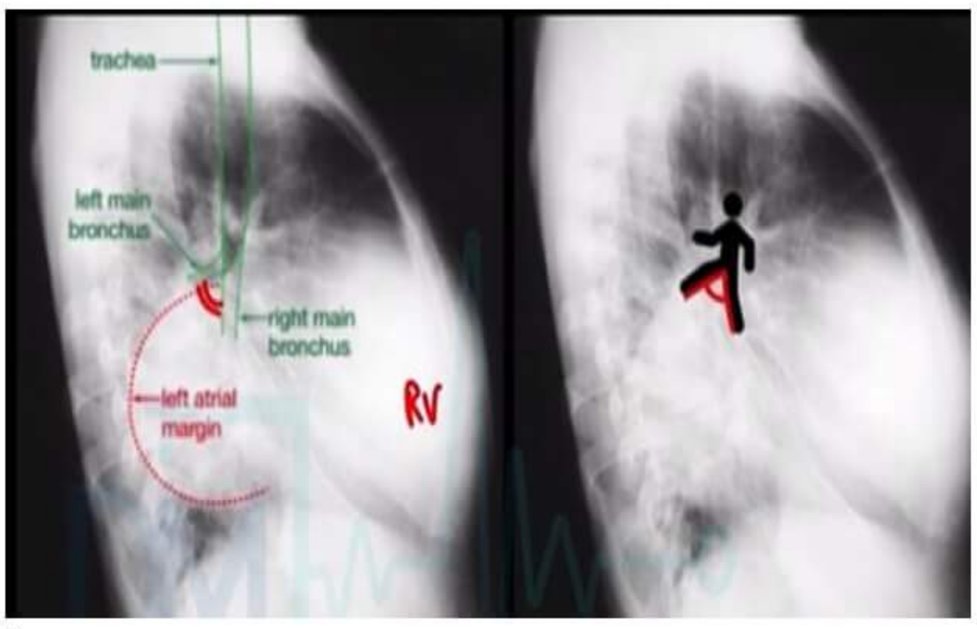
IOC: ECHO

Rx:

Acute MR:

1. Furosemide
2. Sodium Nitroprusside

   (Used in acute onset sudden decompensation that leads to LVF to prevent sudden stress on heart)



PrepLadder

Chronic MR:

Mitral valve repair

- 1. Annuloplasty ring
- 2. Neochords (New chordae tendinae)
- 3. Chord transfer

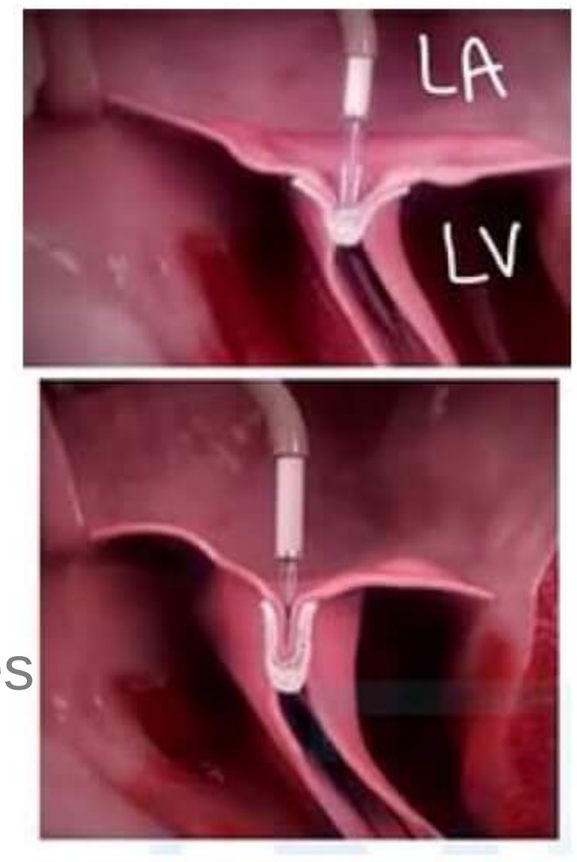
(Mitral valve repair >> mitral valve replacement, as it requires lifelong antiplatelet therapy, which can precipitate warfarin toxicity)

Indication of Mitral valve Repair:

1. Symptomatic severe chronic MR
2. In asymptomatic chronic MR done only if
   a. LVEF < 60%
   b. LVESD >40 mm

Q. New approach:

Trans catheter Mitral valve clip



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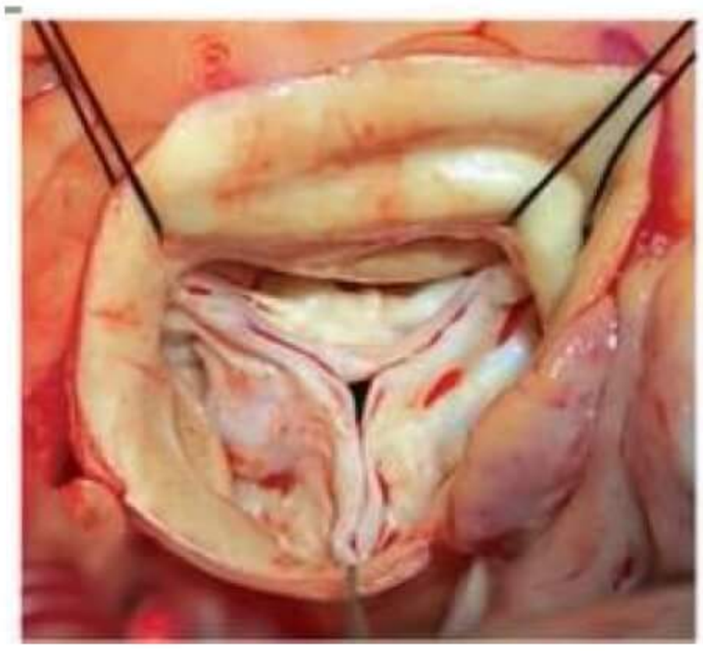
PrepLadder

AORTIC STENOSIS

→ Overall M/C congenital heart **valvular** lesion

→ Most common congenital heart **disease** → Peri membranous Variety of VSD



Normal aortic valve (tricuspid)

(Cross-sectional view)

→ Damage of valves can be due to various causes such as

- Senile Calcification
- Scarring due to RHD

→ Damaged valve can't open & close properly thus leading to aortic stenosis and aortic regurgitation respectively (i.e. defect in valve opening leads to AS & defect in valve closure leads to AR)

→ Etiology of AS

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1. Pediatric presentation→ **Bicuspid Aortic valve**(M/C CVS lesion in Turner syndrome)/ Unicuspid aortic valve.

   -Unicuspid Aortic valve causes more severe disease as compared to bicuspid variety as the ability of valve to allow left ventricular blood to aorta is severely hampered

2. Old age/ senile presentation

→ Degenerative calcification (Associated with atherosclerosis– it leads to involvement of abdominal aorta/root of aorta and the area around the aortic valve-**Fibro calcification** of aortic valve.

→ As the disease progress, there is differentiation of **Fibroblasts / Myofibroblast** into **Osteoblasts**, leading to deposition of bone matrix in valve → **Calcification of valve**

→ **Balloon dilatation & balloon valvoplasty is C/I** in these patients with calcified valves as balloon dilatation would lead the calcified valve cusps to break into small fragments that may get lodged into brain resulting in development of **stroke** in the patients.

3. Rheumatic Fever→ causes commissural fusion & scarring of valve cusps

[Normal aortic valve surface Area → 2.5 – 3 cm^2 & when the surface area of aortic valve is <1 cm^2 leads to **severe AS**]

4. Radiation

e.g. **Mediastinal Radiation** (Radiotherapy) given to a patient of Hodgkin's lymphoma for **hilar lymphadenopathy** or **chest radiotherapy** given to a patient of **breast cancer**.

5. **Shone complex** → Associated with Pediatric AS

PrepLadder

Components of Shone complex

a) Parachute **mitral** valve

b) Supra valvular **mitral** membrane

c) Subvalvular **aortic stenosis**

d) Coarctation of aorta

Extra Edge

Common heart lesion seen in patient of Turner syndrome → Bicuspid aortic valve (MC)>Coarctation of aorta

HOCM is associated with SAM (Systolic Anterior Displacement of mitral valve)

Clinical Features of AS:

→ Male: Female = 2 - 4:1

→ **Bicuspid aortic valve** has **AD** pattern of inheritance

→ **Gene involved** → **NOTCH 1 gene**

→ In old age/ geriatric population → Hypertension may lead to AS.

Symptoms

Triad of AS

S → **Syncope** (On exertion)

A → **Angina** (Secondary to LVH)

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D→ **Dyspnea** (Secondary to increase LV end diastolic pressure)

LV End Diastolic Pressure (LVEDP) increases as a result of hypertrophy of LV

↓

Leads to increased left atrial pressure

↓

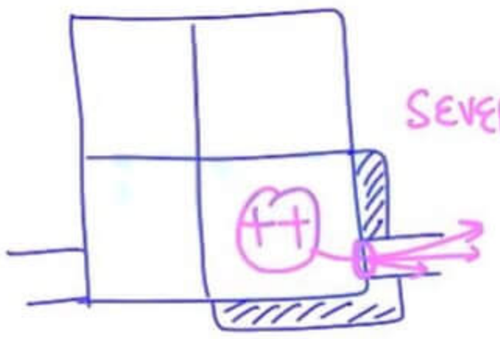
Leads to congestion in lungs & pulmonary edema

↓

Leads to dyspnoea

On examination

1. **Pulsus parvus at tardus - Slow rise pulse** with **delayed peak.**
2. **Anacrotic shudder/carotid thrill** → due to ↑ in ejection velocity



In severe AS

→**Aortic valve area** < 1 cm^2

< 0.6 cm^2/ m^2 BSA (Body Surface Area)

→ Left ventricle has very high pressure. When the blood from LV passes via stenosed aortic valve, there is very much increased turbulence in blood flow.

→ **Volume** of blood going from LV to aorta is **decreased** but **velocity** of blood flow is **increased**

PrepLadder

3. Apex Beat

- Is always displaced
- **Double apical impulse** (Secondary to hypertrophy of LV)

Character → **Heaving** (i.e. impulse hits your finger & lifts it up)

Displacement → To **left** side

- Felt in **both 5th & 6th left intercostal space (ICS)** as it is **double apical impulse.**

4. S_2→ **Narrow split S2** (Narrow as gap b/w A_2 & P_2 is < 30 millisecond)

- **Paradoxical split** i.e. P_2 comes before A2 [Means pulmonary valve has closed on time but aortic valve is closing late i.e. after the pulmonary valve]

6. S_4→**Present**

As patient of AS also have **compensatory left atrial hypertrophy**

↓

Left atria generate more pressure to propel blood into left ventricle

↓

S4 is produced

[If this patient of AS goes to heart failure then S3 would also be ⊕nt. However, initial presentation is S4]

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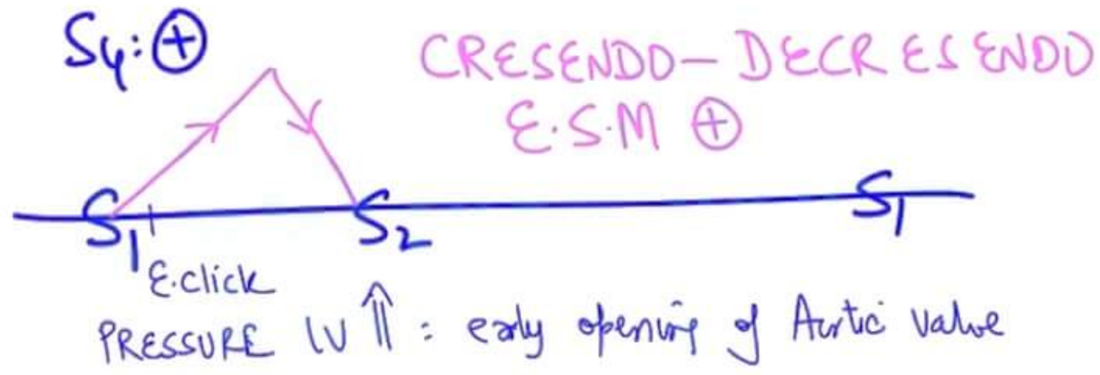
6. Murmur: **Ejection systolic murmur**

→ AKA **crescendo – decrescendo murmur**



7. The murmur of AS radiates to **Carotid artery** known as Carotid Thrill

8. Vibrations of valvular cusps when blood passes from **aortic annulus** leads to murmur to radiate into **Axilla** (K/A Gallaverdin Phenomenon) This radiation into axilla can lead to confuse aortic stenosis with mitral regurgitation as murmur of mitral regurgitation also radiates to axilla.

Work-up of a patient of Aortic stenosis

1. ECG

WORK UP

ECG

$SV_1 + RV_{5|6} > 35mm$

ECG findings

→ Very deep S waves in lead V1

→ Very Tall R waves in lead V5

$[(SV_1 + RV_{5/6})] > 35$ mm is the criteria to call it **Left Ventricular Hypertrophy**

PrepLadder

strain pattern T wave inversion seen in V5 & V6.

2. CXR (Chest X-ray) findings

→ Shows **cardiomegaly**

→ **Cardio – Thoracic ratio** in **increased** (↑ CT ratio)

3. ECHO

→ Used to see valvular morphology

Valve size	Grade Of AS
< 1.5 – 2 cm^2	Mild AS
< 1.0-1.5 cm^2	Moderate AS
< 1.0 cm^2	Severe AS

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4. IOC to see any valvular calcification → CT chest

→ **Coronary Angiography** should also be done in patients of aortic stenosis as most of patients are of old age/ geriatric population & atherosclerosis is very common in these old age patients

→ **Treadmill test and dobutamine stress ECHO are not done** in patients with **severe** aortic stenosis

→ Death in patients of aortic stenosis

- If **syncope/ angina** is present as a symptom → death within **3** years
- If **dyspnea** is present as a symptom → death within **2** years
- If **Congestive Heart Failure (CHF)** Present → death in **1.5-2** years

Highest chances of death seen in patients with Congestive Heart Failure (CHF)

Treatment of valvular aortic stenosis

→ **Treatment is stage based**

Stages of AS

Stage A

→ Risk factors present

→ No narrowing of valve

Stage B

→ Progressive narrowing of valve → (i.e. mild to moderate aortic stenosis)

Stage C

→ Severe aortic stenosis but patient is asymptomatic

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Stage D

→ Severe aortic stenosis & patient is **symptomatic**

Severe aortic stenosis

Definition:

1. Transvalvular pressure gradient of **> 40 mmHg**.

Transvalvular pressure gradient (ΔP) = LV – Aorta

= Pressure difference b/w left ventricle & aorta

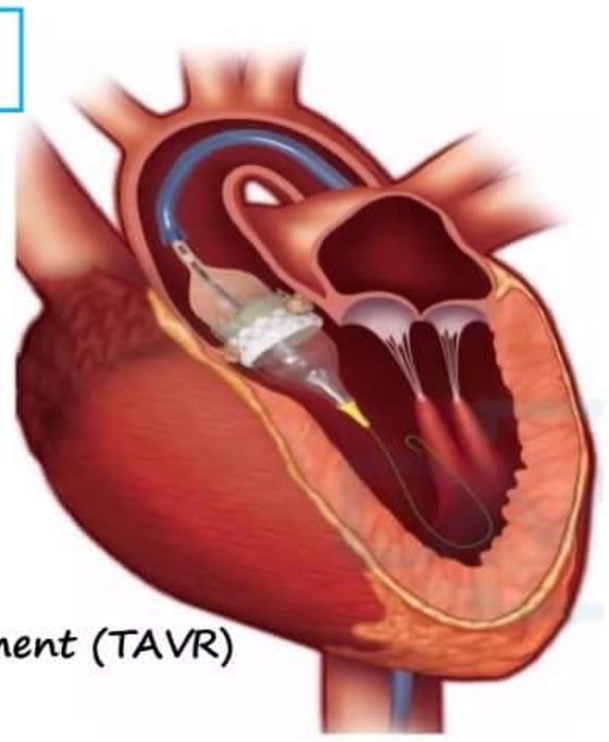
2. Ejection velocity → **>4m/sec** [i.e. 4 times of Normal]

[**Normal Ejection velocity → 1m/sec**]

3. Size of orifice → **< 1 cm^2 / < 0.6 cm^2/ m^2 BSA**

(**BSA** → Body surface area)

Any of these 3-terminology written in MCQ means severe aortic stenosis



Treatment

For stage D→ **Trans catheter aortic valve replacement (TAVR)**

For stage C

- If patient has concomitant risk factors like
  - Concomitant Triple Vessel Disease (TVD)
  - Left ventricular ejection fraction < 50%

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→ In these conditions, treatment is again **Trans catheter aortic valve replacement (TAVR)**

→ Statins are given to prevent further progression of Atherosclerosis & thus Triple Vessel Disease

→ Statins doesn't prevent further progression of calcification

AORTIC REGURGITATION

→ Valvular lesion of aortic valve

↓

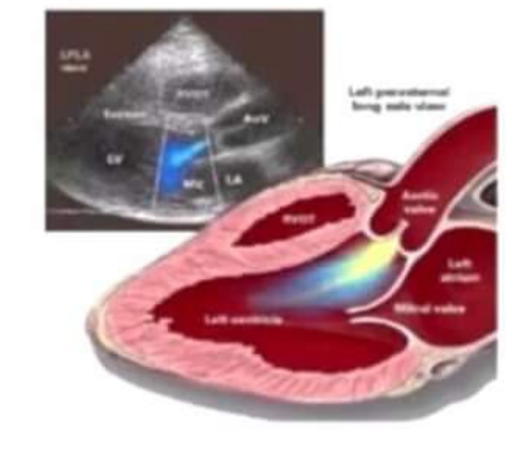
Incompetent valve

↓

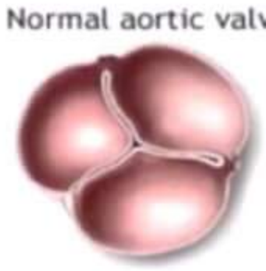
Turbulence created

↓

Diastolic murmur (Decrescendo)



Normal aortic valve



Bicuspid aortic valve

AR → Left ventricle pressure ↑↑

↓

Blood hit the anterior leaflet of mitral valve

↓

Vibrations produced

↓

Murmur

↓

Austin Flint murmur

Murmur of AR a) Diastolic murmur

b) Austin Flint murmur

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Causes of AR

1. Bicuspid aortic valve: defective coaptation
2. Infective endocarditis: perforation
3. RHD (Rheumatic Heart Disease)
4. Myxomatous degeneration of valve
5. Syphilis
6. Ankylosing spondylitis
7. Aortic root dilation
   a) Aortitis
   b) Aortic dissection
   c) HTN
   d) Cystic medial necrosis
   e) Marfan syndrome

→ **Severe AR** → Regurgitant volume **> 60 mL/beat**

→ **Progressive AR** → LVEF **< 50%**

(Left Ventricle End systolic dimension) LVESD **> 50 mm**

(Left Ventricle End diastolic dimension) LVEDD **> 65 mm**

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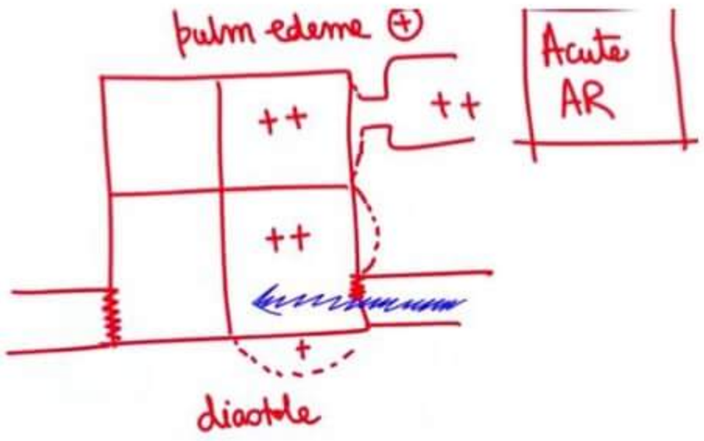
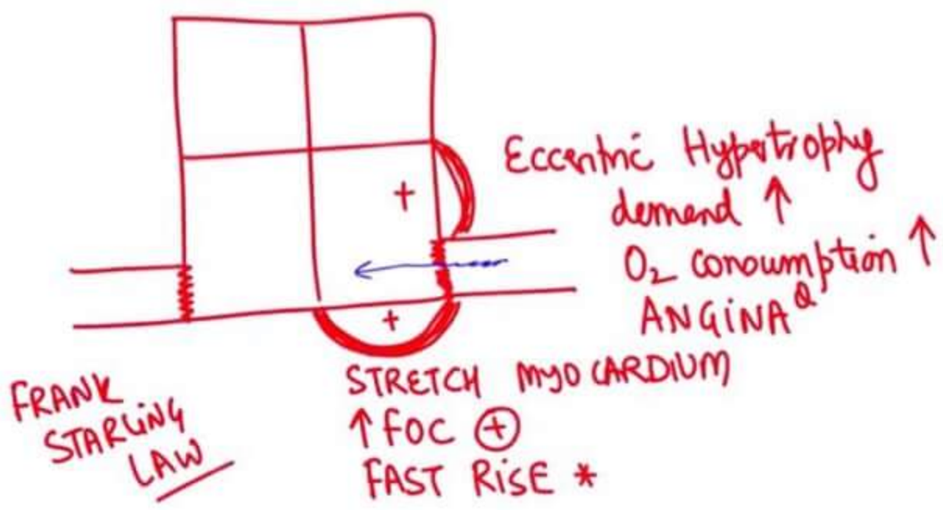


Acute presentation (e.g. Infective Endocarditis)



(Chronic presentation)

Pulse → Corrigan's pulse water hammer pulse

Clinical features:

1. **Angina** → in later stages

↓

Eccentric hypertrophy

↓

Demand ↑↑

O_2 consumption ↑↑

} Mismatch b/w demand & supply → Angina

2. Uncomfortable sensation in supine position
3. Head pounding sensation
4. Development of exertional dyspnea
5. Paroxysmal nocturnal dyspnea
6. Orthopnea / diaphoresis
7. Angina – May be present at rest or on exertion

Sx should be done with 1 year of symptom onset for faster recovery.

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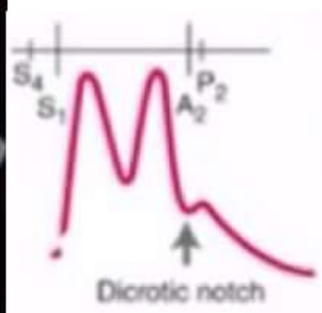
Examination Findings



1. **De-Musset Sign** → Head bobbing to and fro
2. **Muller sign** → Pulsation of uvula
3. **Marfan's** – **Arachnodactyly** (Thumb Sign)

   Ankylosing spondylitis → Schober's test

PrepLadder

4. **Corrigan's pulse /Water hammer pulse/Collapsing pulse**

↓

According to Frank Starling law, as end diastolic volume of LV increases, the force of contraction of LV increases. Seen on arm elevation above level of head.

5. **Quincke's sign** → Flushing and blanching at distal part of nail

6. **Traube Sign** → Pistol shot sounds heard at femoral artery

7. **Duroziez Sign** →

Gently press the femoral artery using stethoscope

↓

Murmur in heart d/t turbulence

↓

To and fro murmur

Extra Mile:

→ **Mill wheel murmur - heard in case of Air embolism**

8. Stroke Volume ↑↑ ┐ Explained by
↓ ├ a) Frank Starling Law
SBP ↑↑, DBP ↓↓ ├ b) Eccentric Hypertrophy
Pulse Pressure ↑↑ ┘

Low DBP values are seen in:

a) AR

b) A-V malformation

c) Aortic Dissection

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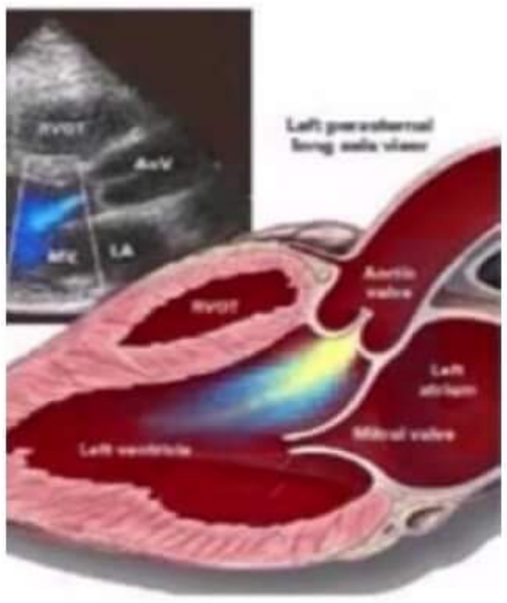
9. BP difference between UL (Upper limb) and lower limb **< 20 mm of Hg (N)**

BP difference **> 20 mm** of Hg is Abnormal and is called as **Hill sign**.



9. **Apex beat** → Heaving (Palpation)

10. **Thrill (Auscultation)** → **diastolic → left lower sternal border**

Systolic → Suprasternal notch.

(AR + AS)

11. S_2 → soft/ single S_2 = A_2 not heard

Ejection click is present if bicuspid aortic valve is present

12. S_4 → present → Left atrial enlargement

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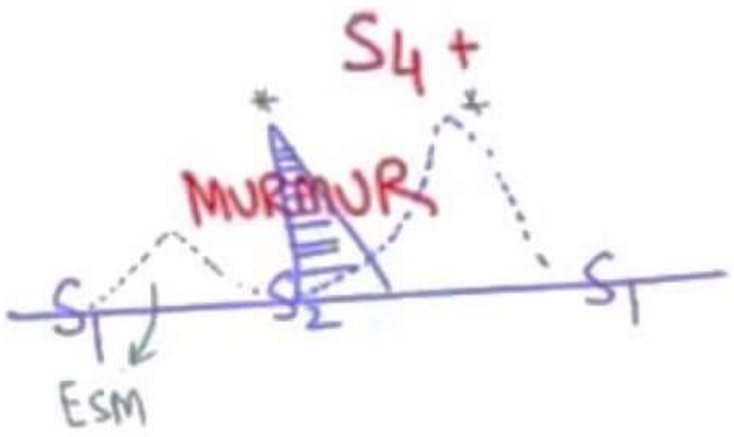
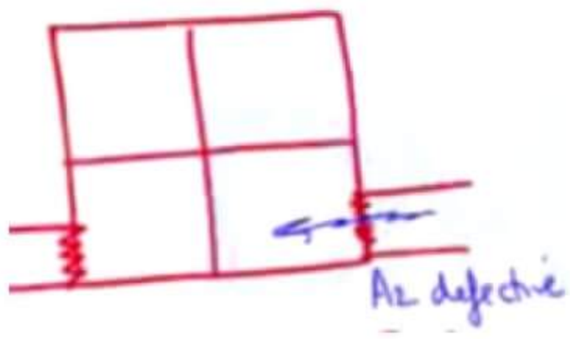
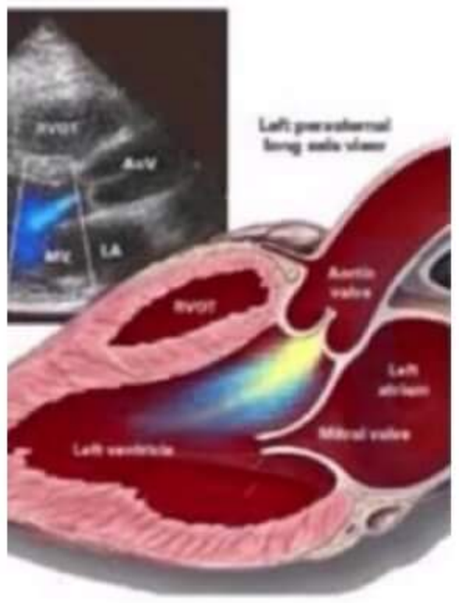
13. Murmur







High pitched **Decrescendo** murmur (Seagull murmur)

Austin Flint murmur → Mid Diastolic Murmur (MDM)

Murmur of AR

1. **Early Diastolic murmur** → Main murmur
2. **Mid Diastolic murmur** → Austin Flint murmur (RHD)
3. **Ejection systolic murmur** → If AS is co-existent

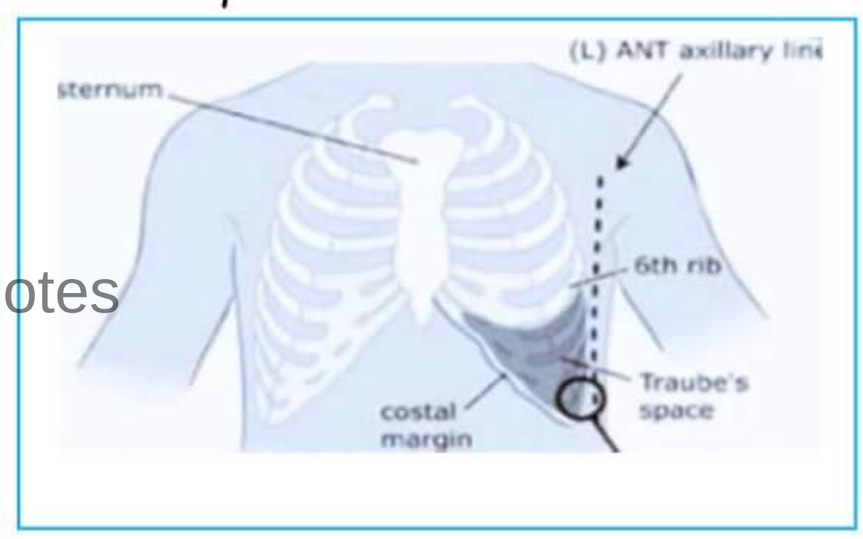
4. **Gerhardt's sign** → Pulsation in spleen
5. **Rosenbach sign** → Pulsation in liver

↓

Also seen in

1. TS (Tricuspid stenosis)
2. TR (Tricuspid regurgitation)
3. AR (Aortic regurgitation)

Traube's space



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Rosenbach sign of eye

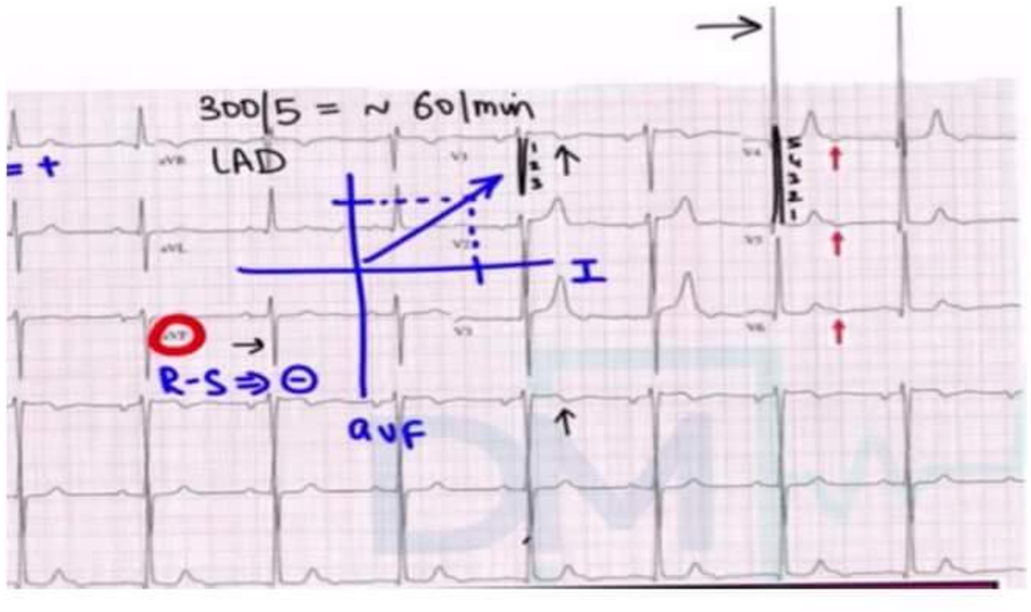
↓

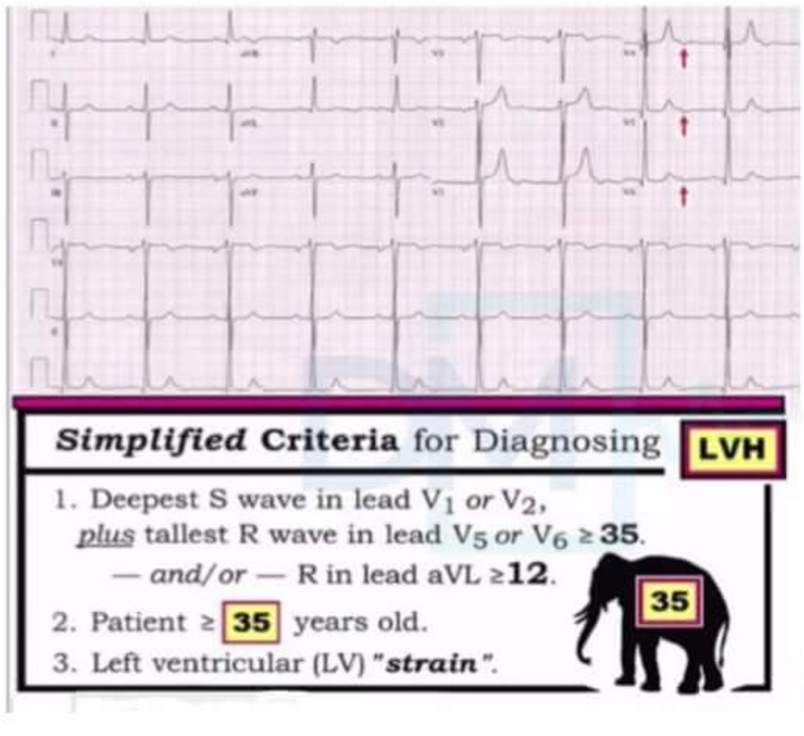
Seen **in Grave's disease** [Tremor of eyelid]

6. **Landolphi sign** → Pulsations in pupil

Work up

1. ECG– 1st line of investigation





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2. Echocardiography – IOC

Severe AR

Criteria

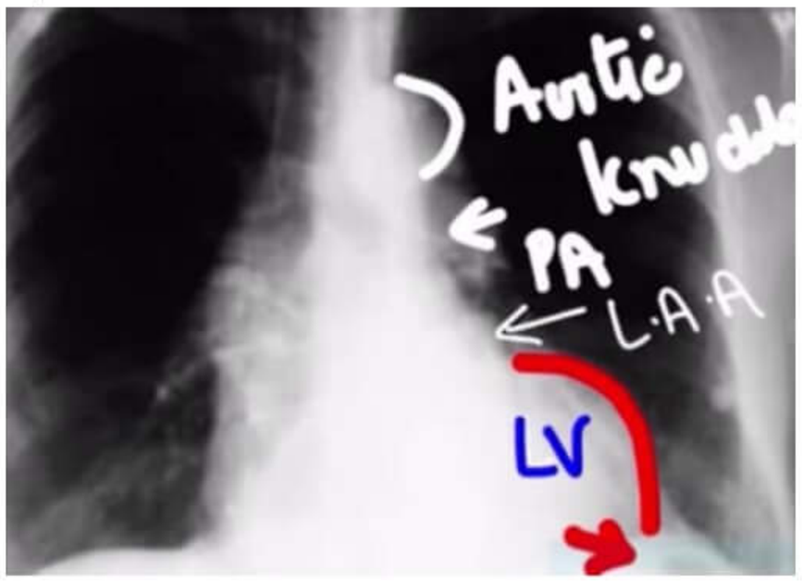
a) Width regurgitant jet > **65% LVOT**

b) Regurgitant volume > **60/ beat**

(Fraction > 50%)

3. CXR → LV enlargement

Apex → Inferolateral



4. **Coronary Angiography** – To know status of coronary arteries

TREATMENT

Acute AR:

a) Loop diuretics

b) Vasodilator – Na Nitroprusside

c) Surgical management within < **24 hours**

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Chronic AR:

a) Diuretics

b) ACE inhibitors

c) CCB

Keep SBP < 140 mm of Hg

→ **↑↑ Stroke volume**

a) Frank Starling law

b) Eccentric

BP = CO x P.R

CO = HR x SV

P.R → Peripheral Resistance

B.P → Blood Pressure

C.O → Cardiac Output

HR → Heart Rate

SV → Stroke volume

d) Nitrates – To treat angina

e) **Penicillin Benzathine → 2.4 MU i.m x 3 shots @ 1 week**

↓

For syphilis

PrepLadder

Extra Mile:

1. β-blockers → absolutely contraindicated in **acute AR**
2. IABP – Intra-Aortic Balloon pump

↓ Contraindicated

↓ Worsens AR

TOC – Aortic valve replacement → Symptomatic

→ Indications of Aortic valve Replacement

a) Symptomatic severe AR
b) Asymptomatic severe AR
c) Symptomatic moderate AR

Surgery should be done with in **1 year.**

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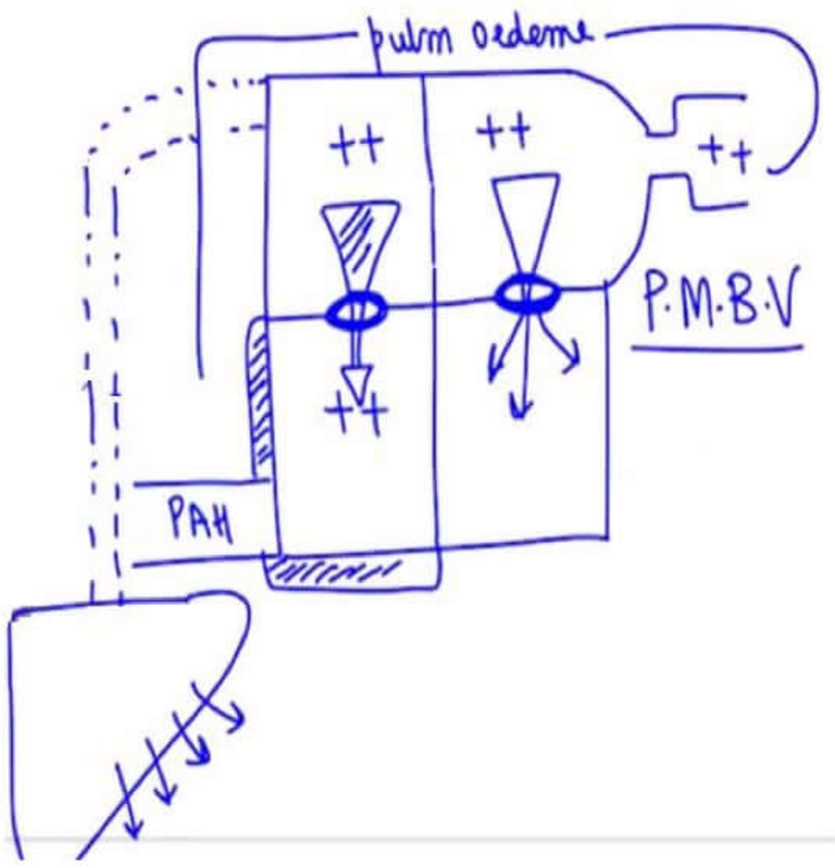
RIGHT SIDED VALVE LESION – TRICUSPID STENOSIS

- Tricuspid stenosis doesn't occur alone but occurs with Mitral stenosis.

In given diagram, both MS and TS diagram are narrowed. So, the amount of blood from RA to RV and from LA to LV is reduced. Mitral stenosis Contribute to left Atrial congestion. Most patients would have structural damage to LA & may cause Atrial Fibrillation



↓

Dilated Left atria transmits pressure to pulmonary veins

↓

Pressure to lungs

C/O Dyspnea on exertion & orthopnea (d/t pulmonary edema)

↓

Pulmonary Artery HTN

↓

Development of **RVH**

- In MS defect on left but hypertrophy seen with Rt. Ventricle,
- Tricuspid stenosis is like blessing in disguise, as it will prevent the transmission of pressure changes in backward direction because the orifice is relatively narrow. Thus the gradient between RA & RV will also change therefore, Back pressure changes, ie. The transmission of Mitral stenosis disease process to the Right side ie. Mainly transmission of pressure changes to SVC & IVC will be lesser, as tricuspid stenosis is acting like barrier.

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Rx of severe type of MS :

By percutaneous Mitral valve balloon valvotomy (PMBV)

↓

C/F of Pulmonary Congestion will disappear & now symptoms of Tricuspid will manifest & amount of blood from RA → RV will be lesser & there would be lot of congestion in RA

↓

Will translate into congestion in SVC & IVC

↓

As pressure transmitted downward to liver these pt will start developing

In a patient of both MS and TS, mostly the symptoms of MS will predominate.
Here, Initial symptoms are – Dyspnoea On Exertion, pulmonary oedema and orthopnoea
Based on it we make dx of MS on ECHO and TS may not be picked up as it may not be severe enough. Now we treat him as a severe case of MS, and after that the patient will still get features of right sided heart failure due to TS. **And he has Clinical features**: Hepatomegaly (Initially),

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Pedal edema and Ascites,

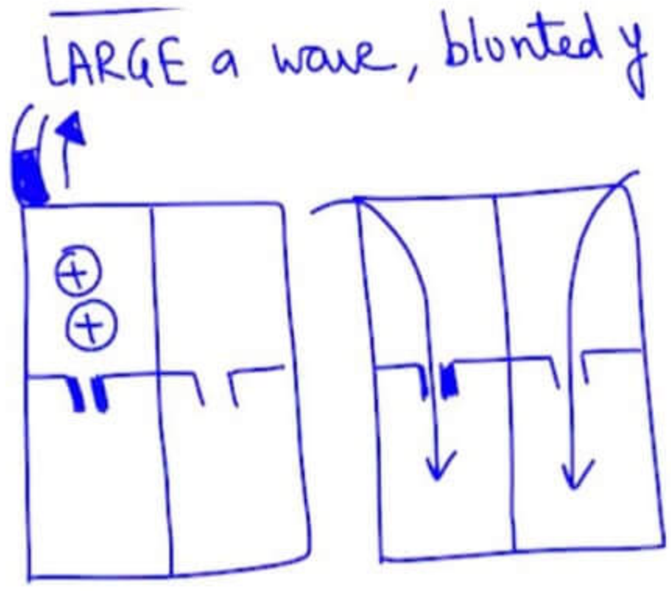
Cardiac cirrhosis (later), Caput Medusae

Here problem lies in the right side of heart

O/E:

1. **On ECG**: **large 'a' wave** (d/t tricuspid stenosis, the RA of pt has to generate more force to push blood in forward Direction)

   Blunted y descent (as stenosis filling in RV is relatively slower)



2. **Presystolic pulsation of liver** (C/F of TS)

   Note - systolic pulsation of liver seen in TR

3. **Murmur**:
   - D/T narrow opening → when blood passes through RA → RV, it creates turbulence
   - Mid diastolic murmur (like mitral stenosis)
     ↓
   - Becomes louder on inspiration
   - Heard on left lower sternal border & radiates to tricuspid area.

     Best appreciated close to xiphoid process.

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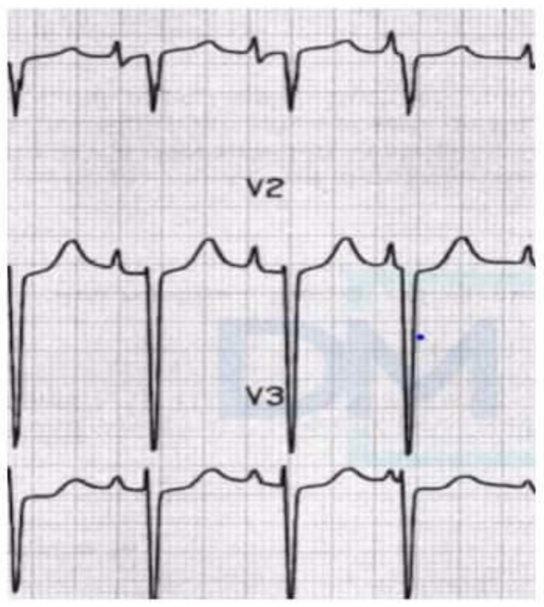
Note - All events on Rt side of heart become louder on inspiration

Work up:

1. ECG with simultaneous Echocardiography: Normal
   - Large P wave: **P- pulmonale** (Peaked p-wave)

     (in limb leads **>2.5cm**)

     (Chest leads **>1.5cm**)
   - Rt axis deviation



2. CXR - RA, SVC } More prominent, enlarged

   Shadow of **Azygous vein enlarged**.

3. **To confirm**: ECHO - Thickened valve. Severe if **<1 cm^2** (Size of orifice)

   Note for MS severe is **< 1.5 cm^2**

   ➢ Time taken by blood to travel from RA → RV will increase

   (Ie T >190 msec.)

PrepLadder

Rx:

- Salt restricted diet
- Diuretics - **Aldosterone antagonist**
- Valve repair (Main treatment)
- Prosthetic valve – metallic or prosthetic valve

  (Disadvantage of Metallic valve – lifelong Anticoagulant therapy needed)

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PrepLadder

TRICUSPID REGURGITATION AND PULMONIC STENOSIS

TR (Tricuspid Regurgitation)

- MCC of tricuspid regurgitation = Functional due to tricuspid annulus dilation
- Secondary causes

1. Severe Pulmonary Arterial Hypertension (Severe PAH > **55mmHg**)
   - Normal Pulmonary Arterial Pressure = 15mmHg
2. Right ventricular pacing
3. Carcinoid Syndrome

mnemonic=TIPS

Tricuspid Insufficiency **Pulmonic Stenosis**

(Two vascular lesions are seen in Carcinoid Heart Disease)

4. Rheumatic Heart Disease (RHD)
5. Radiation exposure
6. Endomyocardial fibroelastosis
7. Infective Endocarditis
8. Ebstein anomaly (Wolf Parkinson White syndrome)- Due to lithium

Symptoms

- Low cardiac output (Effort intolerance)
- Cervical pulsations
- Abdominal fullness
- Asthenia

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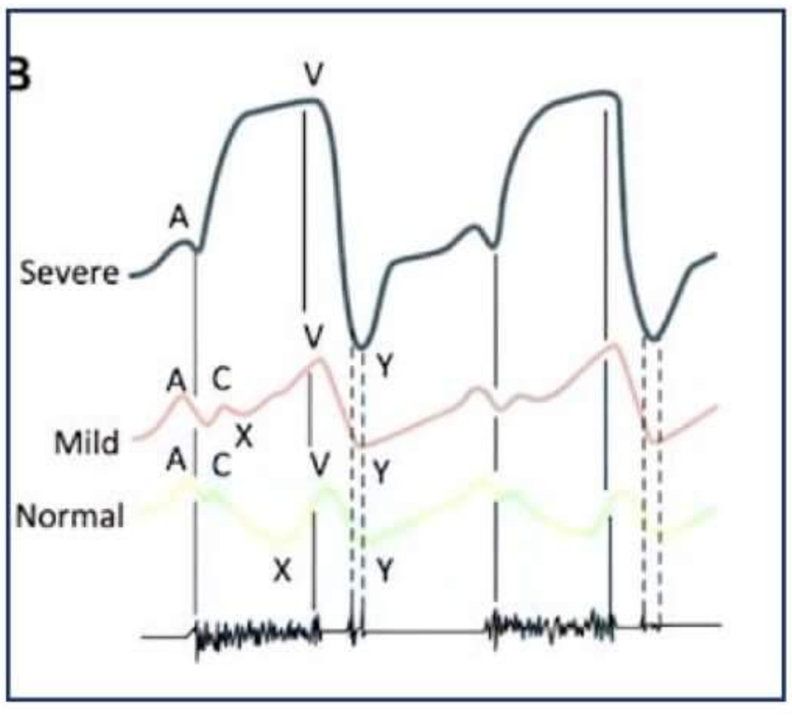
On Examination

- **JVP findings:** Absent x wave
  - CV wave (**LANCISI SIGN**)
  - Steep y descent
- Hepatomegaly
- Pulsatile liver
- Pansystolic murmur
- Right sided event increases during inspiration
  - Pan systolic murmur increases with inspiration (**CARAVALLO SIGN**)



PrepLadder

WORK UP OF THE PATIENT WITH TRICUSPID REGURGITATION

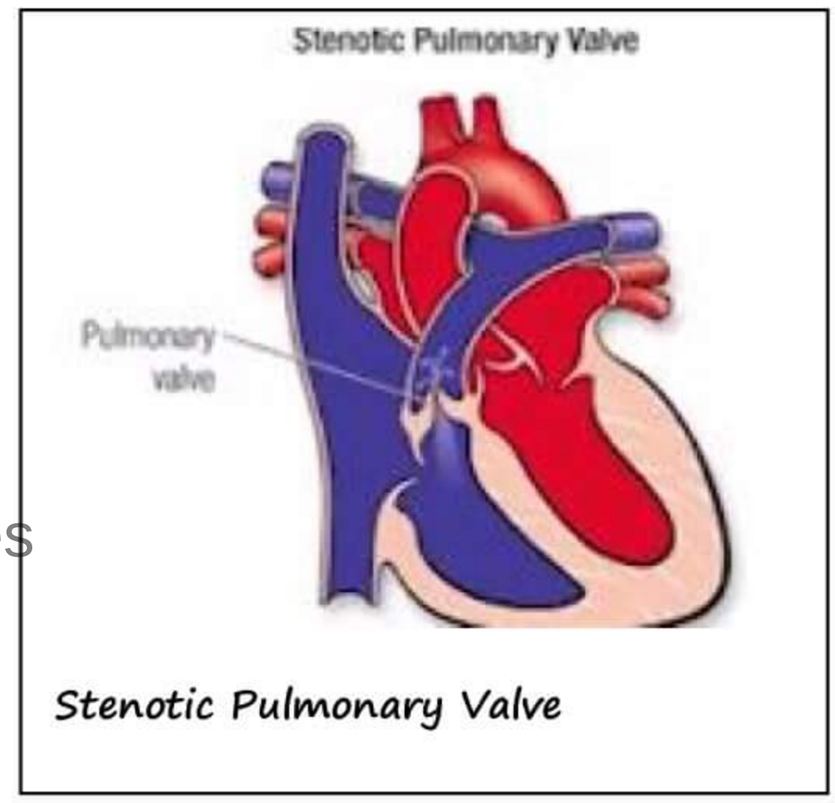
1. **ECG** →Right axis deviation
   P – pulmonale
2. **Chest X-ray** → Cardiomegaly (CT ratio ↑)
   Pulmonary artery segment prominent
   Right atrial enlargement
3. **Echocardiograph**
   - Blood flows from right ventricle to right atria.
   - Reversed systolic flow in the hepatic vein.

Treatment

- Diuretics
- Surgery → Tricuspid valve repair
  Tricuspid valve replacement

Pulmonic Stenosis

- Common in pediatric age group
- Causes–
  1. Congenital
  2. Dysplastic pulmonary valve (**Noonan Syndrome**)
     - **Noonan Syndrome** looks like Turner syndrome except Noonan is **chromosome 12 defect** and Turner is aneuploidy **(45XO)**
     - **Turner Syndrome** (M/C heart lesion) = Bicuspid aortic valve
       (2^{nd} M/C) = Coarctation of Aorta
  3. Carcinoid Syndrome (T.I.P.S)
  4. Rheumatic Heart Disease (Rare)



Stenotic Pulmonary Valve

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Severe Pulmonary Stenosis (> 50 mm Hg)

- Based on pressure gradient

↓

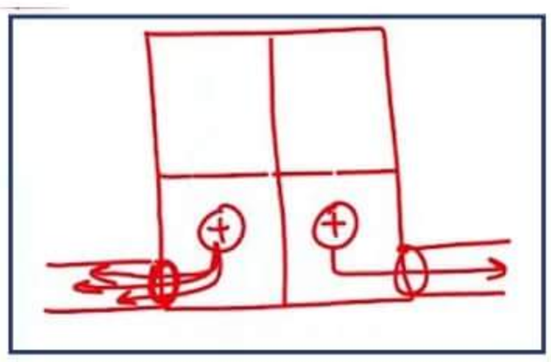
(Between right ventricle & pulmonary artery)

Mild Pulmonary Stenosis / Moderate Pulmonary stenosis

- Mostly asymptomatic

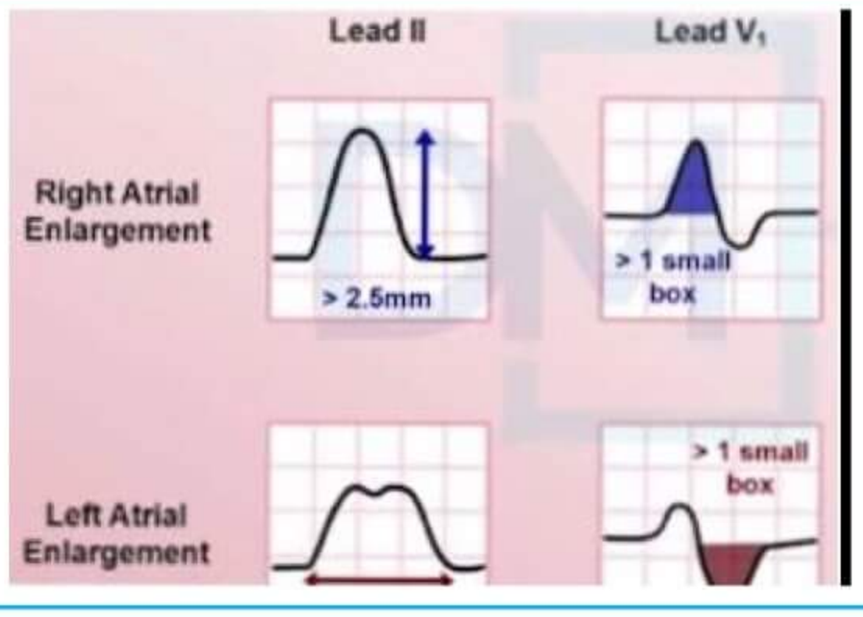
On Examination: **Ejection systolic murmur**

- Severity of Pulmonary Stenosis is $\alpha \frac{1}{S1-Ejection\ click\ gap}$



- ESM +
- Ejection click absent
  Ejection click is less prominent with inspiration in pulmonic stenosis
  All right sided events tend to increase with inspiration except pulmonary ejection click.
- S_2 heart sound
  - A_2 heard normally
  - P_2 soft

PrepLadder



- Loud P2 is hear in Pulmonary Artery Hypertension

➢ S4 heart sound +

Work Up of Patient:

1. **Chest X-ray** → Upturned apex of heart
2. **ECG** → Right axis deviation
   P-pulmonale
3. **Echocardiography** (**IOC**)
   - Tells gradient b/w right ventricle and pulmonary artery **> 50 mm Hg.**
   - Right ventricle hypertrophy (**Eccentric**)

Treatment

➢ Percutaneous pulmonic valve valvotomy

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Pulmonary Regurgitation

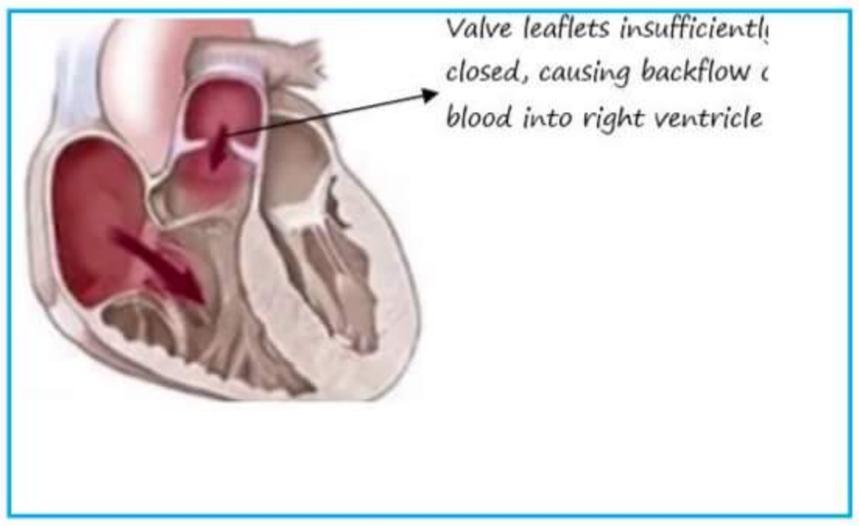
Causes

➢ Annular dilatation of pulmonic valve

↓

Severe Pulmonary Artery Hypertension

➢ Post Tetralogy of Fallot (TOF) repair
➢ Post balloon valvotomy



Pathophysiology

- Right ventricular dilatation

Clinical Feature

→ Exercise intolerance
→ Abdominal fullness
→ Pedal edema

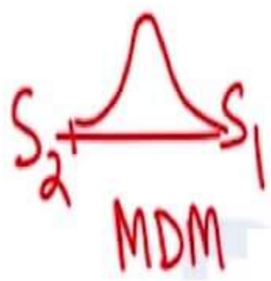
IOC → **Cardiac MRI > Echocardiography**

Treatment

→ Diuretics
→ **Transcatheter pulmonic valve replacement**

PrepLadder

MURMURS

Tricuspid stenosis	Tricuspid regurgitation	Pulmonic stenosis	Pulmonic Regurgitation
→ Large 'a' wave Blunted 'y'	→ CV wave steep 'y' descent	→ Large 'a' wave	→ Large 'a' wave
→ Mid diastolic murmur 	→ pansystolic murmur 	→ Ejection systolic murmur 	→ Graham steel murmur
→ Pre-systolic pulsations	→ Systolic pulsations of liver	→ Ejection click absent.	→ Early diastolic murmur

MITRAL STENOSIS – Orifice of mitral valve becomes relatively smaller

(N – 4-6 cm^2)

- Sever MS < 1.5 cm^2
- Critical < 1 cm^2
- Free flow blood in ventricular cavity hampered

↓

- Lesser blood coming
- Turbulence present

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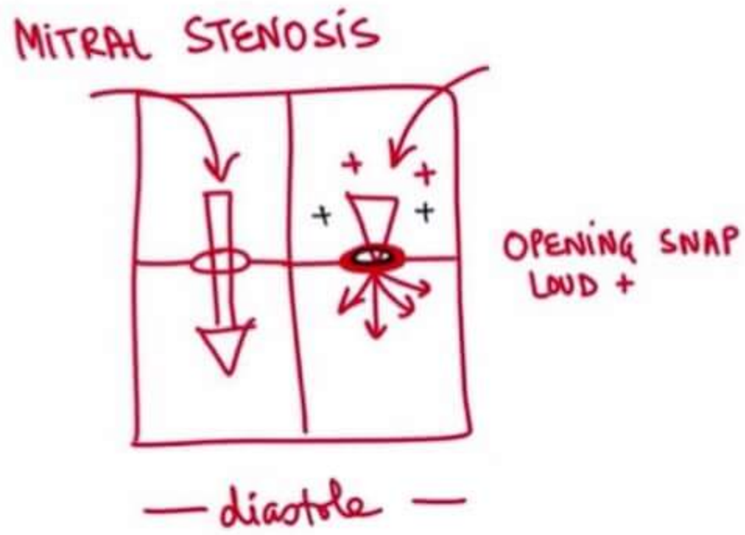
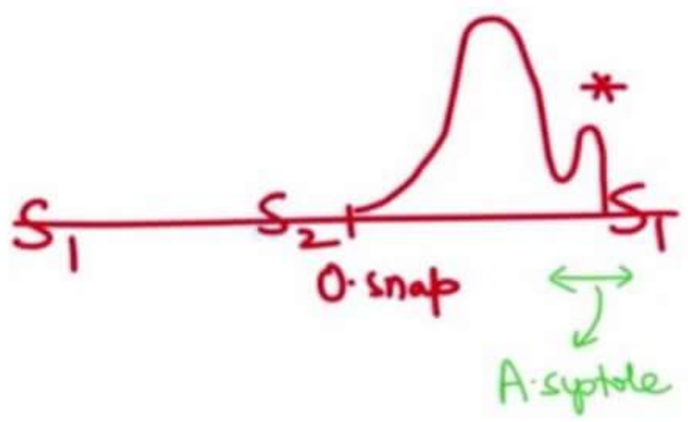


- Murmur appears once mitral valve opens with more force

↓

LOUD OPENING SNAP

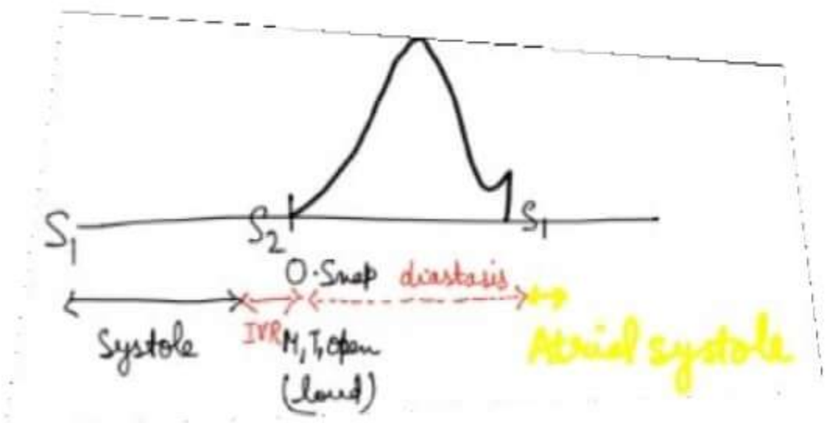


- Murmur in MS – K/A **MID-DIASTOLIC MURMUR**

(Beginning from opening snap)

- Peak at middle of diastole
- Small secondary Spike C/A

PRE-SYSTOLIC ACCENTUATION



* Atrial systole Contributes to pre-systolic accentuation

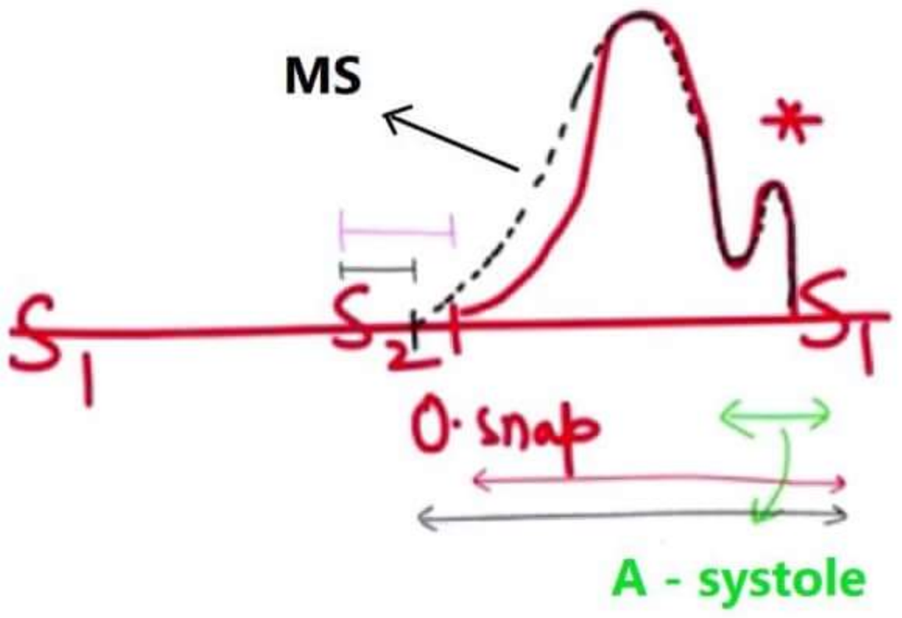
* Pre-systolic Accentuation will disappear

↓

When atrial systole ⊖

↓

In Atrial Fibrillation



Severity of MS

Not decided by – Loud S_1
– Loud P_2
– Intensity of murmur

Decided by – Length of Murmur

Severity MS $\propto \frac{1}{S_2 - O.S\ gap}$

∝ length of murmur

Severe MS

Px - **PERCUTANEOUS MITRAL BALLOON VALVOTOMY**

(Access taken via basilic vein to right atrium, puncture inter – atrial septum, reach left atria and then the stenosed valve)

Contraindications to PMBV

1. Calcified Severe MS
   - PMBV is C/I (forced balloon valve broken
     ↓
     fragments go to brain
     ↓
     Risk of Embolic Stroke

2. Severe MS + MR → PMBV is C/I

3. Severe MS + Left Atrial Appendage Thrombi

* **Murmur of MS** Heard better in **Left Lateral Decubitus**
(**Since** Heart comes closer to chest wall **Murmur is heard better**)

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Severe AR

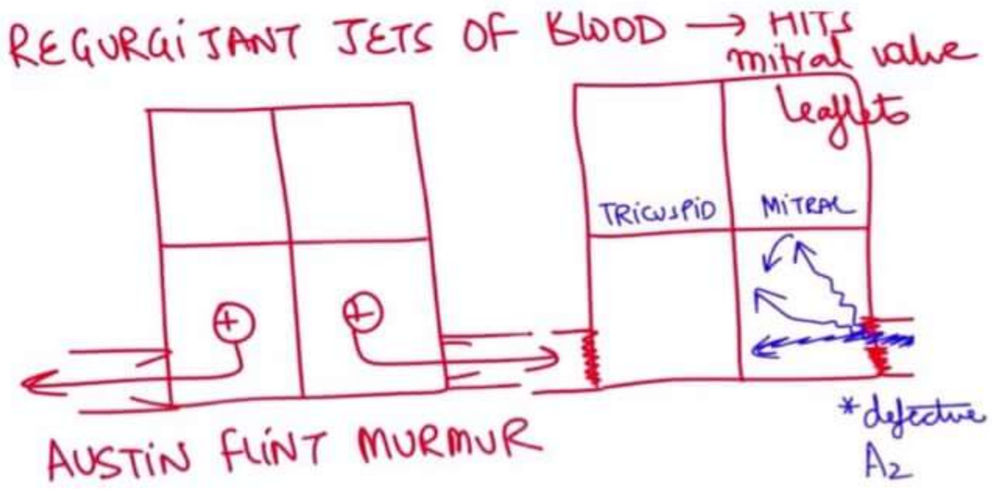
↓

Blood leaking back to left ventricle hits mitral valve leaflets

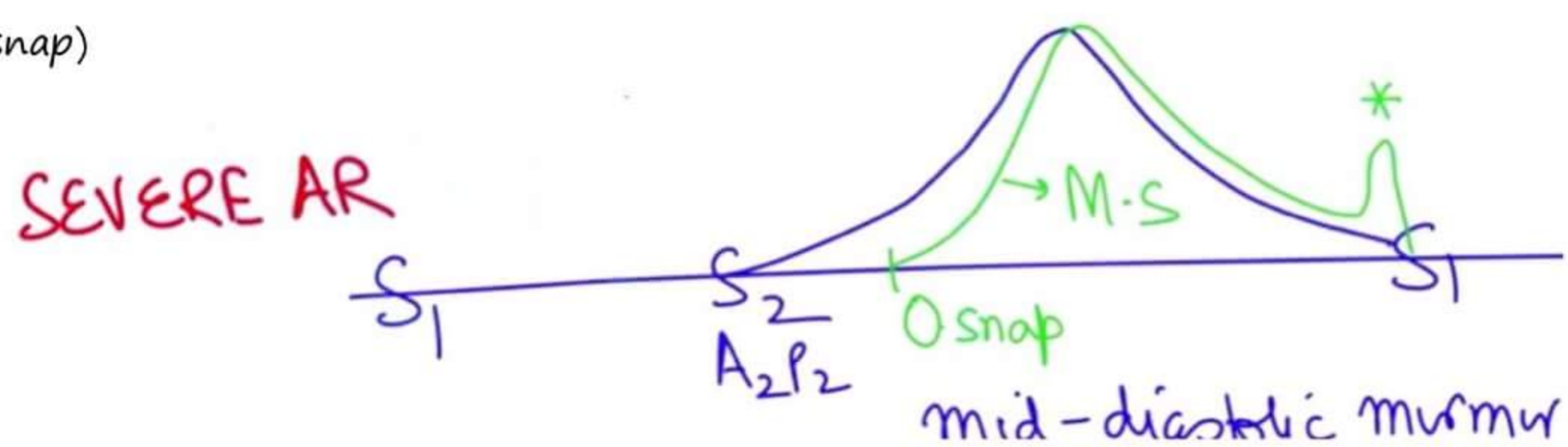
↓

Mid - diastolic murmur

(K/A AUSTIN FLINT MURMUR)



- Start from S2 (Not opening snap)



PrepLadder

Mild AR

- Turbulence begins at A2P2 and Dies down soon
- Triangular configuration

↓

K/A **EARLY DIASTOLIC MURMUR**

- A2 & P2 don't close together

↓

Time lag - 30 millisec

Pt. with Pulmonary A Hypertension (PAH)

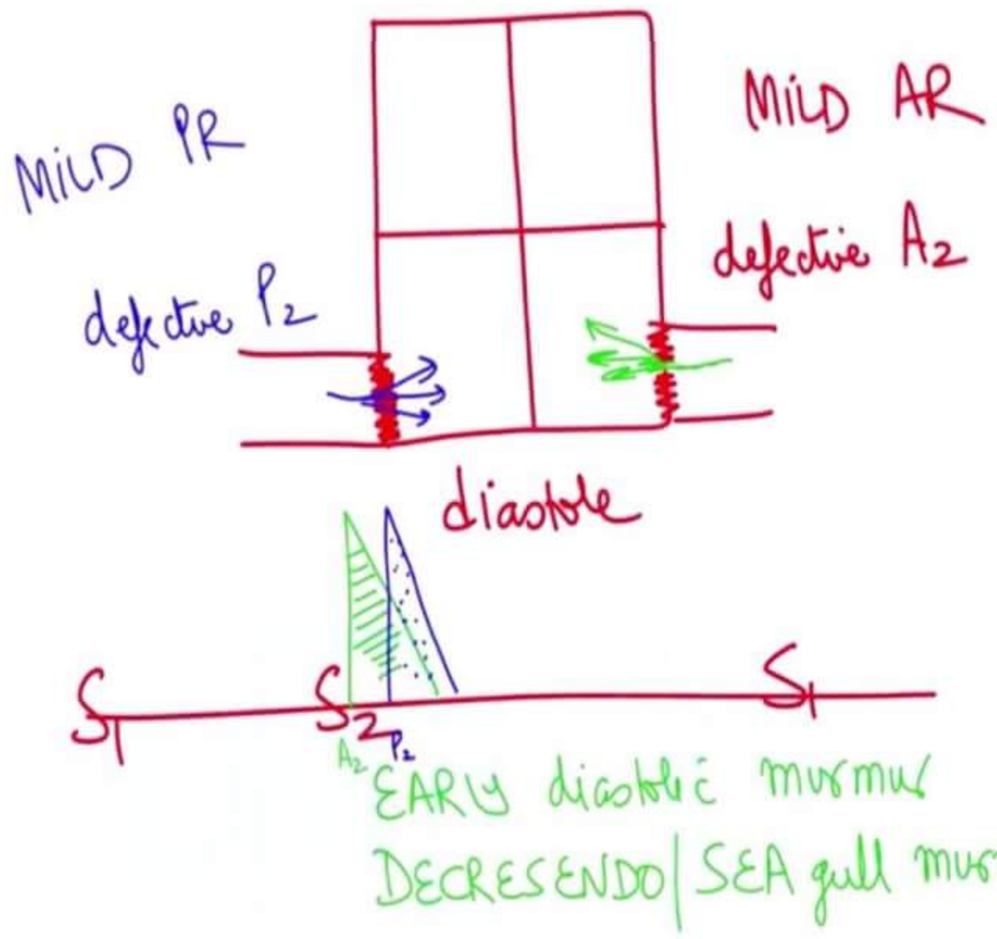
- Development of PR

↓

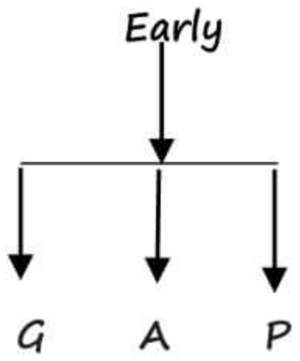
Early Diastolic Murmur

↓

K/A GRAHAM STEELE MURMUR



MURMUR: DIASTOLIC



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- MS
- Austin flint
- Flow Murmur

Rheumatic carditis–Carey coombs murmur

- Graham steel
- AR mild
- PR mild

Flow Murmur

Note: For Carey coombs murmurs if **late diastolic** is not in choices, then answer as **Mid – diastolic murmur.**

ASD LA-RA pressure gradient = 4 mm Hg

- Blood movement ⊕

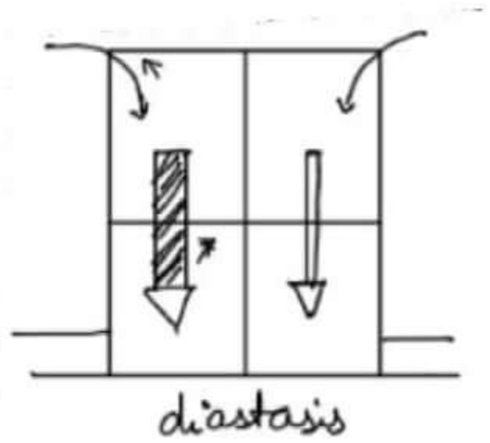
  But No shunt murmur ⊖ due to extremely Low pressure gradient
- More blood flow through tricuspid valve

↓

FLOW MURMUR

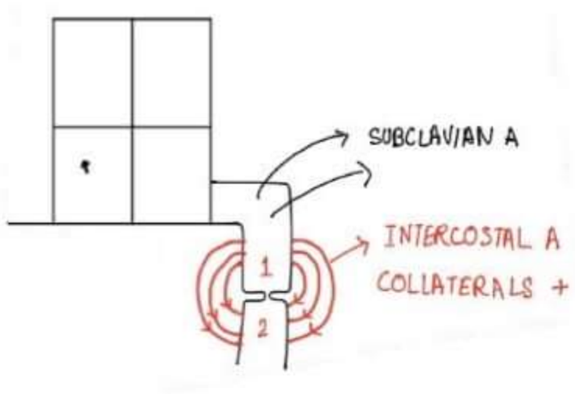
↓

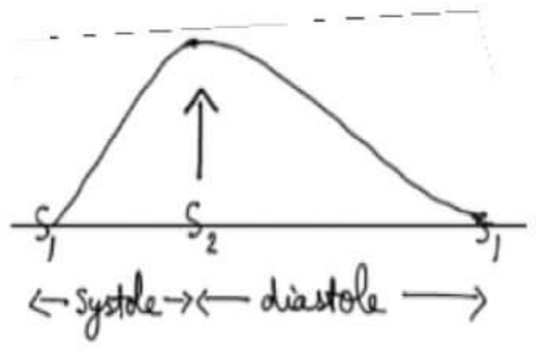
Mid-diastolic Murmur



COARCTION OF AORTA

- M/C site: Distal to origin of Subclavian A
- Murmur heard both systole and diastole
- Peak at S2
- K/A CONTINUOUS MURMUR





PrepLadder

Causes of Continuous Murmur

1. **Coarctation of Aorta** a/w TURNER SYNDROME

   ↓

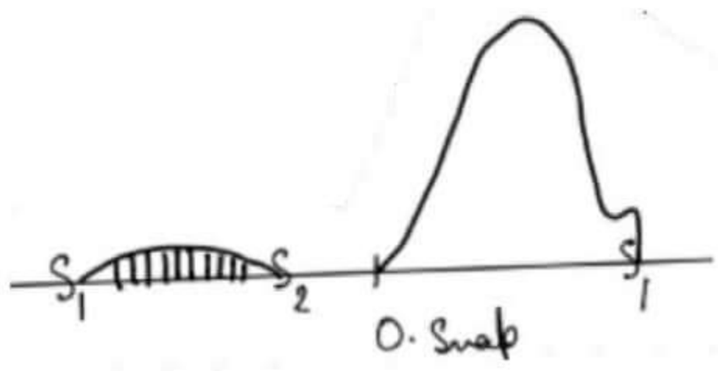
   Commonest cardiac lesion is

   (BICUSPID Aortic valve > Coarctation of Aorta)

2. PDA a/w Congenital Rubella Syndrome
3. **Mammary SOUFFLE** in pregnant lady

   ∵↑ Blood flow (Internal mammary A)
4. **Venous Hump** - dilated veins
5. **Rupture of Sinus of Valsava**
6. **Peripheral pulmonic stenosis**

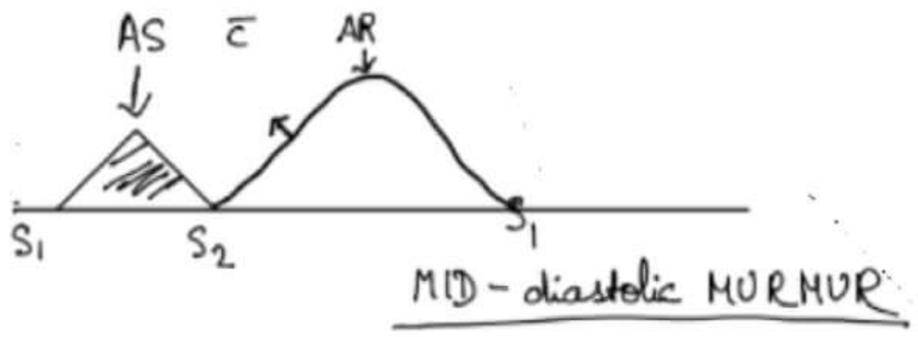
   MS with MR



- Pan systolic murmur

  Intensity - same
- Begins at op. Snap
- Not a continuous murmur

AS with AR



- Ejection systolic murmur
- Non of **combination lesions satisfy the** definition of continuous murmur

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SYSTOLIC MURMURS

↓

Ejection Systolic Murmur	Pan Systolic	Late Systolic
S1 Δ S2	S1 ▱ S2	1. Mitral valve prolapse
1. AS	1. MR	
2. PS	2. TR	
3. HOCM: Sub-valvular Aortic Stenosis		
4. TOF: Sub-valvular PS		

MVP

* Damage to papillary muscle

↓

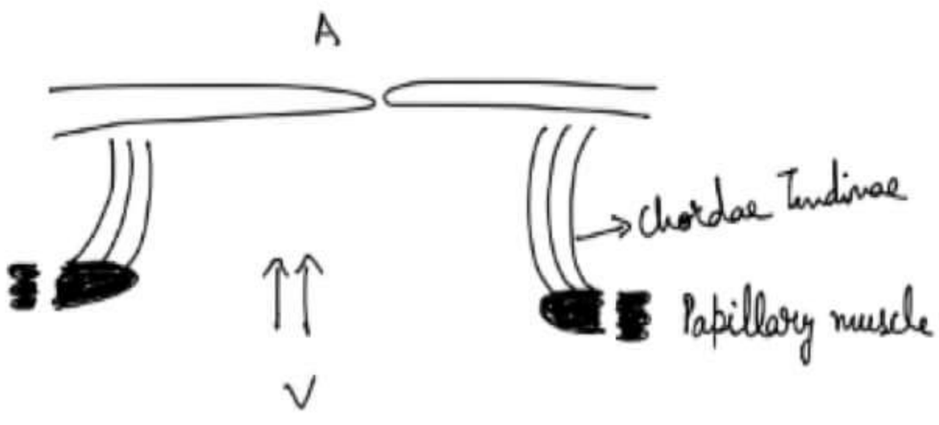
No support to chordae tendinae

↓

↑ Pressure

↓

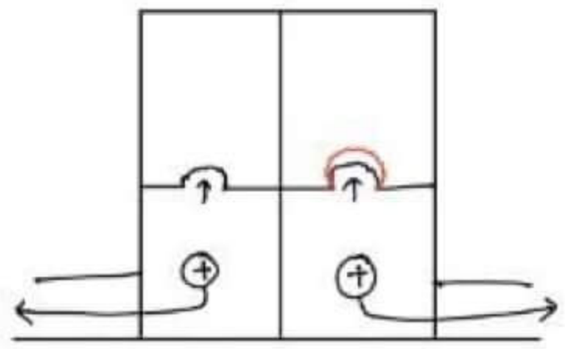
Valve leaflets go higher than Normal



PrepLadder

Cause of MVP:

- Myxomatous degeneration of papillary muscle - (**MC**)
- **Aschoff Nodules** - Rheumatic fever
- MI (Ischemia)
- Infection SABE
- Defect in fibrillin I protein – Marfan Syndrome



Features

- Extra tension in valve leaflets / chordae tendinae
- Auscultatory - mid-systolic clicks

IMPORTANT NAMES

Diastolic → Early: **Graham steel**: PAH
→ Mild: **Austin Flint**: Severe AR
→ Late: **Carey coombs**: Rheumatic

Continuous - → COA
→ PDA
→ Peripheral pulmonary stenosis

Systolic - ESM: AS / PS / HOCM
→ PSM: MR / TR / USD
→ Late SM: MVP

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* All murmurs ↓ in Intensity with Valsalva / Standing / Amyl nitrate inhalation
↓
↓venous return
Except - HOCM - Louder
- MVP - Longer

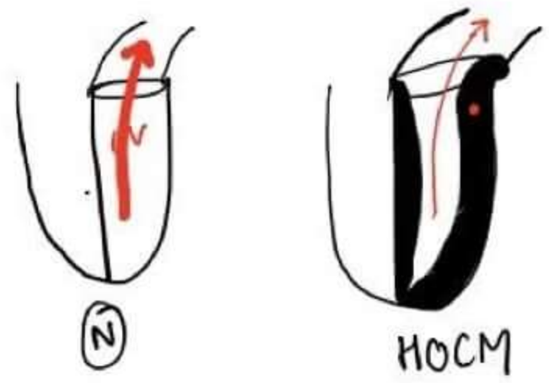
* All murmurs ↑ in intensity with sit ups / hand drip
Except - HOCM - Softer
- MVP - Shorter

PrepLadder

CARDIOMYOPATHIES

HOCM

- AD
- β- myosin gene defect, ch-14
- **Asymmetrical septal hypertrophy**
- **L-VOTO** (Left ventricular outflow tract obstruction)
- Sub valvular AS



C/F: 20yr, male

1. Dysnea – Diastolic malfunction
   - Pooling of blood in lungs
   - Pulmonary Oedema present
2. Chest pain – Sub. Endocardial Ischemia
3. Effort intolerance
4. Sudden collapse / death on exercise/ Running

↓

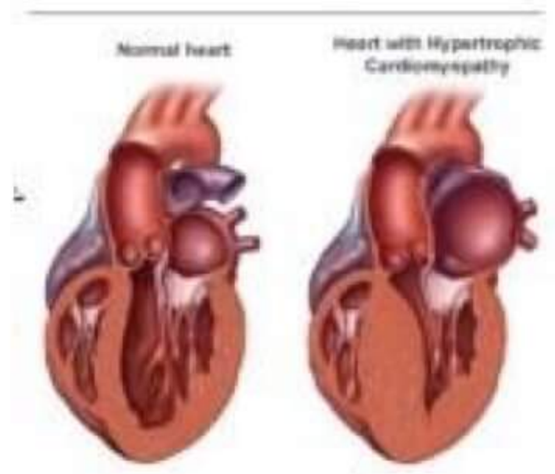
Ischemic ventricular fibrillation

↓

Twitching

↓

Pulse / BP



Notice banana shaped cavity of left ventricle in HOCM

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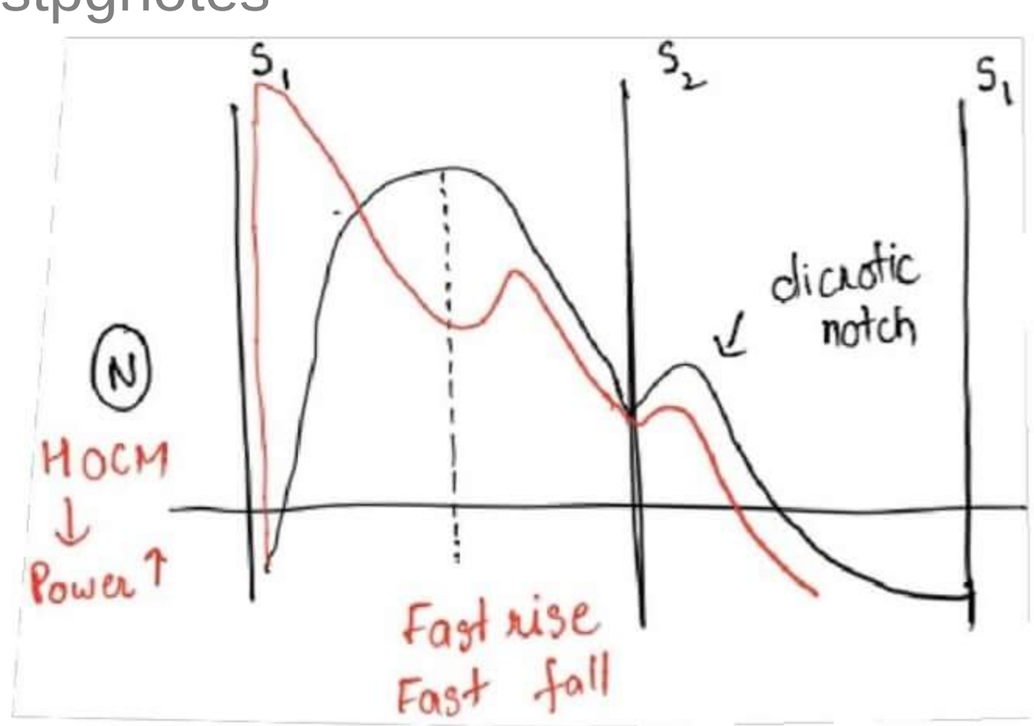
O/E :

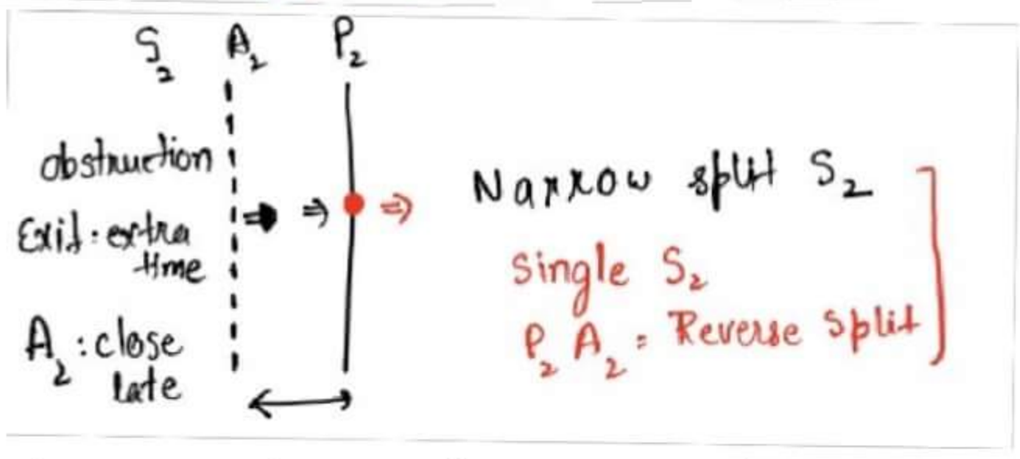
1. Pulsus Bisfiriens (aka) "**Jerky Pulse**"
   - Fast rise initially
   - LVOTO contribution to sudden dip in pressure



2. Apex beat
   - Displaced impulse
   - Double apical impulse

   (5 + 6th I/C space)

3. S_2: Narrow split/ single S_2 / Reverse Split S_2
   - Splitting is best Heard Best in phase of inspiration
   - Heard at ERB'S Point – 3rd I/C Space left parasternal



4. S_4 is heard due to out flow obstruction, left atrial hypertrophy occurs. The extra force generated by left atrium explains occurrence of S_4.

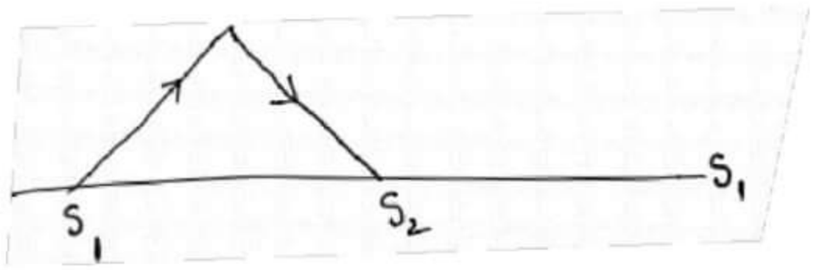
PrepLadder

5. Ejection systolic murmur

↑/↓

- **CRESENDO- DECRESENDO MURMUR**
- ALL Murmur ↓ in intensity with Valsava, Standing, amyl nitrate Except – HOCM = Louder

M.V.P = Longer



Investigation

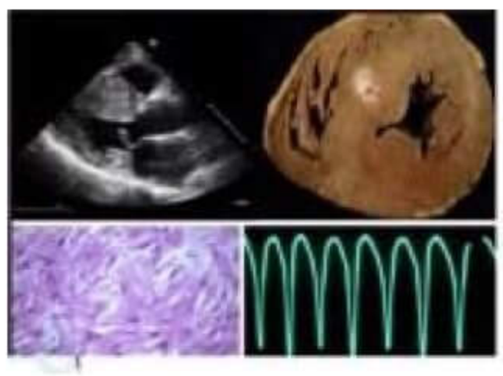
1. ECG – $SV_1 + RV_5 \rightarrow$ >35 mm – indicates Hypertrophy
2. ECtfO – LV Free Wall hypertrophy

↓ **>30 mm**

IOC

- SAM- Systolic anterior movement of mitral valve
- LVEDV ↓ SV↓

Rx - **Propranolol → DOC** - ↓ tfR



INTERVENTIONS AVAILABLE

- Alcohol based septal ablation
- Myomectomy
- ICD (Implantable cardioverter defibrillator): answer it as treatment of choice

↓

1. Family H/O sudden cardiac death
2. LV free wall thickness > **30 mm**
3. R. syncopal attacks

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RESTRICTIVE CARDIOMYOPATHY

- **Rarest cardiomyopathy**

Cause

1. Amyloidosis
2. Sarcoidosis
3. Radiation
4. Endomyocardial fibroelastosis
5. Hypereosinophilia

Compliance ↓ ↓ RV ↓	LV ↓
1. Pedal edema	1. Pulmonary edema due to diastolic malfunction
2. Ascites	2. Effort intolerance
3. Hepatomegaly RUQ discomfort	3. S3 / S4 ⊕
4. Kussmual sign ⊕	

PrepLadder

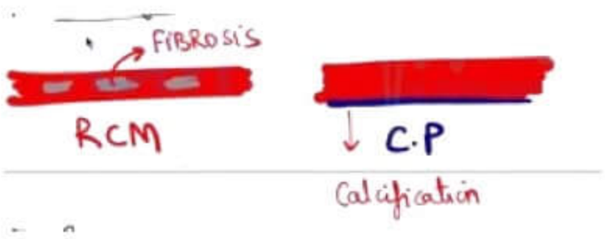
Investigation

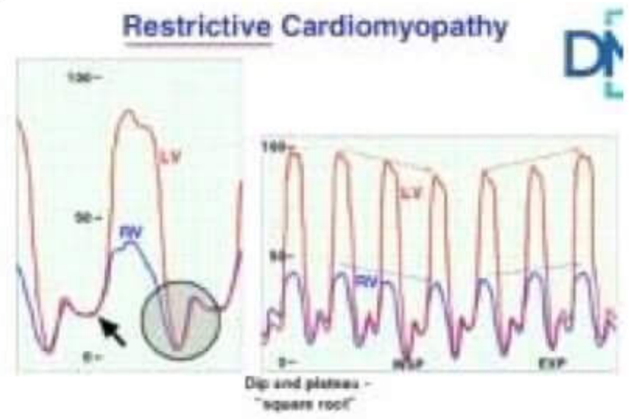
1. CXR- Pulm. Edema ⊕
   - Peri Hilar infiltration
2. ECG-Low Voltage ECG *

Also Seen in
- Myxoedema Heart
- Constrictive pericarditis – Calcification ⊕
- RCM – Fibrosis ⊕

*** R+S = < 5 mm limb lead**
< 10 mm chest lead

3. Doppler = Square root wave sign (also seen in constrictive pericarditis)
4. Endomyocardial Biopsy





5. Cardiac MRI : preferred Imaging modality

Rx- Oral Anti coagulants

↓

↓ Embolic stroke incidence

- Oral diuretics

↓

- Cardiac Transplantation – (TOC)

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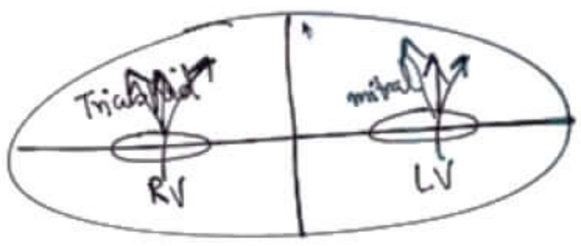
Dilated Cardiomyopathy

*** Causes**

1. Toxin – alcohol
2. Sequalae to coxsackie B myocarditis
3. Sarcoidosis
4. Duchenne's muscular Dystrophy

- Pt has –functional MR, TR



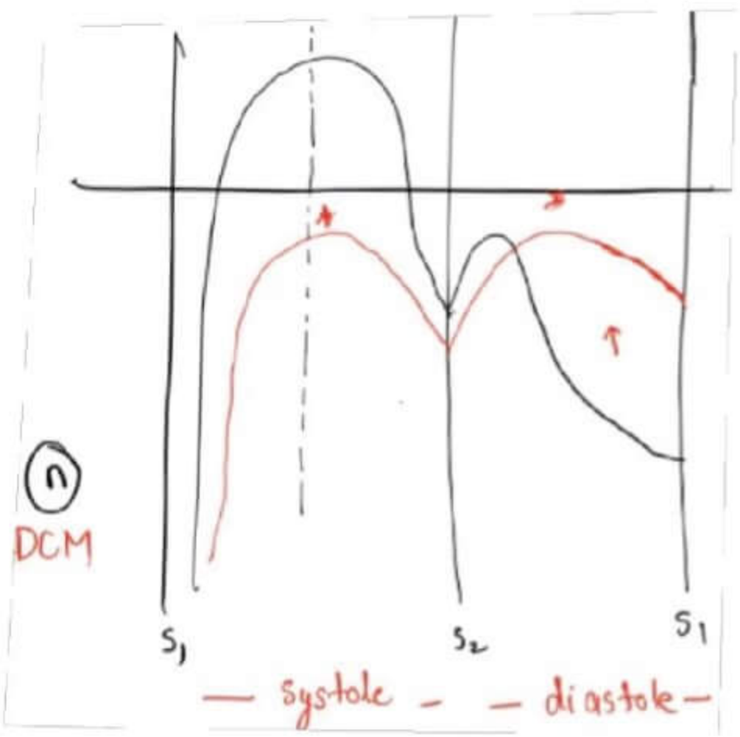
- Pansystolic murmur

O/E 1. Dicrotic Pulse
- Twice beating pulse palpable both in systole as well as diastole.

2. Pansystolic murmur along with features of biventricular failure.

IOC – Echo

Rx- Cardiac transplantation
- ICD can be deployed
- **HOLIDAY HEART SYNDROME**: Sudden death due to Atrial Fibrillation drinking after binge-



PrepLadder

Causes of Sudden Cardiac death

1. WPW/ LGL
2. MI — V. Fibrillation < 1 hr.
   Brady arrhythmia – Mobitz II Block
3. Brugada syndrome – Sodium channel defect
   S-T ↑, V_1 V_2
4. HOCM – ischemic V. Fibrillation
5. DCM - Holiday Heart Syndrome
6. Long QT Syndrome: QT >500 m sec

ROMANO WARD SYNDROME (TORSADES De points) - ⊕infants
Tachyarrhythmia develops in all of them

↓

Device recommended ICD

Extra Mile: ABCD of Pulse

A	Pulsus alternans: LVF Anacrotic pulse: Aortic Stenosis
B	Pulsus bisferiens: HOCM
C	Corrigan/Collapsing: AR
D	Dicrotic Pulse: DCM

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TAKOTSUBO CARDIOMYOPATHY

&

BRUGADA SYNDROME

TTCM is also **called** **Broken Heart Syndrome** and occurs due to **catecholamine toxicity**.

* Life threatening stress

Case based discussion: 60 yrs ♀ trapped in a elevator during an earthquake

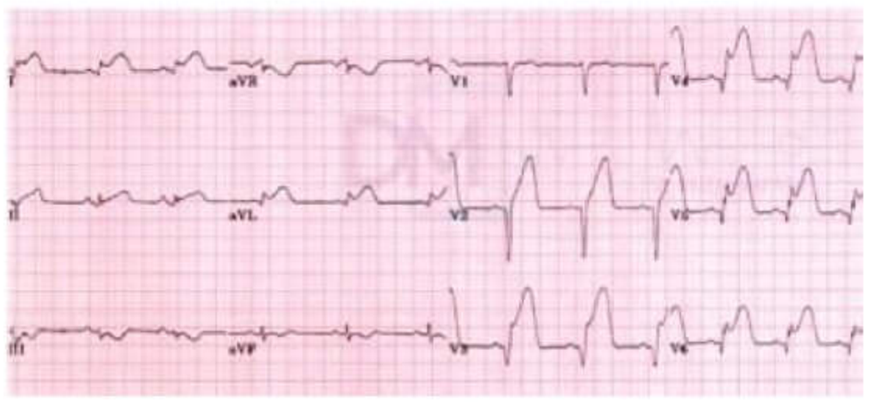
↓ ↓

Emergency crew — Chest pain at rest / diffuse

Rescued her — Diaphoresis

WORK UP

1. ECG :



"TOMB STONE PATTERN" / Pardee sign: Seen in V_2-V_6 leads suggestive of extensive anterior wall MI, due to thrombus in left main coronary artery.

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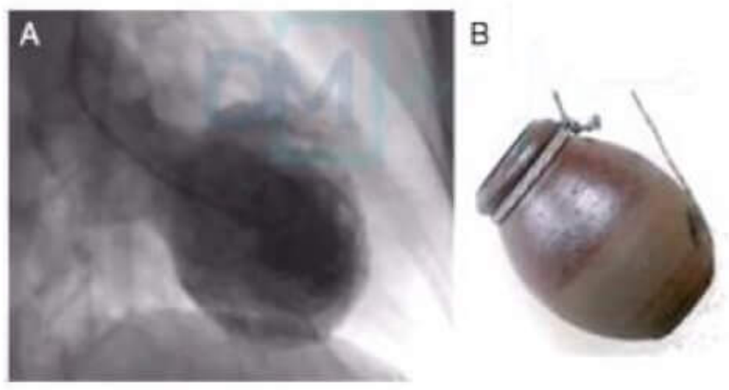
2. **Trop I** : 0.08 mg / dl

3. **Cath. lab** - Coronary angiography normal

Primary PCI: Abandoned

4. ECHO: Alteration of LV shape



Rx: Cardiogenic shock → IABP (Intra – Aortic Balloon Pump)

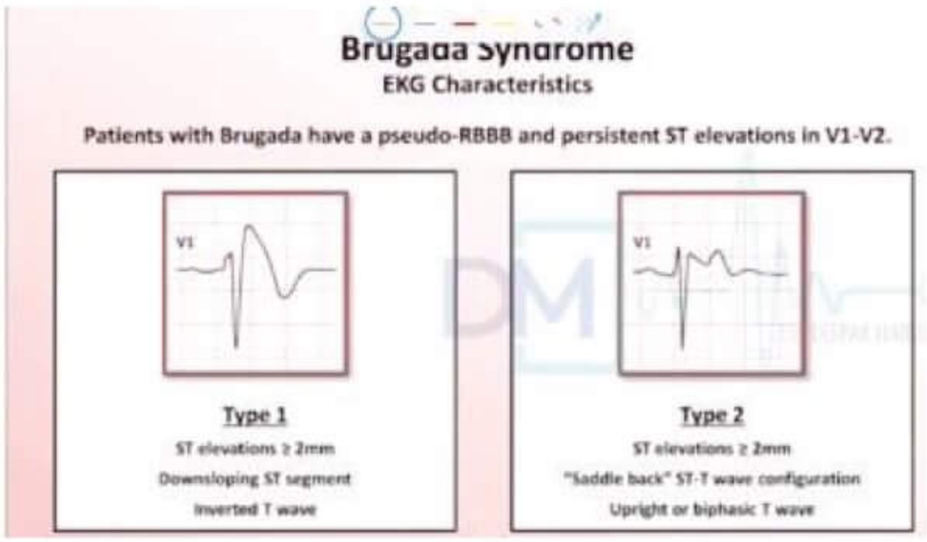
Causative Agent → Catecholamine therefore dopamine, dobutamine should not be given

Must know points for TTCM

1. Acute onset cardiomyopathy
2. Improvement can occurs gradually
3. Mimics STEMI
4. Cath Lab: Normal angiography
5. **(It is differential diagnosis of STEMI and diagnosis is made in cath lab due to normal coronary angiogram.)**

PrepLadder

Brugada Syndrome



- **SCN5A #** → defective Na^+ influx
- RV epicardium
- Voltage gradient → trigger VT / TDP
- ⊕ **Family H/O, H/O syncopal attacks**

↓

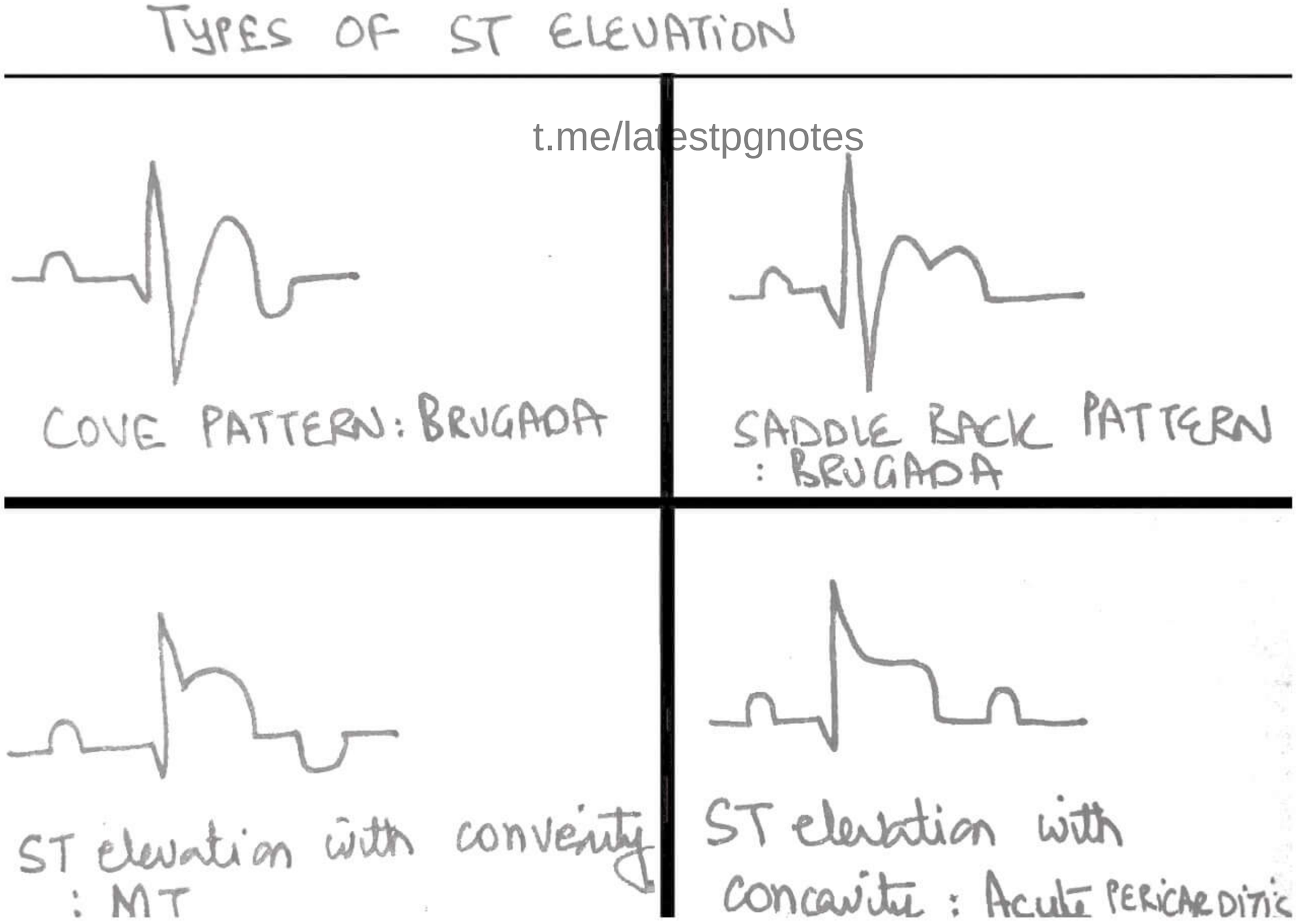
Sudden death in sibling

It is the leading cause of sudden nocturnal death in SE Asian males

- V1 - V3:ST Elevation

Rx : ICD

Cove pattern: Brugada	**Saddle back pattern**: Brugada
ST elevation with concavity: MI	ST elevation with concavity: Acute Pericarditis



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PrepLadder

RHEUMATIC HEART DISEASE

Rheumatic fever

- Organism involved – Group A Beta haemolytic streptococcus
- Antibody cross reacts with connective tissue
  (N-acetyl glucosamine)
- Type II Hypersensitivity / Molecular mimicry
  Formation of Aschoff nodules: Pathognomic feature
  ↓
  Antischkow cells aka caterpillar cells

Modified Jones Criteria (2015 update)

MAJOR criteria

1) Carditis

* Pericarditis (MC)
  - 5-15years, Recurrent Sore throat
  - Chest pain at rest, pericardial friction rule
  - **ECG**- ST ↑, concave upwards present in all leads except aVR.
  - Management- Steroids

* Myocarditis: acute CHF
  M R functional
  T R functional
  Pansystolic murmur

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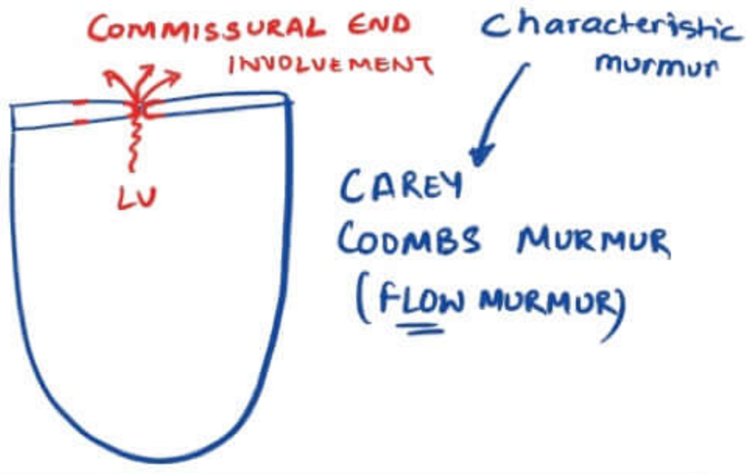
Manifestation- Acute Pulmonary edema

Management- (LMNOP – Mnemonic)
LASIX: Black
Morphine
NTG, O_2
Head high position

Endocarditis

Valve involved	Valvular lesion	Surface
* MC: Mitral	*5 yr, RHD: Mitral Regurgitation	* Commissural end involvement
* Not involved: Pulmonic Valve	*18 yrs, RHD: Mitral Stenosis	
	* Acute Carditis: MR	
	* Carditis: MS	
	* overall: MS	



UPDATE 2020

Echo with Doppler must be done in all cases of confirmed and suspected acute Rheumatic fever as auscultatory findings take time to develop. **Subclinical carditis** seen on echo is now considered a Major diagnostic criteria.

→ Characteristic **Murmur: Carey Coombs Murmur (Flow murmur)**

→ **MC Callum patch**: Characterised by # free wall of left atria

Management

Severe MS (< 1.5 cm^2): Percutaneous mitral balloon valvotomy

MR: Valvuloplasty

2) Arthritis

- Earliest manifestation within 2 weeks with H/O sore throat
- Ankle swelling
  ↓
  Knee Swelling
  ↓
  Elbow swelling

} Migratory polyarthritis

When swelling subsides, no deformity: Non-erosive arthritis

Sometime can cause Erosive arthritis called as **Jacoud's Arthritis**

* **Low endemic (USA)**	* **High endemic (India)**
- Migratory polyarthritis	If single joint involved i.e. **Monoarthritis:-**
	Sufficient for diagnosis of Arthritis

Management

* **Aspirin**

Cx: Reye Syndrome → **Aspirin + Varicella Zoster**

→ **Aspirin + Influenza B**

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Is a type of mitochondrial Encephalopathy

3) Syndenham Chorea (Late neurological feature)

- Damage to caudate nucleus
- Fast, purposeless, involuntary distal movements
- Poor handwriting
- School grades ↓

O/E-

- **Darting Tongue** (Inability to keep tongue in stable position)
- **Milk-maid grip**
- **Hung up reflexes**
  (Hung up ankle jerk – Myxedema)
- **Dysarthria** (unclear speech)

Rx-

- Self limiting condition: <6 months – 12 months

* Valproate
* Haloperidol
* Phenobarbitone
  ↓ If Fails
- Steroids
  ↓ If Fails
  IV Immunoglobulin

PrepLadder

* Medically refractory chorea: IV Ig

* **Atheotosis-** Slow, writing distal involvement involuntary
  Lesion: Globus pallidus

4. Subcutaneous nodules

- Extensor in distribution
  Sites: - Olecranon, occiput, spinous processes of Vx

Don't confuse with RHEUMATOID nodules: - MC extra- articular manifestation of Rheumatoid arthritis

- Extensor, non-tender
- Involve lungs, heart, mononeuritis multiplex

5) **Erythema Marginatum (Not seen in Indian population)**

Minor Criteria-

Fever

Arthralagia

Lab features:

- ESR ↑ — **Low endemic : > 60 mm fall/ 1st hour**; **High endemic**: > 30 mm fall / 1st hour
- CRP: (+)
- Prolonged P-R interval / 1st degree heart block

SAN ⟶ AVN

Aschoff Nodules

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Evidence of preceding Grp A Streptococcus infection

A S O titer > 200 IU/ml suggestion of
Recent streptococcal infection in previous.
< 45 days (Evidence of infection) or Rapid streptococcal antigen test is positive or positive throat swab

- Chorea: late feature

↓

So ASO values can normalize by the time chorea will develop.

Diagnostic Algorithm

* 2 Major criteria + evidence of preceding Grp A Streptococcal infection
* **1 major+ 2 minor criteria evidence of preceding Grp A Streptococcal infection**

Management-

1. Aspirin → Arthritis
2. Steroids → Pericarditis
3. Valproate / haloperidol → Severe chorea
4. Injection Benzathine penicillin I.M. **every 3 weeks**

PrepLadder

Why? => To prevent future sore throats

How Long? => RHD with MR → lifelong basis is ideal but not practical

Hence answer upto 40 yrs of age if valvular lesion is present or 10 yr from date of diagnosis.

Duration of Prophylaxis with Benzathine Penicillin

RHD

RHD with valvular lesion	40 yr	10 yr
RHD without valve lesion	21 yr	10 yr
RF	21 yr	5 yr

* Answer whichever is longer.

Extra Mile

Best for prophylaxis of RF/RHD in penicillin allergic child: **Azithromycin > Sulphadiazine**

Chorea and arthritis cannot co – exists in a single patient

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INFECTIVE ENDOCARDITIS

ABE
- Hospital acquired: S. Aureus
- Community acquired: Streptococcus

SABE- S. viridans

Prosthetic Valve Endocarditis

Early (≤ 60 days) = C. O. N. S Late

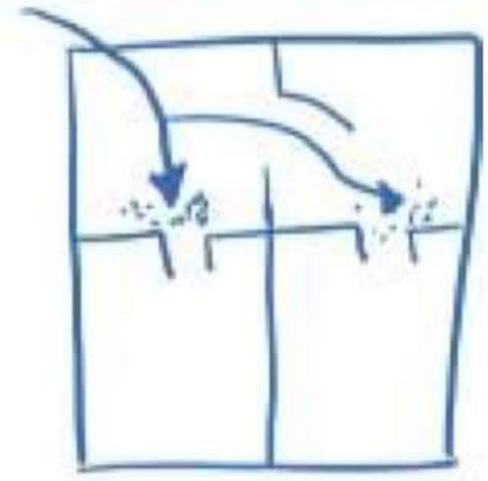
(> 60 days) = Staph. Viridans

I.V drug abuser/ **Right sided** Endocarditis – Staph. Aureus

Association

Left sided Endocarditis → Patent foramen ovale

→ (R→L Shunt)



Organisms responsible
- S. Aureus
- Enterococci

→ Mitral valve is most commonly involved in IE.

- Native value endocarditis → Mitral
- IE incidence is directly proportional to pressure gradient

1. MS: Diastole
2. MR: Systole: LV- VA (Highest pressure gradient so highest incidence of infective endocarditis)
3. AS:LV – Aorta
4. AR: Aorta – LV

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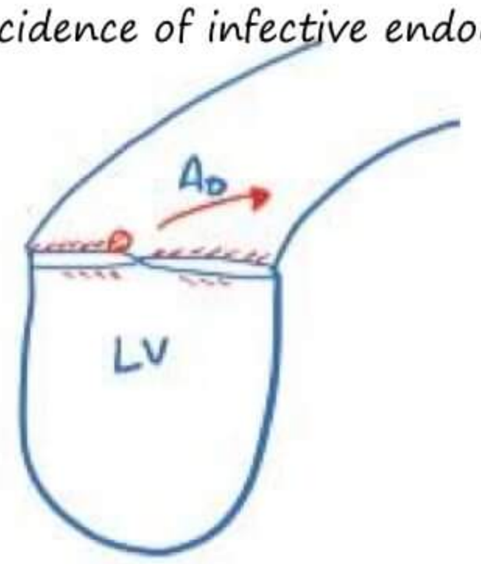


Incidence of IE

- Highest = M.R
- Least = ASD (LA- RA) = 4 mm.
- Highest (Children) = VSD> PDA
- Vegetations = fibrin + Bacteria
- Pt. will be having high grade fever/ chills/ rigors.
- Splenic abscess present: Splenomegaly
- Brain abscess: Hemiplegia
- Clubbing is seen in SABE

Extra Mile

Duke criteria = IE

Duke score = Severity of chronic stable angina.

Duke staging = Colorectal CA

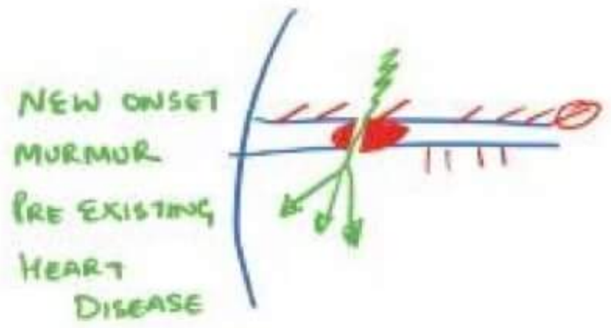
Duke Criteria

Major Criteria

1. Echocardiography: vegetations +
   - Valve abscess / ring abscess
   - Perforation
   - Oscillating intracardiac mass on valve
   - Partial dehiscence of valve

PrepLadder

2. Blood culture: **positive**
   - Out of 3 sets, **2+**/3: Same organism
   - Blood culture drawn = At the gap of 1 hr.
   - **1+**/3: **Coxiella burnetii** = causes **Q Fever**
3. New onset murmur in pre-existing heart disease



Minor Criteria

- **Fever > 38degree Celsius**
- IV drug abuser (IVDA) indicate predisposing condition
- Vascular phenomenon → Arterial emboli
  - Mycotic aneurysm
  - SAH, ICH
  - Conjunctival hemorrhage
  - Janeway lesion
  - Erythematous macules in palms / soles
- Immunological - **Roth spots**: fundus, RA factor +
  - **Osler Nodes**: Pea nodules in tip of fingers, toes
  - G: P. S. G. N → Hematuria

Red – Janeway lesion;

Yellow – Osler nodes

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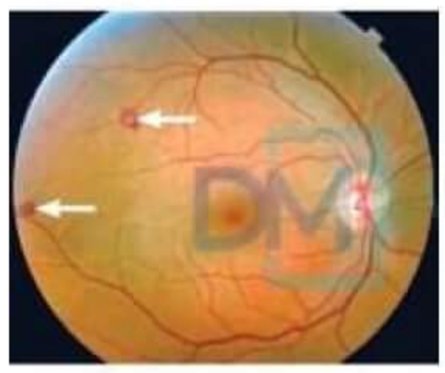
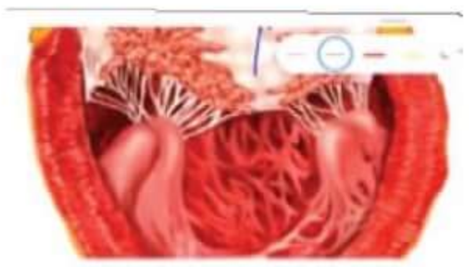


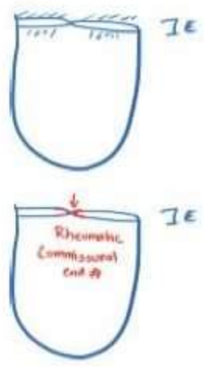
Extra Mile

Roth spots can also seen in
- Lymphoma
- Leukaemia
- Anaemia
- IE



- Non Bacterial thrombotic endocarditis is example of sterile endocarditis also referred as Marantic Endocarditis. Lesions are present on lateral surface of valve

Causes: Malignancy
- GIT, Ovary
- M3 AML



For diagnosis of IE, require 2 major criteria
- 1 major criteria + minor criteria
- 5 minor criteria

PrepLadder

Treatment → Ampicilin + Gentamycin ± Methicillin
Vancomycin

- After 72 hours, culture sensitivity report available, depending upon report, have to give appropriate antibiotics: afebrile **< 7 days**

Tt: 3 Weeks

– Culture negative endocarditis

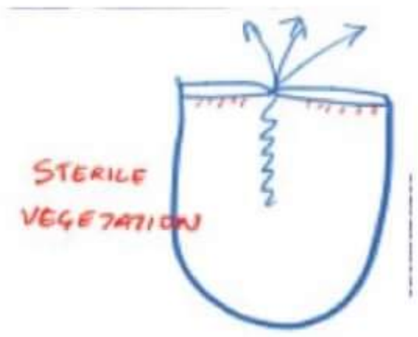
1. Technical considerations
2. Fastidious organisms: **HACEK**

Bacteria present in HACEK group

- **H**emophilus aerophiles
- **A**GGREGATI BCTER species
- **C**ardio bacterium Hominis
- **E**ikinella Corrodens
- **K**ingella

Rx: Ceftriaxone

Libman Sacks Endocarditis



- Predilection under surface of valve
- Mitral Regurgitation
- Rx: Valvuloplasty

* Sterile vegetations are found in:

1. **RHD** – Tip of cusp which is called as commissural end involvement
2. **NBTE** – Line of closure due to Malignancy
3. **LSE** – Undersurface of valve due to SLE

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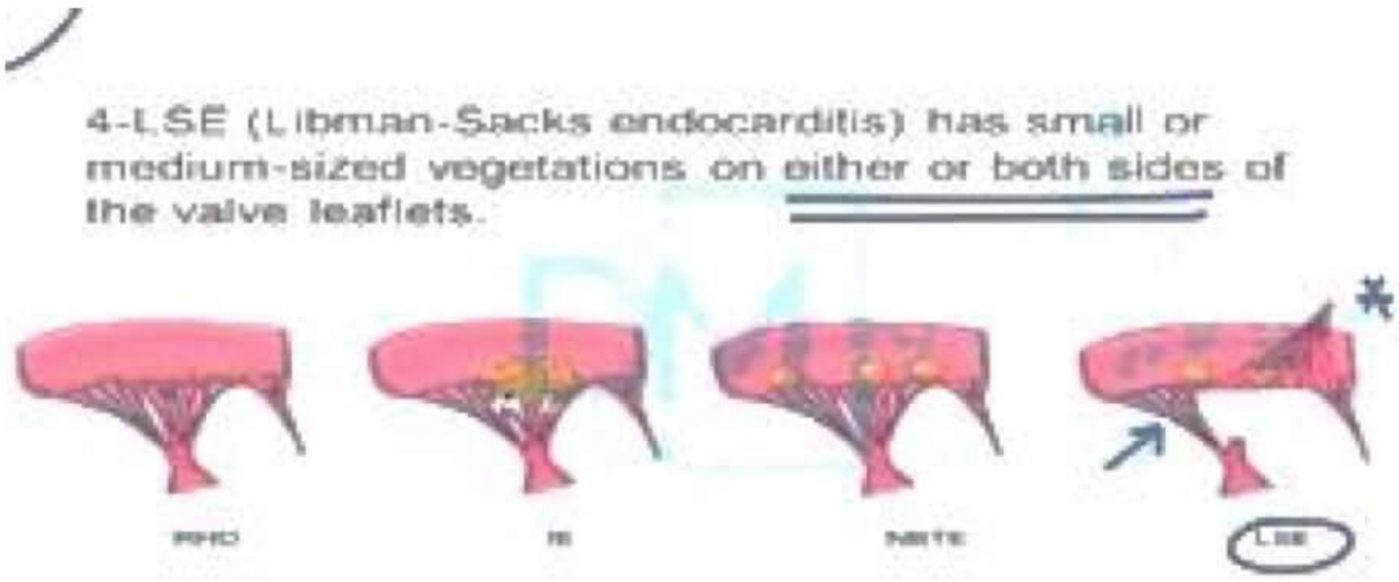


PrepLadder

ECG AND ARRHYTHMIAS PART - 1

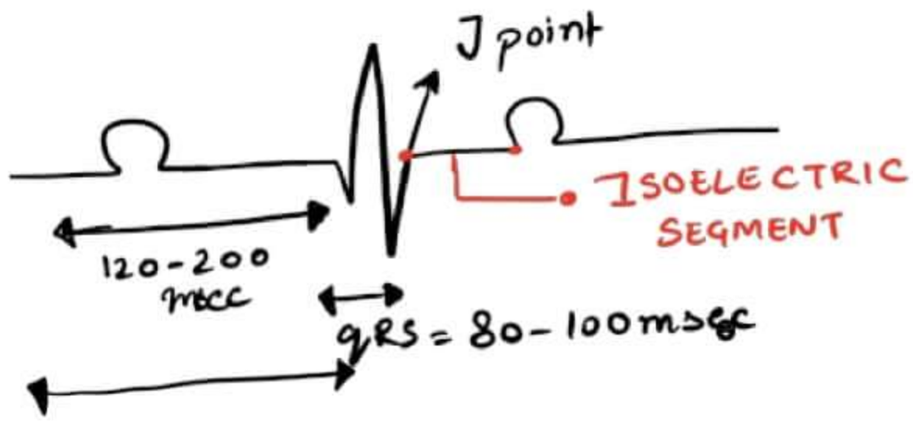
Normal ECG

* P wave = Atrial depolarization (Duration < 120 m sec)
(3 small squares)

* PR = AVN conduction
(Duration 120 - 200 m sec
3-5 small squares)

< 2.5 mm limb leads
< 1.5 mm chest leads
(Vertical Height)

* q wave = septal +: < 40 m sec
< 1mm depth
Depth of q = < 25% R wave
qRS + 80-100 m sec = 2-2.5 small squares



* T waves indicates ventricular repolarization
T = V. repolarization
Height of T wave = < 5 mm limb leads
< 10 mm : Chest leads

Summary

P = AD: < 120 m sec: 3 small squares(ss)

q: septal +: < 40 m sec: 1 ss

qRS: VD: 80-100 m sec: 2-2.5 ss

ST: isoelectric segment

T: Ventricular repolarization

U : Delayed Repolarization of Papillary muscle

QT interval: VD + VR = 360 - 440 m sec : 9-11 ss

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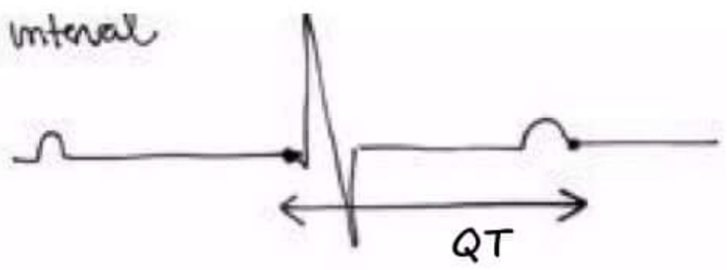


Calculation of heart rate =

- Count squares b/w R-R waves and apply formula: 300/R-R interval

4 Large Squares → 75 / min

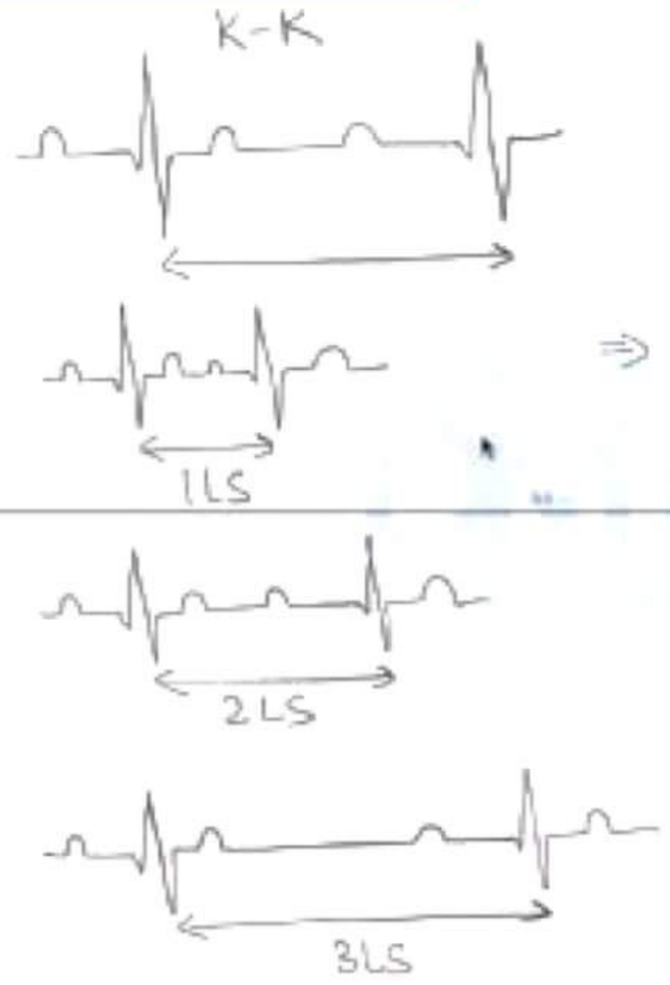
5 Large Squares → 60/min

6 Large Squares → 50/min

7 Large Squares → 40 / min

< 3 Large Squares: > 100 / min → Tachycardia

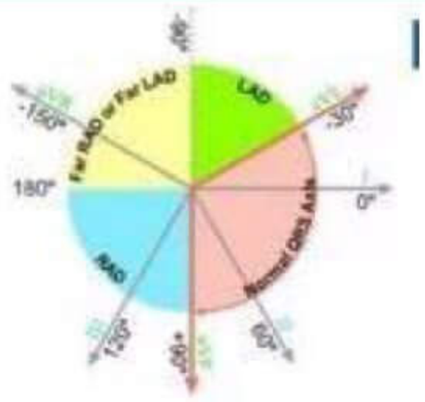
>5 Large Squares: <60/min → Bradycardia

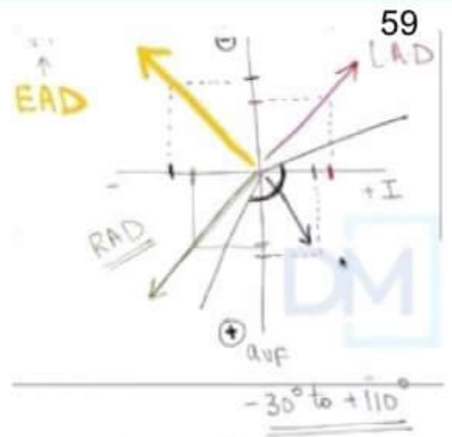


PrepLadder

Axis Calculation:

Normal axis of heart = -30^{o} to $+110^{o}$





Lead I =	R – S → +3	R – S → Θ	R – S → ⊕	R – S → Θ
aVF =	R – S → +3	R – S → Θ	R – S → Θ	R – S → ⊕
	Normal	**Extreme axis deviation**	**Left axis deviation**	**Right axis deviation**

P wave & PR interval abnormalities

- Normally P wave is upright in all leads. But is always inverted / negative in leads aVR and always biphasic in lead V1.
- Mitral stenosis → **LA ⊕** : Enlargement

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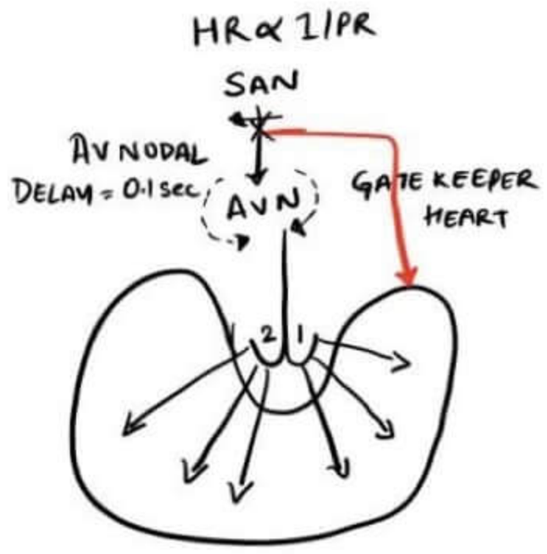
- Hence duration of P wave increases and is called as P – mitrale.
- Once pulmonary artery hypertension occurs then height of P-wave also increases and is called as p – pulmonale.

Wolf Parkinson White Syndrome

→ **Bundle of Kent**

→ **Pre-excitation syndrome**

→ **Low cardiac output**

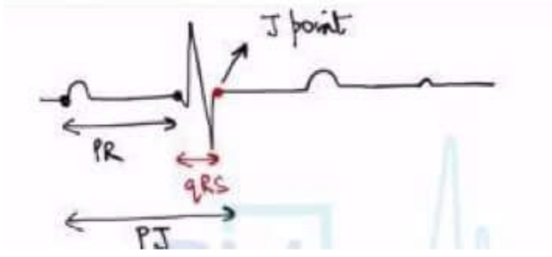


Q: - 25 yr old male complaining of

→ Palpitations, dizziness, vertigo, syncopal attacks (Recurrent)

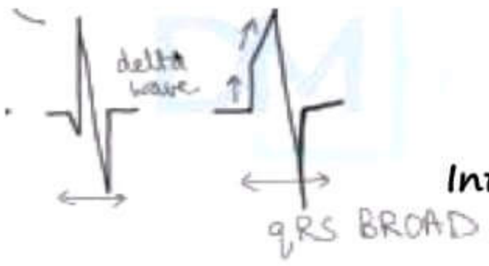
→ Family H/O → sudden cardiac death in siblings

Investigation: ECG

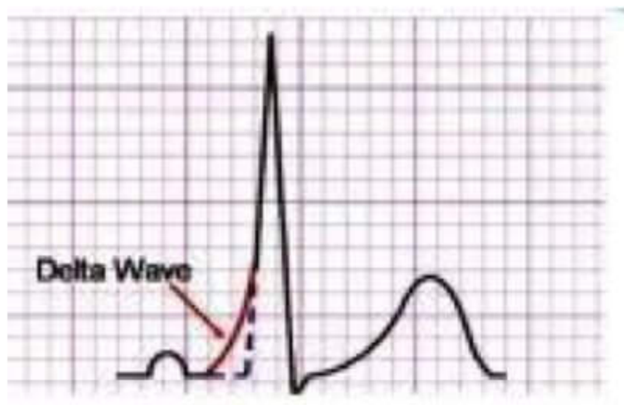


PrepLadder

1. **(Fast conduction: Kent)**: Short P-R interval

2. 

Intermyocyte conduction



3. PJ = PR (Reduced)+qRS (Prolonged) = Normal/ unaffected

* These pts. Are medically unfit for army, pilot, police or jobs that require good fitness levels.

Rx-

DOC → ORAL flecainide to prevent future episodes

TOC → Radio frequency ablation

Emergent Management: IV Procainamide

LOWN - GANONG LEVINE SYNDROME

* Pre excitation syndrome
* Low cardiac output

% Palpitation, dizziness, syncopal attacks: Recurrent

Family H/O: S.C.D in sibling

On ECG

- Short P-R interval
- qRS complex n / ↓
- PJ = PR + qRS = ↓ (n)

Pt. unfit for locomotive driver, commercial pilot, army, police

Rx:-

DOC: Oral flecainide to prevent future episodes

TOC: Radiofrequency ablation

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WPW	L.G.L
BUNDLE OF KENT	JAMES BUNDLE/ MAHAIM FIBERS
Palpitations SCD in sibling	Syncopal attacks (R)
Short P-R interval	
Delta wave PJ Normal	PJ short

Oral flecainide

+

Radiofrequency Ablation

PrepLadder

Extra Mile

Delta waves in EEG: NREM stage 3

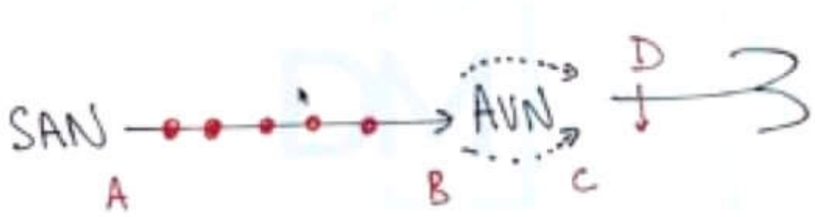
Delta waves in ECG: WPW syndrome

Prolonged PR

Bradycardia

1st Degree Heart Block

1. Athletes (High vagal tone ↑)
2. Rheumatic fever
3. Hemochromatosis
4. Sarcoidosis
5. Endomyocardial fibroelastosis



C/O exercise intolerance

PR = **160 millisec**

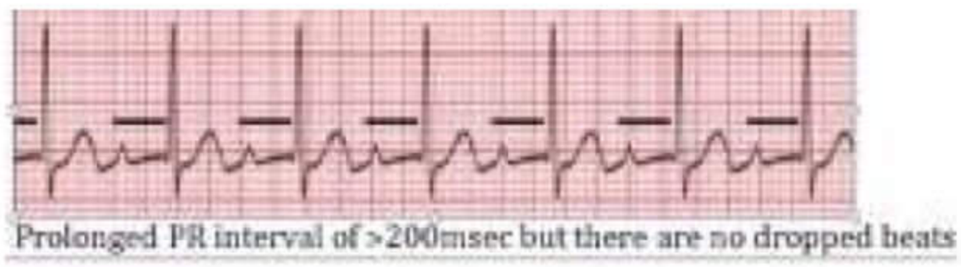
5 sit ups: **HR ↑**

PR = **140 millisec**

PR interval is always inversely related to heart Rate

Investigation- ECG → PR prolonged > **200 millisecs**

Rx- Atropine: oral if can tolerate adverse effects.


Prolonged PR interval of >200msec but there are no dropped beats

2nd Degree Heart Block

* MOBITZ I / **Wenckebach phenomenon**: Serial prolongation of PR interval

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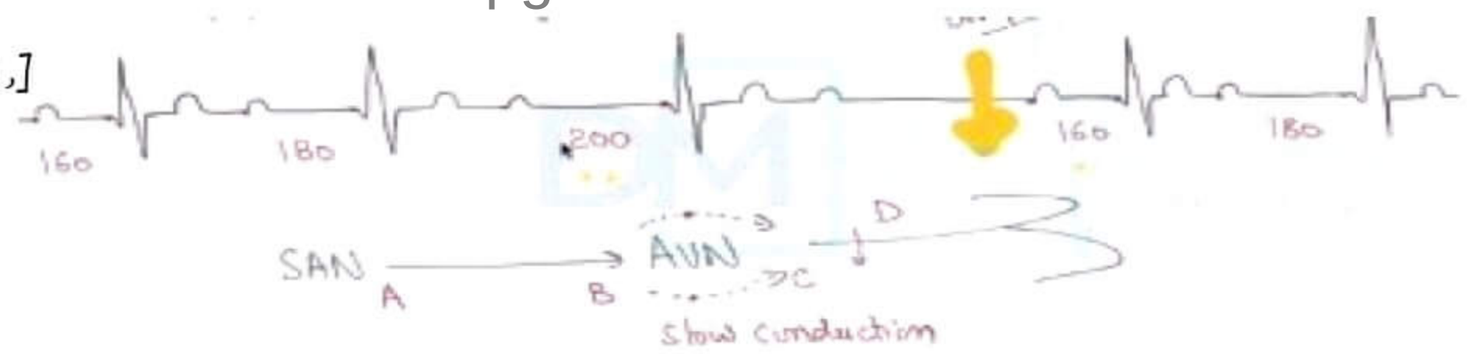
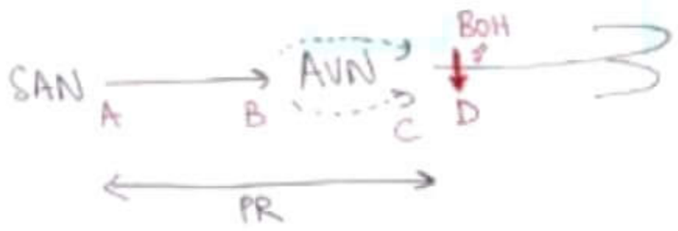
[PR ↑↑↑, Pwave QRS Θ, PR ↑↑↑,]



MOBITZ II



* Life threatening
* MC bradycardia seen post MI

↓

Can contribute to sudden cardiac death overall

MC Arrhythmia seen post-MI = V. Fibrillation

PrepLadder

3rd Degree Heart Block

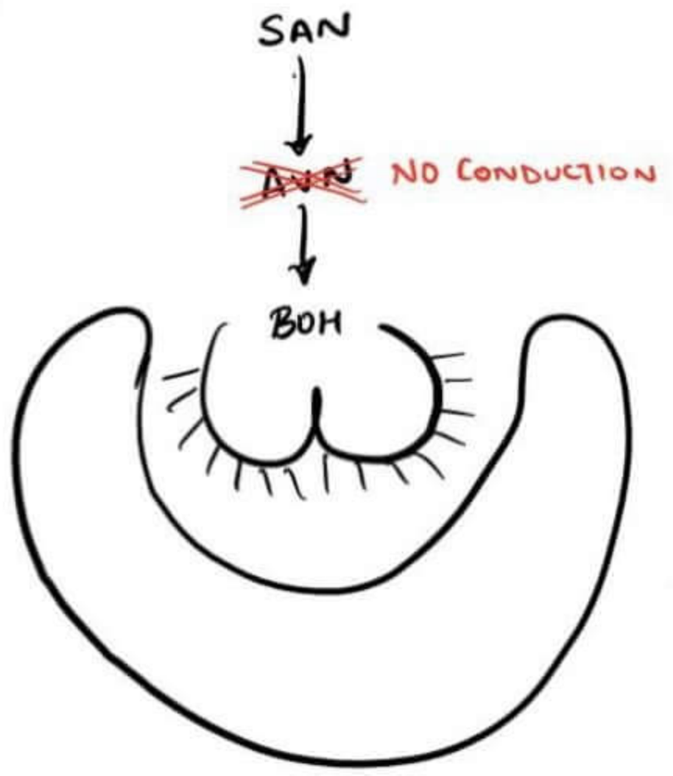
*No conduction by AV Node

SAN → A. rate = 100/min

* BOH → V. Rate = < 40/min

↓

This is called AV dissociation



Cardiac output is drastically reduced due to

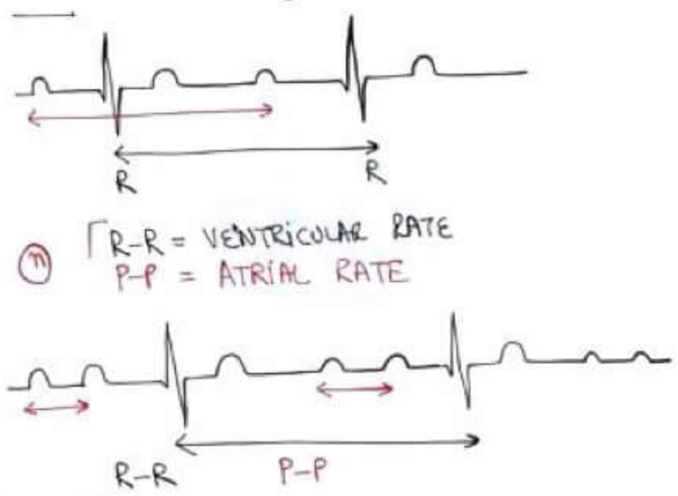
1. Bradycardia
2. Lack of cooperation between atria and ventricles

C/O recurrent syncopal attacks

↓

When pt. stands from supine position

ECG → Stokes adam syndrome



*P-P interval > RR interval

*QRS complexes occur independent of P wave

Rx: - Dual pacing

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1	2	3
* Slow conduction b/w SAN & AVN * PR ↑ > 200 m sec	**Mobitz I** * Problem is in AVN PR ↑↑↑: Missed Beat: PR ↑↑↑	* No conduction by AVN * P-P ≠ R-R It is also called as Stokes **ADAM Syndrome/AV dissociation**
	Mobitz II * Problem in bundle of His AREA PR (N) (N): Dropped Beat: PR (N) (N)	

Pacemaker used in :	Heart Rate
• SAN #: sick sinus syndrome	45-60/min
• AVN #: complete H. block	< 40/min
• BOH #: Mobitz II H. block	15-20/min

Sites of pacemaker's placement

Left → Infraclavicular below skin of chest

Pacing leads: Radio – opaque and can be seen in CXR

RA LA

RV LV

PrepLadder

LEAD CONNECTS TO

In 1950 single lead pacemaker (Introduced): RV

Dual pacing: RA RV

Triple lead pacemaker: RA RV CV

Implantable cardioverter defibrillator (functions) → Read ecg
Analyse ecg
DC shock delivery

Indications of Using I.C.D

Tachy arrhythmias→ Tendency

1. R.C.M / D.C.M
2. LV aneurysm
3. Brugada syndrome: SCN 5A #
   ↓ RV epicardium
   Asymptomatic: ST ↑, V1 V2
   Leading cause of sudden nocturnal death in S. E. Asian males
4. Arrhythmogenic RV dysplasia (ARVD)

Q. Pt. on ICD, C/o electrical shocks in chest first investigation is → Chest x ray.
Reason: Lead malposition/Lead fracture

Q. Pt. on ICD, facial swelling, ↑ supine position: probable diagnosis → SVC thrombosis
due to leads of ICD which are acting like nidus for insitu thrombosis.

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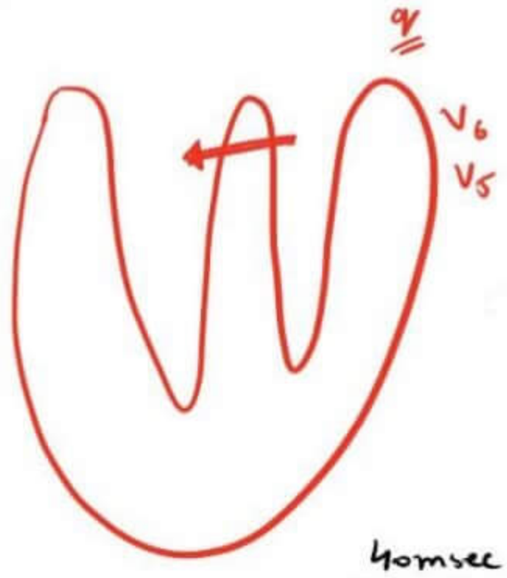
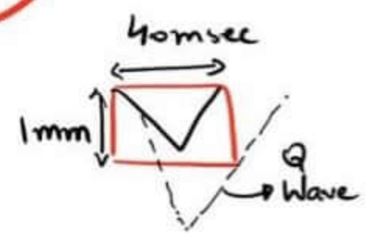
PR

Short	Prolonged
1. WPW	1st Degree H. block
2. LGL	Mobitz I H. block
3. Tachycardia	Complete H. block





Q wave seen in
* MI
* HOCM
* Acute cor pulmonale
↓
S1 Q3 T3

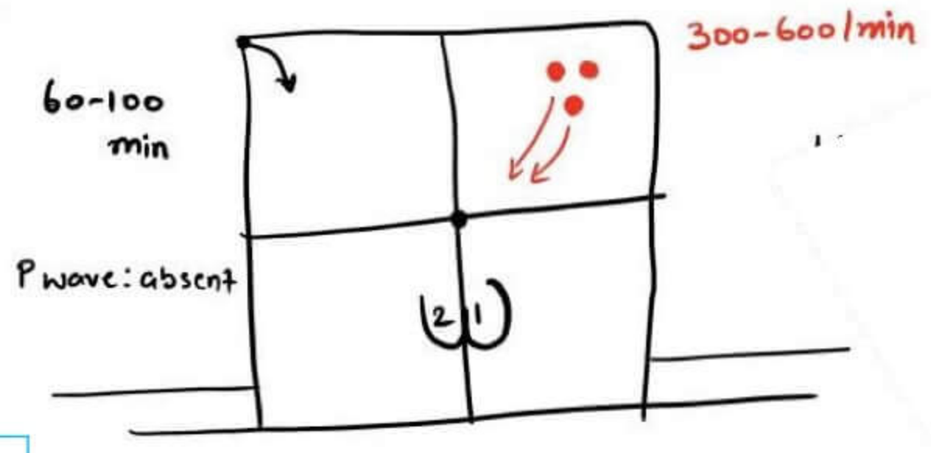
Deep S: Lead I
Deep Q: Lead III
Inverted T: Lead III

Abnormities of qRS complex

Narrow	Wide
SVT	VT

PrepLadder

Atrial Fibrillation



- MC arrhythmia in clinical practice
- MC arrhythmia in HTN
- MC arrhythmia in geriatric population
- MC arrhythmia in DCM (alcohol)
- P wave absent in atrial fibrillation

A:V nodal block	V. Rate
2:1	200
3:1	133
4:1	100

- Irregularly irregular heart rate

MC cause of embolic stroke → non rheumatic A. fibrillation

Q- 40 years old alcoholic (DCM) Binge drinking: Palpitation / dizziness / vertigo syncopal attack

Ans :- O/E: Pulse: Fast

Rhythm: Irregularly irregular

Auscultate - Count H. rate

- Count pulse rate

* When H. rate & pulse rate do not match it is known as **Pulse deficit**

Pulse deficit: > 10 beats / min

BP → 70 / 50 mm Hg

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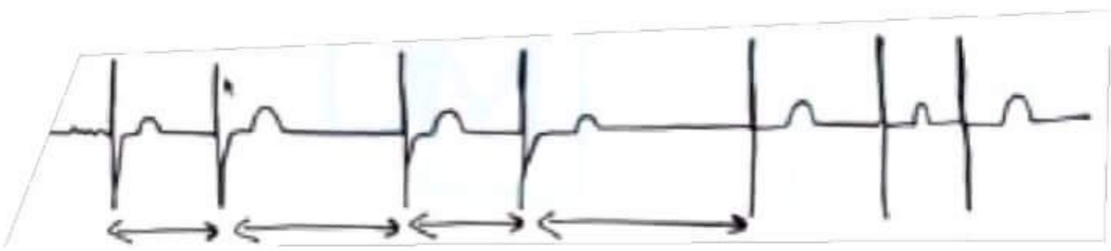
Investigation - ECG

1. P wave
2. R - R: ↓
3. R - R: Irregular
4. qRS: ↓ / ⓝ



Rx- R.A.C.E Mnemonic for management

1. **Rate Control** →
   IV Esomolol/ IV verapamil
   → ↓ HR: ↑diastole time
   ↑ EDV
   ↑ SV ↑ CO ↑BP
2. **Anticoagulation**
   T.E.E: clots ±
   Oral dabigatran, Rivaroxaban
3. **Rhythm Control**
   IV Ibutilide
   Chemical cardioversion
   i.v propofol ↓ fails
4. **Electrical cardioversion**: DC Shock 200 J biphas

PrepLadder

To prevent 1° atrial fibrillation episodes

Oral amiodarone

↓

Ablation catheter

If pt. have CHF + A. Fibrillation = DOC for rate control is digoxin

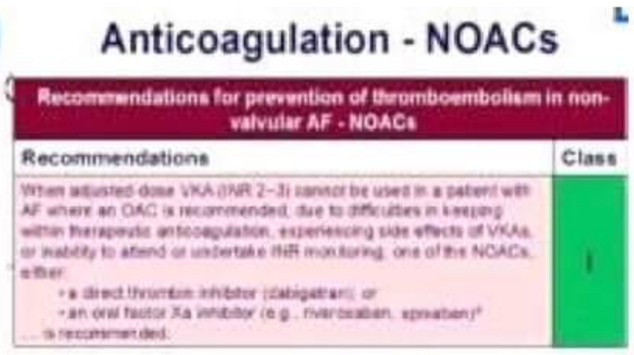
↓

β - blocker: esmolol: Contraindicated

Decision for anticoagulation→

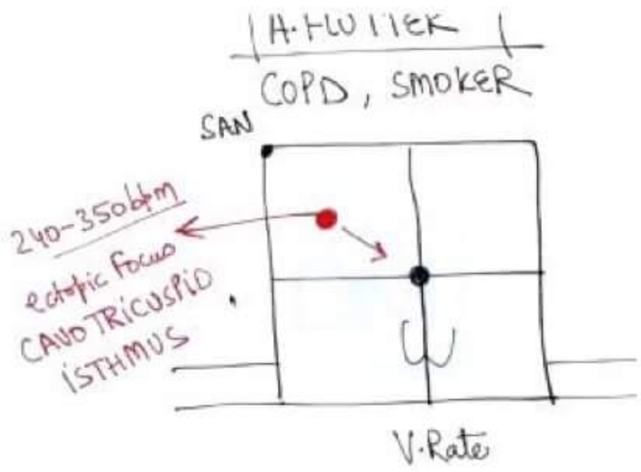
CHADS$_2$ VAS$_c$ SCORE

* DM
* CHF
* HTN
* Age > 75 yr
* Stroke history
* Vascular disease: PAD / CAD / UA
* Age: 65 - 75 year
* Sex category: female
* Clots less than < 2 mm cannot be visualized on TEE



Drugs given→ * Rivaroxaban

* Warfarin (ICH risk)



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Atrial flutter

➢ Pt. will have sudden onset of palpitations, dizziness, loss of consciousness

O/E:

Pulse: 150 / min

Rhythm = regular

BP = 80 / 60

ECG: Lead Ⅱ, Ⅲ, aVF: Ectopic focus: Right sided leads

* Saw tooth pattern
* R - R ↓, regular

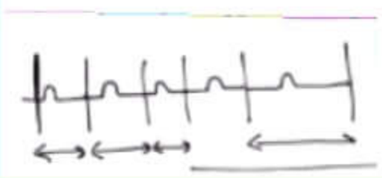
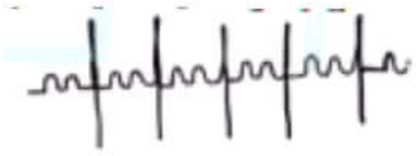
Rx:

1. I.V esmolol (Rate control)/ i.v Verapamil
2. Anticoagulation: 1° pulmonary Embolism
3. Rhythm control: IBUTILIDE iv

↓ fails

4. Electrical cardioversion: 25 - 50 J (Biphasic)

PrepLadder

A. fibrillation	A. flutter
* Multiple ectopic * Foci on L. atria * 300 - 600 /min	* Macro-reentrant circuit * R.A: Cavo tricuspid isthmus * 240 - 350 / min
AV nodal block 4: 1	AV nodal block 2: 1
H. Rate 150 /min	H. Rate 175/min
Alcoholic	COPD
Palpitation, loss of consciousness SBP ↓↓↓ pulse fast	
ECG All leads: Irregular R-R interval 	ECG Rt. sided leads : II, III, aVF 
IV Esmolol DC Shock 200 J, Biphasic	IV Verapamil DC Shock 25 - 50 J, Biphasic

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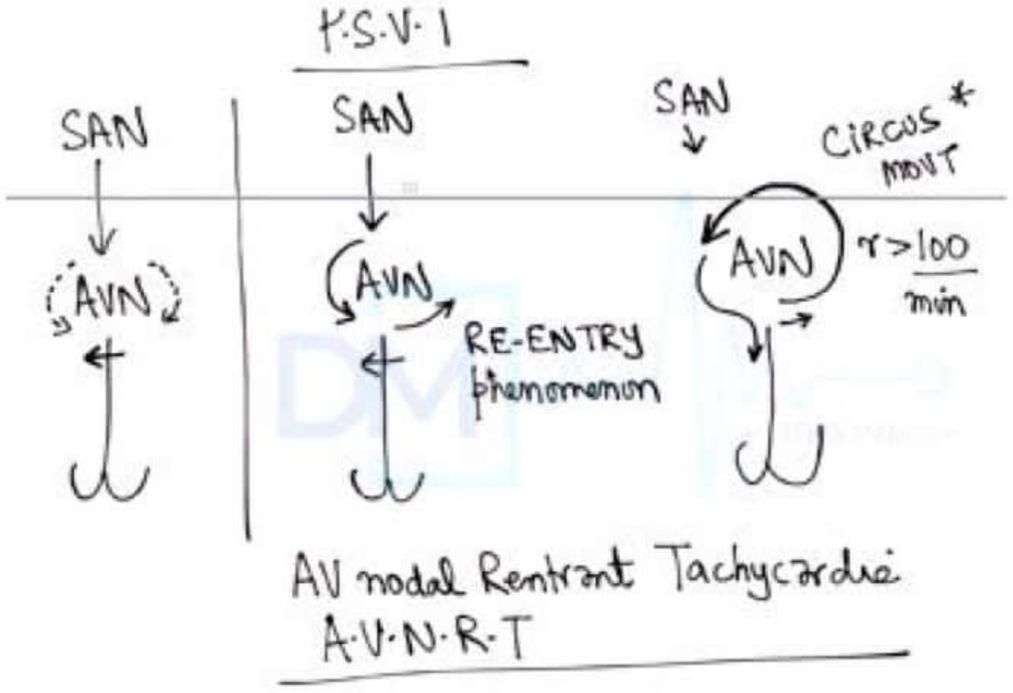
PrepLadder

ECG AND ARRHYTHMIAS 2

PAROXYSMAL SUPRAVENTRICULAR TACHYCARDIA (PSVT)



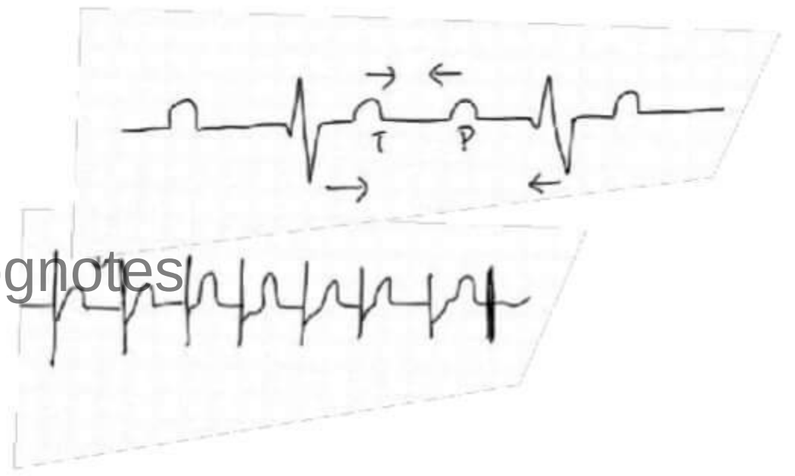
NORMAL DISEASED

E.g. 25 years old lady with recurrent episodes of dizziness and syncopal attacks

Diagnosis:

ECG → Normal when patient is asymptomatic

HOLTER advised - device records ECG for 24 hours



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Findings:

1. Narrow QRS complex
2. ST segment ↓
3. R - R – Regular
4. R - R –Decreased

Management:

Rx

Acute

1) **Carotid Sinus massage**
(Carotid sinus nerve-ix)
↓
Site - perpendicular to angle
Of jaw, burst of 10 seconds

1° episodes (PSVT)

↓
Oral verapamil
↓
Catheter ablation

C/I - Atherosclerosis of internal Carotid artery (Carotid artery bruit).
This is because of Risk of cerebral embolism

PrepLadder

Children: PVST

Rx - Face ice pack

- Valsalva maneuver

2) IV adenosine

6 mg / 12 mg

A-V nodal delay ↑

Circus movement ↓

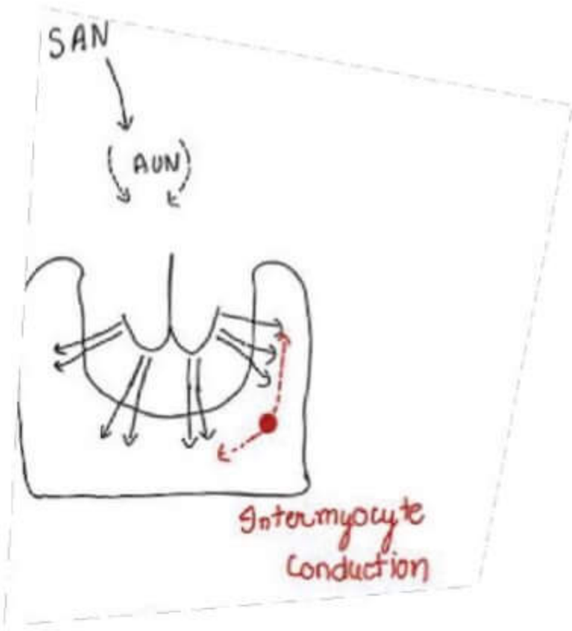
S/E – **Bronchospasm (Self-limiting)**

3) DC Shock

120-200 joules biphasic

Must Know:

Remember that in any MCQ of PSVT where SBP is less than 90 mmHg cardioversion is always to be marked.



Ventricular Tachycardia

- Usually seen Post - MI > 12 hr
- Dispropotionate Tachycardia and lack of coordination between atria – ventricles result in crashing of Blood pressure.

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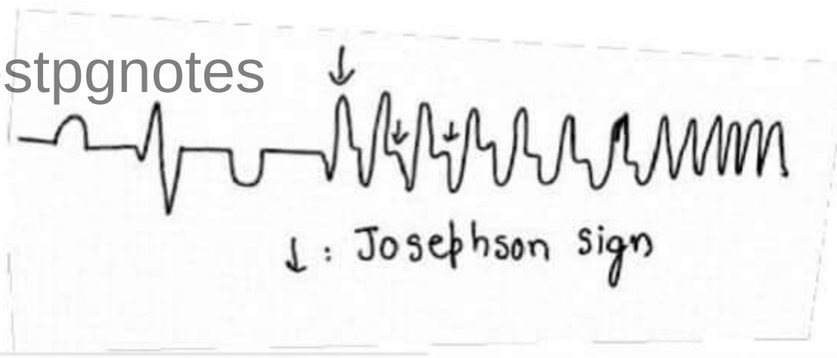
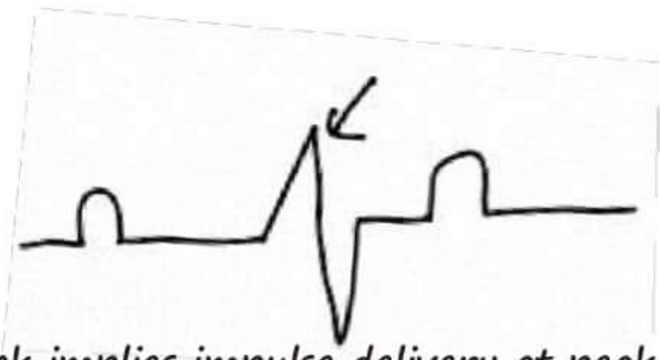
ECG features of V.T

1. PVC > 3 consecutive contractions
2. HR > 100 / min
3. Josephson sign
4. Capture Beat
5. Asymmetrical Rabbit ear appearance



Rx - Pulseless VT

Non-synchronized DC shock

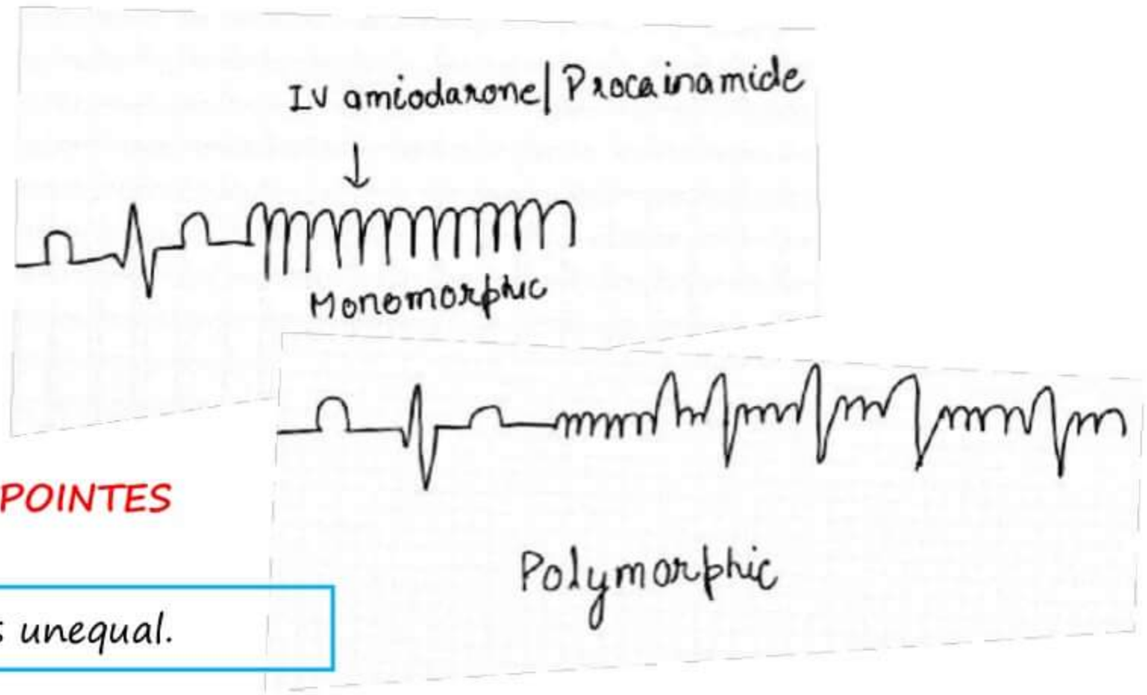


Synchronized DC Shock implies impulse delivery at peak of R wave

PrepLadder

b) Stable Monomorphic VT

IV Amiodarone / Procainamide



→ **POLYMORPHIC VT**

↓

Known by Latin name **TORSADES DE POINTES**

Note: That amplitude of broad qRs in this ecg is unequal.

TORSADES DE POINTES

Causes –

1. K ↓
2. Mg ↓
3. Erythromycin + Terfenadine
   Erythromycin + Astemizole
   Erythromycin+ Ketoconazole
   Erythromycin + Cisapride

Hypomagnesemia
Hypokalemia
Hypocalcemia
Hypothermia
Subarachnoid Hemorrhage
Intracranial Hemorrhage
Hereditary Long QT syndromes

Diagnosis:

ECG criteria – QTC ↑ Prolongation

Where,

QTC = QT / √ R-R

DOC T.D.P – Magnesium SO4 IV

TDP + BP ↓↓ – DC shock

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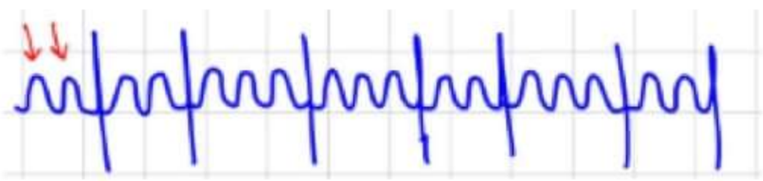
TACHYARRHYTHMIAS

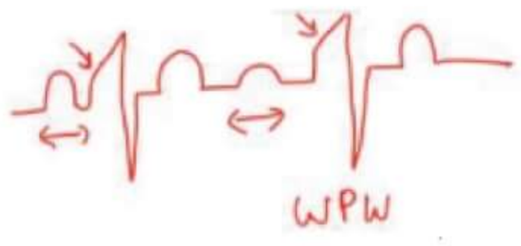
Atrial Fibrillation

Atrial Flutter

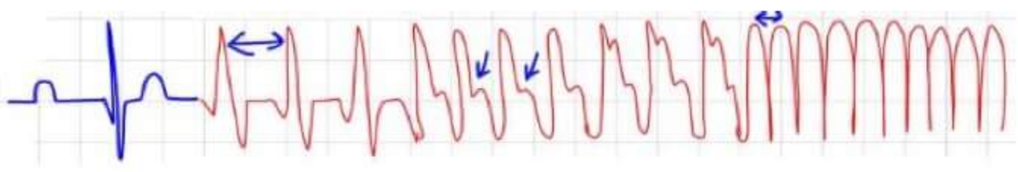


AVNRT

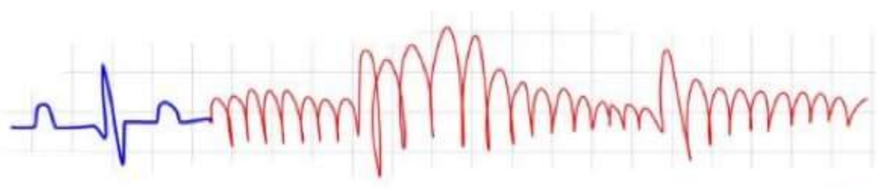
WPW



VT



TDP



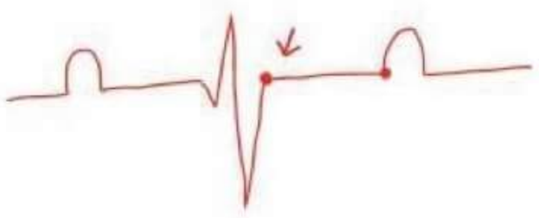
PrepLadder

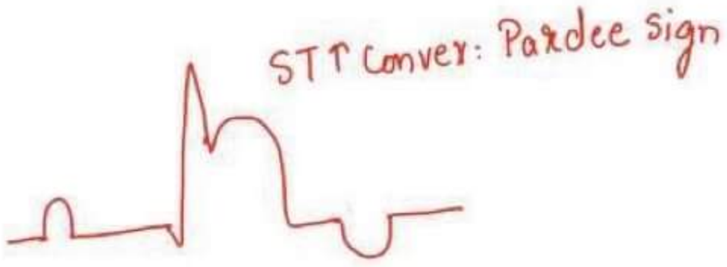
V. Fibrillation

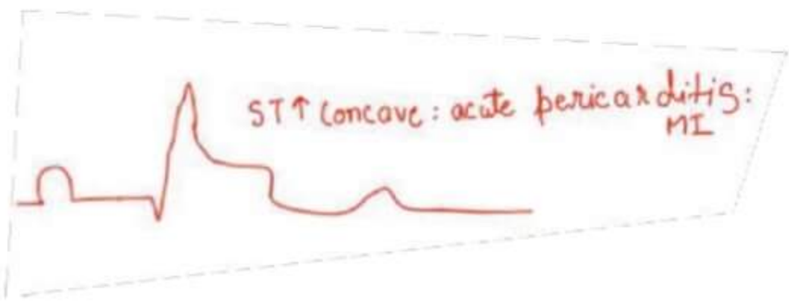
Abnormalities of ST segment

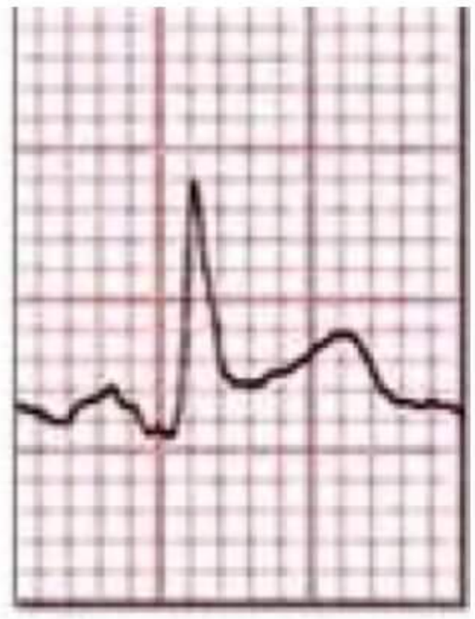
ST Segment Elevation

- ST ↑ convex - pardee sign (MI)
- ST ↑ concave - acute pericarditis









Causes: Mnemonic: **ELEVATION - AB**

1. **E**lectrolyte imbalance = K ↑
2. **L**BBB
3. **E**arly Repolarization Variant
4. **V**entricular **A**neurysm
5. **T**rauma: Pericardiocentesis
6. **I**schemia Injury: MI
7. **O**sbourne wave: Hypothermia (core temp. < 35° C)

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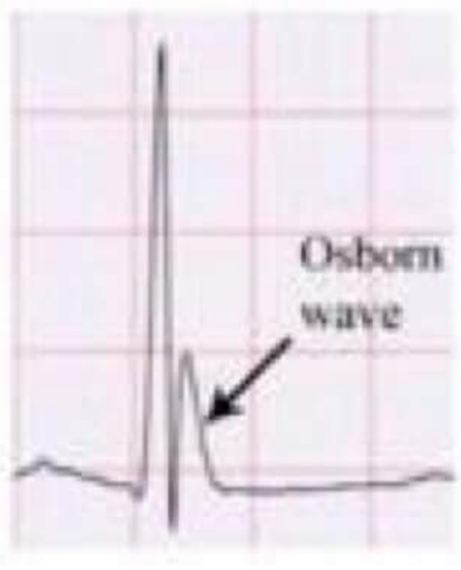
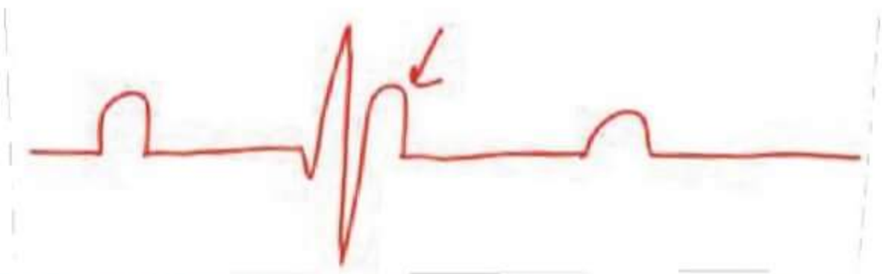




8. **N** - Non- Occlusive Vasospasm - Prinzmetal Angina / Variant Angina
9. **A** - Acute Pericarditis
10. **B** - Brugada Syndrome: SCN5A defect
    - Sudden cardiac death: TDP
    - Asymptomatic→ ECG ST ↑: V_1, V_2

* ST SEGMENT DEPRESSION

Causes:

1. Chronic stable angina / Hibernating Myocardium
    * **70% # Blockage of coronary artery**
    * Chest Pain on Exercise / Emotion
    * Post - prandial angina
    * TMT → ST ↓ ≥ 1 mm ≥ 80 m sec: 2 contiguous leads

2. LVH: ↑ demand leading to subendocardial ischemia

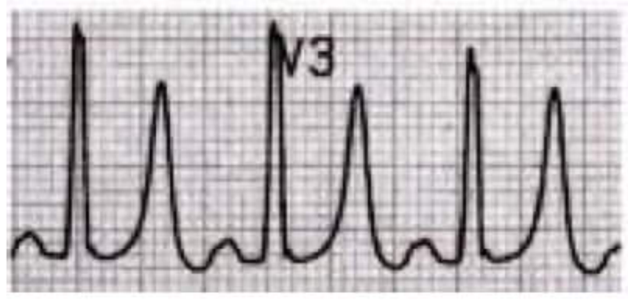
PrepLadder

Coronary artery supply - normal

- HTN, AS, HOCM

3. Normal size Heart, Oxy-Hb availability ↓
   Severe anaemia / cocaine overdosage

4. Digoxin - ST ↓ → **Hockey stick sign**



5. K ↓ - Hypokalemia

Abnormalities of QT interval

$$QT \propto \frac{1}{\text{Calcium, Mg ++}}$$

Normal - 360 - 440 m sec
- 9 - 11 small squares

Hypocalcaemic crisis (Possible systolic arrest)

Malignancy

1. Ca breast
2. Squamous Cell Ca lung - PTH – rp (Related Peptide)
3. Sarcoidosis
4. Vit. D_3 intoxication

Diagnosis

1. ECG→ QT ↓
2. Ionised Ca++ - ↑
3. Total Ca++ - ↑
4. s. albumin- Normal

Extra Mile

- ECG changes with diagnosis

1. PR Prolongation
2. ST depression / Hockey stick sign
3. QT shortening

- T Wave always follows potassium levels

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Treatment

1. IV fluids - Normal saline – Hydration (First line management)
2. Furosemide drip (Causes Calcium loss in urine)
3. **IV Ibandronate (DOC)**
4. Calcitonin Nasal Spray

Tetany

- Thyroid surgery after 72 Hours
- S. Calcium < 7 mg %

C/F:

1. Perioral paresthesias
2. Inflate BP Cuff - SBP + 20 mm Hg
   ↓ 3 min
   - Carpopedal spasm
   - Obstetrician Hand

   } Trousseau's sign
3. **Chvostek sign** – Tap on Facial nerve
   - Irritability
   - Facial Grimace

Risus sardonicus = Tetanus

PrepLadder

4. Death → Laryngospasm

Investigations: ECG - QT ↑
S. calcium = ↓
Ionized Ca ++ = ↓
S. albumin = n

Treatment of Tetany:

IV calcium gluconate

But if he will ask: Surgery induced Hypoparathyroidism. **Then answer as [**Injection Teriparatide (PTH)**]**

ECG Findings of K & Ca Abnormalities

K^+ ↑	Tall tented T, ST ↑	Diastolic arrest
K^+ ↓	Prominent U, ST	Respiratory paralysis
Ca ↑	↓QT↓	Systolic arrest
Ca ↓	QT ↑	Laryngospasm
K^+ ↑	Calcium gluconate	
K^+ ↓	KCl	
Ca ↑	Bisphosphonate	
Ca ↓	Calcium gluconate	

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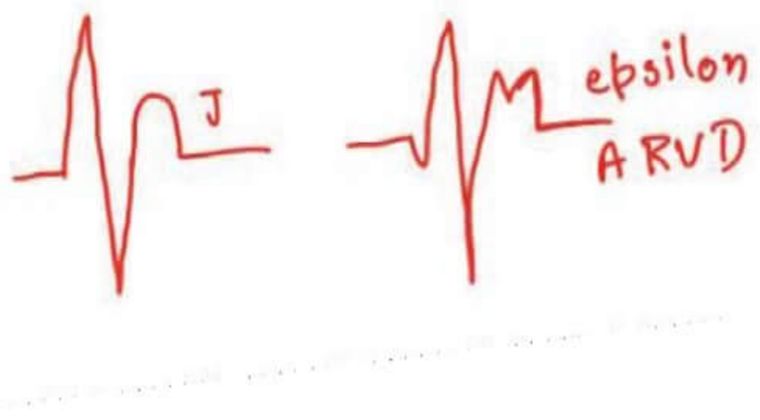
Abnormalities in ECG Summary

P wave → Mitrale, pulmonale

PR → WPW, LGL (Shortening)
→ H. Blocks (Prolongation)

qRS → Narrow - SVT : AVNRT, A. Fib, A flutter
→ Wide - VT
→ Delta – WPW

ST → ELEVATION-AB
→ Depression: CSA, LVH, Cocaine, Digoxin



T → Hyperacute - MI
→ Tall tented - K
→ T wave inversion – MI, K ↓

U Prominent - K ↓

PrepLadder

MULTIFOCAL ATRIAL TACHYCARDIA

- Transient rhythm between atrial fibrillation and atrial flutter.

Etiology

1. COPD (**MC cause**)
2. Theophylline Toxicity
3. Sepsis

ECG Features

1. 3 different morphologies of P wave
2. Isoelectric baseline present between P wave
3. P- P, P-R interval → variable

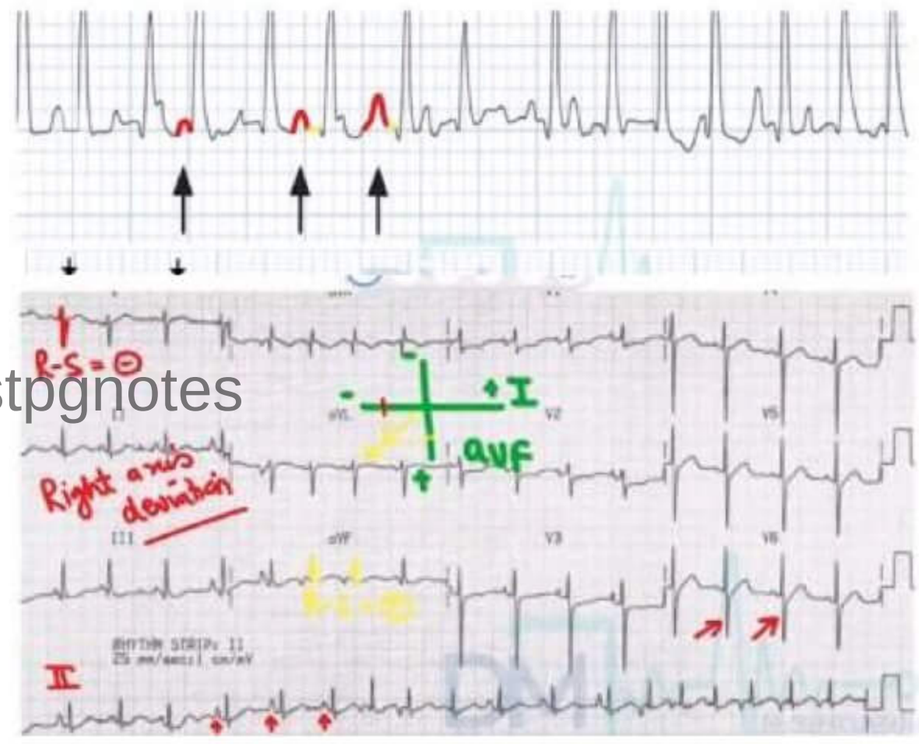
Clinical Feature

Example – Smoker, 60-year, light headness, Palpitations, syncope

O/E – HR ↑
BP ↓ ↓

ECG features

1. Three different amplitudes of P wave
2. RAD
3. Deep S in V_6
4. HR = 100-125/min (Variable)



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Treatment

1. Manage respiratory failure
2. Cardioversion is NOT helpful
3. For acute episode - Metoprolol / Verapamil
4. For Recurrent episodes – Oral Verapamil

Extra Mile

IRREGULAR R-R INTERVAL CAUSES

1. Atrial Fibrillation: **Absent P waves**
2. Multifocal Atrial Tachycardia: **Three Different Morphology P waves**

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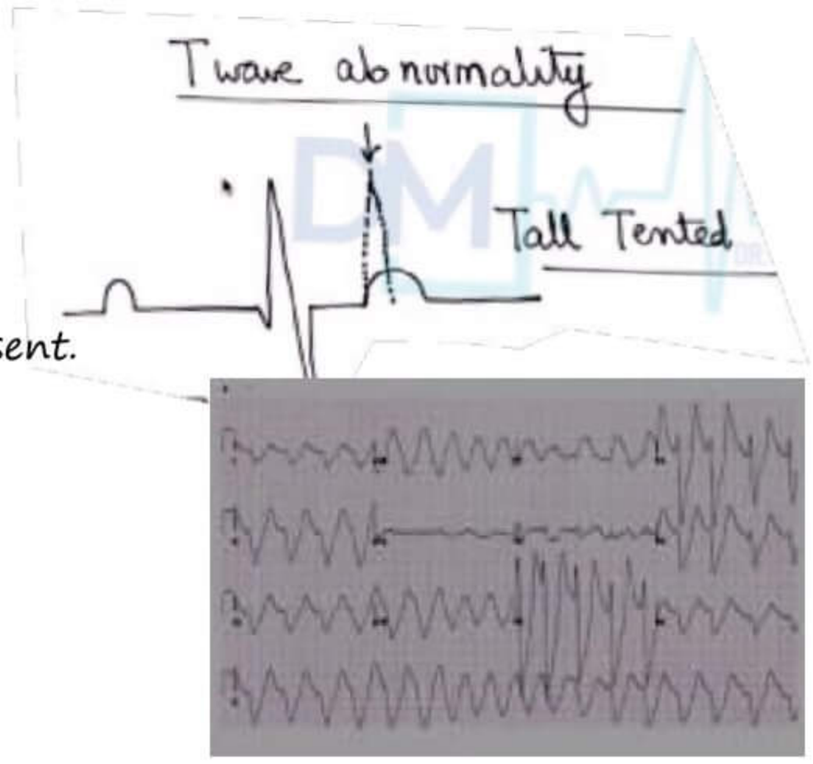
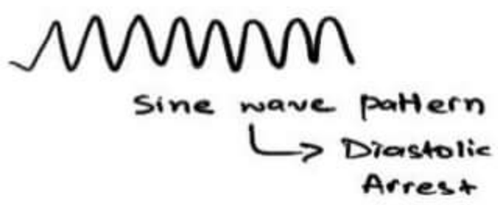
ECG CHANGES IN HYPERKALEMIA AND HYPOKALEMIA

T wave abnormality



$K^+ \uparrow \rightarrow$ T wave: repolarization α K^+

1. Tall tented T wave
2. ST elevation
3. P wave: Amplitude/ duration decreases and becomes absent.
4. qRS complex broad
5. >8.0 meq/dl



Rx:

1. IV calcium gluconate /$CaCl_2$ DOC

   * never Calcium Carbonate

2. (0.5 – 1 meq ↓/ HR): **Insulin drip** (Regular)] Redistribution of K^+
3. Salbutamol/ nebulization
4. IV furosemide: Kaliuria
5. Hemodialysis: Most effective method
6. K^+ binding resin: Enema

↓

Not used in Emergency management because it takes sometime to show response

* Not used routinely in K ↑ Management – Soda-bicarbonate

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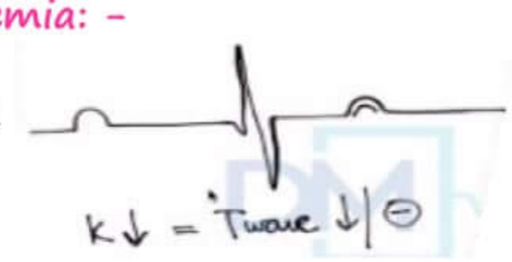
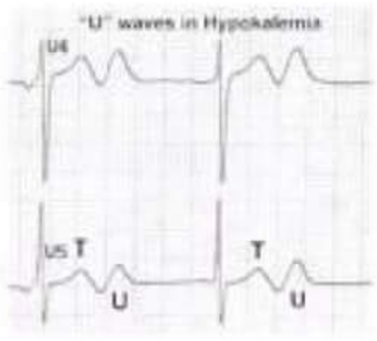
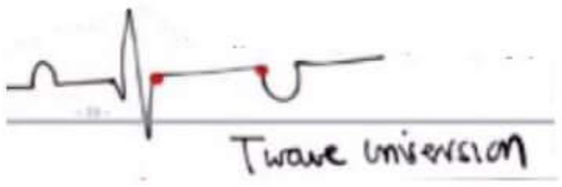
Hypokalaemia: –

1





2.



3. ST ↓
4. Prominent U wave
5. Prolonged QU interval

Death → Respiratory paralysis

Rx= KCl + IV Fluids

PrepLadder

ACUTE CORONARY SYNDROME (PART-1)

ATHEROSCLEROSIS

* Order of involvement of blood vessels in decreasing order

* Abdominal aorta (MC) > Coronary A > popliteal A (M/C peripheral) > Circle of willis (STROKE) (ACP)

- Least common: **Internal mammary artery**
  (Preferred bypass conduit: CABG)
- Abdominal Aorta → AA aneurysm

Size > 5.5 cm

↓

Spontaneous rupture at any time coronary Artery involvement in Atherosclerosis leads to:

1. Chronic stable angina > 70% blockage in any one coronary Artery results in chest pain on exercise, emotion or combination.

Chest pain at rest

2. Unstable Angina
3. MI
4. Prinzmetal angina

Markers for Atherosclerosis

1. **High sensitivity CRP**: If positive: Predictor for future coronary events
2. Total Cholesterol ↑ > 3.5 → ↑ risk of atherosclerosis
   HDL ↓
3. Lipoprotein A : ↑ (Risk of coronary artery disease)
   Apolipoprotein B
4. Homocysteinemia: Autosomal recessive, seen in young coronary artery thrombosis (India) Risk factor for PREMATURE ATHEROSCLEROSIS
5. HDL ↓
6. LDL ↑

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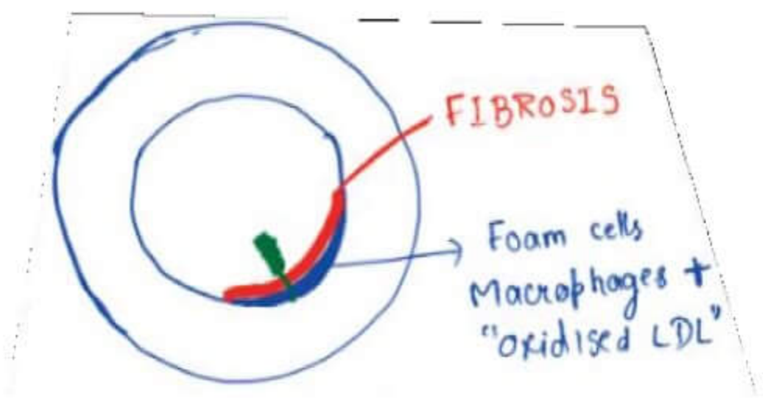
IMAGING for Atherosclerosis

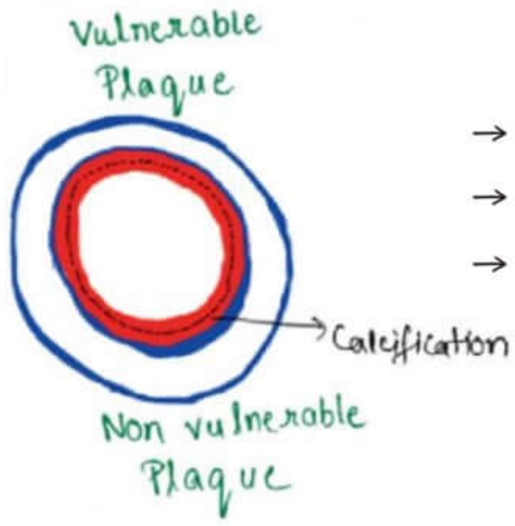


Foam cells
= macrophages +
Oxidised LDL

- Oxidised LDL
- Smoking, sedentary lifestyle, lack of exercise
- Fibrosis
- K/A VULNERABLE PLAQUE

Tear → platelets stick → Thrombus formation
→ OCCLUSION OF
LUMEN

PrepLadder



→ More atherosclerosis
→ More fibrosis
→ K/A **NON VULNERABLE PLAQUE**

- Multidetector CT scan (MDCT)
  - Imaging modality
  - Non-invasive method
  - Differentiates b/w vulnerable & non vulnerable plaque

Calcification

- Seen in later stages
- **AGATSON Score** amount of calcification in **Coronary Arteries**

CHRONIC STABLE ANGINA / REVERSIBLE ISCHEMIA OR HIBERNATING MYOCARDIUM

60 yr, smoker, HTN (Non-compliant)

↓

- CHEST PAIN ON EXERTION, emotion
- Excruciating pain
  - LEVINE SIGN (Patient putting his hand on left side of chest to describe the diffuse chest pain)

  Radiating pain

  > 70% blockage
- PALPITATIONS, Diaphoresis + Duration: ~ 10 minutes
- RELIEF ON REST
- POST PRANDIAL ANGINA
- Vasoconstriction ↑ in morning (Therefore episodes occur in morning)

ECG:

- Asymptomatic → ST normal

STRESS TEST

- **Symptomatic**, ST depression
  ↓
  Sublingual nitroglycerin
  ↓
  Relief
  ↓
  Repeat ECG (15 min) = ST normal

} Reversible Ischemia

STRESS TEST

1. **Treadmill test [BRUCE MODIFIED PROTOCOL]**
   - Non invasive test

   ↑ speed, ↑ incline

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(1.7 mph → 2mph------6 mph) (mph→ miles per hr)
Increase speed every 3 mins
- Continuous ECG and BP monitoring
- TARGET HR = 85% of maximum possible physiologically
= 85% [220 - Age]

* no ECG finding → no blockage

* ECG finding ST ↓ ≥ 1mm > 80 m sec : 2 contiguous leads
(Down sloping)
↓
Indicates Blockage in coronary Arteries

* Resting, ECG after 3 mins of termination of test post exercise ST segment depression
↓
Indicate BLOCKAGE in coronary Arteries
* Sensitivity 75%

Contraindications for performing Tread mill test:

1. Morbid obesity (BMi > 40)
2. Severe aortic stenosis
↓
Fixed obstruction
Cardiac Output ↓
3. Non healing ulcer - SOLE
4. DVT (Risk of embolization)
5. CHARCOT JOINTS
6. B/L severe osteoarthritis knee
7. BUERGER / TAO (Thromboangitis Obliterans)
8. MI < 48 hrs
9. Unstable angina (acute)

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2. Stress echocardiography
- Morbid obesity with CSA symptoms
- IV Dobutamine; receptor activation, HR ↑
↑ O_2 consumption

ECG: ST ↓ ≥ 1mm ≥ 80 m sec: 2 contiguous leads
Echocardiography: REGIONAL Hypokinesia
(Contractibility on lower side)
Sensitivity = 80%

3. Myocardial perfusion imaging (MPI)
(i) → Thallium scan
→ Gamma camera
Thallium - 201
Dobutamine
Plaque cause luminal obstruction ≥ 70% blockage

(ii) Technetium 99 / SESTAMIBI SCAN
Sensitivity = 90%

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Gold Standard investigation to identify coronary A blockages

- CORONARY ANGIOGRAPHY
- Real time evidence
- % blockage
- Site of blockage
- Number of blockages

Diagnosis

- PET scan > 95% - BEST test to identify viability of Myocardium. It helps to differentiate scar vs ischemic Hibernating myocardium
- Thallium scan = 90%
- Stress Echocardiography = 80%
- TMT = 75% - 1st to be done

Treatment: DOC CSA: β blocker Metoprolol (↓ HR)
Mortality ↓ drug = Metoprolol

1. Tab Aspirin 75 mg OD (↓ mortality)
   (or)
   Clopidogrel 75 mg OD
2. SL NTG emergency USE
   Buccal spray (Wider surface area)
   Transdermal patch
   - No mortality reduction seen with Nitrates.
3. Tab Isorbide mononitrate (Post prandial angina)
   Disadvantage: Tolerance
   Drug holiday: 8 hours everyday
   - No mortality ↓
4. Tab metoprolol
   ↓ mortality,
   CI in HR < 60 / min
   Sick sinus syndrome: SAN #
   Complete heart block: AVN #
   Mobitz II heart block: BOH #
   * acute CHF
   OR
5. Tab Amlodipine
6. Tab Rosuvastatin (duration of action 19hr)
   Atorvastatin (Duration of action 14 hr)
   HMG COA reductase inhibitors
   (Bed time dose)
   Mortality ↓
7. Smoking Cessation
8. Vitamin B6 / 9 / 12 (Homocystinemia)
   Best : B6
9. New drugs:

- IVABRADINE: Inhibits funny current
- Ranolazine
- Trimetazidine

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- Nicorandil

If Failure of medical therapy

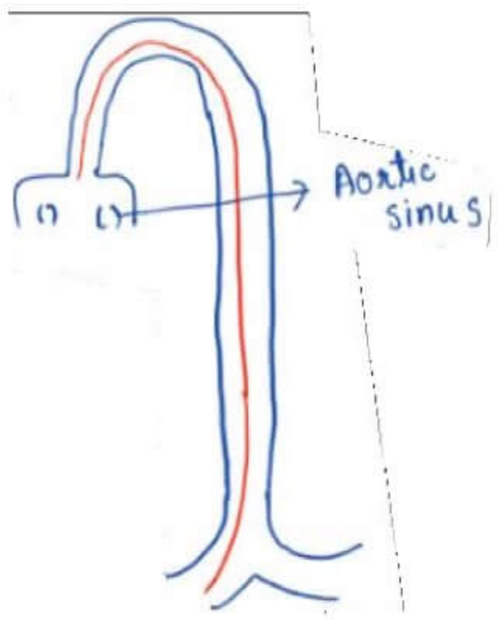
- Perform Coronary angiography (Invasive)
- Via Radial / femoral artery access
- Guidewire : Fluoroscopic guidance

* SELDINGER TECHNIQUE - puncturing radial artery

* Triple vessel disease: Rx - CABG

* Single vessel disease: Rx - Percutaneous coronary intervention (PCI) + Stenting

* Double vessel disease: Rx - PCI + stenting



Triple Vessel Disease (TVD)

Left anterior descending artery blockage (Anterior wall)

Left circumflex artery blockage (Lateral wall)

Right coronary artery blockage (Inferior wall)

- Poor or no response to medication
  - Advise CABG

Graft

1. Internal mammary artery
2. Radial artery
3. Great Saphenous vein
4. Gastroepiploic artery

Note: Arterial graft is always superior to venous graft.

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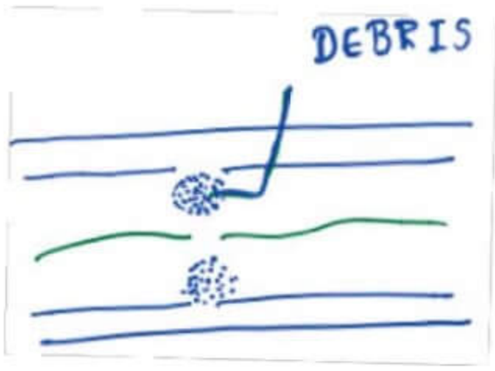
Single Vessel Disease

Treatment: PCI + Stenting (To prevent Re-development)



Steel wire Balloon

↓

Destruction of atherosclerosis plaque

↓

Disintegration

↓

Debris + guide wire

↓

Acts as magnet for platelets

↓

Platelet plug formation

↓

Type 4A MI

↓

↑ troponin I X 5 times

To prevent such an event of patient having Mi while undergoing P.C.I

* **Pre-op:** Anti-platelets drugs: **TICAGRELOR/ PRASUGEL/ TICLOPIDINE**

(Prevent formation of thrombus)

Anti-clotting: Enoxaparin

* **Intra-op:** **Abciximab / Eptifibatide / Tirofiban**

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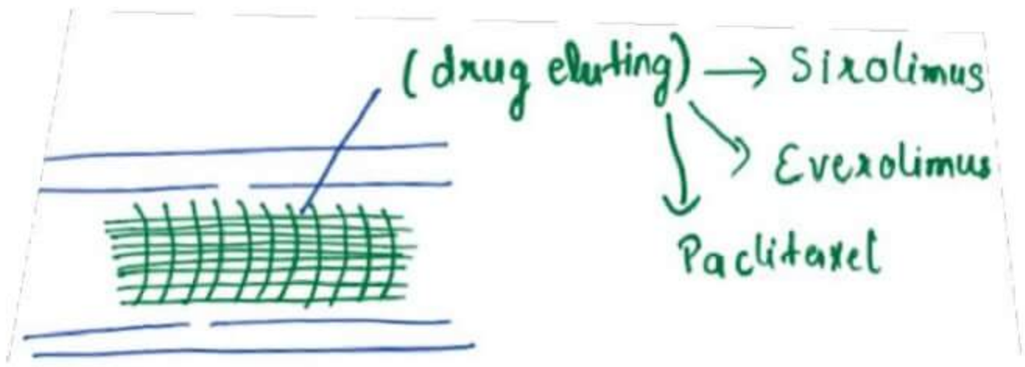
* Stenting is done to avoid redevelopment of atherosclerotic lesion

Drug eluting stent, **biodegradable**

→ **SIROLIMUS**

→ **Everolimus**

→ **Paclitaxel**

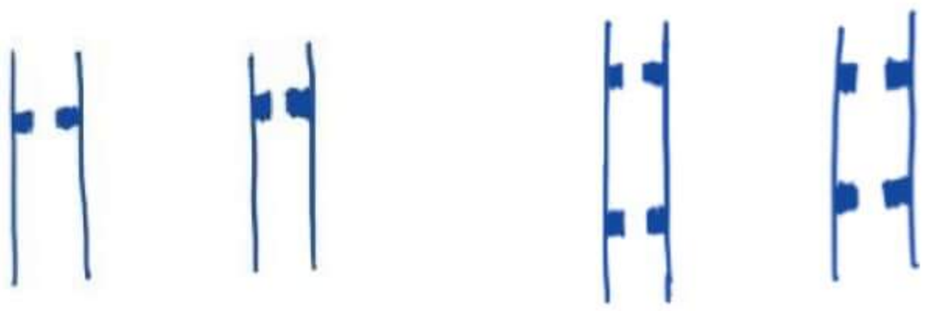


Double Vessel Disease

PCI + Stenting

Cost ↑ 2 stents

If Multiple blockages in both vessels advise CABG



Double vessel disease, PCI + STENTING

Double vessel Disease without multi site # =CABG

Must know

If in a Q, only L.A.D Blockage is given with ejection fraction < 40%, then answer TOC as CABG

Revascularization of hibernating myocardium

PCI + Stenting

- Single vessel D
- Double vessel D

CABG

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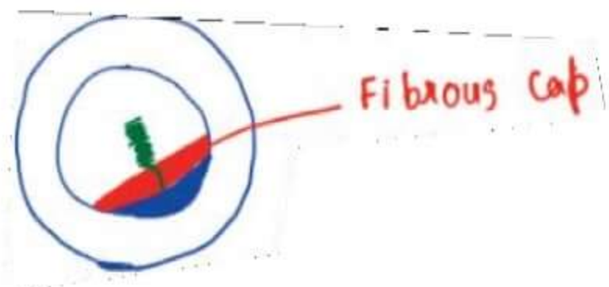
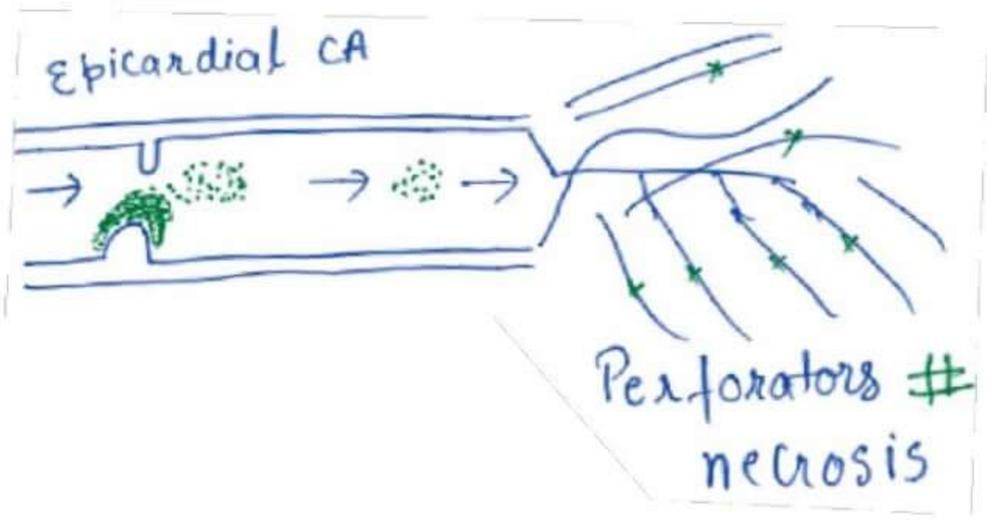
STUNNED MYOCARDIUM = MI

UNSTABLE ANGINA



- Perforators
- Micro occlusions
- Necrosis
- Atheroembolism
- Chest pain at rest / Levine sign
- Diaphoresis / palpitations
- Dyspnea
- 3 hours

- Plaque fissure
- Causing collagen exposure
- Platelet plug : Thrombus
- Protein C / S / AT III



O/E

ECG = ST normal in 50%

ST ↓ = 25%

T wave inversion = 25%

PrepLadder

Cardiac Marker

C Troponin I = Normal/ elevation (Mild to moderate) (Normal < 0.04 mg / dl)

In MI, troponin ↑ x2, x3, x5, x10

Treatment

ABE-MOAN: Mnemonic

IV **A**BCIXIMAB

β - blockers: Metoprolol I/V

Enoxaparin SC

Morphine, **O2**-**a**spirin, **N**TG drip

(325 mg chewable)

↓

Inhibits TxA_2 Production

DOC: IV NTG drip > Enoxaparin

If patient does not improve

Monitor: SpO_2: ↓↓

BP : ↓

Crepitations: ++

TIMI score Thrombolysis in MI score

Treatment: Delayed percutaneous coronary intervention thrombolysis is contraindicated in case of unstable angina.

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PRINZMETAL ANGINA

Spasm of epicardial coronary artery In normal individual, Normal Acetylcholine → coronary vasodilation Liberation of NO

In PA,

Ach = Coronary vasoconstriction, NO↓

Arginine $\xrightarrow[NOS\ 3]{\text{nitric oxide synthase 3}}$ **NO (In coronaries)**

↓

Malfunction due to damage to coronary endothelium

Presentation,

Female, 60 yrs, chest pain at rest

3-4 hours persisting in especially morning hours

Diurnal variation of chest pain

Multiple attacks and more in winter months

Past medical history: H/O **Raynaud's Phenomenon**

Cold H_2O exposure → Vaso Constriction of blood vessels of Tip of fingers, Toes

White ↓ **Blue** ↓ **Red**

Both **Prinzmental Angina and Raynaud Phenomenon** are vasospastic disorders and can co-exist in same patient

PrepLadder

ECG: ST ↑ (Variant angina)

Cardiac Troponin I = Normal (< 0.04 ng/dl)

2 Treatment: IV NTG drip (DOC)

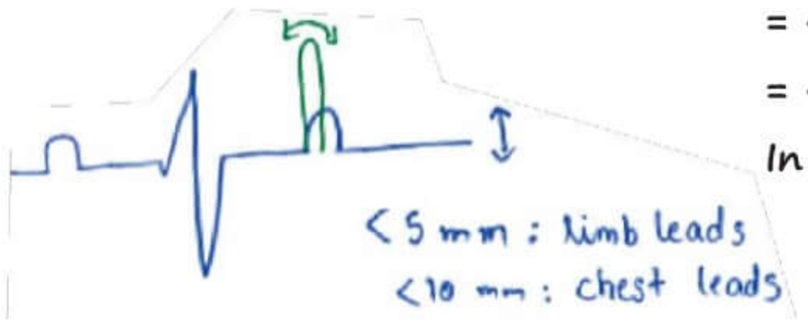
Tab isorbide mononitrate

+ amlodipine

3. Work up for hibernating myocardium

MYOCARDIAL INFARCTION

* ECG findings: Normal vertical height of T wave



= < 5 mm: Limb leads

= < 10 mm: Chest leads

In MI, T wave will become bigger

Rounded appearance

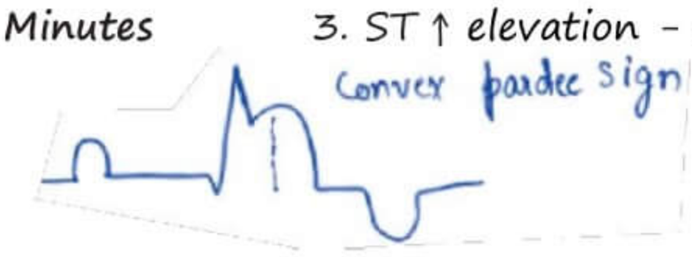
Height > Breadth

Seconds → 1. Hyperacute T wave (Indicates severe myocardial ischemia)

↓

2. T wave inversion

Minutes 3. ST ↑ elevation - convex in upper direction (Indicates myocardial injury)



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Pardee sign/ Tomb stone pattern

Chest leads

≥ 2mm for males

≥ 1.5 mm for females

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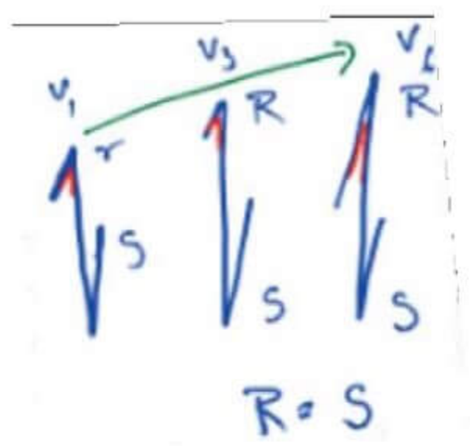
4. Hours (> 1 hr) = Deep Q waves

= INDICATES cell death

= Persists for whole life

= Old MI / previous MI



5. Poor progression V_1 of R wave

→ Localization of surface involved in MI

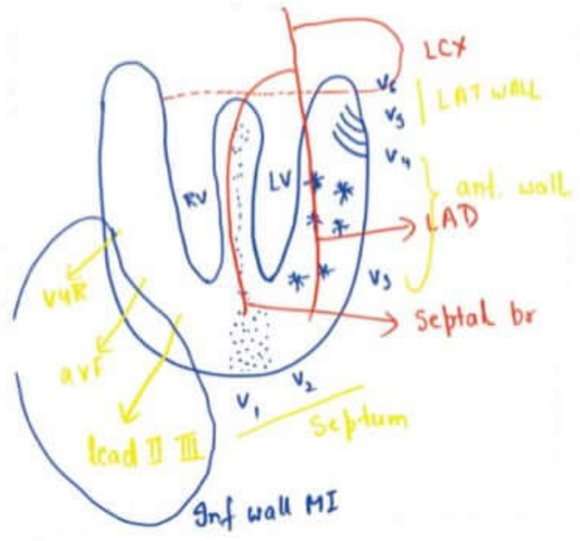
- R not increasing with normal magnitude
- Non progression of R
- ECG poor at localising right ventricle ischemia and LCX artery ischemic

V1V2 SEPTAL ISCHEMIA

V3V4 ANTERIOR WALL

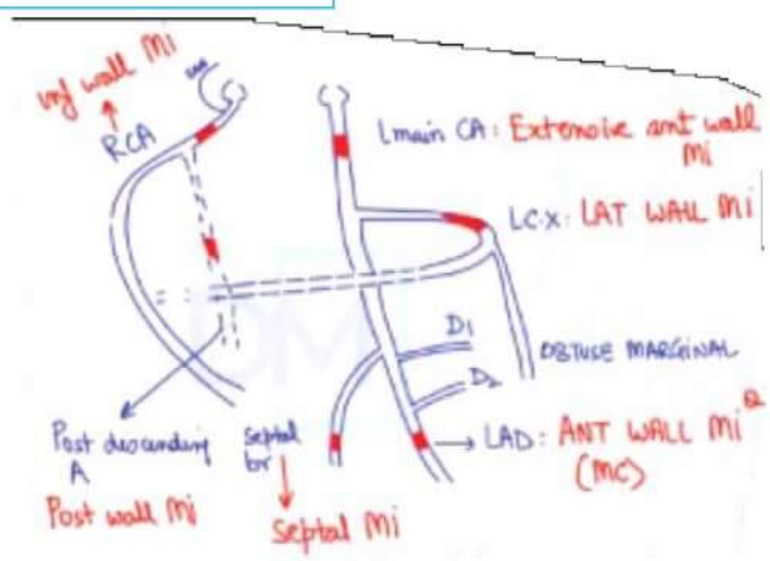
V5V6 LATERAL WALL

- RV forms inferior surface of heart
- For RV ischemia use the following leads
  1. V4R
  2. aVF
  3. Lead II, III



PrepLadder

BV #	INFARCT	ECG finding
1. LCX	LAT WALL	V_5V_6 I_{aVL}
2.SEPTAL BRANCH	SEPTAL MI	V_1V_2 I_{aVL}
3. LAD	Anterior Wall MI	V_1-V_4 I_{aVL}
4. L main CA	Extensive Wall MI	V_1-V_6 I_{aVL}
5. PDA (Intraventricular)	Posterior Wall MI	V_1-V_4 → ST ↓ V_7, V_8, V_9 → ST ↑ (Reciprocal changes)
6. LAD	NSTEMI ant wall MI	V_1-V_4 → ST ↓
7. Inferior wall MI	Inferior wall MI	lead I, II, aVF



First branch of:

AORTA: Coronary Artery

Aortic arch: Brachiocephalic trunk

* CARDIAC BIOMARKERS

1 CPK-MB (Older): Creatine phosphokinase myocardial band

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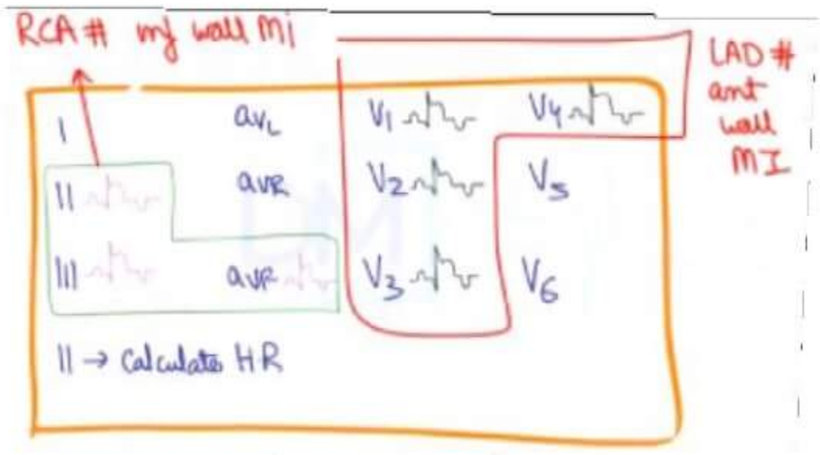
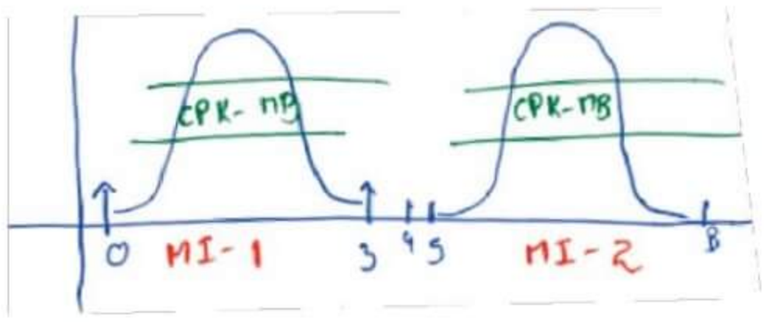
Marker	Rise	Peak	Fall
CPK-MB	4-6 hrs	12-24 hrs	48-72 hrs
Trop T	3 hr	24 hr	14 days
Trop I	3 hr	24 hr	10 days



1st to rise in MI = Heart fatty acid binding protein (HFABP)

Old data = Myoglobin

- BEST / IOC / SENSITIVE / SPECIFIC } Cardiac Troponin-I
  IOC MI in ATHLETES }
- Reinfarction > 72 hr: CPK-MB
- Reinfarction > 1 hr: Troponin I: ↑↑ 20% admission base line value



- Reinfarction: Troponin I
- Last to rise in MI: LDH. (Lactate dehydrogenase)

- MI: Normal Troponin I < 0.04 ng/dl
  (Minimum) x2, x3, x5, x10
- Troponin I Does not rise immediately
- SERIAL TROPONIN I: Admission value: Normal
  3hr value: ↑↑

PrepLadder

For diagnosis of myocardial infarction in a case

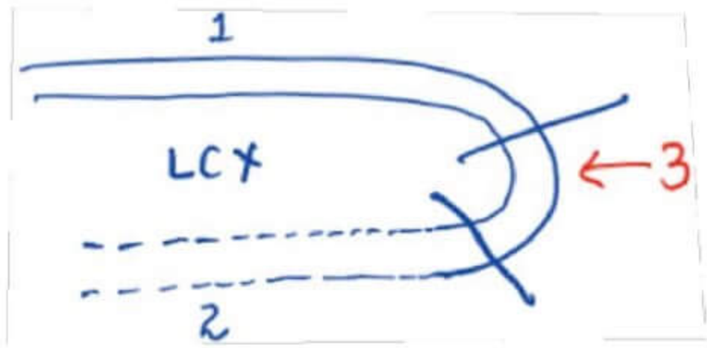
* LEVINE SIGN positive x 3hr

1. ELEVATED CARDIO BIOMARKERS → Cardiac Troponins are more reliable

and / or

2. ECG changes:

- 1st done in any case of chest pain



Limitations

1. Poor at localizing right ventricular ischemia
2. Ischemia of left circumflex artery

and/or

3. Intra-op MI → SpO_2 ↓, BP ↓, crepitations ++

→ Trans-esophageal echocardiography

T.E.E

Stunned myocardium

- If any of these are positive, it indicates myocardial injury due to coronary artery thrombosis.
- It asked to select one, **elevated cardio biomarkers are most reliable for diagnosis**.

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ACUTE CORONARY SYNDROME (PART 2)

Diagnosis + management in STEM I

60 yr old male smoker, HTN (Non-compliant),

Levine sign +,

Diaphoresis +,

Dysnea minimal activity – grade III,

Orthopnea,

Pink frothy sputum,

O/E: HR – 160/min, BP – 180/100 mm of Hg, JPV ↑, neck veins full, Kussmual sign+, S1 - Loud (Tachycardia), S2 – ERB's point – splitting

Narrow split S_2: LVF

Wide split S_2: RVF

S_3: low pitch / ventricular gallop rhythm

Bi - Basilar Crepitations → Interstitial lung disease / Idiopathic pulmonary fibrosis

Chest- B/L fine crepitations

ECG → V_1 - V_4: ST ↑: 3mm

T wave inversion

Troponin I → x 2

STEMI/ Ant wall / LVF

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Rx:

MOAN → **Morphine, Oxygen, Aspirin, Nitrates**

1. **O_2**: SpO_2 < 95%

2. **Tab Aspirin 325 mg** (Chewable)
(Absorbed from buccal cavity mucosa when crushed between teeth)

↓

Inhibit TxA_2 production

Clopidogrel: P_2Y_{12} receptor → inhibit platelet aggregation

3. Sublingual nitroglycerine →

Causes pooling of blood in vein S/E: SBP ↓

Contraindicated: SBP < 80 mm Hg

4. **Morphine** → SC / IM / IV

↓ **Pulmonary edema**

↓ **Air hunger**

↓ **Infarct size**

↓ **Pain**

5. **IV metoprolol** : ↓ HR ↓ O_2 consumption

↓ **Infarct size**

PrepLadder

6. Inj enaxaparin SC (Prevent clot which has already developed in coronary artery of patient)

7. Pulmonary edema → IV furosemide
ACE inhibitor
Nitroglycerine drip

8. Cath lab : Percutaneous coronary intervention

Door to balloon time → Angiography, Balloon angioplasty

< 90 minutes

Cath Lab: Not available → Thrombolysis Door to needle time < 30 mins

- Alteplase - Preferred in stemi
- Reteplase - Acute ischemic attack
- Tenecteplase
- STK (Streptokinase)

Mechanism of action - Plasmin **Fibrin insoluble** -----→ **Fibrin soluble**

MC complication of thrombolysis → Bleeding

Antidote of STK Toxicity → Epsilon amino caproic acid

STK : Group C Streptococcus

↓

Streptococcus Equisimilis

Allergic reactions / anaphylactic shock (Type I)

(Reuse of STK - after 6 months)

↓

Mortality due to → **Laryngeal edema**

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Rx of Anaphylaxis - IM adrenaline 0.5 ml
Undiluted (1:1000)

Cytokines in anaphylactic shock → **IL-4**

Cell responsible for histamine release → **Basophil**

IOC - **Serum Tryptase level**

Thrombolysis is contraindicated in -

1. **Recent stroke** (< 3 months)
2. Bleeding diathesis
   - **Platelet count < 1 lac**
   - **Prothrombin / International normalized ratio → ↑↑ (11-16 sec)**
   - **aPTT → ↑↑ (30-40 sec)**
   - **Single donor platelets are given**
   - **Fresh frozen plasma**
3. Unstable angina / Prinzmetal angina → spasm NSTEMI
4. Aorta dissection
5. SBP > 185 DBP > 110 mm Hg - Labetalol
6. CPR > 10 minutes (Prolonged)
7. Pregnancy
8. **Known case of** Brain Tumor → ↑ hemorrhage Risk

PrepLadder

9. **Known case of A-V** aneurysm → ↑ hemorrhage Risk

10. Recent major vascular surgery

Same clinical presentation but note the change in ECG finding

ECG → T wave inversion V_1 - V_4

cTrop I → x2

NSTEMI / ant wall of heart

Rx → IV abciximab

IV β blocker (↓ HR)

Inj enoxaparin (SC)

Morphine - O_2 - Aspirin clopidogrel - IV NTG drip

STEMI + unstable angina → ABE - MOAN

DOC = IV NTG drip

Fails to respond = SpO_2 ↓ BP ↓ CREPTS ++

Delayed PCI

Unstable angina / NSTEMI

↓ ↓

ST normal ST normal

Trop I ↑ Trop I x2 fails

Rx - ABE-MOAN -----→ delayed PCI

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MI

STEMI

Cath lab - 1^0 PCI

D2B time < 90 min

Or

Cath lab - not available

Thrombolysis

D2N time < 30 min

NSTEMI (Thrombolysis contraindicated)

↓

ABE-MOAN

↓ Fails

delayed PCI

Updates 2020

In case of failure of thrombolysis, Rescue PCI is done within 90 minutes of starting Thrombolysis. Note that this 90 minutes is not from entry into hospital but initiation of Thrombolysis

COMPLICATIONS OF MI

1. Arrhythmias (MC)

Ventricular fibrillation: Twitching, pulseless / BP ↓↓ (< 1 hr) : Golden period

Sudden cardiac death

* MC bradyarrythmia SCD Post M

→ Mobitz 11 H Block

V. Fib - ECG = Twitching activity

PrepLadder

< 5 min (Onset of V. fib) = DC shock 200 J biphasic

> 5 min (Onset of V. Fib) = 1st step is chest compressions as brain stem is having severe ischemia and by the time DC shock is delivered it may be too late

- Chest compression

  30:2 → rescue breaths at 100-120 / min

- Sternal depression = 5 cm lower 1/3rd of sternum

  MC solid organ traumatised during CPR → Liver

  MC RIB # during CPR → 4-6th ribs

* BLS Paediatrics, CPR Ratio

Single Rescuer – 30:2

Two rescuers – 15: 2

* Neonatal resuscitation – 3:1 CPR Ratio

Mandatory → 2 rescuers

V. Fib = > 5 minutes (Onset)

1. CPR = 30: 2 x 2 minutes
2. AED =DC → 200 j Biphasic
3. CPR – DC shock x 3 times
4. IV – adrenaline → ↑ Coronary perfusion
   ↓ Hypoxia

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V. Tachycardia

- MI after 12 hours
- Ectopic focus = 200-300 / min: V rate
- Exhibits Inter Myocyte conduction

(Slower than conduction in Purkinje)

- Hence qRS is broad
- A rate = 100 / min, While V. Rate is 200-300/min

↓ Leading to

AV dissociation

Pulseless VT — AV dissociation (Lack of co-ordination)

V rate ↑: Reduced duration of end diastolic volume

SV ↓

Cardiac output ↓

SBP ↓

PrepLadder

EGG Criteria of V. Tachycardia

Notice : M shaped appearance/Rabbit ear: At peak of R wave

1. Broad qRS - 80-100 m sec = 2-2.5 ss small square
2. Premature V. contraction > 3 PVC, HR > 100/ min
3. Plateau shaped appearance at start of S wave called as **Josephson sign**
   - Capture beats
   - Spindle appearance
4. Extreme Axis deviation

Rx – Pulseless VT → Cardioversion: DC shock 200 J
Stable VT → IV Amiodarone
IV Lignocaine

2. Cardiogenic Shock In - Hospital Mortality

Rx: Norepinephrine - DBP ↑ coronary perfusion ↑
Dopamine: D1 Receptor and ↑ GFR
Dobutamine B1, Cardiac output ↑ HR
↑: ↑ O_2 consumption
Refractory Cardiogenic Shock = Impella > Intra Aortic Balloon pump

3. Cardiac Rupture: Transmural MI

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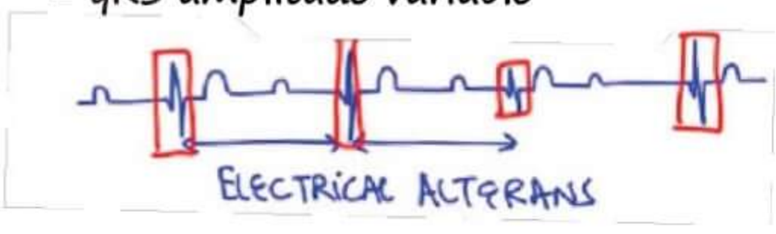
Normal pericardial fluid = 20-50 ml
Cardiac tamponade: Intrapericardial pressure >> LVED
EDV ↓↓ SV ↓↓ → CO ↓↓→BP ↓↓

Electro
Mechanical dissociation
DC Shock : CI

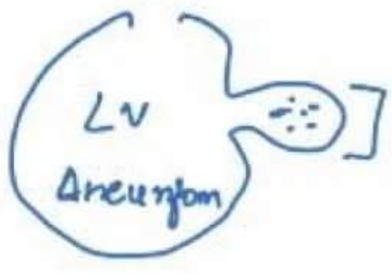
C. Tamponade : HR ↑ = R-R ↓ P-R ↓, low voltage ECG

= qRS amplitude variable



4. LV Aneurysm - Damaged part

↓ Contractility
CO↓
Stasis: clots
Embolic stroke



PrepLadder

Dx - Echocardiography

Rx - WARFARIN + inj Heparin

↓ (Discontinue after 5 days)

Lifetime

↓

Same brand (because different brands have different bioavailability)

Warfarin → INR monitoring

5. DRESSLER Syndrome

- Autoimmune Pericarditis which present as diffuse chest pain at rest after 3-6 weeks of discharge of patient of MI.

3-6 weeks later

- Radiation of pain→ **Left shoulder**
- Relief = **Sitting position**

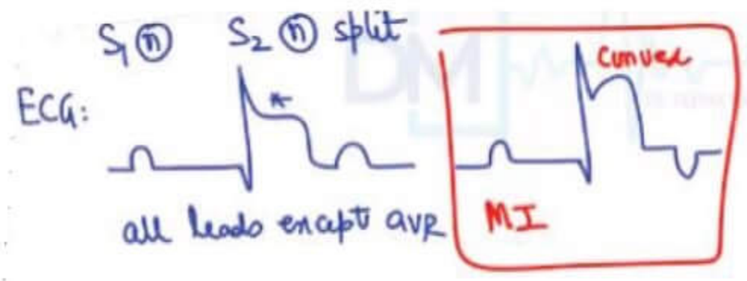
O/E: Pericardial Friction Rub → Inspiration + expiration

(Pleural rub → inspiration)

S1n S2n split

Troponin I - normal / ↑

Rx → Aspirin 650 mg TDS x 3 days



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6. Valvular damage

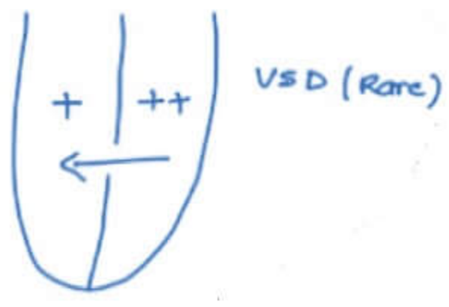
MC → Mitral regurgitation

Never seen post MI - AR

Aorta → Aortic valve

7. Ventricular Septal Defect

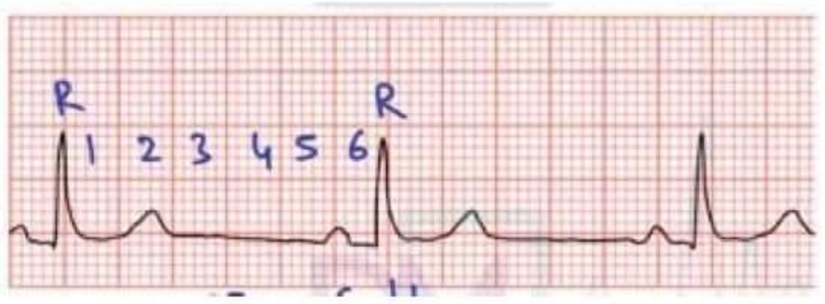
(Rare)



PrepLadder

SYMPTOMATIC BRADYCARDIA WITH PULSE

R – R (5 to 6 large square) → HR: 50-60 bpm



C/F – Cut off < 60 bpm (Bradycardia)

Symptomatic patient

1. Dizziness
2. ↓ BP
3. Altered mental status
4. Pulmonary congestion
5. Chest pain CHF

Treatment

- Patent airway
- Assist Breathing
- Monitor SpO_2
- IV Access
- Search for contributing factor (e.g coronary event)

If perfusion → **Normal → keep patient under observation**

Low → Immediate intervention is required (TCP)

Transcutaneous pacing

- Best method for symptomatic bradycarida patients

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  - 1^{st} electrode → below right Clavicle
  - 2^{nd} electrode → Near Axilla of Patient / below the left nipple
- Stickon pads on chest of Patients
- Oxygen with reservoir

Steps:-

1 Apply PADS
2 Sedation ±
3 Set HR = 60 – 80 bpm
4 Mode – Synchronous
5 10 m A ↑ until capture occurs
6 Broad complex qRS → Corresponding to → Carotid Impulse

On display we can see many

MA of voltage we are using

Management algorithm of symptomatic bradycardia

1 IV atropine 0.5 mg every 3-5 min

Maximum dose = 3 mg

[6 dosages of 0.5g]

If Atropine fails then→ TCP

2 IV epinephrine drip

- Activates β1 in the heart
- Dose → 2-10μ g/minute

PrepLadder

3. IV Dobutamine (2-20µg/Kg/ min)
   - Activate β1, D1 receptors

4. Transcutaneous Pacing

5. Transvenous pacing

(Remember first line is atropine but we will not wait to first give 6 dosage and then go to pacing. If no response to atropine and heart rate is low, start T.C.P.)

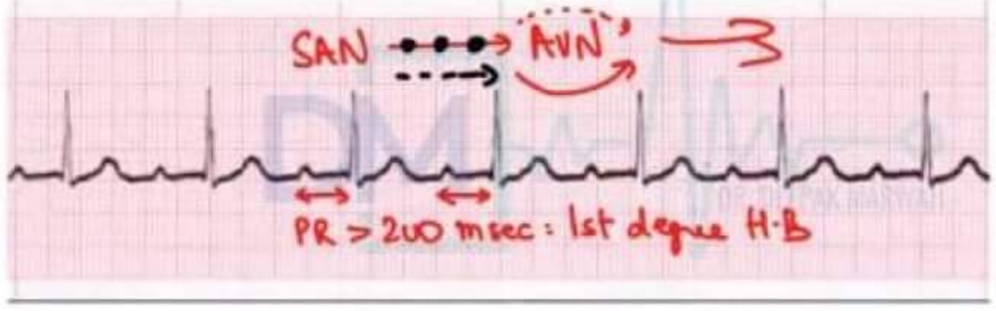
1st Degree Heart Block →

- ↑↑ PR Interval (> 200 m sec) → Presence of 1 degree heart block

SAN $\xrightarrow{\text{slow conduction}}$ AVN→ Bundle of His

Seen in Rheumatic Fever

Most common cause is physiological → Marathon runners



2nd Degree Heart Block

MOBITZ I/WENCKEBACH

- Serial ↑in PR Interval
- Dropped QRS (Missed Beat)
- PR interval before missed Beat is longer than after.
- Intra nodal defect

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MOBITZ II

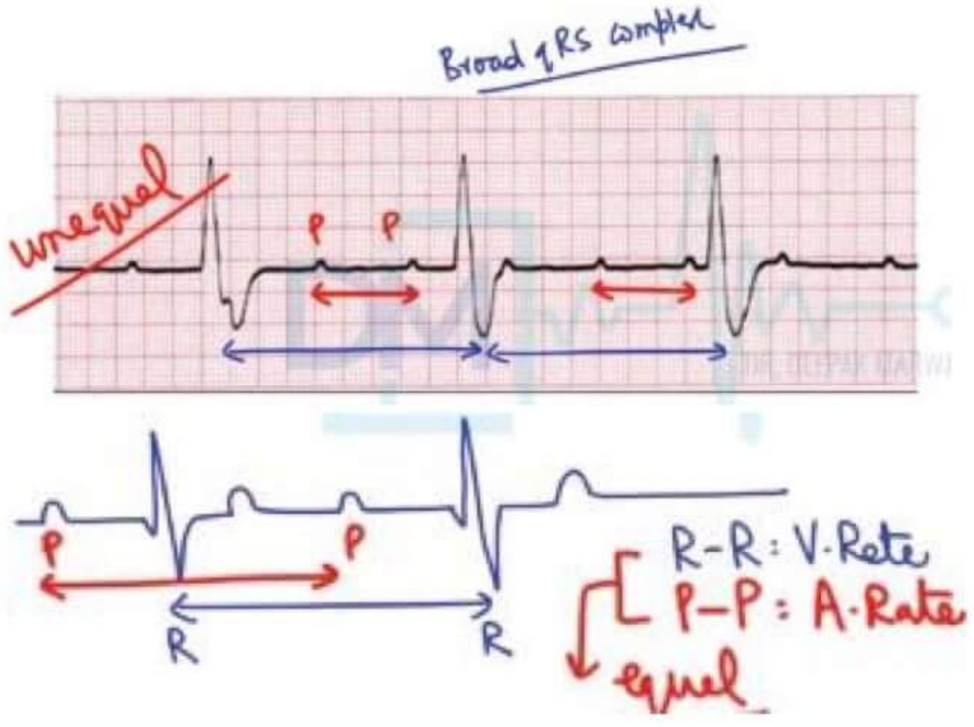
- Infra nodal defect
- Bundle of His (Refuses to conduct)
- PR Interval is constant
- Missed beat present
- PR before and after missed beat is equal

  2:1 BLOCK
- Alternatively conducted impulse & non conducted impulse
- Dropped beat is present alternatively unlike in mobitz II where multiple impulses are conducted followed by a drop.

3rd Degree Heart Block

- Broad Q RS complex
- PR internal is ↑↑
- PP interval is not matching RR interval
- RR interval (Ventricular Rate)
- PP Interval (Atrial Rate)

MC bradyarrhythmia seen post – MI: **MOBIT2 II heart block**



CONGENITAL HEART DISEASE

Nadas criteria

Major →

- CHF (L→R shunt)
- Cyanosis (R→ L shunt)
- Diastolic murmur
- Systolic murmur
  ≥ grade III

Minor →

- Systolic murmur grade I/grade II
- Abnormal S2
- Abnormal ECG
- Abnormal CXR
- Abnormal BP

1 Major or 2 Minor Criteria

Tetralogy of fallot:-

Pathophysiology

Defects present – (hallmark) ← Subpulmonic stenosis
Concentric R.V.H.
VSD (R→L Shunt)
Over riding aorta

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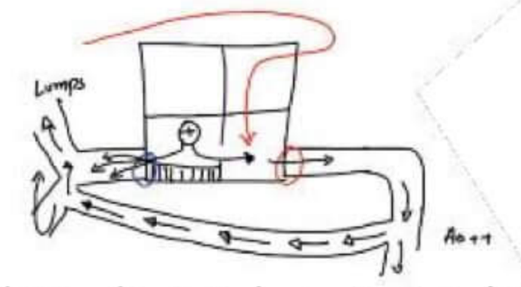
Tetralogy of fallot	Triology of fallot	Pentalogy of fallot
1. Subpulmonic stenosis 2. Concentric R.V. H 3. VSD (R→ L shunt) 4. Over riding aorta	Same Same ASD	T.O.F + ASD

- Central cyanosis in a body on day 0 – TGA
- Central cyanosis in Tetralogy of Fallot **develops on** day 7



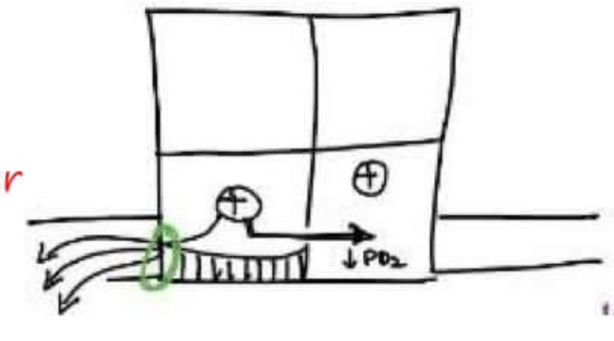
Ductal dependent pulmonic circulation

Rx

Drug of choice – Alprostadil (Maintain ductal Patency): **PGE1**

Palliative surgery – Blalock Taussig shunt

Ejection systolic
murmur intensity = lesser



Tet spells / hyper cyanotic spells
Lips: blue → black, murmur: softer

In Pts. Suffering from Tet spells intensity of murmur become less, murmur will become softer

Knee – chest position

Management:-

1. Knee- chest position
   ↑ P. resistance
   R→L shunting ↓
2. Morphine
3. Soda bicarbonate
4. Methoxamine
   SBP ↑ : ↑ P. resistance

T.O.F Clinical Features:

- Most common CHD (Cyanotic)
- Central cyanosis day 7
- Tet spells / F.T.T

O/E:

1. Clubbing
2. Shunt murmur of VSD is not heard.
3. Flow murmur → E.S.M
4. Rt. Para Sternal heave + → due to RVH

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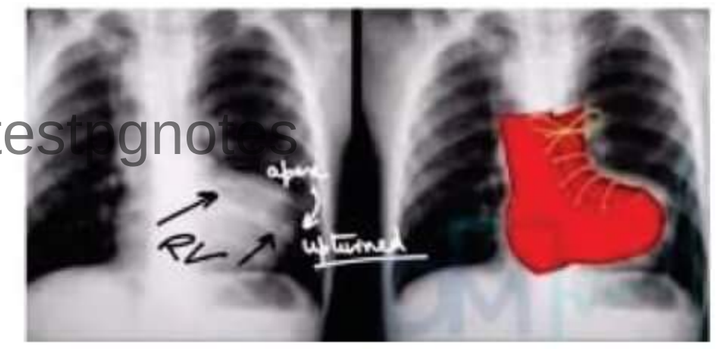


Work up: Chest X-ray →

1. Pulm oligaemia
2. RV enlargement (Boot shaped heart)
3. Rt sided aortic arch (30%)

"COER – EN- SABOT"

Investigation of choice: Echo

Squatting episode

Rx:-

Alprostadil / Blalock- taussing shunt

Pink Tet- Milder subpulmonic stenosis

Old children with T.O.F – Squatting episode

Central cyanosis + (N) size heart = CT ratio = N

Tricuspid atresia

Central cyanosis – day 0

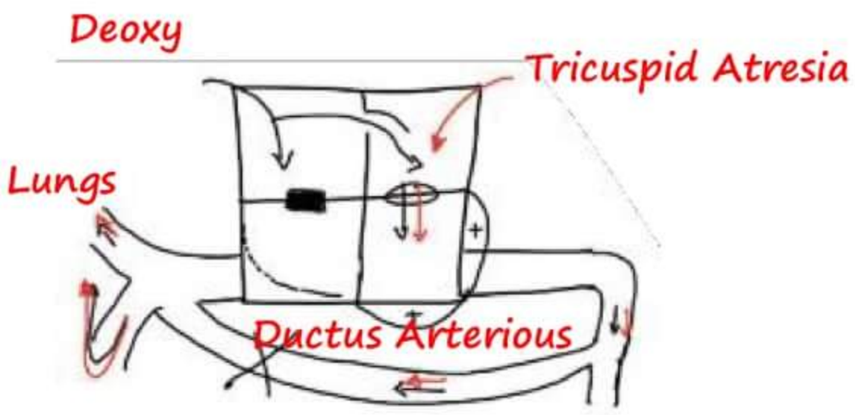
Death – day 7

Chest X-ray: CT ratio ↑ (Left sided)

S1 = M1 louder (Single)

T1 absent

S2 = A2 normal (Single)



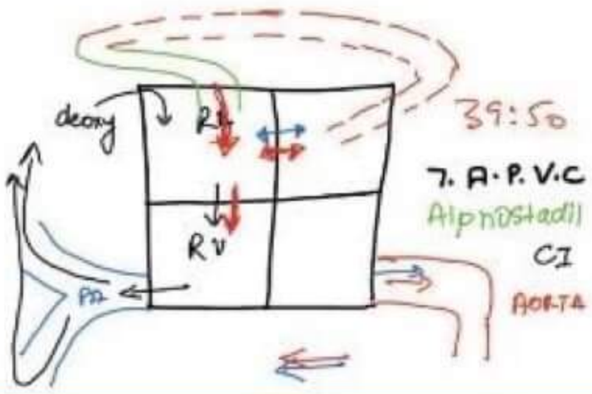
PrepLadder

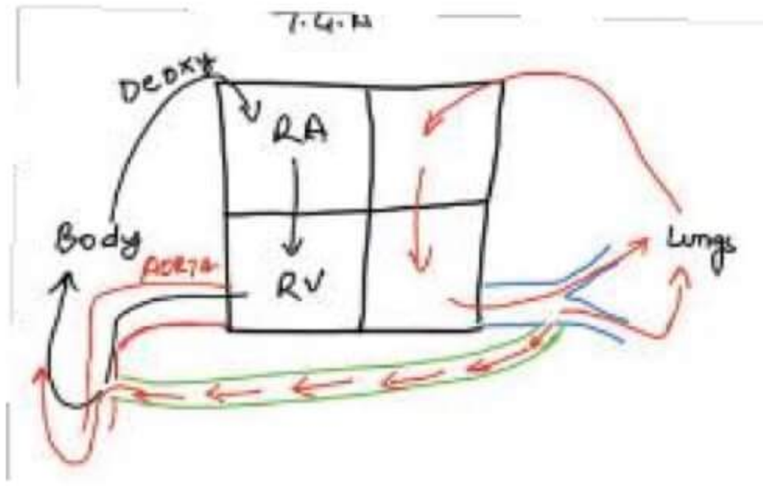
You can keep patient alive by giving drug alprostadil Iv

Ductus arteriosus = Patency alprostadil

Immediate = atrial septostomy → switch operation

Central cyanosis – day O





Ductal dependent pulmonary circulation

1. T.O.F
2. T.A
3. TGA with intact VSD

TAPVC

Abnormal Vein → SVC : Supracardiac

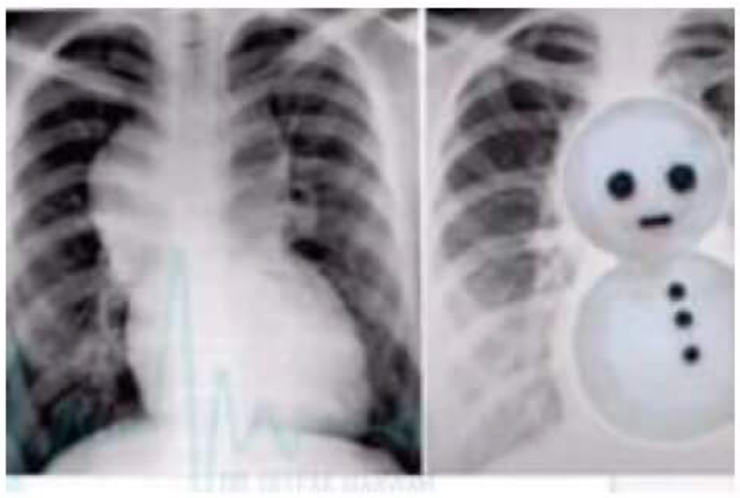
Most common : Fig of 8 appearance of CXR

Abnormal vein → RA : Cardiac

Abnormal vein → IVC : Infracardiac

↓

"Ground glass appearance" on CXR



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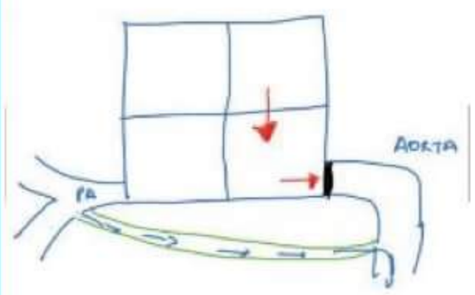
Neonate: Shock cynosis

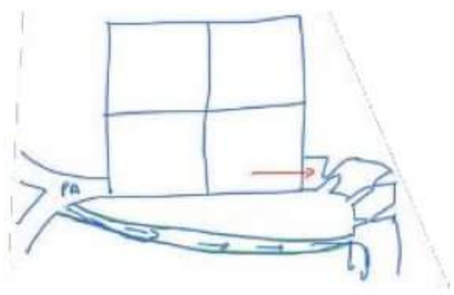
- Ductal patency maintained by alprostadil IV

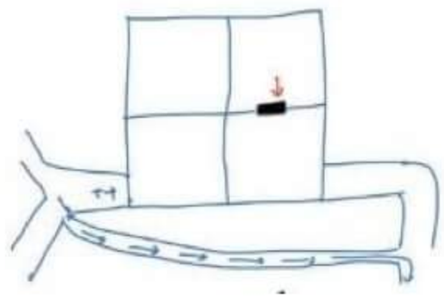
Ductal dependent systemic circulation

1. Interrupted aortic arch
   Neonate: Shock cyanosis
   - Alprostadil IV

2. Mitral Atresia
3. Aortic Atresia

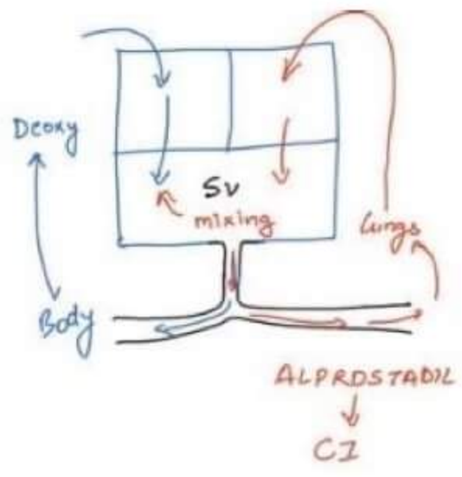






Truncus arteriosus

- Co – Truncal abnormality
- Alprostadil C/I
- Ductal dependent circulation



PrepLadder

Pulmonary	Systemic
1. TOF 2. Tricuspid atresia 3. T.G.A with intact VSD	1. Mitral atresia 2. Hypoplastic left heart syndrome 3. Aortic atresia 4. Interrupted aortic arch.

Ductal independent circulation

1. TAPVC
2. Truncus arteriosus
3. Kawasaki disease

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PrepLadder

METABOLIC SYNDROME X AND SYNDROME Z

Syndrome X vs Syndrome Z

Metabolic Syndrome (Syndrome X)

1. **Centripetal obesity** →Visceral/ abdominal fat → Heart disease

(Sumo Wrestlers → SUBCUTANEOUS fat → No heart disease)

+

+

Exercise

Measured by → Abdominal circumference

Female	> 88 cm	**If Indian Female > 80 cm**
Male	> 102 cm	**Indian Male > 90cm**

2. **↑ Insulin Resistance**

FBS = 100-125 mg% (On medication for sugar ↑)

IGT (Impaired glucose Tolerance Range)

if patient on medication (Eg. Metformin) for hyperglycemia → component of metabolic syndrome

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3. **↑ Peripheral Resistance → ↑ BP**

HTN: > 130 / 85 mm Hg (On medication for HTN)

4. **TG > 150 mg%** [Or on medication] for hyperlipidemia

5. **HDL < 40 mg** (Males) <50 mg/dl (Females) [On Medication]

For diagnosis of metabolic syndrome 3 out of 5 components should be present.

6. **Obstructive sleep apnea [Syndrome Z : Syndrome X + O.S.A]**

* Apnea cutoff- 10 sec
* 5 episodes / hour

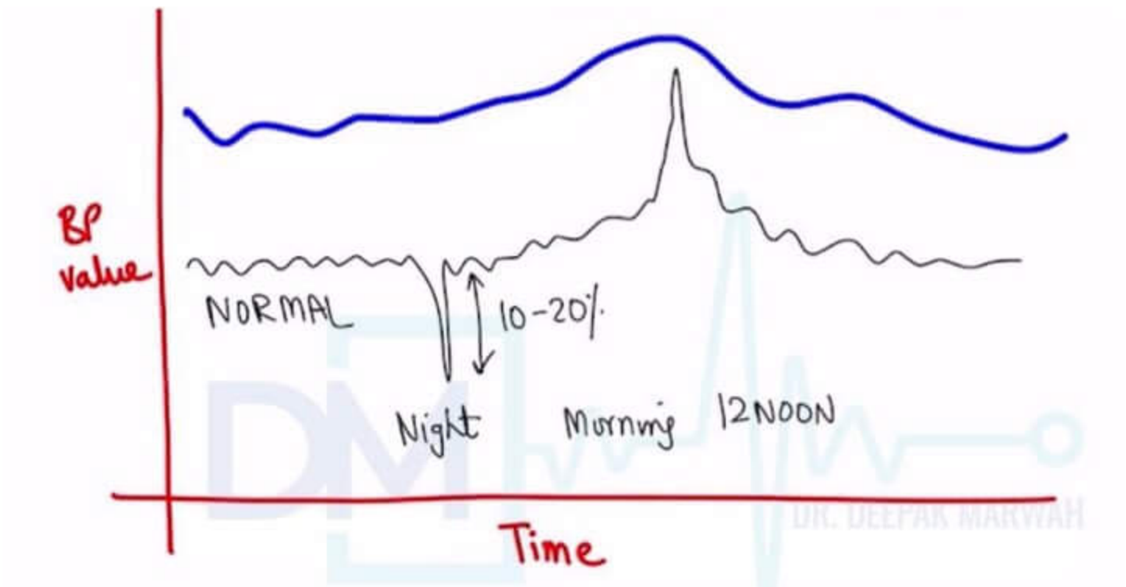
↑ C V mortality of Patient

LDL ↑ is not a component of both Syndrome X and Syndrome Z

PrepLadder

HYPERTENSION

Normally there is fall in BP at night when the muscles are relaxed – Nocturnal Dip is there with approx 10-20% of fall in BP. The BP values are higher at 12:00 noon w.r.t diurnal variation.



Ambulatory BP recording for normal person (**Black tracing**), and HTN patient (**Blue tracing**).

→ No nocturnal dip at nighttime in HTN patient, if there is attenuated nocturnal dip → there is ↑ risk of cardiovascular mortality in HTN patient.

Note- Antihypertensives should be taken either in early morning or at night , so that morning ↑↑ in BP due to vasoconstriction can be prevented.

→In patient with **good control HTN:**

- Acute coronary syndrome to be ↓↓ by 25%
- Stroke to be ↓↓ by 30%
- Heart failure to be ↓↓ by 50%

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Note: Normal value of BP generally varies for all, but if BP $>\frac{115}{75}$ mm of Hg and current scenario shows that if SBP > 20 mm of Hg or DBP > 10 mm of Hg is associated with ↑↑ cardiovascular mortality

Pre HTN = 120-139/80-89 mmHg
Stage 1 = 140-159/90-99 mmHg
Stage 2 = > 160/100 mmHg

} According to Harrison

According to AHA guidelines:-

Elevated = 120-129/ < 80 mm of Hg
Stage-1 = 130-139/ 80-89 mm of Hg
Stage-2 = > 140/90 mm of Hg

Ambulatory BP recording-

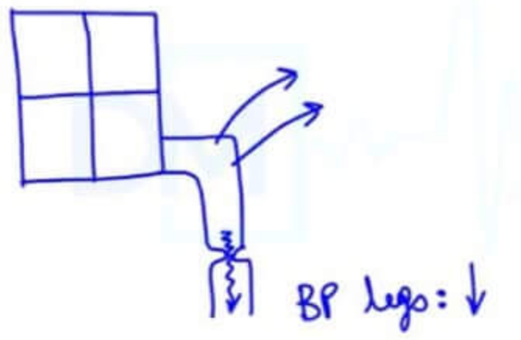
Average awake BP = > 135/85 mm of Hg
Average sleep BP = > 120/75 mm of Hg

The above values correspond to the **clinic BP** = > 140/90 mm of Hg

PrepLadder

→ Most common cause of HTN → Primary/ Essential

→ Most common cause of 2° HTN → Renal causes



2° HTN (America) → Obstructive sleep apnea

- Congenital cardiovascular causes of HTN → **Coarctation of Aorta**

In Coarctation of Aorta (Post ductal variety) = BP in upper limb ↑↑ and BP in lower limbs ↓↓, there is muscle wasting present in lower limbs.

BP = CO x P. resistance

Note: Normally BP in upper limb = < 120/80, & BP in lower limb < 140/80 but the reverse scenario is seen in coarctation of aorta, where BP in legs ↓↓ and upper limb ↑↑.

Unequal BP left/right arm is seen in:

1) Takayasu's arteritis (Imp causes of renal artery stenosis in India)
2) Supravalvular AS (Aortic Stenosis)
3) Coarctation of Aorta (Pre ductal variety)

Secondary causes of HTN-

→Renal parenchymal disorder → Chronic Kidney disease

→ Obstructive uropathy

→ Renovascular causes → Fibromuscular dysplasia, Atherosclerosis

→ Metabolic syndrome

a) Centripetal obesity

b) Insulin resistance

c) Hyperlipidaemia

d) HTN

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→ Obstructive Sleep Apnea (OSA): Fluctuation of heart rate during sleep ↑↑ the stress on the heart and that manifests into HTN, LVH

- During apnea episode there is bradycardia (O_2 cut off from body) and due to hypoxia the person tries to breathe in and then there is cortical arousal – O2 goes inside and there is sudden increase in the HR.

→ Endocrinological causes → Hypothyroidism (Isolated diastolic HTN)

→ Thyrotoxicosis

→ 1° Aldosteronism

→ Neurogenic → Spinal cord transection (At T6 or above → unopposed sympathomimetic outflow to heart)

→ Raised ICP

→ Porphyria

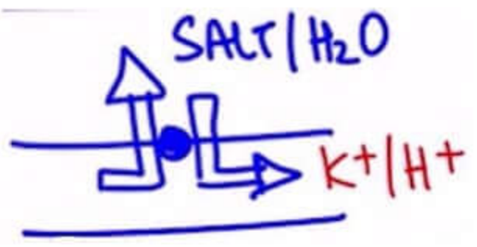
→ Lead poisoning (↑↑ activity of ACE)

→ Mendelian causes:

a) **Liddle syndrome (Autosomal Dominant)**

* Overactivity of ENac – causes more salt/H2O to retain in the body
* HTN with loss of K+/H+ causing hypokalaemia alkalosis.

Treatment → **Amiloride (ENac blocker)**



PrepLadder

b) Gordan syndrome

* AD

* WNK-1/ WNK-4: gain of function - Thiazide dependent Na/Cl cotransport in DCT

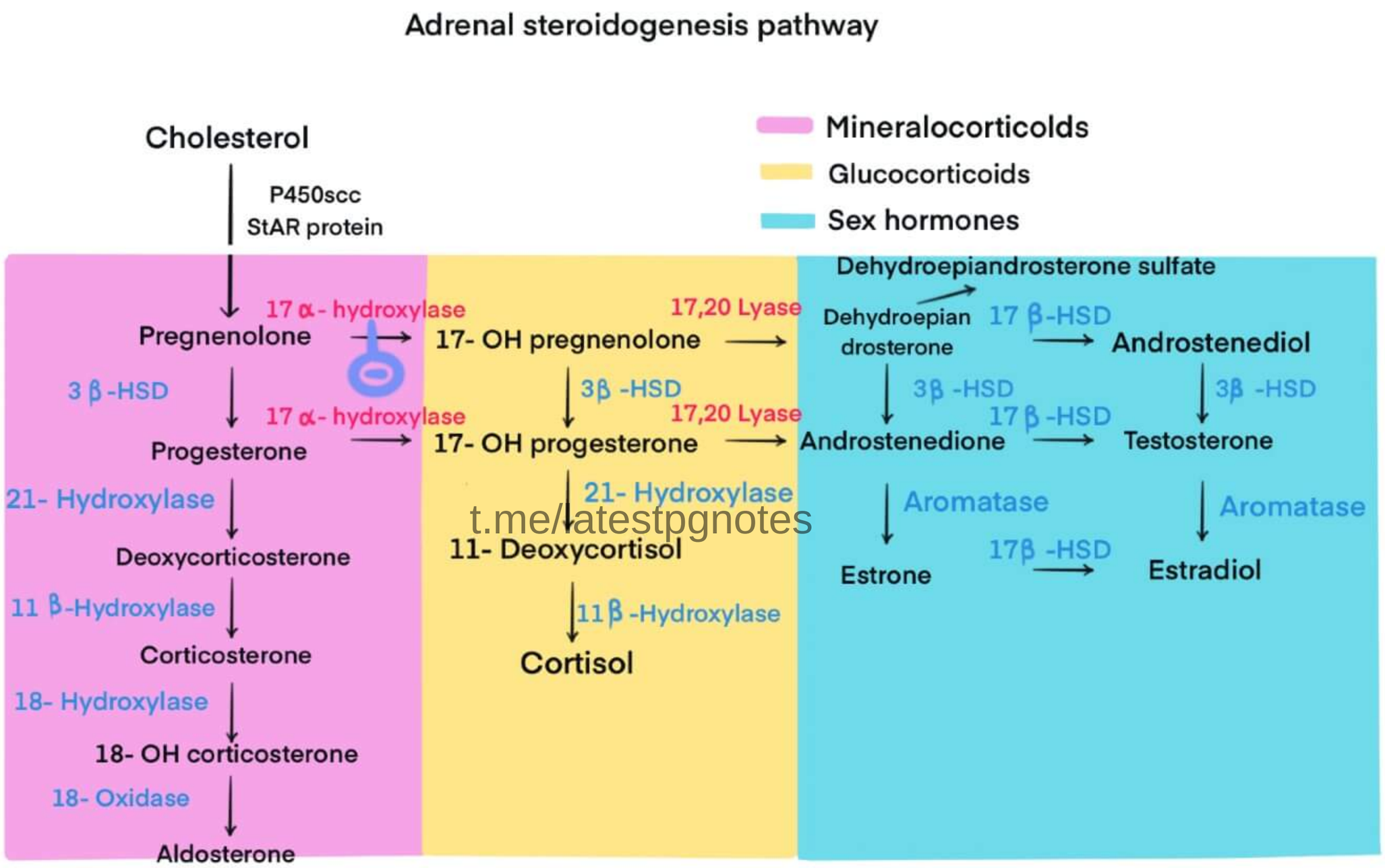
* HTN due to more Na/Cl retaining in the body

c) Polycystic kidneys: AD, AR (AD- adults, AR- paediatrics) and then the destruction of parenchyma in kidney causes ↓↓ GFR and Renin levels ↑↑ resulting in HTN.

d) Pheochromocytoma (AD):- Assoc with MEN-2A, MEN-2B, VHL, NF-1

e) 17-α hydroxylase deficiency (AR)

f) 11 – β hydroxylase deficiency (AR)



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Work up for newly diagnosed HTN patients:-

1) Echocardiography → Left ventricular hypertrophy

2) Fasting blood sugar, lipids

3) Serum electrolytes

4) TSH

5) Urine microscopy, Albumin Excretion Rate (AER) -30-300 mg/gm, BUN, Serum creatinine

Treatment:

1) Life style modification

a) D.A.S.H:-Intake of Na↓↓, K↑↑

b) Physical activity

2) If the patient is HTN despite the lifestyle modifications then switch to drugs

PrepLadder

Young: < 55 years → "**ACE inhibitor**", in case of dry cough, angioedema then switch to "**ARB**"

Old: > 55 years → **CCB**

Resistant HTN: Uncontrolled HTN with three classes of Antihypertensive drug and the drugs given should include "**Thiazides**".

Ex: **Patient on** → ACE Inhibitor + CCB + Thiazides and BP still not controlled then, add "**α- Blocker**" or "**β – Blocker**"

Uses of Antihypertensive: Drugs for various scenarios

1. ACE inhibitors:-

a) Acute coronary syndrome -post MI

b) Diabetic nephropathy

c) Ischemic nephropathy (Unilateral RAS)

d) HF with ↓↓ EF

2. β- Blockers (Cardioselective):-

a) CHF due to systolic malfunction.

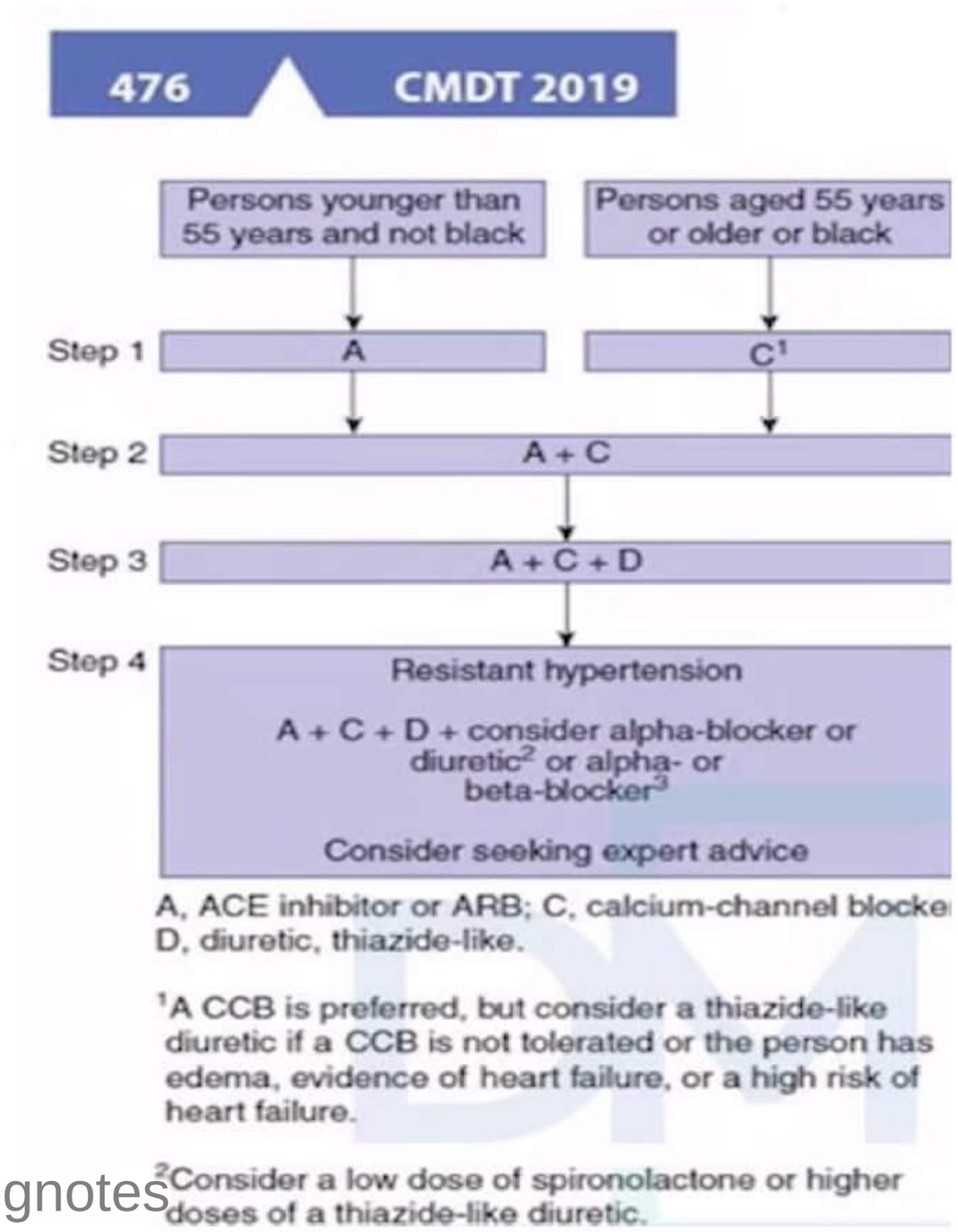
b) Chronic stable angina.

3. Aldosterone antagonist → Used in patients of heart failure with preserved ejection fraction

4. α- Blockers:

a) HTN in patients having BPH

b) Pheochromocytoma



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Hypertensive Urgency:

If BP > 220/125 mm of Hg but life threatening end-organ damage is absent.

Hypertensive emergency/ crisis:

If BP > 220/125 mm of Hg + target organ damage is present.

Goal/ Objective: Reduce MAP by 25% within 2 hrs (Mean Arterial Pressure) OR maintain BP $\frac{160}{100}$ mmHg

Malignant HTN: → Fibrinoid necrosis occurs in the vessels supplying various parts in the body and the mortality rate ↑↑ by 50% in 6-12 months

Retina → Papilledema

Brain → Encephalopathy

Kidney → KFT deranged

Blood vessel → Microangiopathic hemolytic anemia

Note: If a known patient of HTN on medications with an episode of abrupt rise of BP as the patient is becoming older. There can be 2 scenarios:

PrepLadder

→ Atherosclerotic narrowing of the ostia of renal artery can be present, and rule out the possibility of B/L Renal artery stenosis by Doppler – Always omit the use of ACE-inhibitors if B/L RAS is present because the BP will fall all of sudden and there can be AKI.

→ Malignant HTN

So, in these patients we have to initiate the aggressive treatment, and always rule out the cocaine abuse and recreational drug abuse before starting the treatment.

Treatment of Malignant Hypertension:-

a) Labetalol

b) Nicardipine

c) Sodium Nitroprusside

d) Enalaprilat (**ACE inhibitor given IV**)

Note:- In patient with HTN encephalopathy → **Na Nitroprusside** is given as first choice, but in case of the Malignant HTN (Especially in old people) the first choice should be **Labetalol** because **Na Nitroprusside** can cause fall in BP all of sudden and there is possibility that coronary ischemia might be triggered in the patient.

- **In patients of Acute Ischemic Stroke** with **HTN** > $\frac{185}{110}$ → **Na Nitroprusside** is not preferred because, the moment we administer the drug, BP will fall fast and results in fall of CPP (Cerebral perfusion pressure) as **C.P.P = MAP – ICP,** normal CPP = 60-80 mmHg). In these patients, thrombolysis cannot be done immediately, because first we need to lower down the BP using drugs.

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Drugs used: Nicardipine > Labetalol > Sodium Nitroprusside

→ **Candidate for thrombolysis in AIS:** If the patient comes to you within 4.5 hours.

Cut off value intervention= > $\frac{185}{110}$, first lower the BP then initiate thrombolysis because thrombolysis itself can cause brain hemorrhage and the high BP can be fatal

→ **Not a candidate for thrombolysis:** If the patient presents late after 4.5 hours. Then we have to lower the BP only when it is > $\frac{220}{130}$ mm of Hg by using antihypertensive.

- In patients with **postoperative HTN / MI/ Unstable Angina/ Acute decompensated CHF** → DOC is I.V Nitro-glycerine.
- In patients of "**Adrenergic Crisis**" in Pheochromocytoma surgery → **Nitroprusside** is used along with **Phentolamine**
- Target BP/ Goal to be maintained in patients with HTN: < 135-140/ 85-90 mm of Hg
- Target HTN along with Diabetic nephropathy = < 130/80 mm of Hg
- BP Malignant HTN → 160/100 mm of Hg to be maintained by using antihypertensives or MAP should be ↓ by 25% over 2 hours.

PrepLadder

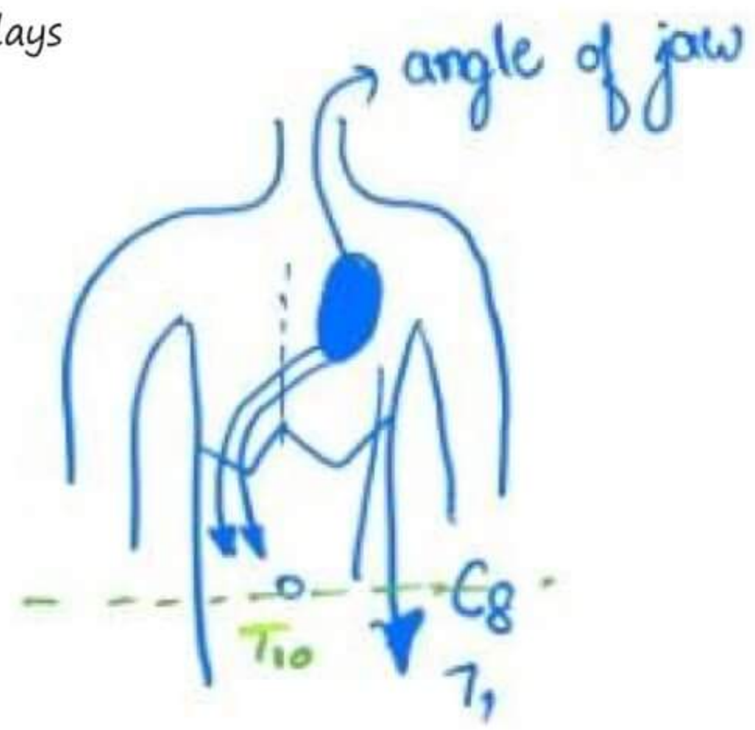
DISEASES OF PERICARDIUM

ACUTE PERICARDITIS

Etiology:

- Idiopathic **(Most common)**
- Viral
- Rheumatic
- **Dressler Syndrome:** Autoimmune pericarditis seen post MI
- Uremia
- Malignancies / 2^{o}: Oat cell ca lung

-Patient presents with diffuse chest pain at rest for hours - days
-Radiation to left shoulder (Phrenic nerve involvement)
-Relief: - on sitting
-Pericardial friction rub heard on auscultation



LEVINE SIGN (MI): Chest pain (L>R) radiating to -

1. Medial side of arm and forearm (C8, T1 dermatome)
2. Epigastrium up to umbilicus- pain due to coronary etiology can extend up to T10 dermatome
3. Angle of jaw

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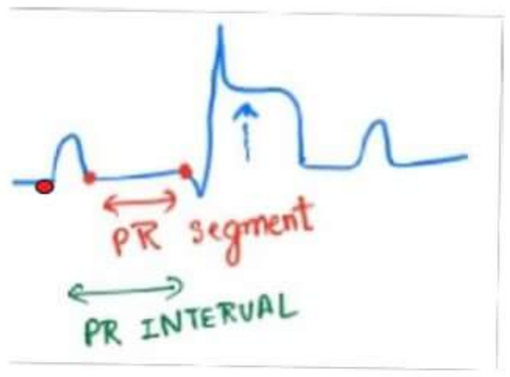
Nerves involved in chest pain of MI / Angina

1. Superior cervical cardiac nerve
2. **Inferior cervical cardiac nerve**
3. Thoracic splanchnic nerve

Investigation:

ECG: ST ↑ concave upwards, all leads except aVR: ST ↓
PR segment depression, all leads except aVR = **PR segment elevation**



Rx: -

- Viral Pericarditis = **NSAIDS**
- Rheumatic Pericarditis =**STEROIDS**
- TB Pericarditis = **ATT + short course of steroids**
- 2° Pericarditis = **CHEMOTHERAPY**
- Uremic Pericarditis = **Hemodialysis**

PrepLadder

Complications: - Pericardial effusion

- Normal fluid in pericardial space= 20-50 ml
- Pericardial effusion- fluid accumulation in pericardial space >50ml.
- **ECG reveals low voltage ECG (R + S < 5 mm - Limb leads, < 10 mm = Chest leads)**

Extra Mile

Causes of Low Voltage ECG

1. Restrictive cardiomyopathy
2. Myxoedema heart
3. Constrictive pericarditis
4. Pericardial effusion

ELECTRICAL ALTERANS

↓

Ⓝ axis = -30 to +110°

CXR: - Narrow vascular pedicle, Money bag appearance, water bottle appearance with increased CT ratio.

IOC: - Minimal pericardial effusion: - Echocardiography

Rx: - T/t for specific cause

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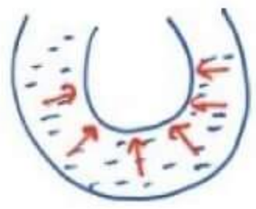
Cardiac Tamponade



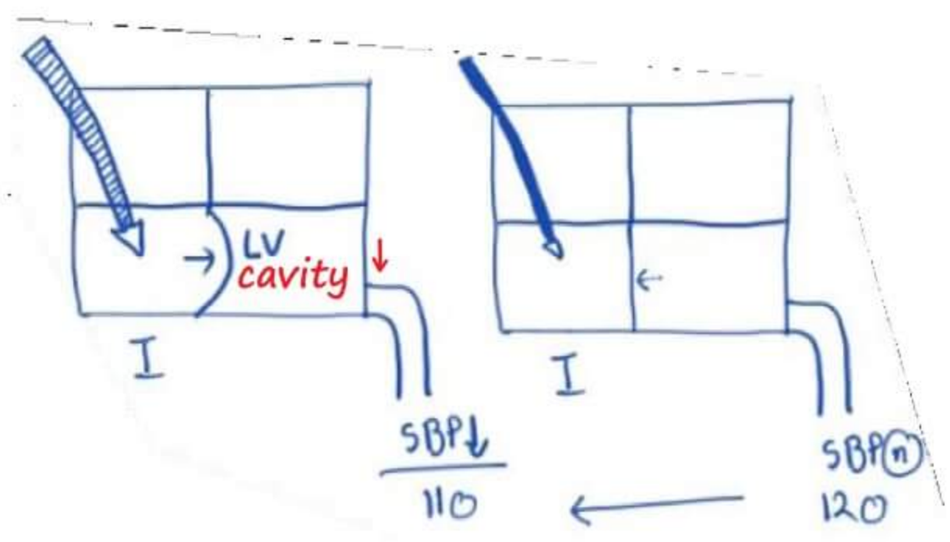
Intrapericardial pressure >> LVEDP (Left ventricular end diastolic pressure)

→ Diastolic collapse of ventricles

EDV ↓ → SV ↓ → CO ↓ → BP ↓

Pulse becomes so weak ↔ disappear! (**Pulsus paradoxus**)

Normal SBP ↓ < 10 mm Hg on deep inspiration



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* In cardiac tamponade, there is an exaggerated septal deviation leading to reduction in LV cavity size. This reduces EDV, stroke volume and leads to crashing blood pressure.

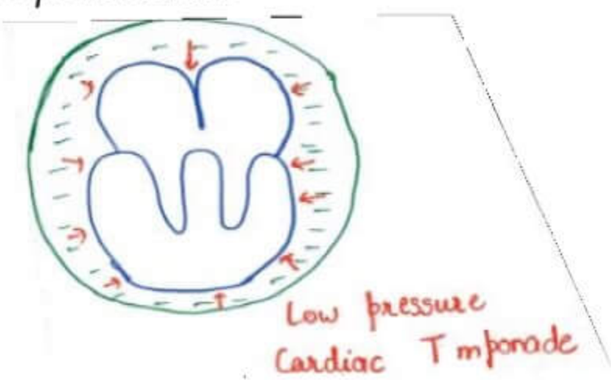
* In cardiac tamponade, in inspiration SBP ↓ > 10 mm Hg – Pulsus paradoxus
* Low pressure cardiac tamponade - atrial collapse

30% ↓ filling of ventricles → HYPOTENSION

Cardiac tamponade: Atrial + ventricular collapse

BP decreased (unrecordable)

* Pulsus paradoxus is not seen in low pressure cardiac tamponade and Massive pericardial effusion.



Massive Pericardial Effusion

Seen in: Hypothyroidism = Myxedema

Lymphedema +++ (20 ml / yr)

- Gradual accumulation of fluid in pericardial space. Hence ventricles adjust to this gradual rise of intrapericardial space pressure.
- So pulsus paradoxus is absent

Cardiac tamponade Summary

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1. Exaggerated septal deviation ++
2. Pulsus Paradoxus: SBP ↓↓, Hence an example of obstructive shock
3. * **BECK'S TRIAD:** – MUFFLED S_1S_2

   HYPOTENSION

   Congested neck veins: Non pulsatile ↑ JVP

   ↑

   Also in **SVC syndrome**

4. Pulsus Paradoxus + Electrical Alternans = Cardiac Tamponade

If electrical Alternans is given alone in a MCQ, answer as Pericardial Effusion

5. Kussmaul sign absent
6. Electrical alternans present
7. Money bag appearance+
8. **TOC**: – Echo guided Pericardiocentesis (Xiphisternal approach)

PrepLadder

Constrictive Pericarditis

Sequelae: - Pyopericardium

- TB Pericarditis

Compliance is decreased

Right Ventricle	Left Ventricle
1. Pedal Oedema	1. Pooling of blood in the lungs
2. Hepatomegaly (RUQ discomfort)	2. Pulmonary edema
3. Ascites	3. Dyspnea
	4. Low CO
	5. Effort intolerance

O/E: - **1. Pulsus Paradoxus (Rare)**

2. JVP: - Kussmaul sign (+)

(Paradoxical rise of JVP)

Prominent x, prominent y descent

3. Pericardial shudder / knock/ shock

4. Liver span ↑

5. B/L fine crepts +

6. Puddle sign + Ascites

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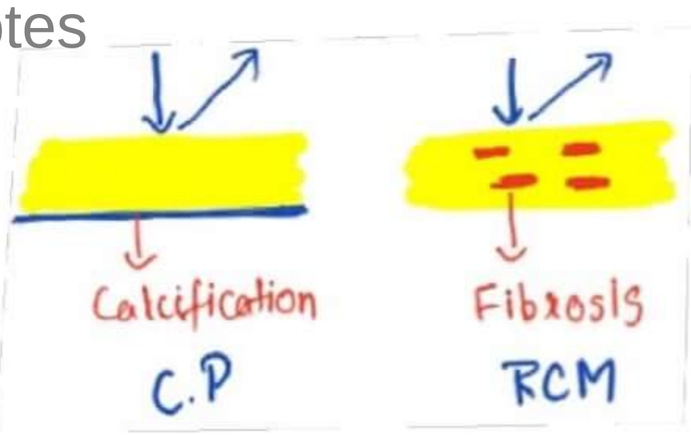

Diagnosis - C. Pericarditis
Vs
RCM

Compliance ↓- calcification in C. pericarditis

Fibrosis in RCM

* **CXR:** - Egg in a cup appearance

Egg on side appearance = **TGA**

* **ECG:** - Low voltage ECG

Electrical alterans :- absent

* **CT chest → calcification outside the heart of the patient**

* **Cardiac MRI**

* **Doppler →** SQUARE ROOT WAVE SIGN

* **Endomyocardial Biopsy →** Gold Standard investigation to differentiate RCM from constrictive pericarditis

PrepLadder

Treatment: - Pericardial stripping

	Acute pericarditis	Pleural effusion	Cardiac tamponade	Constrictive pericarditis
ECG:	ST ↑ Concave	Electrical alternans	Electrical alternans + Pulsus paradoxus	Low voltage ECG + Pulsus paradoxus
	Kussmaul sign ⊖	Kussmaul sign ⊖	Kussmaul sign ⊖	Kussmaul sign⊕
JVP:			Absent y	Prominent y
			Prominent x	
			BECK's Triad	
Treatment	Cause specific		Pericardiocentesis	Pericardial stripping

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CONGESTIVE HEART FAILURE

Cardiac output = Heart rate X stroke volume

↑ HR → ↑ Sympathetic drive

Clinical features:

1) Palpitations
2) Diaphoresis
3) Dyspnea on exertion
4) Nocturnal cough
5) Paroxysmal nocturnal dyspnea (Orthopnea)
6) Pink frothy sputum

On examination:

→ Tachycardia

- Maximum HR = 220 - Age

Left ventricular failure	Right ventricular failure
1) ↓ SBP leads to oliguria 2) S_3 present: Ventricular gallop rhythm 3) B/L fine crepitations 4) Reduced air entry B/L	[m/c/c of RVF is LVF] 5) JVP ↑ 6) Kussmaul signs → JVP ↑ on inspiration 7) Abdomino + jugular reflux ⊕ 8) Tender hepatomegaly 9) B/L pitting pedal edema [Chronic CCF]

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→ The diagnostic criteria used for diagnosis CHF is **Framingham criteria**

Minor Criteria:

1. Dyspnea On exertion
2. Nocturnal cough
3. Tachycardia
4. Pleural effusion
5. ↓ Vital capacity > 1/3rd
6. Tender hepatomegaly
7. Pitting pedal edema
8. Oliguria

Major Criteria= Rest all are major criteria.

For Dx → 2 major criteria should be present

Or

1 major + 2 minor

PrepLadder

Stage of CHF – (According to ACC):

Stage A → No structural damage, high risk of developing symptoms

Stage B → Structural heart disease + No symptoms of CHF

Stage C → Structural heart disease + Symptoms of CHF

Stage D → Refractory heart failure

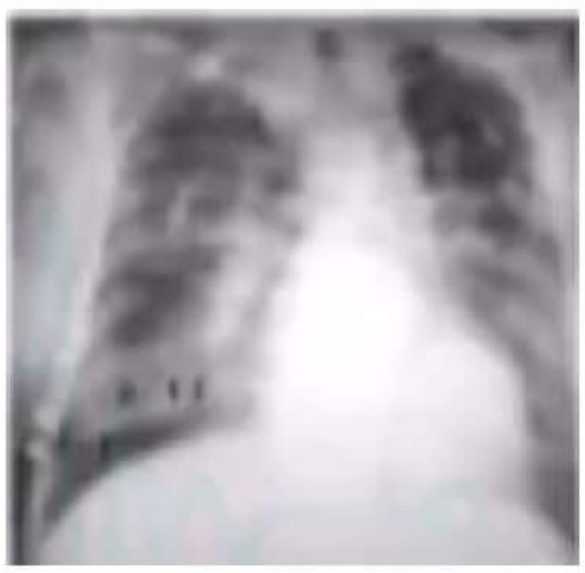
Work up of patients:

1) BNP levels / N-terminal Pro BNP

→ Released from ventricles of heart

→ If > 100 pg/ ml – It differentiate from non-cardiogenic causes of breathlessness

2) Chest X-ray



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A. Earliest radiological finding: Prominent upper lobe veins / Antler sign or Reverse moustache sign

B. CT ratio increased > 0.5

C. **Bat wing pulmonary edema**

D. **Costo – phrenic angle blunting**

E. **Kerley B lines** → Perpendicular to pleural surface. Due to thickened interlobular septa.

- Also seen in lymphangitis carcinomatosis

(Kerley A lines: Present in the periphery of hila

- Due to distension of anastomotic channels between central and peripheral lymphatics

Kerley C lines: Reticular opacities at lung base.)

3) Echocardiography

Ejection fraction = $\frac{Stroke\ volume}{End\ diatolic\ volume}$

In systolic malfunction = EF ↓

In diastolic malfunction = EF can be normal

In HTN patient → Left ventricular end diastolic pressure increased

↓

Pooling of blood in lungs

PrepLadder

4) Cardiac MRI

It identifies:

1) Subtype of CHF

2) Etiology of CHF

5) BORG Scale → Tells functional assessment of the patients

RPE Scale	Rate of Perceived Exertion
10	**Max Effort Activity** Feels almost impossible to keep going. Completely out of breath, unable to talk. Cannot maintain for more than a very short time.
9	**Very Hard Activity** Very difficult to maintain exercise intensity. Can barely breath and speak only a few words
7-8	**Vigorous Activity** Borderline uncomfortable. Short of breath, can speak a sentence.
4-6	**Moderate Activity** Breathing heavily, can hold short conversation. Still somewhat comfortable, but becoming noticeably more challenging.
2-3	**Light Activity** Feels like you can maintain for hours. Easy to breathe and carry a conversation
1	**Very Light Activity** Hardly any exertion, but more than sleeping, watching TV, etc

Treatment of Heart failure with preserved ejection fractions [Means EF > 40%]

1) Angiotensin Receptor blocker and sacubitril [ARNI]

2) Aldosterone antagonist

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General Therapeutic Principles	Specific Therapy Targets (Beyond general management)
→ Reduce the congestive state - Caution to not reduced preload excessively → Control blood pressure - Central aortic blood pressure control may be more relevant → Maintain atrial contraction and prevent tachycardia - Efforts to maintain sinus rhythm in atrial fibrillation may be beneficial → Treat and prevent myocardial ischemia - May mimic HF as an "angina equivalent" → Detect and treat sleep apnea - Common co-morbidity causing systemic hypertension, pulmonary hypertension and right heart dysfunction (adaptive servo-ventilation infective)	→ Renin-angiotensin-aldosterone-directed therapy - ACE's and AFE's ineffective (Except in 'prevention') - Aldosterone antagonists (May be beneficial) → Digoxin - Ineffective (May reduce hospitalization) → Beta blockers and calcium channel blockers - Ineffective (Useful in preventing tachycardia) → Phosphodiesterase – 5 inhibitors - Sildenafil ineffective → Novel Therapy - ARNIs show early promise - Isosorbide Mononitrate ineffective (Reduces activity tolerance) → Chronotropic insufficiency - Target pacing (Unproven)

PrepLadder

Preserved Ejection Fraction (>40-50%)	
Pathologic hypertrophy - Primary (Hypertrophic cardiomyopathies) - Secondary (Hypertension) Aging Endomyocardial disorders	Restrictive cardiomyopathy - Infiltrative disorder (Amyloidosis, sarcoidosis) - Storage diseases (Hemochromatosis) Fibrosis

Depressed Ejection Fraction (< 40%)	
Coronary artery disease - Myocardial infarction - Myocardial ischemia Chronic pressure overload - Hypertensions - Obstructive valvular disease Chronic volume overload - Regurgitant valvular disease - Intracardiac (Left to right) shunting - Extracardiac shunting Chronic lung disease - Cor pulmonale - Pulmonary vascular disorders	Nonischemic dilated cardiomyopathy - Familial/ genetic disorders - Infiltrative disorders Toxic/ drug induced damage - Metabolic disorder - Viral Chagas's disease Disorders of rate and rhythm - Chronic bradyarrhythmias - Chronic tachyarrhythmias

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→ Treatment of acute pulmonary edema with reduced ejection fraction:

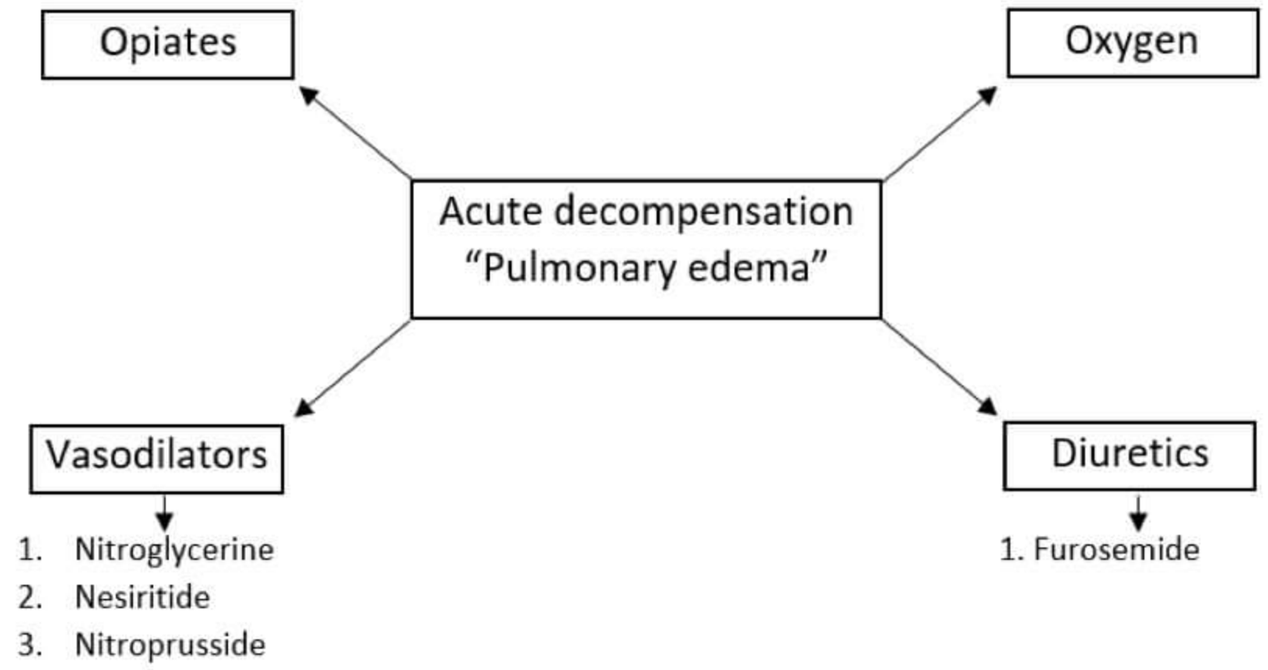
L → Lasix (Furosemide)

M → Morphine (↓ Pulmonary edema)

N → Nitro-glycerine

O → Oxygen (NIV)

P → Positioning



Nesiritide = BNP Analogue

PrepLadder

Treatment of Acute Decompensation with Cardiogenic shock:

→ Inotropic therapy

- Dobutamine
- Milrinone
- Levosimendan
- Omecamtiv mecarbil

→ Nor Epinephrine is reasonable as the first line vasopressor based on randomized trials compared to dopamine.

→ Vasopressors

1) NE
2) Dopamine
3) Dobutamine (β1): Increase HR

Milrinone

→ Inodilator

→ Used in Acute RVF

→ Medically refractory cardiogenic shock:

1. **Impella**: Intravascular Micro axial blood pump to support patient's circulatory system.
2. Intra-aortic balloon pump [IABP]

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↓

Generate counter pulsation

↓

↑ Coronary blood flow

3. Left ventricular assist device [LVAD]
4. Ultrafiltration

Summary of management for HFrEF (Reduced EF)

1) Acute pulmonary edema

L → Lasix
M → Morphine
N → NTG
O → Oxygen
P → Positioning

2) Cardiogenic shock/ Pump failure due to MI/ Myocarditis

- NE
- Dopamine
- Dobutamine
- IABP
- LVAD (Heart mate)
- Ultrafiltration

PrepLadder

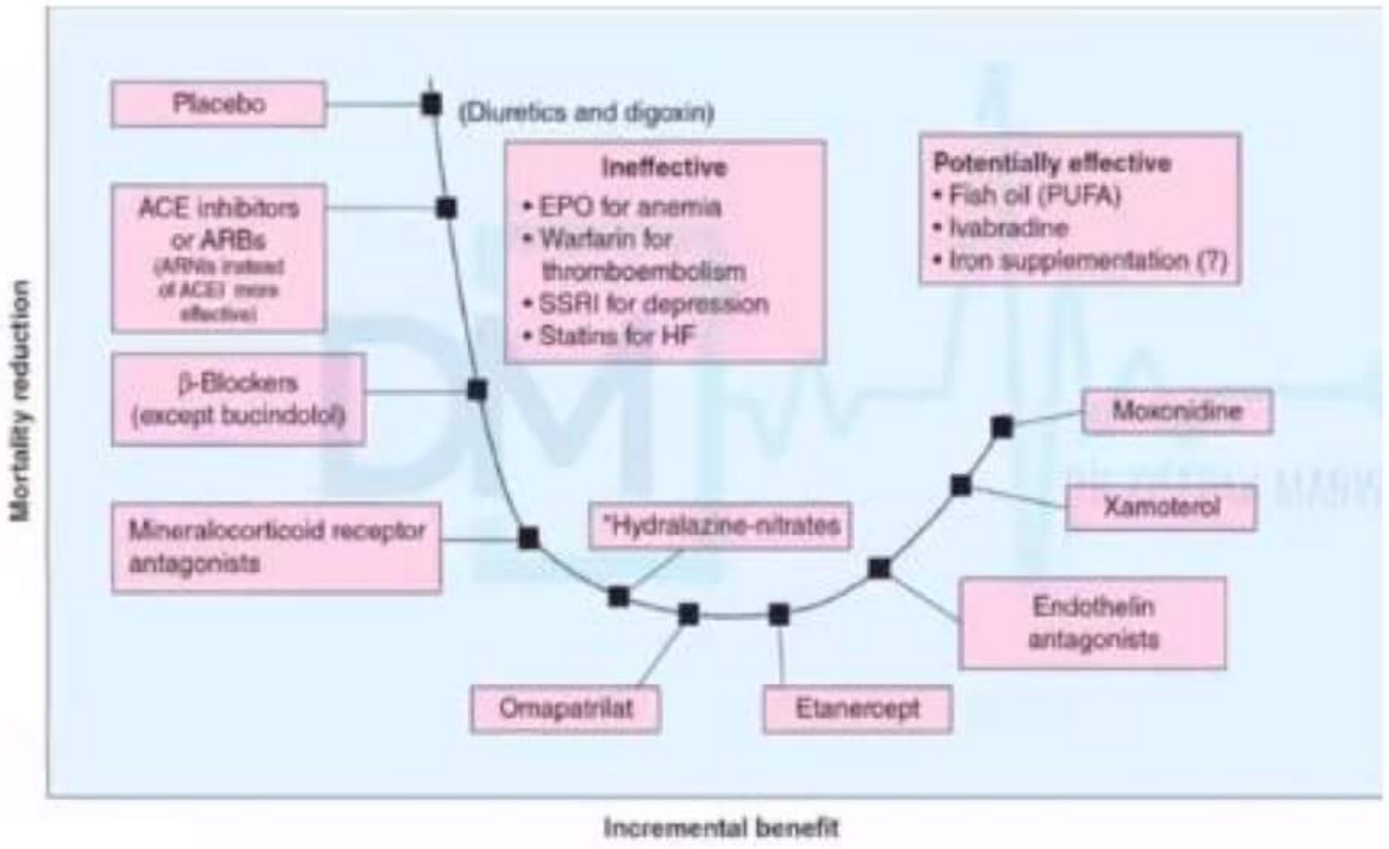
For Follow Up:

1) ARNI

2) ACE inhibitors + β blockers (Metoprolol, Carvedilol, Bisoprolol)

3) Spironolactone/ Eplerenone

→ ARNI = ARB (Valsartan) + Neprilysin inhibitors → (sacubitril) [Inhibit degradation of BNP natriuresis]



4. **Ivabradine**: Inhibitor of If current (Funny current inhibitor)

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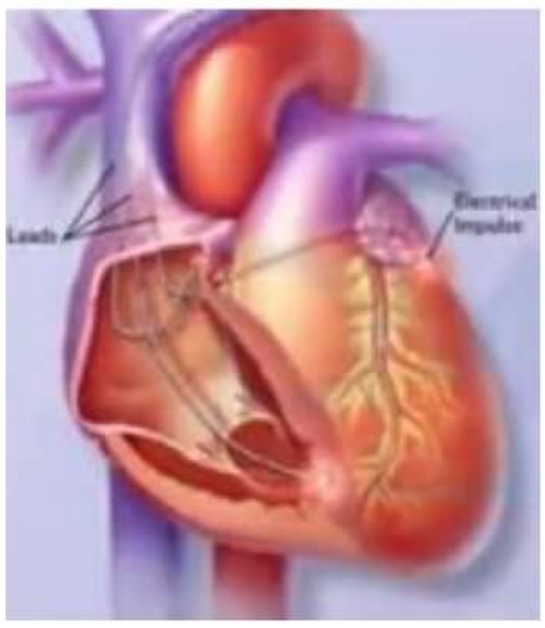
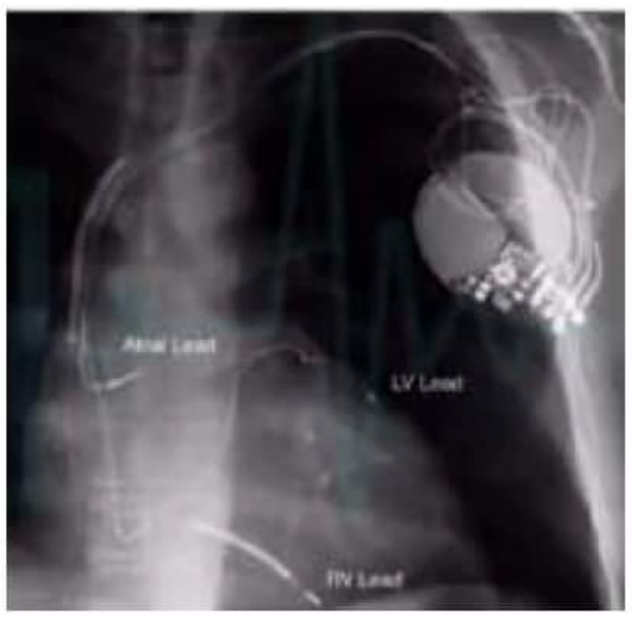
- It reduced hospitalization and the combined end point of cardiovascular related death.

5. **Cardiac Resynchronization therapy**

- Both ventricles contract at the same time in normal person, while in chronic heart failure due to cardiomyopathy both ventricles contract independently. CRT ensures simultaneous contraction of ventricles.





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Note:

Heart failure	
HF with preserved ejection fraction	**HF with reduced ejection fraction**
Causes → HTN → Restrictive cardiomyopathy → Amyloidosis → Hemochromatosis → Endomyocardial fibroelastosis **Survival Benefit** 1) ARNI 2) Aldosterone antagonist 3) ACE Inhibitors	**Causes** → CAD → Dilated cardiomyopathy → Ischaemic cardiomyopathy → Coxsackie B myocarditis → Chagas Disease **Survival benefit:** In Acute decompensated heart failure → Pulmonary edema - LMNOP → Pump failure - Vasopressor - IABP - LVAD - Ultrafiltration → **On long term basis:** ARNI or A + B + spironolactone ↓ if not working CRT/ICD/LVAD

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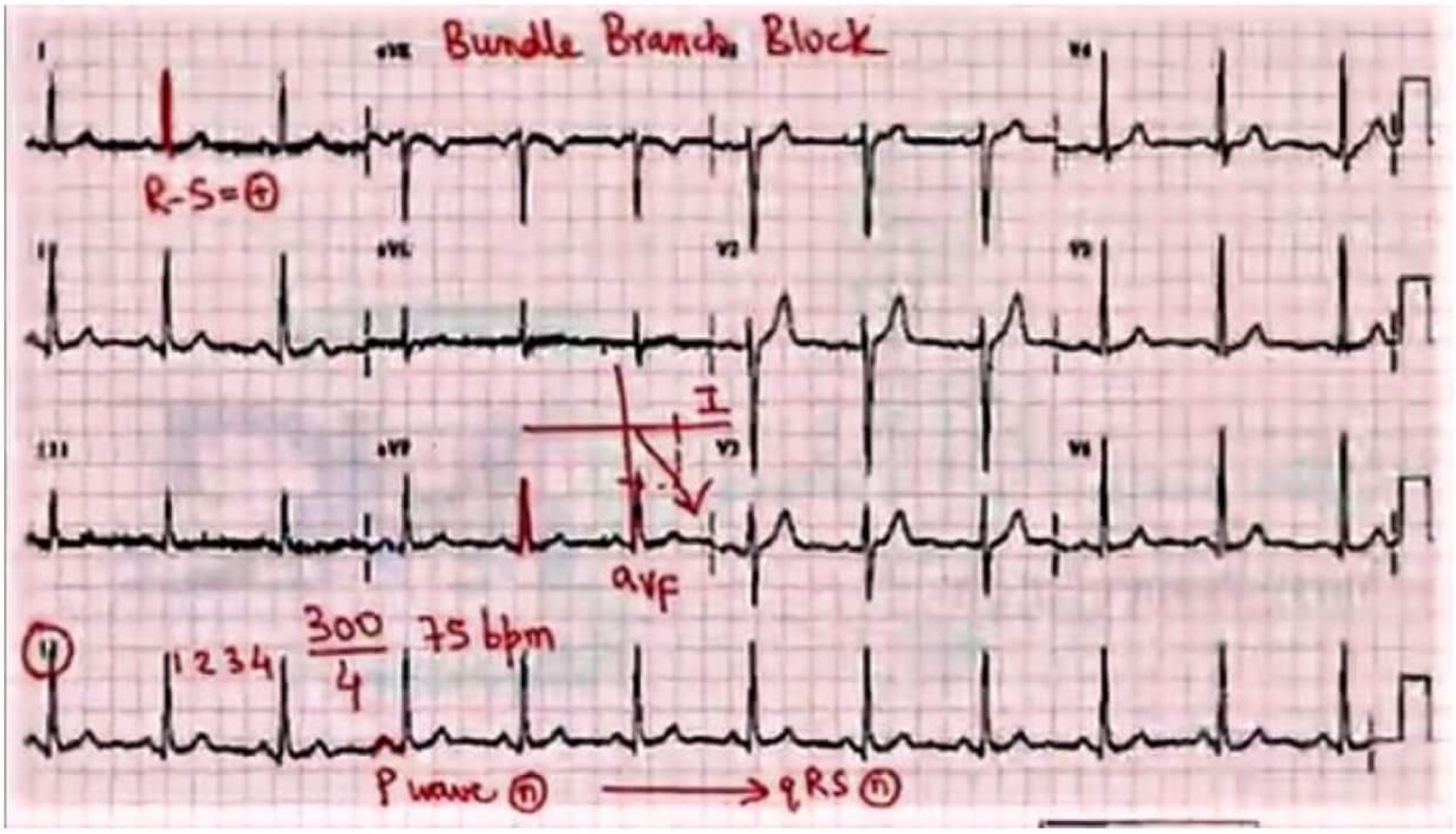
PrepLadder

Bundle Branch Block



In Normal ECG-

1) **Check HR** - Calculate R-R interval by looking at long lead II by counting no. of large squares then,

$$\frac{300}{No.of\ large\ squares} = \text{No. of beats/min}$$

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2) **Calculate Axis**

In given ECG **Lead I** – R wave is much bigger than S wave so, R-S = +ve and R-S = +ve in **aVF** → ECG shows normal axis.

3) **Check if every P wave followed by QRS** (Normal P wave = < 120 msec).

In the given **lead II** - P wave is three small squares and vertical height is < 2.5 mm → Normal and also check R-R interval is constant or not

4) **Check for ST segment** changes like ST – elevation, depression, coving

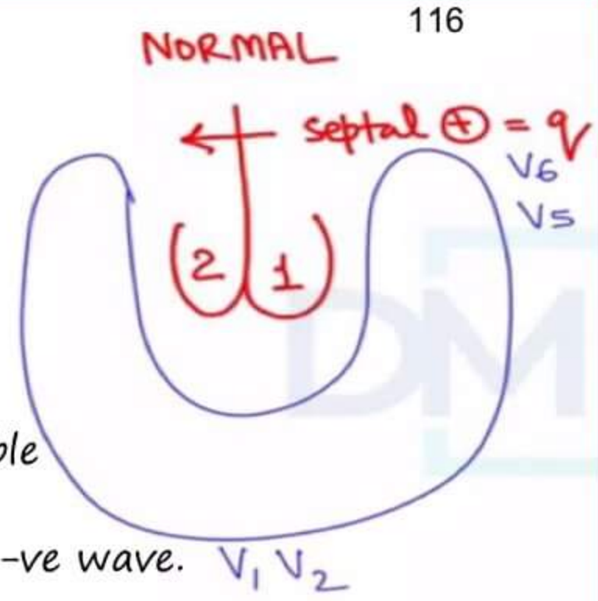
5) **Height of T wave in precordial lead** should be < 10 mm

Note: Height of T wave In limb leads = < 5 mm and In chest leads = < 10 mm

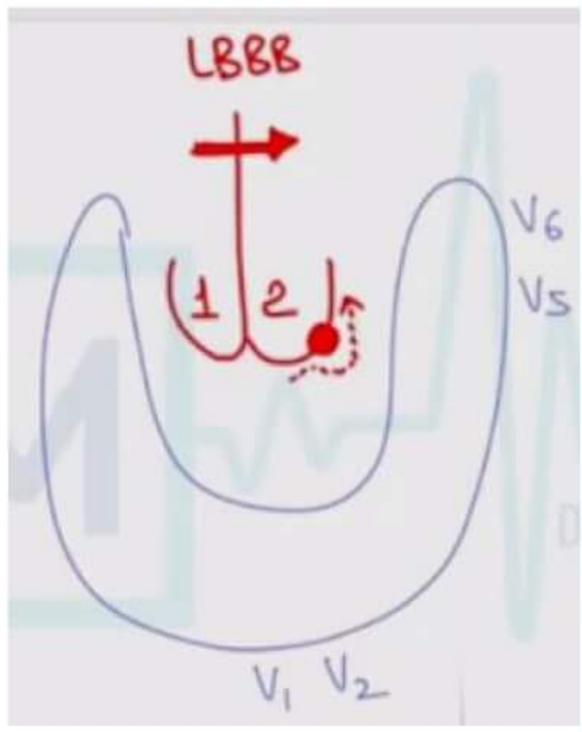
7) **Check for QT interval**, and Look for **'q' wave in V_5 & V_6**

8) Look for progression of R & S wave in V_1 to V_3 leads from V_1 to V_3 → R & S become equal in amplitude in lead V_3 and from $V_3 \rightarrow V_6$, **R becomes bigger than S** (progression of R wave)

PrepLadder



Normally – In Bundle of His- current goes to left fascicle and later on to right fascicle - Red arrow (Vector) signifies septal activation which is responsible for generation of 'q' wave, which is away from lead V_5 & V_6. So it is becomes -ve wave.



In LBBB

→ Damage in left fascicle so refractory period of left side is more than right

→ Current will go to right side first

→ Vector changes w.r.t. change in septal activation (towards right side)

C/F

→ Absent 'q' wave in lead V_5 and V_6

→ Tall R wave in V_5 and V_6 (lateral leads)

→ In the peak of 'R' wave -**Rabbit ear appearance** seen. This is due to:-

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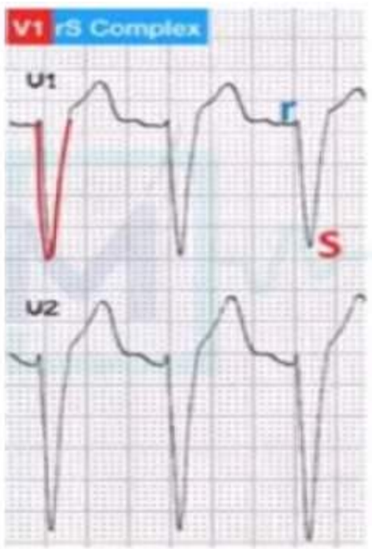
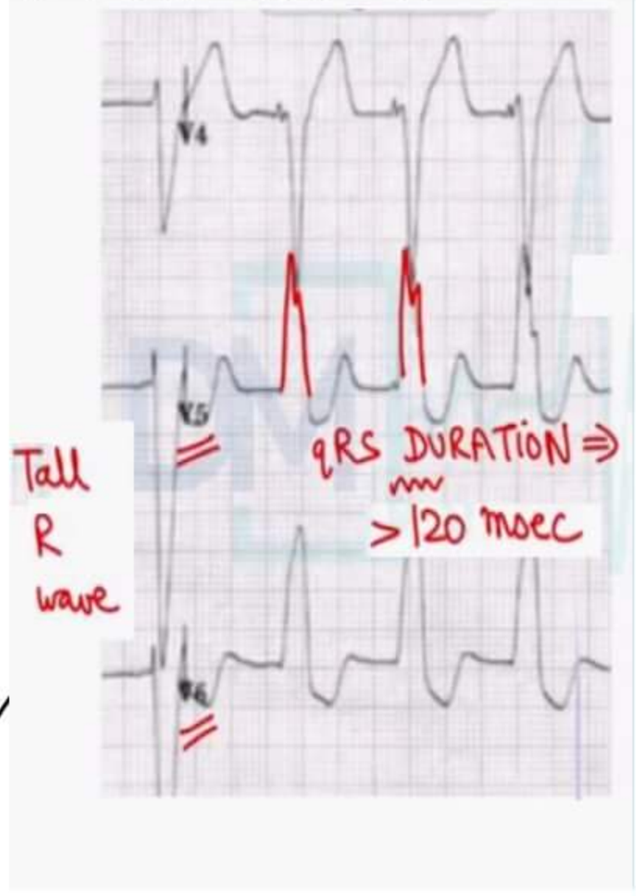
- Current travelling via Intermyocyte pathway.
- Sequential activation of ventricles (instead of simultaneous activation which occurs normally), so the ventricles contract independent of each other → results in pooling of blood in lungs → pulmonary edema → **LBBB is lethal**

Note→ A new onset LBBB is suggestive of MI as anterior wall MI → damage conduction system of heart → LBBB



→ **On ECG → deep 'S' in V_1& V_2** as the abnormal current is **going away from V_1 & V_2**

→ **Non discordant ST-T segment changes** (due to abnormal repolarization)

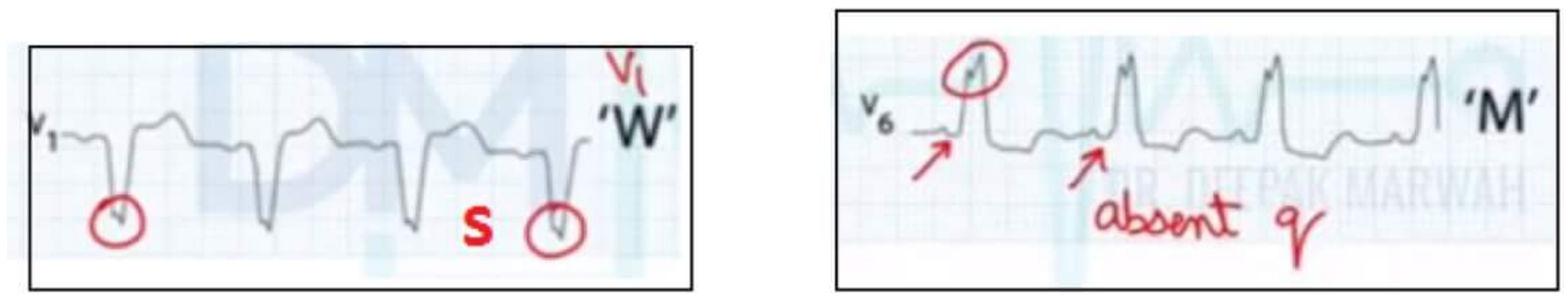


→ ST/T wave move opposite to the predominant qRS vector

e.g. in V_5/V_6 → **Tall R wave is seen** and also **ST depression is seen and in V_1/** deep 'S' and ST segment elevation is also seen.

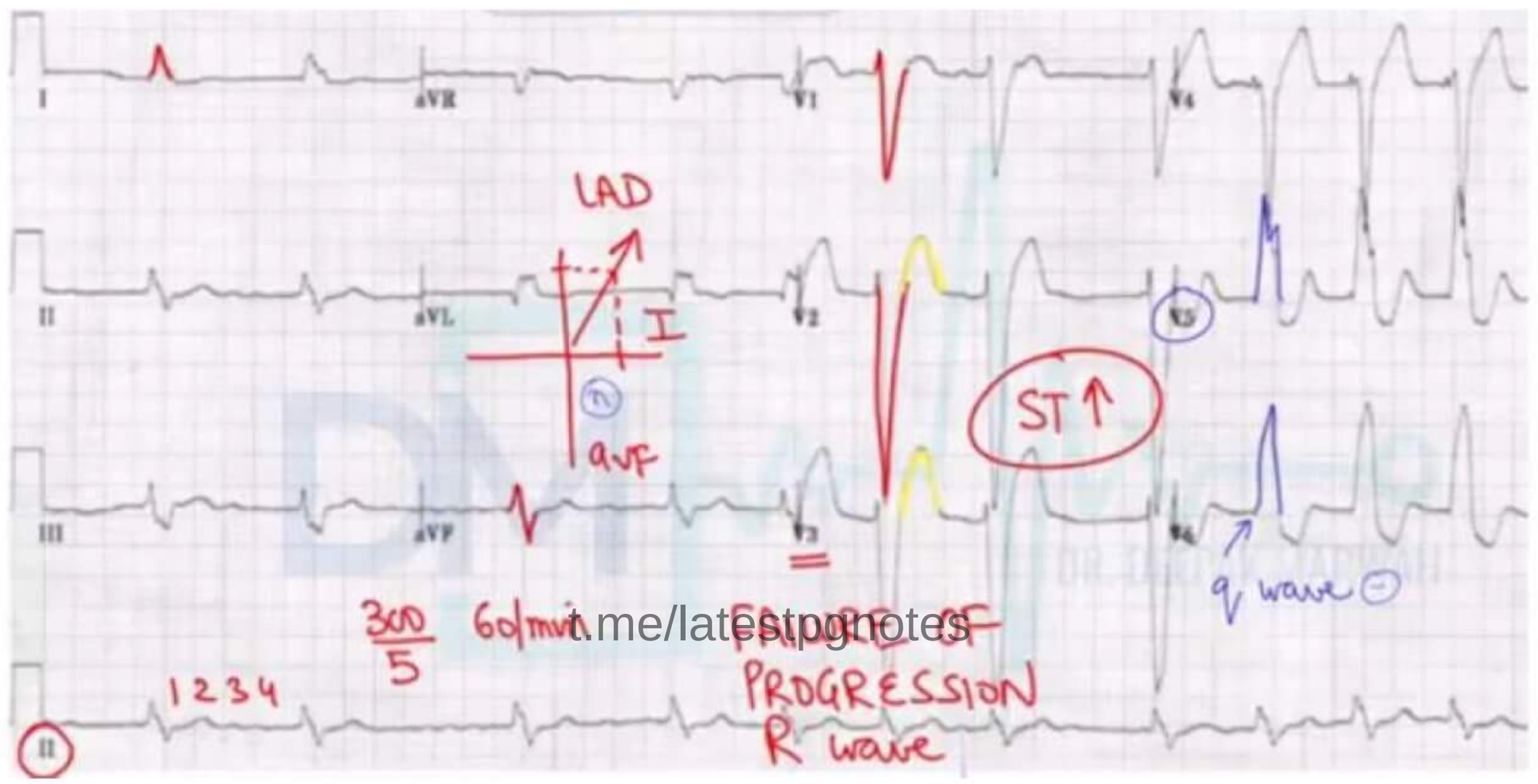
→ qRS duration is increased d/t wastage of time (Normal qRS = 80-100 ms)

PrepLadder



In ECG having Broad qRS –due to conduction delay, HR= Normal and there is presence of William pattern seen → "**Rabbit ear" in dominant S & peak of R,** W is seen at V_1, M is seen at V_6

Clinical scenario- ECG



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→ HR = 60/min (300/5-small squares between R-R interval)

→ Lead 1 is positive and lead aVf is negative, so Axis = LAD (Left Axis elevation)

→In precordial leads – **Deep/Dominant - S wave in V_1& V_2**

→ Rabbit ear appearance in V_5

→ Dominant R wave in V_6 and **absence of q wave**

→ Failure of progression of R wave – presence of BBB in the patient

→ Non discordant ST elevation seen in $V_1/V_2/V_3$., tall T wave also seen.

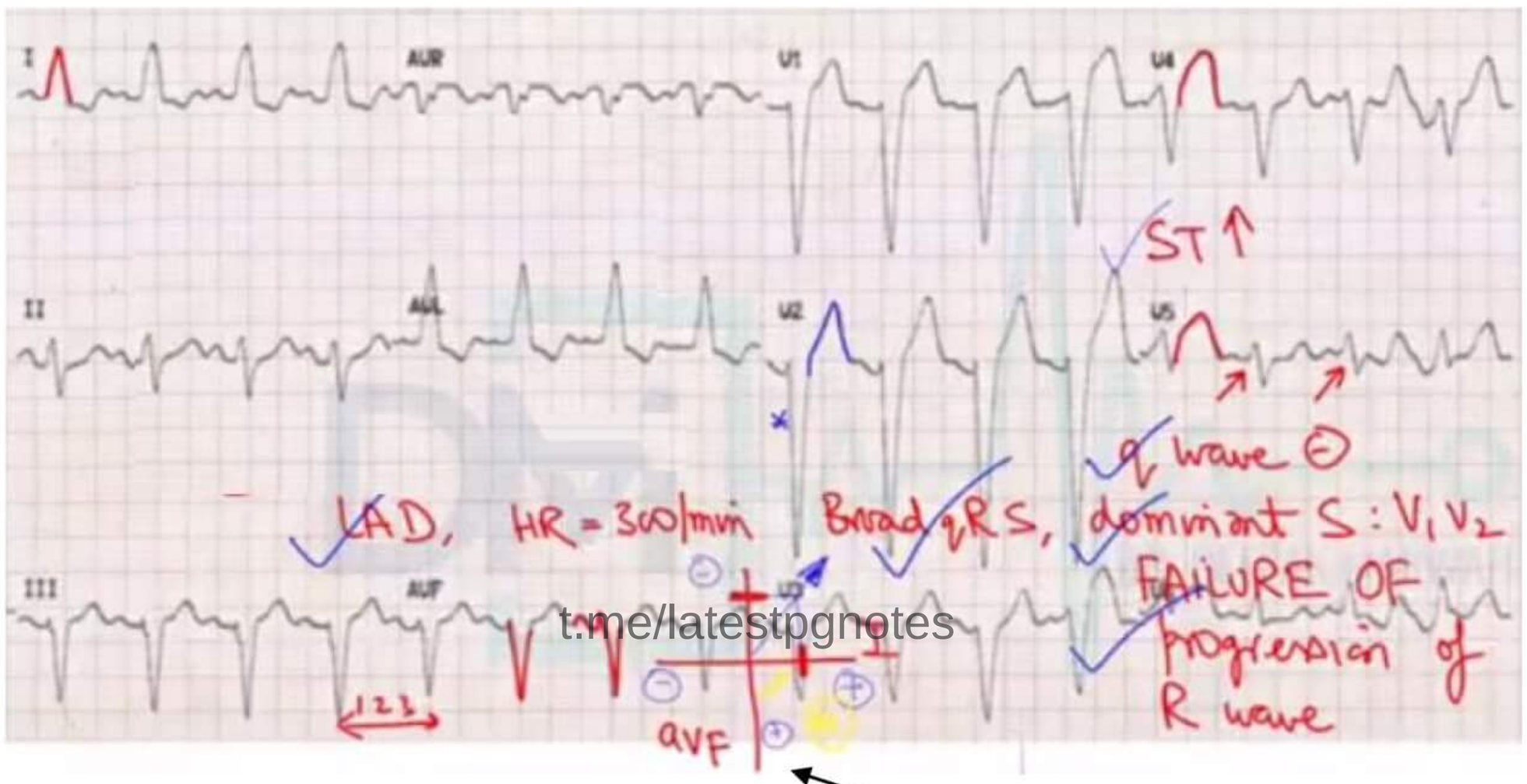
All these point to LBBB

PrepLadder

Causes of LBBB (mnemonic A_2,D_2,H_2)

- Aortic Stenosis
- Ant wall MI
- Digoxin Toxicity (most common – Ventricular bigeminy)
- Dilated cardiomyopathy
- HTN
- Hyperkalemia

Clinical scenario- ECG (LBBB)



- HR = 300/ min
- Lead I = +ve, aVF = -ve so there is LAD (always plot the axis to rule out the axis)
- Broad qRS complex
- In precordial leads- **Dominant 'S' lead V_1& V_2**
- Failure of progression of R wave
- **Broad dominant R wave in V_5 & V_6**
- Absent q wave
- **Note**- William' is not always applicable

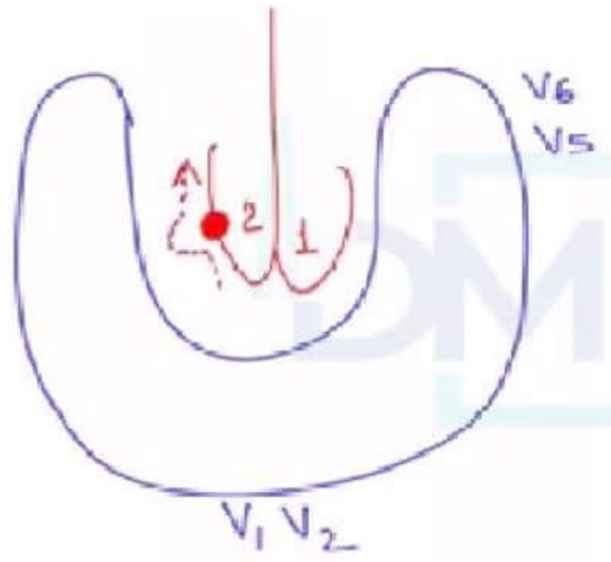
Sgarbossa criteria

→ To diagnose an MI when LBBB is present.

Note→ New onset LBBB could be present in MI & MI diagnosis can be missed in the patient having LBBB. The patient can have MI as a cause of LBBB

PrepLadder

Right Bundle Branch Block (RBBB)



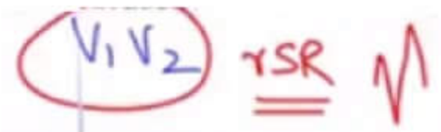
→ Defect in Right bundle branch

→ Left ventricle activated normally

→ But right side is having a delay in activation - Leading to →

C/F:

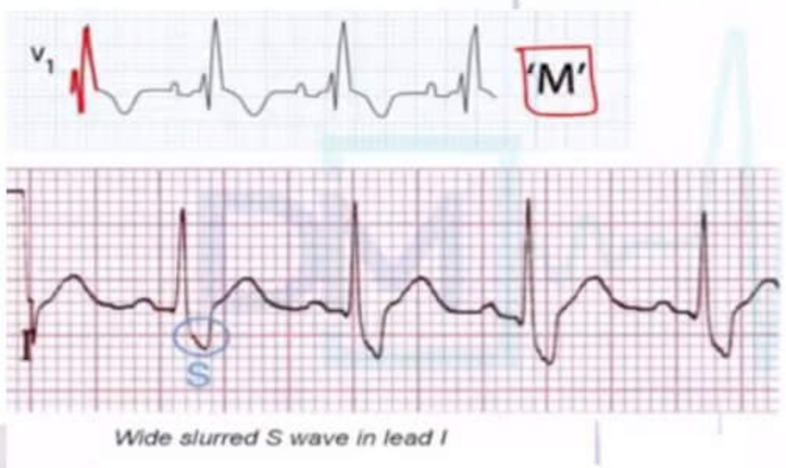
1) **rSR pattern in V_1& V_2.** It is also looking like a rabbit ear appearance.



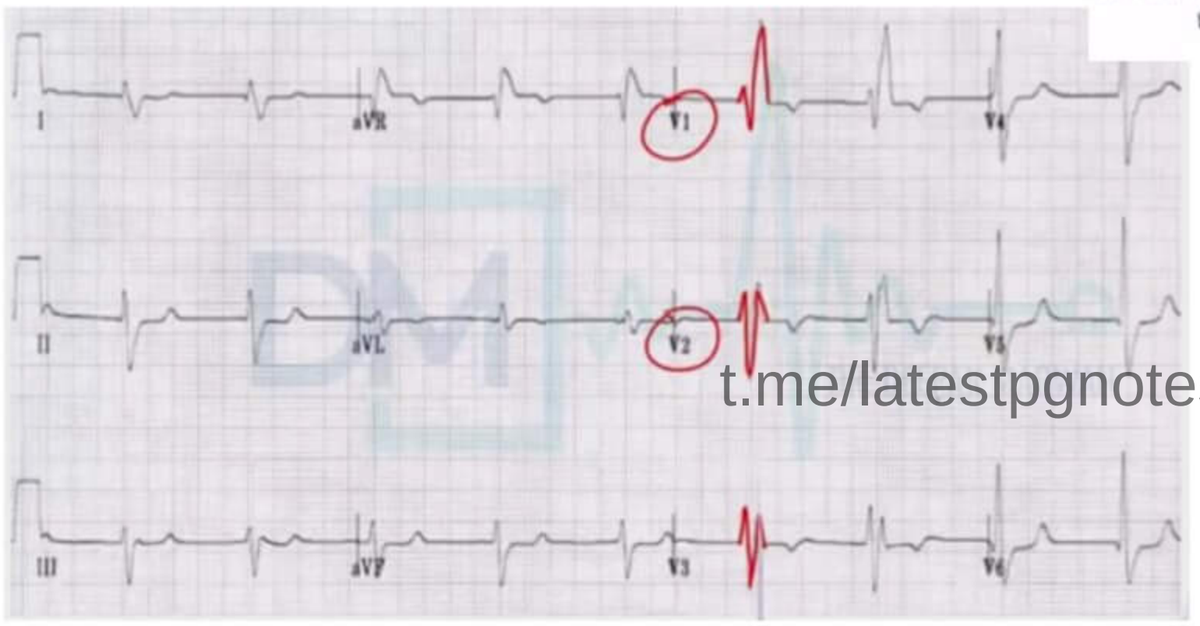
Note - But here no blood pooling of blood in lungs.

2) V_5/V_6 → W pattern and **"M pattern" in V_1/V_2**

3) Dominant S in V_5/V_6



ECG



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→ **rSR pattern in V_1& V_2** – due to intermyocyte conduction wrt Right fascicle to the patient

Shortcuts for BBB

→ qRS duration ↑ in both LBBB & RBBB i.e. > 120mq

LBBB	RBBB
→ Dominant S in V_1 V_2 - Tall R in V_5/V_6 - Rabbit ear - Absent q wave → More dangerous	→ rSR in V_1/V_2 → Dominant S in V_6 → Can be physiological

Cause of RBBB

- RVH
- Pulmonary embolism
- Cor pulmonale
- IHD, RHD, Cardiomyopathy.

PrepLadder

BASIC LIFE SUPPORT

Definition:

→ Out of hospital care to a person who has suddenly become unresponsive & pulseless.

Any cardiac event occurring out of Hospital in western countries

→ Survival Rate ≡ **10%**

Any cardiac event occurring out of Hospital & Patient was provided Bystander CPR

→ Survival Rate ≡ **20%**

Cardiac Arrest

1. **Unresponsive** person [As there is no cerebral Blood flow]
2. **Pulseless** [Carotid pulse is checked as it is closest to heart & last one to go in case of cardiac arrest]
3. **Apnea/ Gasping Respiration/ Agonal Rhythm**

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Pulseless conditions

→ Ventricular Fibrillation

→ Ventricular Tachycardia

→ Asystole

→ Pulseless Electrical Activity [PEA]

Shockable Rhythms

Ventricular Fibrillation and Ventricular Tachycardia

→ Treatment is **Cardioversion**

→ Survival chances are higher

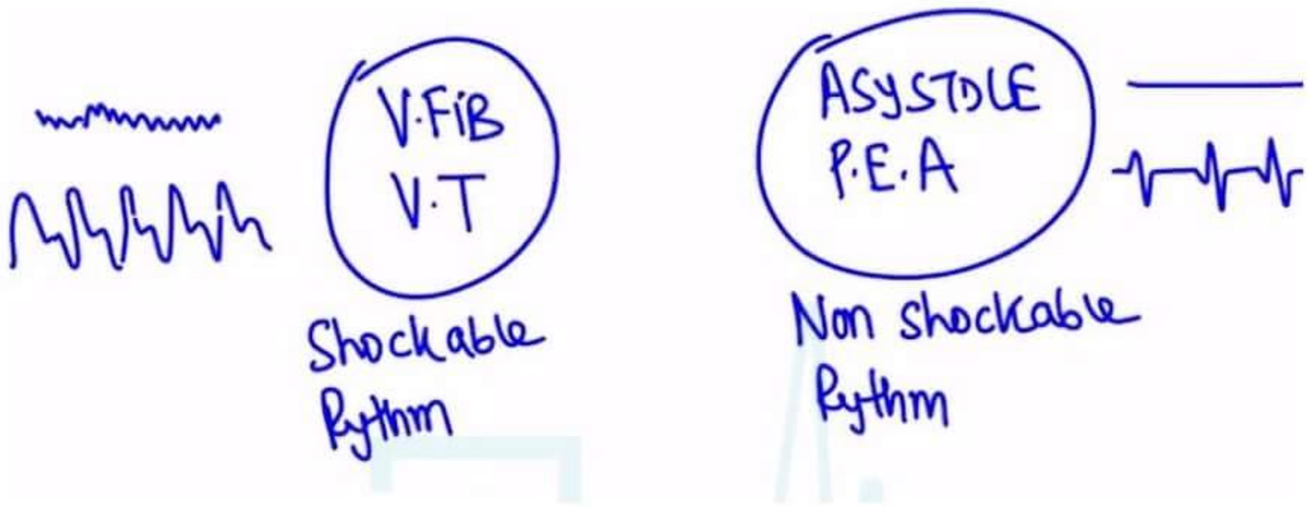
Non – shockable Rhythms

Asystole and Pulseless Electrical Activity

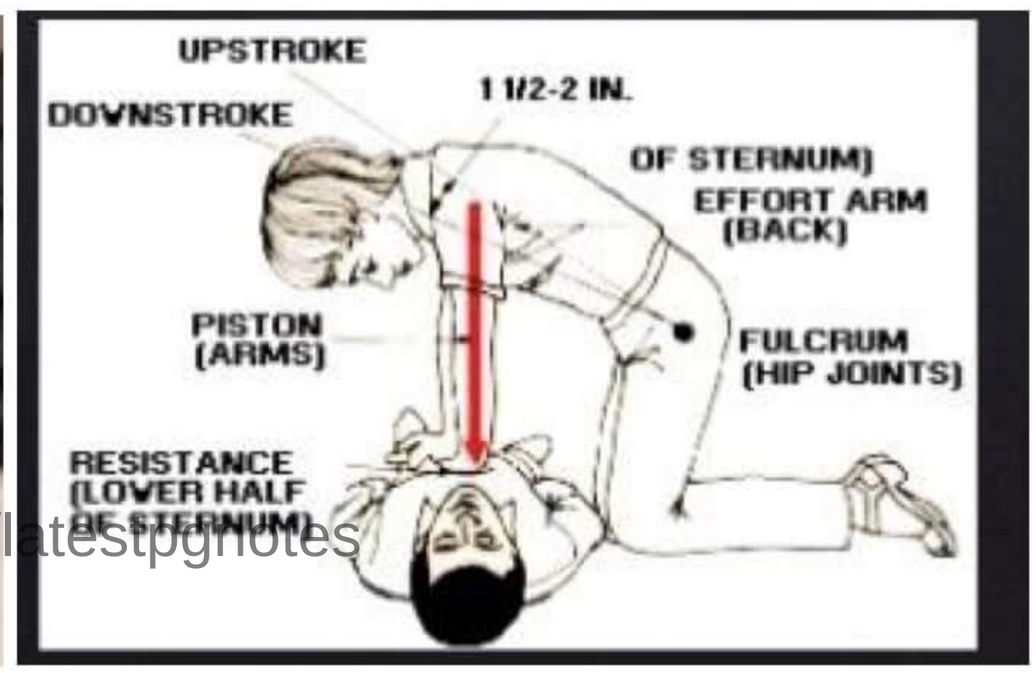
→ Survival chances are low

PrepLadder

Both Shockable & non-shockable Rhythms are inter convertible. i.e. Ventricular Fibrillation may convert into Asystole & vice versa.



Cardio Pulmonary Resuscitation (CPR)



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Q. An elderly male collapsed suddenly in an airport at the boarding gate. What will be the correct management of the patient?

Steps of giving Cardio Pulmonary Resuscitation (CPR)

1st step → Check **scene safety** (Take the patient to a flat surface)

2nd step → Check **unresponsiveness** of patient. (Tapping the shoulder)

3rd Step → Call for **Help**

4th step → **Activate** emergency response

5th step → Check **pulse** → carotid pulse

→ Check **breathing effort** → Look for

- Chest rise and fall
- Feel the breath sounds of the person

PrepLadder

Case scenarios of a collapsed person

1. Pulse → Present

   Respiratory effort → Absent

↓

Respiratory Arrest

↓

Treatment → Rescue breaths at the rate of 10-12/min (1 breath/second)

2. Pulse → Absent

   Respiratory effort → Absent

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↓

Cardio-Pulmonary Arrest

↓

Treatment → Cardiopulmonary Resuscitation at a rate of 30 : 2

(Chest compressions) ← 30 : 2 → (Rescue Breaths).

→ One cycle of CPR is of 2 mins

3. Pulse → Present

   Respiratory effort → Present

Treatment → Monitor the patient

PrepLadder

Case – 1 → An elderly man, who is 60 years old collapsed suddenly at the airport boarding gate. How will you manage this case?

Management

Follow steps 1 to 5 of cardiopulmonary Resuscitation

↓

Give a CPR cycle for 2 mins

↓

Look for an Automated Electrical Defibrillator Device (AED)

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↓

If AED available

↓

Put chest leads & look for Rhythm

If Shockable Rhythm

↓

Press button of AED

AED will give a DC shock of 200 J

↓

After shock is delivered, check for return of Pulse & Respiration

If Non-shockable

↓

Continue CPR till Medical health team arrives.

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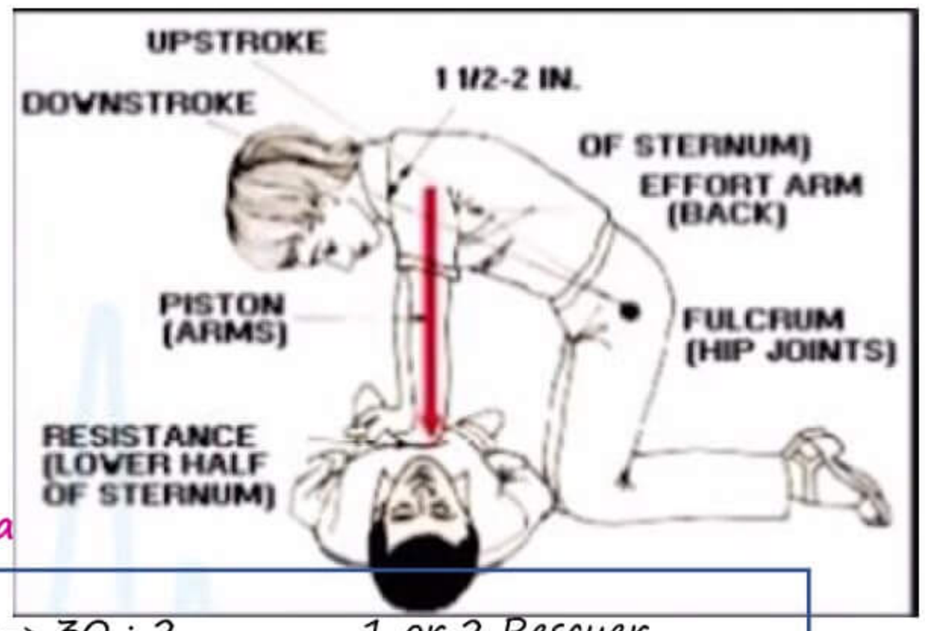

Ratio of CPR administra

Adult	→ 30 : 2	1 or 2 Rescuer
Paediatrics (Child)	→ 30 : 2	1 Rescuer
	→ 15 : 2	2 Rescuer
Neonate	→ 3 : 1	2 Rescuer mandatory

Sternal Depression

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Adults → 5cm

Child → 2 cm

Neonate → 1 cm

→ Allow for proper recoil of chest so that

- Heart can get filled with blood
- Coronary blood flow can be ensured

→ **Chest compressions** are given at a rate of **100 – 120 / min.**

→ Place hands on **lower 1/3rd of sternum** while giving chest compressions

→ Very forceful & aggressive chest compressions can lead to pressure over Xiphisternum

- As Xiphisternum is pointed → It causes damage to **Liver.**

-Most common solid organ traumatized in CPR → Liver (Not lungs)

-Lung is not a solid organ

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-**Hip joint** acts as **fulcrum** while giving CPR

-**Most common ribs damaged** while giving CPR → **4th to 6th** Ribs

-Do not discontinue CPR even if the Ribs are fractured.

Airway management by Bag & Mask Ventilation (BMV)

-By **AMBU Bag**

-Ensure → Head **tilt**

→ Chin **lift**

Head tilt & chin lift ensure patency of airways so that air can enter r into lungs during BMV

- Position of patient → **Sniffing position**

→ **Correct application of mask** -The Mask should be held b/w **thumb & an index finger of a left hand** in a '**C**' **shaped manner** so that air does not leak.

-Remaining **3 fingers** are kept in an '**E**' **shaped** manner, so as to stabilize the lower part of mandible

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→ With the **right hand** we press AMBU bag & give rescue breaths.

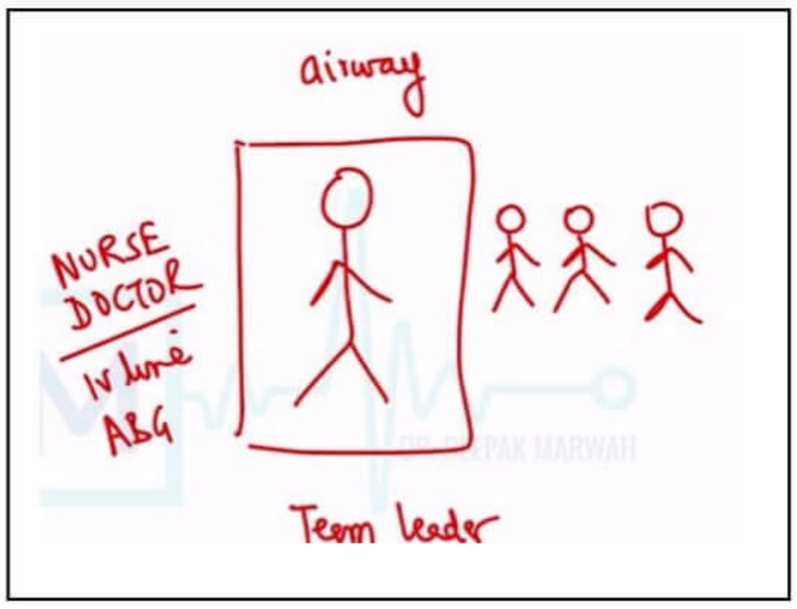
→ The person who provides **airway support** stands at **head end** of patient

→ Team **leader** stands at **foot end** of the patient

→ On the **right-hand** side is a team of 2-3 doctors and paramedical staff to provide simultaneous chest compressions after every 2 minutes.

→On the **left-hand** side is the nurse/doctor to secure an I.V. line and collect blood samples for ABG

→ Coordination of team members is an important component in CPR



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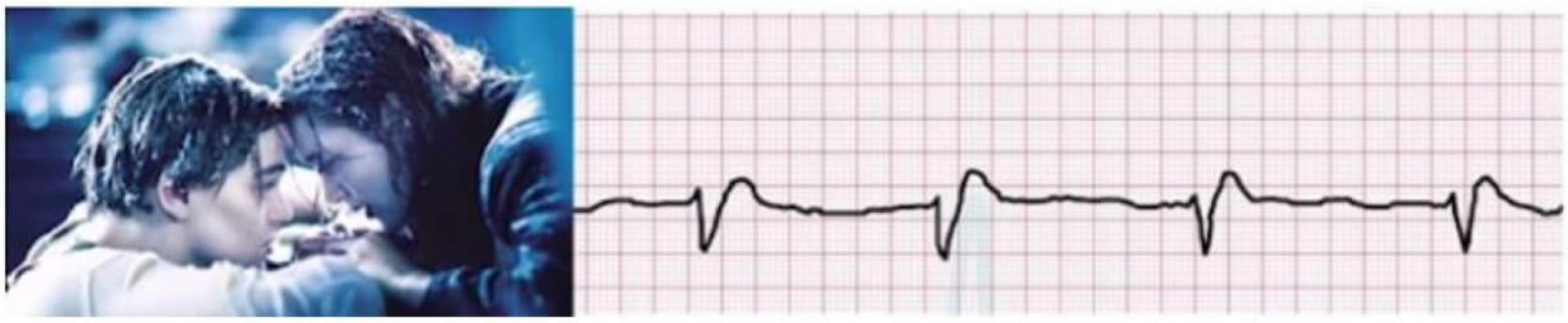
PULSELESS ELECTRICAL ACTIVITY (PEA)

Electrical activity of heart i.e. **SAN, AVN, Bundle of His** are **normal** but pulse is absent



Code outcome by diagnosis (code blue)

Diagnosis	Survival	
Unstable VT	65-70% (Pulseless)	shockable - rhythm
V-Fib	25-40%	
PEA	11%	non shockable rhythm
Asystole	0.2%	

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Rx -cause specific Rx.

PEA

Causes:

1)Empty Heart a) Hypovolemia

↓

eg Bullet injury to the abdomen causing ripping of aorta / superior mesenteric artery/ inferior mesenteric artery

↓

Patient can have hypovolemia → resulting in decompensatory shock → pulselessness

- here, even though muscle of heart is working fine, there is no blood to be pumped

(b) **Tension pneumothorax** - Eg Bullet injury to the chest causing air rush into the chest cavity- increased +ve pressure- lung collapse - kinking of SVC & IVC.→ venous return is compromised → cardiac output is compromised → pulselessness

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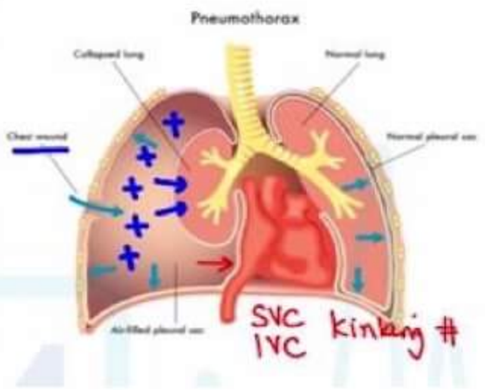
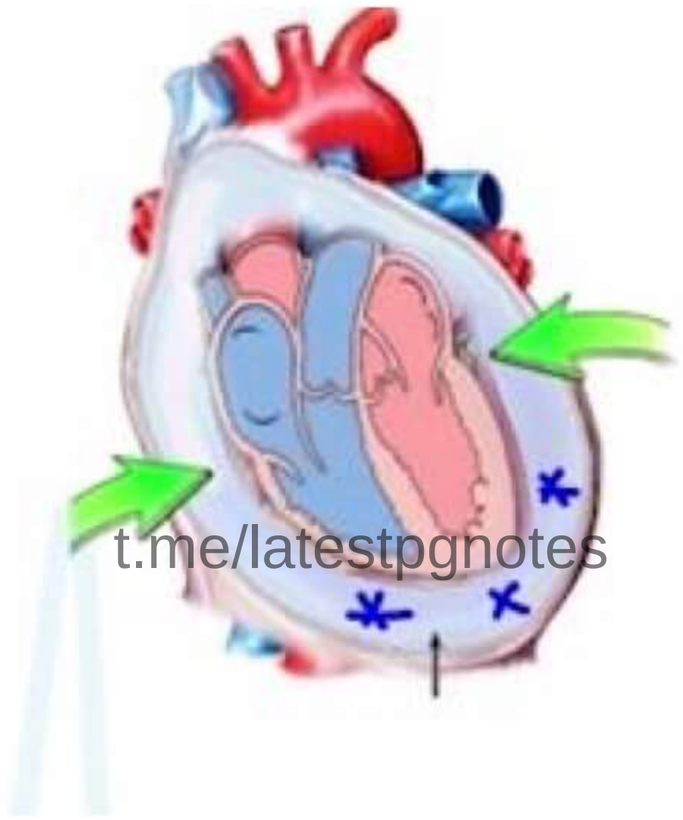


(c) **Cardiac tamponade** – fluid in pericardial space which exerts pressure on heart from outside → venous return to heart is compromised → Cardiac output is compromised → pulselessness



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2) **Electromechanical dissociation** – Conduction normal

Eg. **Acute MI** → stunned myocardium (hypoxia) (extensive ant. wall MI)

(no effective contractions – ↓ CO)

E.g. **Pulmonary embolism**
Postpartum patient

develop deep vein thrombosis d/t immobilization→

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Orthopedic surgery eg. THR, TKR resulting in pulmonary embolism → which causes severe **hypoxia** & right sided heart failure → pulselessness

Echocardiogram → shows dilated right ventricle

Treatable causes of cardiac arrest

5H's	5T's
Hypoxia (AMI)	Toxins
Hypovolemia (Aortic rupture)	Tamponade (cardiac)
Hydrogen ion excess (acidosis)	Tension pneumothorax
Hypo / Hyperkalemia	Thrombosis, Pulmonary
Hypothermia (Causes BCT < 35°C)	Thrombosis, Coronary

- Hyperkalemia → K+: >8.0m Eq/L → causes diastolic arrest → pulselessness
- Hypokalemia → causes Diaphragmatic paralysis → resulting in hypoxia → which decreases function of heart
- Hypothermia (T < 35°C)
- Toxins : TCA Toxicity
- Tamponade(cardiac)
- Tension Pneumothorax
- Thrombosis (Pulmonary embolism)

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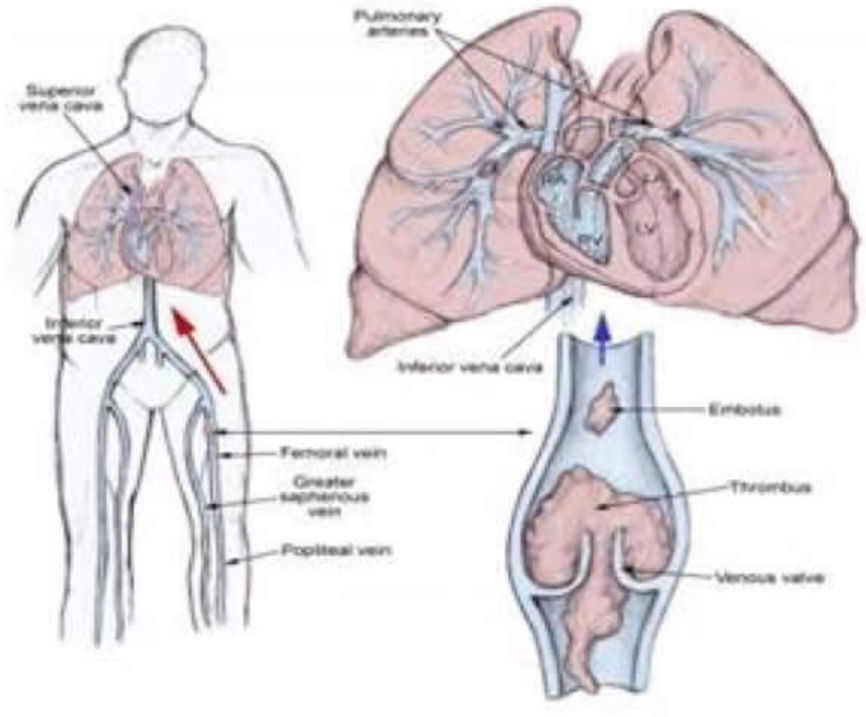

- Thrombosis, (Coronary- Myocardial Infarction)

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Revise causes

HEART	CONDITION	LUNG
Hypovolemia	Not enough blood	Hypoxia
Cardiac Tamponade	Squeezed	Tension pneumothorax
Acute MI	Killed	Massive pulmonary embolism

Note: Way to remember the causes Reversible of Cardiac arrest

H	Hypothermia
E	Electrolyte Imbalance (↑ K^+ / ↓ K^+)
A	acidosis
P	Poisoning

Intervention

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Rapid infuser → having a in line warmer so that it can prevent the development of hypothermia.

Echocardiography guided Pericardiocentesis

managing cardiac tamponade

wide bore needle in 2nd intercostal space

managing tension pneumothorax

PrepLadder

➔ if the soldier with tension pneumothorax has bullet proof vest in place/males with big pectoral muscles →then, needle is placed in **5th intercostal space, in mid-axillary line**

AIR BLANKET → TREAT HYPOTHERMIA

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ADVANCED CARDIAC LIFE SUPPORT

Q. How ACLS is different from BLS ?

A. In **ACLS** the differential diagnosis(d/d) of the causes of pulselessness are listed (we do Airway Breathing Circulation **D/d** i.e. ABCD) and manage the patient accordingly

-in **BLS** the main aim is to maintain brain perfusion by giving chest compressions

D/D of Pulselessness

1. **Ventricular Tachycardia**
2. **Asystole**
3. **Pulseless Electrical Activity**
   a. Hypovolemia
   b. Tension Pneumothorax

- **Defibrillator** -measures the rhythm, but the **physician** decides whether shock should be given
- **AED (Automated)** → Decision is made by the **machine**
- **Advanced Airway** →1 breath is given every 6 seconds (10 breaths /min)

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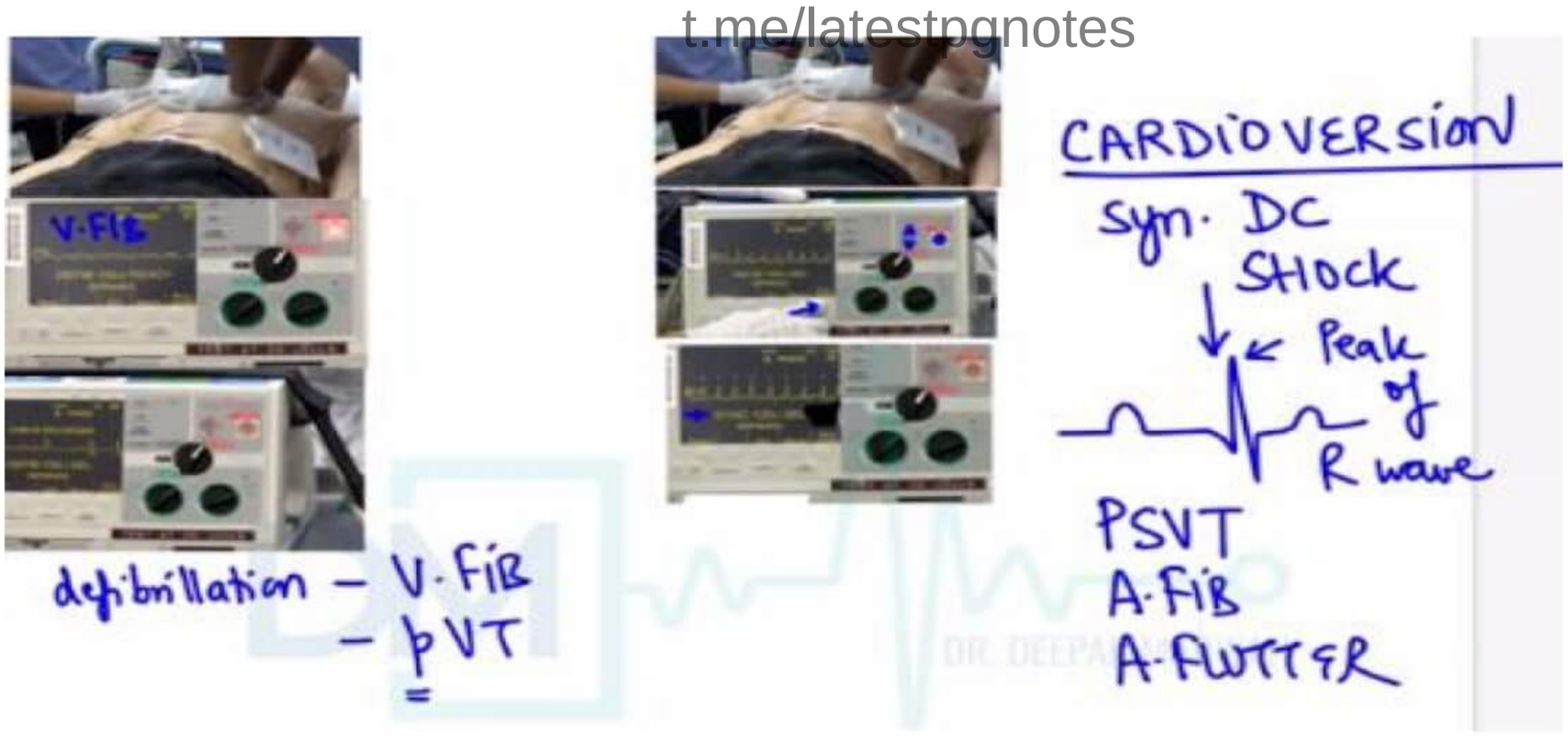


Q. Difference b/w **Defibrillation** & **Cardioversion**

A. Cardioversion

↓

Synchronized DC shock at the peak of R Wave

i.e.

- Impulse is fired at the **peak of R Wave**

↓

As R wave is the time at which heart is contracting abnormally

PrepLadder

So, it makes the heart relax, so that, at the next beat SA node takes over

↓

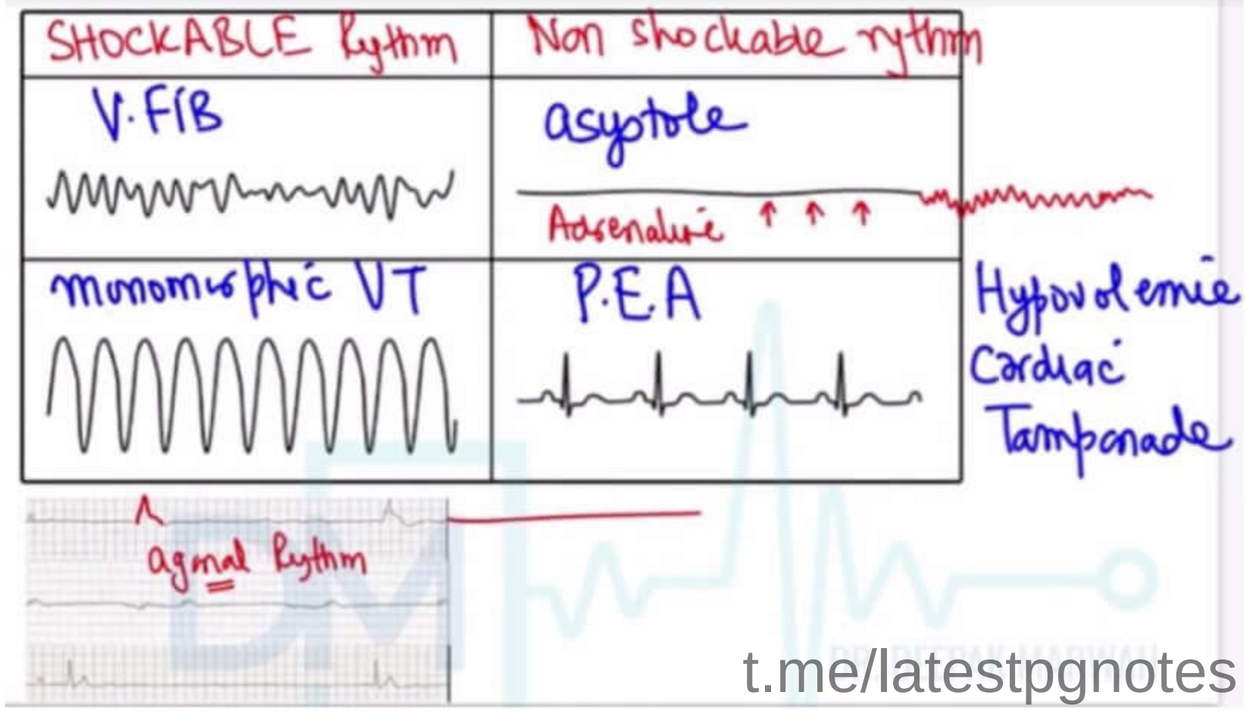
Return of spontaneous circulation

Done for → **PSVT, A. fibrillation, A. flutter**

Defibrillation → Impulse will be fixed irrespective of peak of R wave

Done for

- **V. Fibrillation**
- **Pulseless Ventricular TachyCardia (PVT)** Eg monomorphic VT



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- Both Shockable & Non-shockable Rhythms are inter-convertible. i.e. Ventricular Fibrillation may be converted into Asystole & vice versa.

Agonal Rhythm → Few last breaths of a person (efforts of brain stem)

→ Irregular Broad QRS due to firing of bundle of HIS

↓

After this Asystole

PrepLadder

Treatment of Reversible Causes

-5 H

&

-5 T

H	Hypovolemia	Hypoxia	Hydrogen Ion (acidosis)	Hypo/Hyper-kalemia	Hypothermia
	Loss of fluid volume in the circulatory system. Look for obvious blood loss. Most important intervention is to obtain IV access and administer IV fluids. Use a fluid challenge to determine if the arrest is related to hypovolemia	Deprivation of an adequate oxygen supply can be a significant contributing cause of cardiac arrest. Ensure that the airway is open. Ensure adequate ventilation, and bilateral breath sounds. Ensure oxygen supply is connected properly.	Obtain an arterial blood gas to determine respiratory acidosis. Provide adequate ventilations. Use sodium bicarbonate to prevent metabolic acidosis if necessary.	Both a high and low K+ can cause cardiac arrest. Signs of high K+ include taller, peaked T-waves, and widening of the QRS complex. Signs of low K+ include flattened T-waves, prominent U-waves and possibly widened QRS complex. Never give undiluted intravenous potassium.	If a patient has been exposed to the cold, warming measures should be taken. Core temp. should be raised above 86 F and 30 C as soon as possible. The patient may not respond to drug or electrical therapy while hypothermic.

T	Toxins	Tamponade	Tension Pneumothorax	Thrombosis (heart: acute, massive MI)	Thrombosis (lungs: massive PE)
	Accidental overdose : Some of the most common include: tricyclics, digoxin, betablockers, and calcium channel blockers). Cocaine is the most common street drug that increases incidence of pulseless arrest. Physical signs include bradycardia, pupil symptoms, and other neurological changes. Poison control can be utilized to obtain information about toxins and reversing agents.	Fluid build-up in the pericardium results in ineffective pumping of the blood which can lead to pulseless arrest. ECG symptoms: Narrow QRS complex and **rapid heart rate.** Physical signs: jugular vein distention (JVD), no pulse or difficulty palpating a pulse, and muffled heart sounds. Perform: pericardiocentesis to reverse.	Tension pneumothorax shifts in the intrathroacic structure and can rapidly lead to cardiovascular collapse and death. ECG signs: Narrow QRS complexes and **slow heart rate.** Physical signs: JVD, tracheal deviation, unequal breath sounds, difficulty with ventilation, and no pulse felt with CPR. Treatment: Needle decompression.	Causes acute myocardial infarction. ECG signs: 12 lead ECG with ST-segment changes, T-wave inversions, and/or Q waves. Physical signs: elevated cardiac markers on lab tests, and chest pain/pressure. Treatments: use of fibrinolytic therapy, PCI (percutaneous coronary intervention). The most common PCI procedure is coronary angioplasty with or without stent placement.	Can rapidly lead to respiratory collapse and sudden death. ECG signs of PE: Narrow QRS Complex and rapid heart rate. Physical signs: No pulse felt with CPR. distended neck veins, positive d-dimer test, prior positive test for DVT or PE. Treatment: surgical intervention (pulmonary thrombectomy) and fibrinolytic therapy.

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- **Hypokalemia** → *Results in TORSADES DE POINTES, Diaphragmatic paralysis*
- **Hyperkalemia** →*Bradycardia* →*ASYSTOLE*
- **Tamponade** → *identified by electrical alternans of ECG*
- **Tension pneumothorax** → *identified by absent breath sounds on ipsilateral side*
- **Coronary Artery Disease** → *ST elevation*
- **Massive pulmonary embolism** → *have right ventricular failure* [$S_1Q_3T_3$] & **Kussmaul's sign**

PrepLadder

Mx of patient who had suddenly collapsed →CPR, O_2,and Defibrillator attached

If PVT(premature ventricular tachycardia)/V.fib (ventricular fibrillation)	If PEA(pulseless electrical activity) / Asystole
↓ **Non synchronized DC Shock** ⇩⇩⇩⇩⇩ CPR x 2 min, I.V / I.O line Fails ↓ **Repeat Non synchronized DC Shock** CPR x 2 min, IV / IO epinephrine 1 mg in 1:10000 dilution Advanced Airway, Capnography **Breathing: 1 breath / 6 Sec after Endotracheal Intubation** Fails ↓ **3rd Shock repeated** CPR x 2 min IV amiodarone **Treat reversible cause [hypoxia, toxins acidosis etc]**	↓ CPR x 2 min IV/IO [tibia /sternum] epinephrine Advanced Airway & Capnography ↓ fails CPR x 2 min Repeat epinephrine Treat reversible causes mainly Hypovolemia Epinephrine can be repeated every 3-5 minutes .

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Amiodarone 3 doses can be given

1st dose = **300** mg
2nd dose = **150** mg after 3-5 mins
Amiodarone is useful for VT as well as shock refractory VT
ROSC (Return of Spontaneous Circulation)

PrepLadder

↓

TTM (Target Temperature Management) or

Therapeutic Hypothermia (limit the progress but can't reverse damage)

- -Cardioprotective
- -Neuroprotective

Prognosis of these patients isn't good

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PrepLadder

MECHANICAL VENTILATION STRATEGY

- **TIDAL VOLUME [V_T]:** 12-12 Rule

  V_T = 12ml / Kg (lean body weight) → i.e Fat component is subtracted

  RR= 12/min

Note: **But, in ARDS patient, we don't follow 12-12 Rule**

In ARDS : V_T = 6 ml /kg (lean body weight) → to minimize **volutrauma** in the pt

- In ARDS, there is inflammation in alveoli → if we inflate these alveoli in standard fashion, it leads to barotrauma to the alveoli → which worsens the situation
- A person having any neurological cause [GBS / Transverse myelitis etc] with diaphragmatic paralysis → there is no inflammation in the lungs → so, this person can be ventilated at tidal volume of 12mg/kg

- **RR :** | **Minute volume = (V_T x RR ↑↑)** |

  - **Conditions in which we increase the respiratory rate & make the person hyperventilate are:**
    - ➔ **Raised intracranial pressure**
      Hyperventilation causes vasoconstriction of cerebral blood vessels resulting in decreased production of CSF → decrease ICP
    - ➔ **DKA (Diabetic ketoacidosis)**
      Hyperventilation is a Compensatory mechanism to clear acidosis in DKA patient

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- **FiO_2** → 1.0 = 100% of O_2

  → 0.6 = 60% of O_2; 0.4 =40% O_2

  - **Objective** of giving O_2 [starting from FiO_2 0.4] to the pt, is to maintain oxygen saturation = **paO_2 > 60 mm Hg & spO_2 > 90%**

PrepLadder

PEEP (Peak End Expiratory Pressure)

- There would always be a baseline pressure in the lungs, so whatever the inflation/ deflation that would be done should be always above this base-line pressure.
- Hence after applying PEEP, Recruitment of alveoli will be maintained (more surface area of alveoli is available for gas exchange)

↓

Better gas exchange of respiratory gases both during inspiration and expiration

↓

Hence, better O_2 saturation will be maintained.

- **DISADVANTAGE OF PEEP** -At PEEP of 5 cm H_2O, Recruitment of alveoli is ensured
  - But, if PEEP ↑↑ → it increases pressure on great veins of the chest leading to reduction in venous return to heart → decreases B.P
  - Higher PEEP is a disaster for the hypotensive patients
    - ✓ Eg. Pulmonary embolism (RVF & hypotension)
    - ✓ Inferior wall MI (RVF)
    - ✓ Therefore, PEEP must be kept 3-5 cm of water

EXAMPLE:

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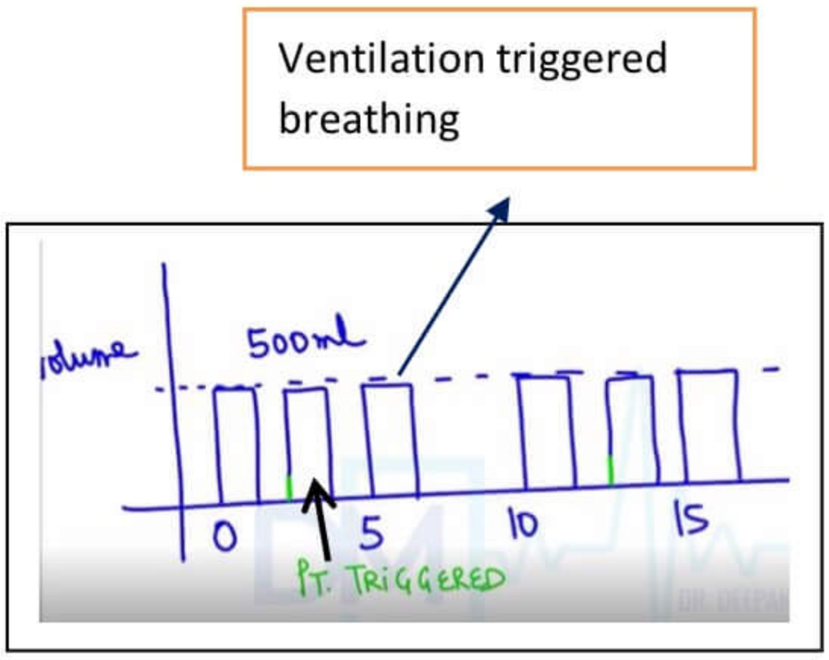
ABG parameters

(A) Patient	(B) Patient
pH = 7.40 (normal)	pH = 7.20
pO_2 = 60 (**deficient**)	pO_2 = 100(normal)
pCO_2 = 40 (normal)	pCO_2 = 60 (↑↑ **ed**) (respiratory acidosis)
Management : ↑FiO_2	**Management:** Change the RR ↑↑↑
↑PEEP → Recruitment is Better	Minute Volume ↑↑
	[result in CO2 washout & correct acidosis]
In **hypoxia,** parameters to be Taken care of are **FiO_2 & PEEP.**	In **Respiratory acidosis,** take care of **RR & Minute Volume** of the ventilator.

PrepLadder

ASSISTED CONTROL MECHANICAL VENTILATION (ACMV)



RR = 12 /min [1 breath every 5 sec]

V_T = 500 ml

FiO_2 = 0.4(40%)

- ADVANTAGE- Used In patients with no spontaneous breathing
  - Patient triggered breaths are also assisted by ventilator.
- ACMV is **Most common** mode used in invasive mechanical ventilation.
- S/E of ACMV → **HYPERVENTILATION (only with ACMV)**

↓ causes

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Respiratory Alkalosis

↓ resulting in

HYPOCALCEMIA (TETANY)

↓

LARYNGOSPASM

↓

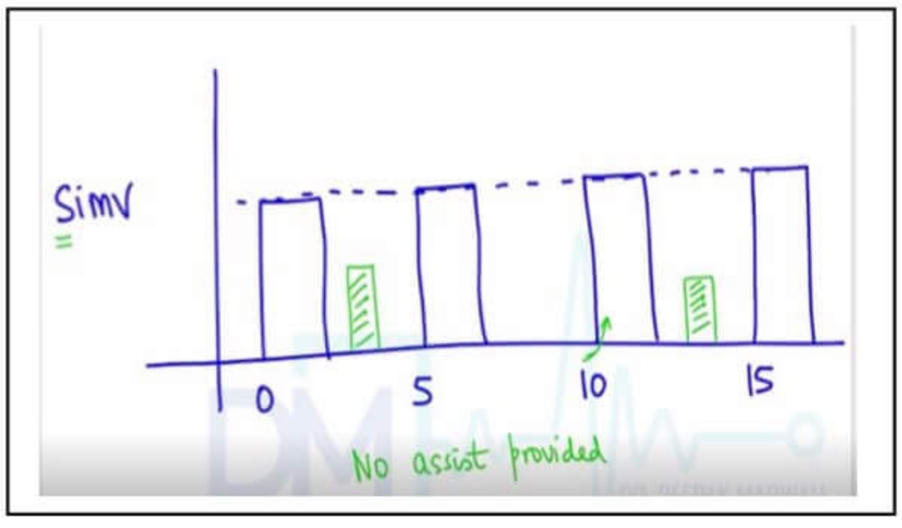
HYPOXIA

↓

seizures & myoclonus

SIMV (SYNCHRONIZED INTERMITTENT MANDATORY VENTILATION):

- The breathing is synchronized but **not assisted by the ventilator**
- Advantage → support or wean off the patient from ventilator.
  - Ensured minute volume is provided
- Disadvantage of SIMV → HYPOVENTILATION



↓

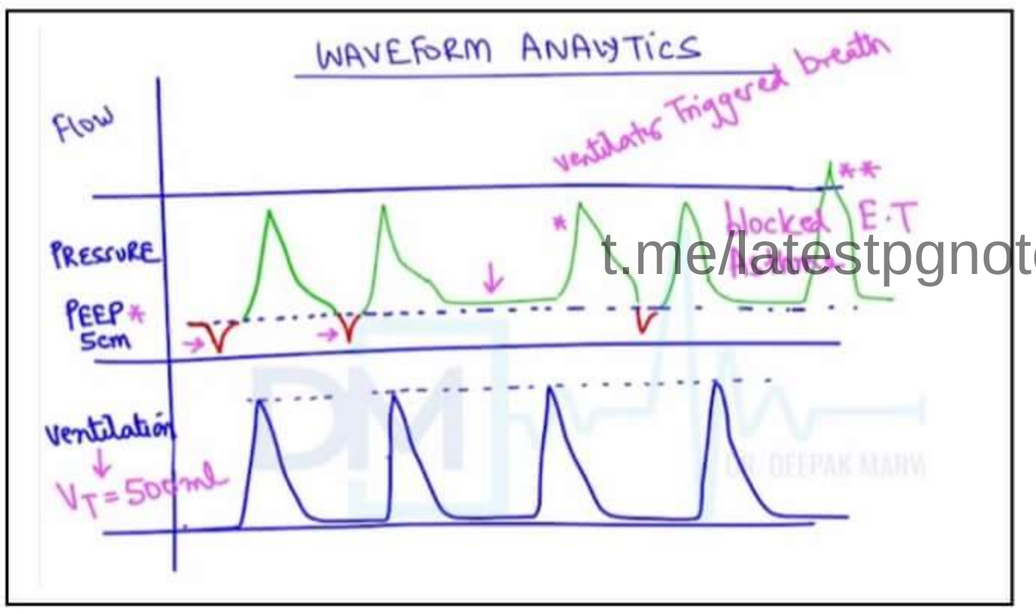
If patient's breathing effort is occurring at the same time as that of mechanical ventilator breath, → it results in inhibition of ventilatory drive & total Minute Ventilation will be reduced

Note: DO NOT USE SIMV, if patient has tachypnea

- **Asynchrony** [lack of coordination b/w ventilator & person] can also result in hypoventilation

WAVEFORM ANALYTIC PRESSURE SUPPORT VENTILATION:

- Negative spike (red)- Inspiratory effort of the patient (**pt. triggered breath**)
- Flat line – **Ventilatory triggered breath**
- ** Spike of waveform due to
    - Blocked Endotracheal tube
    - Asthma



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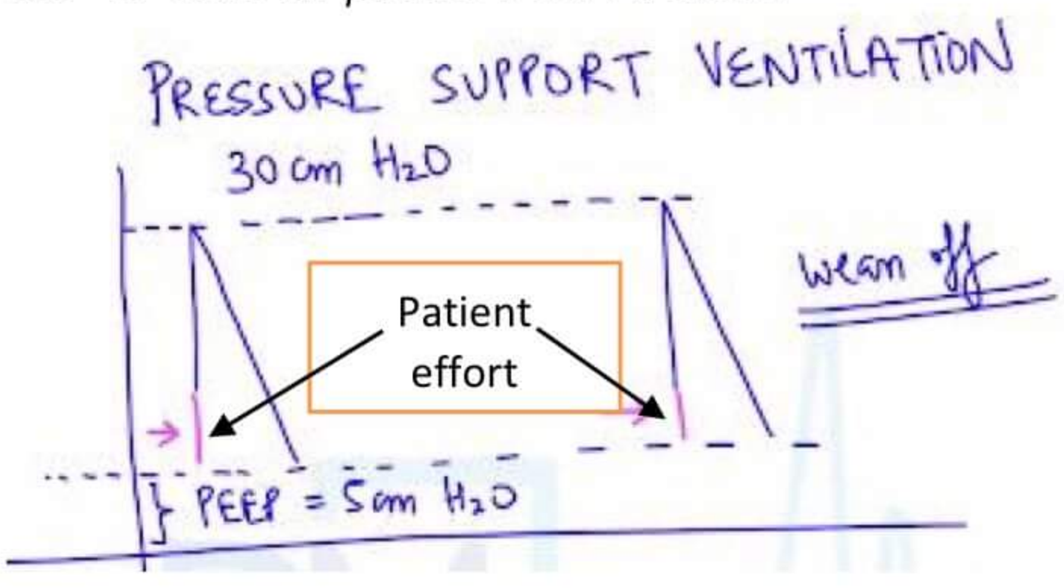
PRESSURE SUPPORT VENTILATION:

- Only pressure support is given
- No guaranteed /backup ventilation
- **Use**- to wean off patient from ventilator



NOTE :

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- **ACMV**- To put patient **ON** ventilator
- **SIMV and PSV** – To wean **OFF** patient from ventilator

PRESSURE CONTROL VENTILATION:

INDICATIONS:

- Pre-existing Barotrauma (pt with pneumothorax on ventilator)
- Patient undergone cardiothoracic Vascular surgery (to reduce shear stress over the surgical scar)
- ' **CONTROL** ' means to limit further inflation of lungs to a level where it may cause worsening of pre-existing barotrauma in a person

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PROTECTIVE VENTILATOR STRATEGY:

➔ Any person who has gone into respiratory failure, 4 basic rules are to be followed while treating that person to increase chance of survival

BASIC RULES OF VENTILATION:

1. **Tidal Volume** IN ARDS = **6** ml /kg (6-8 ml/kg)
2. **Peak pressure** = **30** cm of H_2O (to limit barotrauma component)
3. **FiO_2** = **0.4** (initiated and then gradually upgraded)
   a. **SaO_2** > **90 %**
   b. **pO_2** > **60** ($pO2 < 60$ is Hypoxia)
4. **PEEP** = **5cm** of H_2O (to decreases the venous return and recruitment of alveoli simultaneously)

NIV (Non-Invasive Ventilation) **VS** **CPAP** (Continuous Positive Airway Pressure)

✓ Both gives good O_2 delivery → by tight fitting face mask

PrepLadder

NIV	CPAP
-**Positive pressure** generated which Varies in phase of **inspiration [i PAP]** and **expiration [e PAP]** [to decrease the load on accessory muscles of respiration	-**Constant positive pressure**, maintained both in inspiration and expiration -Acc to Harrison- CPAP not exact form of ventilation * Splinting of airways [force to keep the airway open]
INDICATIONS -COPD exacerbation **(Resp acidosis)** (PH- 7.25- 7.35) - Intubation is avoided bcoz there is a chance of developing ventilator associated pneumonia & local trauma to the airways of pt - Hence NIV is recommended for patients with Type-2 resp failure [COPD exacerbation with resp acidosis]	INDICATIONS -Hyaline Membrane disease -Obstructive sleep apnea [always feel sleepy] * CPAP is initiated if there are **>15 apneic episodes/hr** (minimum) -Cardiogenic pulmonary edema (CPAP is a supportive measure)
Advantage- ↓ incidence of VAP [pseudomonas > staph aureus] ↓ Tracheo-laryngeal trauma	

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It is a type of **Pressure Support Ventilation (PSV) without intubation**	
Monitor – ↓ Respiratory rate ↓ use of accessory muscles of respiration	
C/I – Encephalopathy/ ppl who Can't protect their airways -Cardio-Respiratory Arrest -GIT bleeding -Unstable Angina /MI [any acute pulmonary syndrome] -Facial surgery -Upper airway obstruction	

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SUMMARY:

- **CPAP**:
  - It is the splint that keeps the airways open [method of non-invasive ventilation]
  - **INDICATIONS**: Hyaline Membrane Disease, Obstructive Sleep Apnea
- **BiPAP / NIV**: variation in **iPAP, ePAP**
  - **Indication**: **COPD** Exacerbation
- **INVASIVE MODE (IMV)** → **ACMV**: Most common modality of ventilation used.
  - Initiation of ventilation
  - S/E → **Hyperventilation**, respiratory alkalosis, **seizures, myoclonus**

SIMV → used for weaning off the pt from ventilation

PSV → **S/E** (Respiratory Acidosis- ↑CO2) → hypoventilation

PCV → CTVS (Cardiothoracic Vascular Sx), Barotrauma (Pre Existing)

→ **S/E** (Respiratory Acidosis- ↑CO2) → hypoventilation

PrepLadder

MASSIVE TRANSFUSION PROTOCOL

DEFINITION → Replacement of the Entire blood volume of patient in a 24 hr period

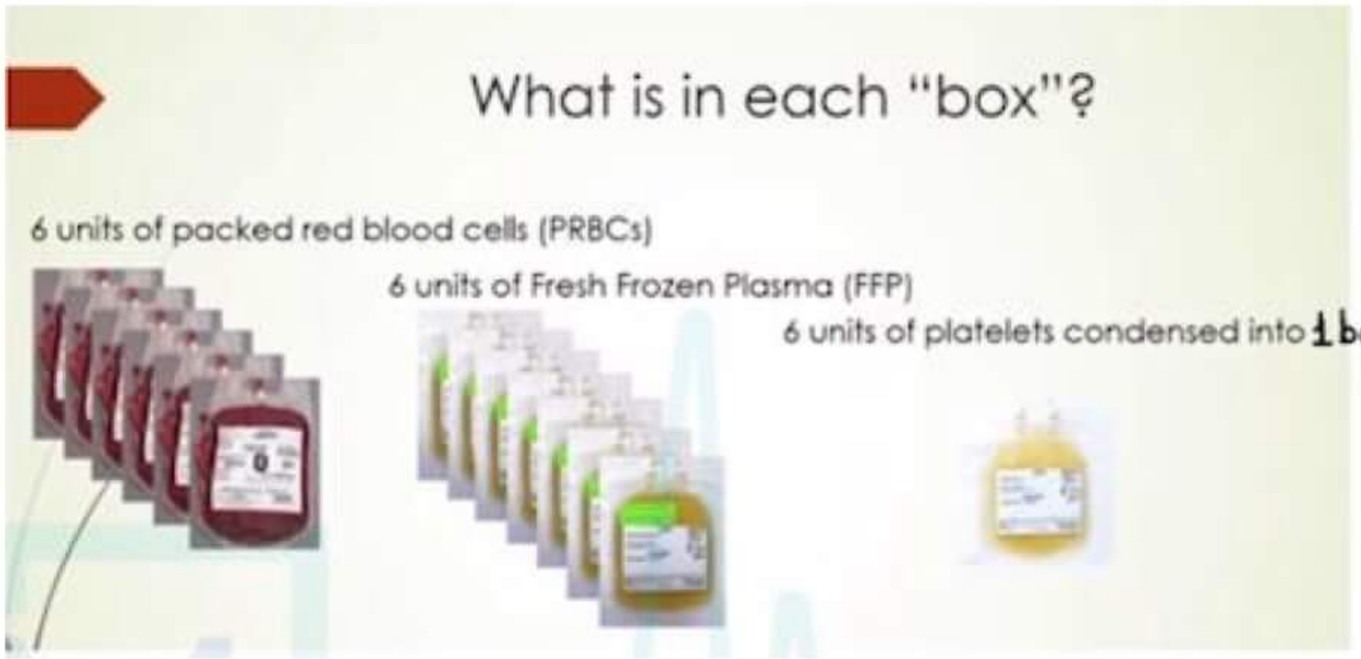
Or

> 10 Units of whole blood within 24 hrs

Or

> 2.5 L [5 units] of whole blood given within 4 hrs period

--> 6 units of Packed RBC / 6 units of FFP / 6 units of PRP can be given to the patient



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* 6 units of platelet rich plasma is condensed into single bag and is available as SDP (Single donor Platelet) which is Prepared by **Apheresis**
* Efficacy of SDP= 6 Units Of Platelet Rich Plasma (PRP)
* **Ratio of administration = PRBC: FFP : PRP = 1:1:1**
    * In a bleeding patient, there would be hypoxia & acidosis d/t blood loss.
    * **First thing** to be administered in these patients is **Packed RBC** **[f/b FFP & PRP]** →which carry oxygen & neutralize the acidosis component.
    * Acidosis impair the ability of blood to clot, which may worsen the coagulopathy of the patient. Hence, platelets shouldn't be given first

RED COOLER BAG

* Have **6 units** of packed RBC
* Plasma is stored at -30 degree C
* Plasma would be initially stored inside but then it is kept outside to thaw the plasma and bring it to room temperature
* Platelets are not kept in cooler bags → these are stored at room temp → 20-24 degree C
* Trauma in patient causes blood loss, resulting in
*
    - loss of clotting factors
    - Hypothermia [d/t loss of heat]

  } leading to **TRAUMA INDUCED COAGULOPATHY**

PrepLadder

TRAUMA INDUCED COAGULOPATHY:

THE HUMAN COAGULATION SYSTEM IS SLOW AND WEAK

→ Clotting takes time (2-10 minutes in the best circumstances)

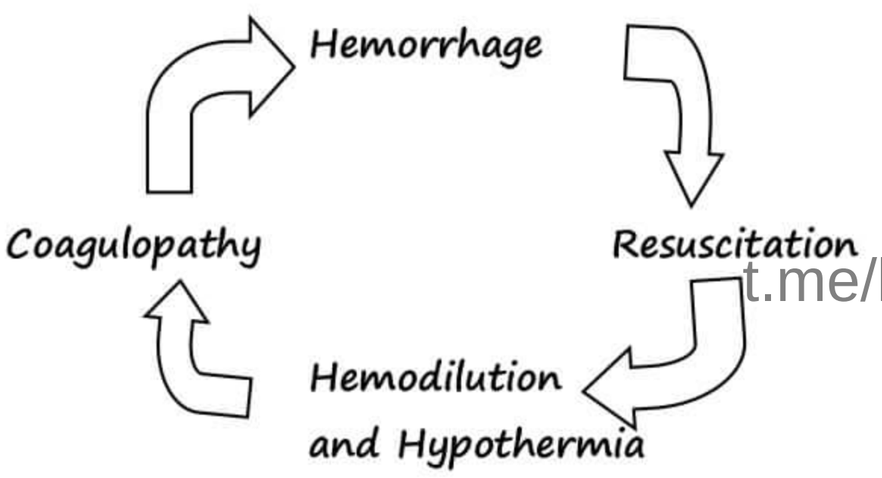
→ Clots are physically weak

→ There is limited clotting material to work with (even in the whole body) :

* **10 g of fibrinogen** total
* **15 ml of platelets total in normal individuals**

➔ If we give packed RBC which are stored at 4 degree C to these patients → hypothermia worsens → which further result in coagulopathy

BLOODY VICIOUS CYCLE:



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* **Poor circulation** results in **metabolic acidosis** [because cells are in **anaerobic** respiration]
* Giving **cold blood components** triggers → **Hypothermia** interferes with clotting process **leading to coagulopathy**
* Triad of **acidosis + hypothermia + coagulation** → difficult to manage
* To minimize hypothermia → ensure in-line warmers in rapid infusion pump
* **Eg** → In **obstetric hemorrhage**, resuscitation of pt with massive transfusion protocol,
  - When so much of **crystalloid** fluids followed by blood transfusion is given,→ **hemodilution** occurs→ hypothermia → interferes with coagulation process & worsens coagulopathy
  - ensure **in-line warmers** in rapid infusion pump→ components are warmed to sufficient temperature to minimize the hypothermia component
* If there is **150 ml blood loss/min** in a patient → within 20 min,→ depletion of circulating volume → decompensated shock (↓↓ BP) → Death
  * In a bleeding patient, infused blood = output i.e blood loss (to prevent the patient from going into decompensated shock)

PrepLadder

* **TRIGGERS of massive transfusion protocol:**

ASSESSMENT OF BLOOD COMPONENT SCORE (ABC SCORE)

Components	Points
1. Penetrating Injury	1
2. FAST positive	1
3. HR > 100 / min	1
4. SBP < 90 mm Hg	1

* If ABC score ≥ 2 then there is **75% accuracy in prediction** of Massive Transfusion Protocol [MTP]
*

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SETUP REQUIRED FOR INITIATING MTP IN A PATIENT:

Pressurized Rapid Transfusion (PRT)

* Ensures that the blood components reach into the body of patient on time
* Ensures that infusion matches output & chances of survival increases
* has **in-Line Warmer** → chances of Hypothermia ↓ hence coagulation problems are taken care of and hemostasis achieved.
* **Tranexamic Acid**
  - ✧ Antifibrinolytic agent
  - ✧ stabilize the clot → hemodynamic stability

PrepLadder

ADULT MASSIVE TRANSFUSION PROTOCOL:

TRIGGERS:

* ABC Score (ABC > 2)
* Surgery [trauma to major blood vessel]
* Hematemesis d/t PUD (Peptic Ulcer Disease)
* PPH (Postpartum Hemorrhage)
* Penetrating traumatic Injury
* + Low BP

ROUND 1:

* Call Blood Bank & inform MTP protocol to be initiated
* Assign Team Members to do **specific** tasks

- Divide Teams into A, B, C.

FUNCTIONS OF TEAMS:

A = **A**dminister blood Components to patients (not be responsible for drawing, labeling blood sample or writing notes in a file about units of blood sample given)

B = **Record** Keeping, Sampling, labeling of samples, entry in the file of units of blood etc, so that proper documentation is maintained.

-blood Sample - CBC / CMP
- PT /aPTT
- ABG [from radial artery]

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C = Runner → go to blood bank & get cooler bag/blood units to hospital

Team A:

* Give **1g** of **Tranexamic** acid to patient I.V Stat, then given 8 hourly
* Connect the pressurized rapid transfuser to the patient
* Give **4** Units of **PRBC** (O-VE) & **2** units **FFP** (AB +)

After Round 1, Reassess the patient
↓
If NO Improvement
↓
ROUND 2

ROUND 2:

Infuse - **4** units **PRBC**
4 units **FFP**
1 Unit **SDP** [Single Donor Platelet]

Team B → Resend blood to Lab → so that we can evaluate coagulopathy & metabolic acidosis component.

PrepLadder

* **Calcium gluconate** given to prevent tetany [caused by citrate in PRBC].
* **Cryoprecipitate** given → If the **fibrinogen** < 100 mg/L

↓ If No Improvement

ROUND 3

ROUND 3:

Repeat Round 2

+

Factor VII a

-Indications to administer Factor **VII a** :

- Surgical hemostasis,
- **temperature**-37 degree celsius (stabilized),
- **pH**-7.35 (stabilized) has been achieved but pt is still bleeding

CHALLENGES DURING MASSIVE TRANSFUSION PROTOCOL:

1. **Hypovolemia**
   * A major challenge
   * All efforts should be made to stop the bleeding rather than replace blood loss.
   * The loss of 150 ml of blood per minute results in loss of half the blood volume in 20 Minutes

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2. **Hypothermia**
   * Because Erythrocytes are stored at 1°C-6°C rapid blood product administration can lead to hypothermia which leads to coagulopathy
   * 6 Units of RBC will decrease body temp. by 1°C.

3. **Hypo-coagulopathy**
   * There is dilution effect from infusion of crystalloid volume expanders.
   * Hypothermia reduces the activity of coagulation proteins and prevents activation of platelet.

COMPLICATIONS OF MASSIVE TRANSFUSION PROTOCOL:

1. **Coagulopathy** → minimized by Pressurized Rapid Transfusion within line warmer
2. **TRALI (Transfusion Related Acute lung injury)** → Respiratory Distress [non-cardiogenic pulmonary edema] + BP normal + BNP normal
3. **TACO (Transfusion Associated Circulatory Overload)** → Respiratory Distress (cardiogenic pulmonary edema) + BP ↑ + BNP ↑
4. **Hyperkalemia** → packed R.B.C are stored at lower temp, near expiry date → Na^{+2}- k+ pump is shut down which leads to hyperkalemia → causes **Diastolic arrest (Bradycardia)**

PrepLadder

5. **Hypocalcemia** → Laryngospasm (Difficulty in breathing, stridor in clear chest)

RESPIRATORY DISTRESS CAN BE DUE TO:

* **TRALI** → Pulmonary edema [non-cardiogenic pulmonary edema]
* **TACO** → Pulmonary edema (cardiogenic pulmonary edema)
* **Laryngospasm** → chest is B/L clear but adventitious sounds are heard
  - (adventitious sounds are the sounds from upper airway)

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ACUTE RESPIRATORY DISTRESS SYNDROME

CARDIOGENIC PULMONARY EDEMA → ↑ left atrial pressure secondary to LVF → edematous fluid is TRANSUDATE

Acute Respiratory Distress syndrome is due to **NON-CARDIOGENIC PULMONARY EDEMA**

NON-CARDIOGENIC PULMONARY EDEMA

Eg: ARDS occurs secondary to swine flu/bird flu. Because swine flu virus ultimately damages Pneumocytes. That will end up in ARDS.

↓

Collapse of alveoli

↓

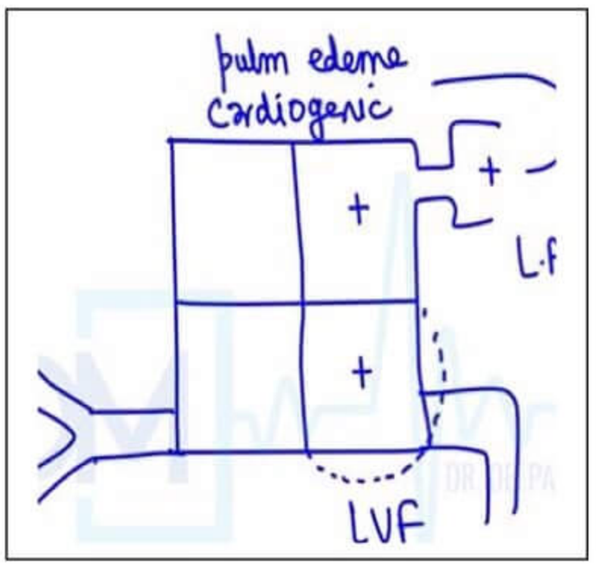
Hypoxia

↓

Damage of **Endothelium** (damage to gap junctions)

↓

Leakage of fluids from pulmonary capillary Into alveoli



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- ARDS occurs in **10% of ICU patients**
- **Sudden onset Respiratory distress**
- \+ **CXR B/L infiltrates** (no cardiac cause found)
- \+ **↓ pO2** (demonstrable hypoxia)
- \+ **Normal** left atrial pressure (LAP)

Triggers for ARDS:

Direct (M/C)	Indirect
• Pneumonia (H1N1)	- **Sepsis**
• **Mendelson** syndrome	- Trauma (multiple bone fracture)
• Toxic gas inhalation	- Flail chest
• Pulmonary contusion	- Head injury
• Near drowning	- Burns
	- Multiple blood transfusion /TRALI
	- Acute pancreatitis
	- Post cardio pulmonary bypass

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- Mendelson syndrome – Aspiration of stomach acid (Chemical Pneumonitis)

Important one liners:

- **Both pneumonia > sepsis** are the leading causes of ARDS
- Leading cause of death after blood transfusion – **TRALI**
- All of the followings are the causes of ARDS **except**:
  - **Status asthmaticus** (disease of airway)
- There would be **no CXR findings** in fat embolism

Clinical Presentation

EXUDATIVE PHASE (0-7 days)

Triggers ⟶ symptoms begin

In 12-36 hrs

-**Type 1 pneumocytes** –covers **90% of surface area** – (injured during adult ARDS)

-**Type 2 pneumocytes** – produce surfactant (**most abundant cell of alveoli**)

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IN ARDS,

Type 1 pneumocytes are affected

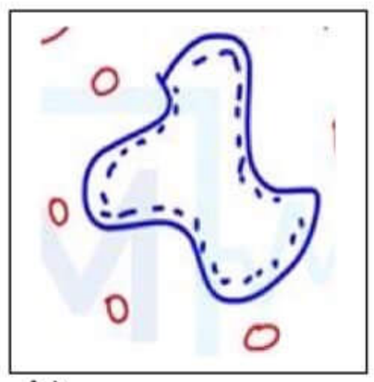
Type 2 pneumocytes are not affected

Normal surfactant with reduced surface area of alveoli for gas exchange

↓

Ventilation and perfusion imbalance

(perfusion is secondary to hypoxia component)



(**Hypoxia** causes **dilatation** of all blood vessels in body **except** **vessels of pulmonary circuit**)

↓

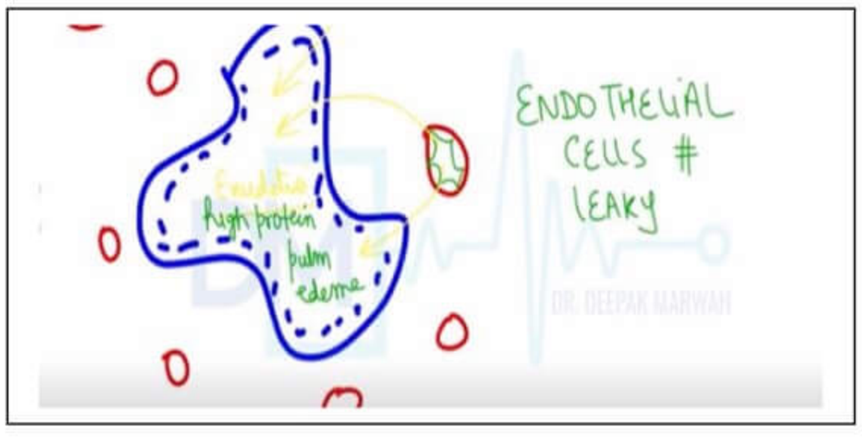
Most vulnerable cells/most damaged cells in ARDS – endothelial cells of alveoli – d/t Hypoxia

↓ Endothelial cells become LEAKY RESULTING IN

Exudative, high protein pulmonary edema

↓ forming a layer resulting in

Further ↓ of gas exchange



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- In heart failure → **low protein** pulmonary edema

FEATURES: (**Sudden onset Respiratory Distress**)

EXUDATIVE PHASE → (0-7 days)

12-36 hrs

Triggers

PROLIFERATIVE PHASE → (7-21 days)

[able to wean off the ventilator]

↓

proliferation of **type 2** pneumocytes

↓

Some differentiate into **type- 1** pneumocytes

[recovery is possible]

FIBROTIC PHASE OF LUNGS (>21 days)

require supplemental oxygen for rest of their life

[requirement varies from case to case]

-it results in pulmonary artery hypertension

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INTRAPULMONARY SHUNTING

[blood is getting wasted in the lungs→ d/t alveolar collapse/endothelial injury]

there is sudden onset of distress,

- ↑ work of breathing: ↓ **CO2**
- ↓ pO2, ↑ pCO2 **(Refractory hypoxia)**
- Dead space ↑

} **Type 2 Respiratory failure / Respiratory acidosis**

➔ In **initial** phase of ARDS → There will be **Respiratory alkalosis (CO2 washout)**

→In **acute asthma** → **type-1** respiratory failure & **respiratory alkalosis** → d/t CO_2 washout

→In **status asthamaticus** -**type-2** respiratory failure & **Respiratory acidosis** d/t CO2 overproduction in lungs

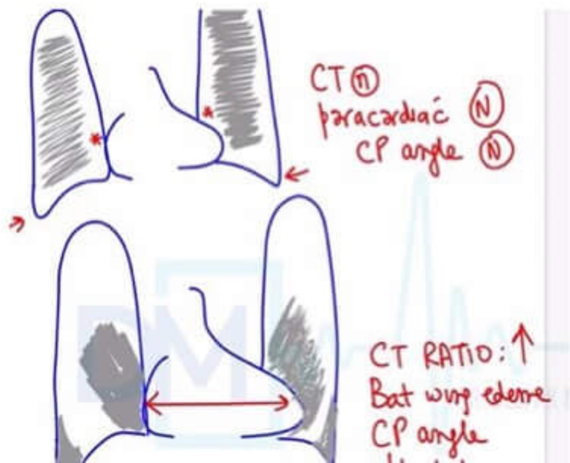
➔ When Pco_2 = **60mm** of Hg, then the **compensatory mechanisms begin to fail.**

Note :

Bulla/blebs along with **fibrosis and (PAH)** pulmonary artery hypertension are seen in **ARDS.**

Work -up:

1. CXR – B/L extensive infiltrates



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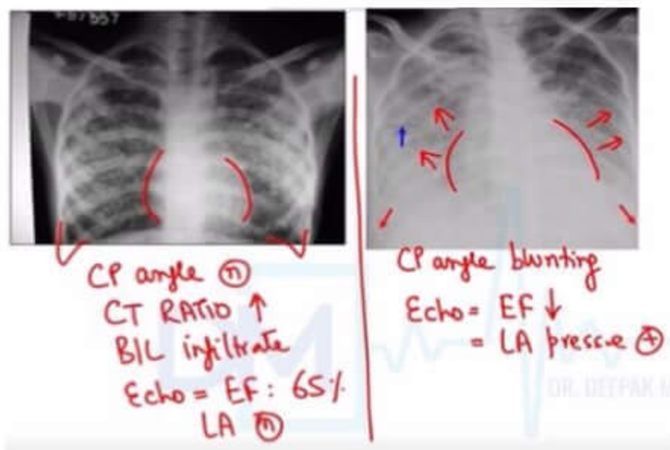
- Cardiothoracic ratio – normal
- **Para cardiac area** sparing
- CP angle – normal

In cardiogenic pulmonary edema

- Cardio thoracic ratio – **increased**
- **Bat wing** edema
- **CP angle** blunted

2. Echo- ejection fraction is normal, LA pressure – normal



In cardiogenic pulmonary edema, echo shows

- Decrease ejection fraction
- LA pressure increased

3. ABG – ↓ pO2, ↑ pCo2 [ventilation, perfusion imbalance]

Key words: – essentials of diagnosis:

1. Sudden onset resp. distress

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After **multiple** Bone fractures/ Massive blood transfusion → ARDS

central line insertion → Pneumothorax

S. Aureus pneumonia → receiving i.v Vancomycin for 2 day → **Pneumatocele** rupture resulting in Pneumothorax

2. CXR: B/L pulmonary infiltrates
3. **Pao2 / Fio_2 < 300** → **most imp** diagnostic criteria for ARDS
4. **Absence** of LA Hypertension

Above mentioned keywords with case of H1N1 / multiple blood transfusion / acute pancreatitis – confirm diagnosis of ARDS.

PrepLadder

GRADING:

ARDS	Pao2 / Fio2
- Mild	<300
- Moderate	<200
- Severe	<100

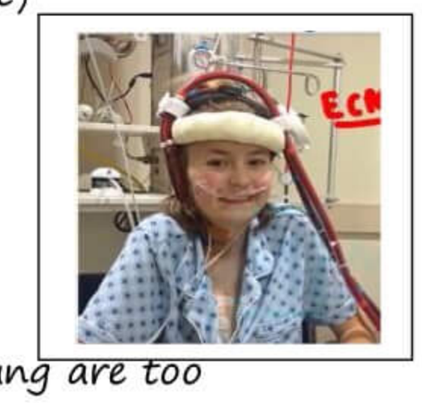
*BERLIN Criteria – 1+2+3+4

Rx of VOLUTRAUMA – seen in high/normal volume ventilation resulting in **PNEUMOTHORAX**

➔ 1. **Low volume ventilation** = 6 ml/kg → to minimize BAROTRAUMA to chest.
(Normal tidal volume = 12 ml/kg - Maintained in diaphragmatic paralysis Etc)

- **Plateau pressure** of ventilator = **<30 cm H2o**
- **Respiratory rate** of ventilator = **<35/min**

2. **Prone** position ventilation
   - Risk of **extubation**, CVP line lost, **orthopedic injuries**



3. Extracorporeal membrane oxygenation **(ECMO)**- Pt. In which heart and lung are too weak for ventilation
4. **Limited fluids** & diuretics – To maintain normal LA pressure
5. **Ensure neuromuscular paralysis**: Cisatracurium (for effective ventilation)

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➔ Steroids, surfactant therapy & high frequency jet ventilation (HFJV) have **no role** in treatment

➔ **m/c cause** of **death** in ARDS: **Sepsis** (non-pulmonary causes)

Congestive heart failure	ARDS
1.**Transudative** pulmonary edema	**Exudative** pulmonary edema
2.Hydrostatic pressure **increases**	Hydrostatic pressure normal
3.LA pressure **increased**	LA pressure normal
4.Low protein pulmonary edema	**High** protein pulmonary edema
5. BNP **increased**	BNP normal

PrepLadder

SNAKE BITE

STANDARD SNAKES FOUND IN INDIA:

1. Cobra } Contribute to **Neurotoxicity**
2. Krait }
3. Russel viper } Contribute to **hemotoxicity**
4. Saw scaled viper }
5. Humped nose viper

- can also cause hemotoxicity
- **Anti-snake venom available in India is ineffective**
- bleeding manifestation can go as long as upto **3 weeks**

- Bite of poisonous snake and non-poisonous snake becomes difficult to identify due to local edema of soft tissue.
- About **50K deaths /yr** in India are d/t snake bite.
- About **50 million people** are exposed to risk of getting a snake bite especially increased during monsoon/ harvesting season.
- However, **70% of bites** that occur are **non-venomous**
- Bite from venomous snake might be a **dry bite** (i.e. The snake might bite at an angle that it is able to inject its teeth/ fangs into body of person but may not be able the inject the poison, as person might perceive pain & withdraw the arm away)
- **50% bites**: venomous snake bite is Dry bite.

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Management in case of snake bite we follow first aid component

mnemonic "RIGHT"

- R- **Reassure** the patient. 70% snake bites – nonvenomous species. Only 50% of bites by venomous species envenomate the pt.
- I – **Immobilize** → which prevent faster spread of venom.
  - DO NOT APPLY TORNIQUET → to avoid **pressure necrosis**
    - **If tourniquet is already applied** then, don't cut tourniquet, as it may cause extensive spread of poison resulting in

PrepLadder

        - Diaphragm paralysis
        - Sudden onset **hypo-tension** d/t histamine release

    -So, apply B.P cuff proximal to tourniquet & Inflate it to the pressure almost equivalent to the tourniquet & then cut the tourniquet → Then gradually deflate the B.P cuff

  - **No CUTTING / ELECTROCAUTERY** of that area & **no walking** as well
  - **NITROGESIC ointment- nitrate ointment/ nitrate spray can be applied locally → but didn't show any efficacy on clinical trials**

- **GH** – **G**et to the **h**ospital immediately
- **T** – **T**ell the doctor of any systemic symptoms that manifest on way to hosp.
- **Cobra bite** (neurotoxic) → affects **post synaptic transmission.** it hampers action of Ach at neuro-muscular junction
- **Krait** → mainly affects **presynaptic transmission** i.e. Release of Ach at neuro-muscular junction is affected
- **Russel viper** → acute kidney injury/ renal failure/ Acute tubular necrosis/ uremia
- **Hump nosed viper** → can cause **hemorrhagic** manifestations which can persist for weeks
- **ASV** should be given **within 4 hrs** of snake bite
    - **ASV: Bite to needle. Time < 4 hrs**

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VIPER ENVENOMATION MANIFESTATIONS:

- Local pain, tender lymphadenopathy
    - Noticed with viper bite
    - Not noticed with cobra bite, krait bite
- One of the **earliest bleeding** manifestations → **subconjunctival hemorrhage**
    → Epistaxis
    → Gum bleeding

- Severe abdominal pain (d/t bleeding in mucosa of stomach)
- **BP↓** (d/t combination of histamine release, bleeding & vomiting)
- **Purpura** (I.e. Palpable bleeding on skin)
- Retro peritoneal bleeding
- Kidney: Acute tubular necrosis, flank pain/ tenderness in costovertebral junction, **Black/dark urine** (d/t **hemoglobinuria**)

PrepLadder

ELAPID ENVENOMATION MANIFESTATIONS (by Krait/ cobra)

→ 4P's

- Paralysis of Levator Palpebrae Superior & Extra ocular muscles

  ↓ ↓

  Ptosis Diplopia / ophthalmoplegia

- Paralysis of **jaw/ tongue** →inability to swallow saliva, resulting in frothing /
- pooling of secretions → cause aspiration & can die d/t aspirational pneumonia.
- Paradoxical Respiration

→ 4D's

  - Diplopia
  - Dysphagia
  - Dysarthria/ dysphonia
  - Dyspnea

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→ There is development of DESCENDING PARALYSIS in patient

20 Whole Blood Clotting Test (WBCT)		
Draw 2 mL of venous blood and transfer directly into a lean and dry glass tube. Leave it upright, open, undisturbed for 20 and/or 30 minutes at room temp	After exactly 20 minutes, pick up the tube and invert it. If a solid clot is retained, the test indicates normal coagulation.	It **clot breaks** down quickly upon inversion of the tube or fails to coagulate, the test indicates a coagulopathy

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Collection: a blood sample for 20 WBCT testing immediately after collection.	Normal: a solid clot is retained on inversion of the tube at 20 or 30 minutes (Grade 0, no coagulopathy)	**Abnormal**: clot degrades rapidly (**Grade 1**, friable clot) or fails to coagulate whatsoever (**Grade-2**)

Work up:

1. 20min Whole Blood Clotting Test

   Repeat for every **30 min** for **first 3 hrs of the admission** [then after giving ASV it can be done on 1hr basis]
2. CBC
3. LFT
4. KFT (baseline serum creatinine)
5. Coagulogram: BT, PT/ aPTT

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MANAGEMENT:

1. Pain: Paracetamol
2. BP cuff (above the level of tourniquet)
3. Polyvalent ASV→ No effect against humped nose viper
   - **Dose** => 10 – 30 vials – same for adult/ pregnant/ child.
   - **T1/2** of ASV ≈ 90hrs.
   - **Re-administration** of Indian ASV → **not required**

   → **1 vial** can **neutralize** 6 mg of Russel viper venom

   → Bite to needle time **< 4 hrs**

➔ As ASV can result in **anaphylactic** shock → keep the **adrenaline** ready in syringe

➔ **Anaphylactic shock** can be recognized by **presence** of

- Stridor
- Cyanosis
- Crashing of blood pressure etc

PrepLadder

INDICATIONS OF ASV:

1. Coagulopathy
2. **Neurotoxicity**: 4P's

Ask patient

→ To raise neck

→ Count numbers in one single breath

In **neurotoxicity**, the patient **can't do these**

3. **CVS** abnormalities: BP ↓, tachy arrhythmia
4. **GIT** -Severe vomiting + abdominal pain → may be d/t retroperitoneal bleeding → diagnosed by CT/MRI abdomen
5. **Local** swelling: ≥ ½ circumference of arm /leg
6. Swelling has extended rapidly above the level of waist (after cutting tourniquet)

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To prevent reaction to ASV = Administer Hydrocortisone, H_1 Blockers

Any indication of anaphylaxis = **IV adrenaline (1:1000)**

Signs:

- Laryngeal edema
- BP↓
- Stridor
- Cyanosis
- ↓ SpO2

I.M ADRENALINE is **avoided** because it causes

- Muscle hematoma in-case of viper bite
- BP too less so absorption may not occur

Clinical features of snakebite					
Feature	Cobra (post synaptic)	Krait (pre synaptic)	Russell viper	Saw scaled viper	Humped nose viper
Local Pain/ Tissue damage	Yes	No	Yes	Yes	Yes
Ptosis,	Yes	Yes	No*	No	No

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Neurological sign					
Hemostatic abnormality	No	May Occur	Yes	Yes	Yes
Renal complication	No	No	Yes	No	Yes
Response to neostigmine	Yes	+/-	No	No	No
Response to ASV	Yes	Yes	Yes	No	No

- ❖ Neostigmine + Atropine → more useful in neurotoxic cases [mainly cobra poisoning]

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Recovery Phase

If an adequate dose of appropriate anti-venom has been administered, the following responses may be seen:

1. Spontaneous systemic bleeding such as gum bleeding usually stops within 15-30 minutes.
2. Blood coagulability is usually restored in 6 hours. Principal test is 20 min WBCT.
3. Post synaptic neurotoxic envenoming such as **Cobra** may begin to improve as early as 30 minutes after antivenom but can take several hours.
4. Presynaptic neurotoxic envenoming such as the **Krait** usually takes a considerable time to improve reflecting the need for the body to generate new acetylcholine emitters.
5. Active hemolysis and rhabdomyolysis may cease within a few hours and the urine returns to its normal color.
6. In patients who were in shock, blood pressure may increase after 30 minutes.

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NEUROENDOCRINE TUMORS

INSULINOMA:

- **It is Pancreatic Neuroendocrine Tumor**
- Overall number **1** functioning Pancreatic Neuroendocrine Tumor.

→ Overall number 1 non-functioning Pancreatic Neuroendocrine Tumor = PP-OMA (pancreatic polypeptide)

Doesn't cause any symptoms from perspective of hormones but will produce mass effect, which can contribute to obstructive jaundice & other features that can mimic features of pancreatic adenocarcinoma.

Insulinoma:

- Insulin high
- Sugar lever fall < 54 mg% – patient will have symptoms of Hypoglycemia
- Normally, When Blood sugar < 70 mg% - Insulin production stops & Counter regulatory hormone glucagon, Catecholamines, growth hormone → Neutralize blood sugar.

C/F:

- Eccentric psychiatric behavior
- Emotional outburst: mis dx as personality disorder.

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INCIDENCE:

- Rare 5-15 % Malignant
- size at dx < 2 cm → good prognosis
- Equal distribution in all areas: Head, neck tail of Pancreas.

GLUCAGONOMA:

- Malignant
- size of tumor is 5-10 cm
- Mc location at Tail of Pancreas

INSULINOMATOSIS: Patient has multiple micro or macro adenomas/ island of tumor in Pancreas behaving like Insulinoma.

NESIDIOBLASTOSIS: it is a pediatric precursor of Insulinoma characterized by excessive insulin (hyperinsulinism) concomitant with Hypoglycemia

- Usual age of presentation of insulinoma : 40-50 years of age

C/F OF NEUROGLYCOPENIA:

1. Concentration Span ↓
2. Irritability
3. Rage attacks
4. Visual disturbance
5. Irrational behavior
6. Symptoms of sympathomimetics

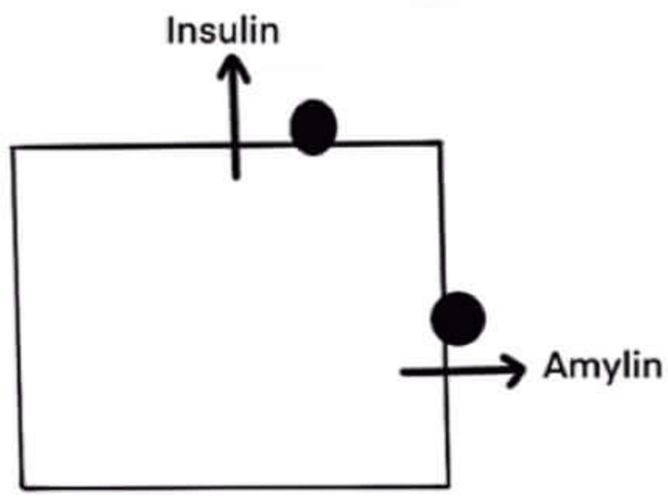
   i.e tremors, heart racing, diaphoresis, palpitations etc

PrepLadder

WORK UP:

- **IOC:** 72 hour prolonged fasting test:
  Every 4 hrs check Blood sugar

1. Blood sugar > **40 mg%** [Insulin by RIA < **6 µu/ml]** → **normal person**
2. In **Insulinoma** RIA insulin elevated > **6 µu/ml & low blood sugar levels - < 40 mg%**
3. C peptide elevated
4. Proinsulin elevated
5. Insulin/ **glucose** ratio = > 0.3 [Normal value < 0.3]
6. Low plasma β OH butyrate values



Beta pancreatic cells

- Insulin produced by Pancreas comes into circulation along with **amylin** & **C-peptide**
- **Insulin has 51 amino acids**
  - A chain = 20 AA
  - B chain = 31 AA
  - C-peptide = 33 AA ,is a interlinking chain
- insulin coming in blood is pro insulin (inactive) form.

- Check for Urine/ Plasma Sulfonylureas (to r/o factitious hypoglycemia as Sulfonylureas causes hypoglycemia like features)

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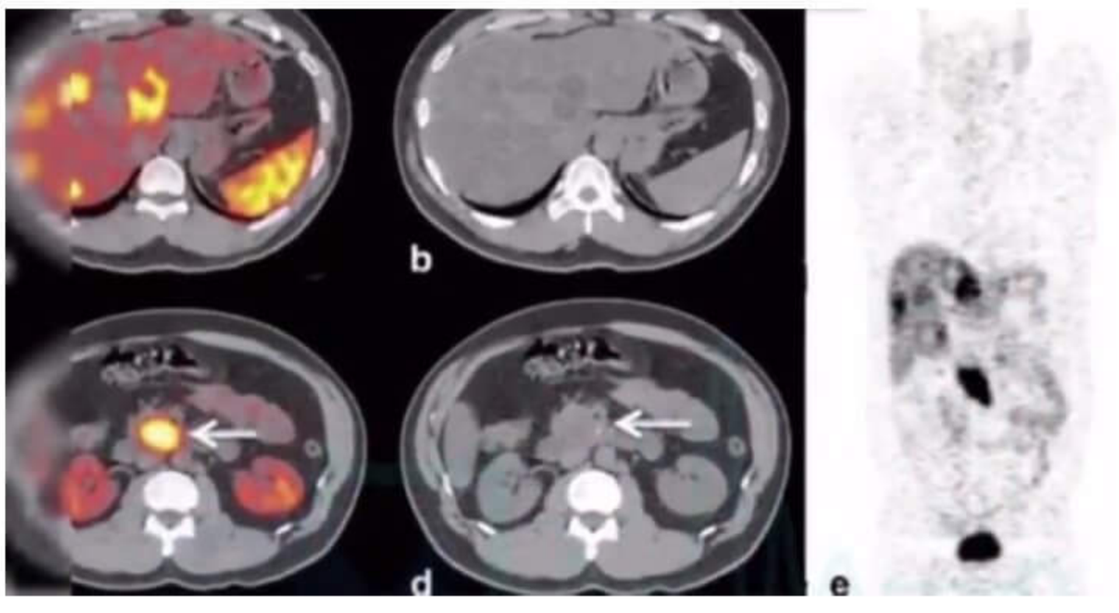
TUMOR LOCALIZATION FOR INSULINOMA:

Harrisons: "**Endoscopic Ultrasound** →Highly sensitive technique for identifying Insulinoma."

- **SRI** → somatostatin receptor Scintigraphy Based on Somatostatin analogs
- Somatostatin Receptor scintigraphy (imaging) useful in localizing pancreatic Neuroendocrine tumor including GI endocrine tumors **Except Insulinoma** (as they are small & have low densities of Somatostatin receptors)

*Tumor localization of pancreatic neuroendocrine Tumor: somatostatin receptor image SRI

***Insulinomas:** - Endoscopic ultrasound techniques
- PET CT -gallium 68
- MRI/CT abdomen → for tumors >2cms



(e) Pet scan

(a), (c), (b) CT scan

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RxOC: Surgical resection

MEDICAL MANAGEMENT:

Octreotide (somatostatin analog) + **Diazoxide**

↓ ↓

Inhibit production of growth hormone → sugar ↓ → Counter regulatory Stimulation of α cells: Production of glucagon → ↑ insulin → Therefore, it worsens hypoglycemia

Insulin production ↓ from β cells

Thus, DOC for insulinoma : Diazoxide

If metastasized → Chemotherapy palliative care, no role of surgery

GLUCAGONOMA:

→ Mostly located in Tail of Pancreas.

→ Tumor is malignant; 5-10 cm in size

→ Characteristic finding in skin: **necrolytic migratory erythema**.

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CLINICAL FEATURES:

→ Impaired glucose Tolerance

→ D/D – HSP in child. (If no glucose tolerance)

→ Necrobiosis lipoidica diabeticorum characterized by erythematous lesion with central clearing usually on shin.

→Acanthosis Nigricans:

Present on buttocks, back of thighs, gluteal region, back of popliteal fossa

CONFIRMATION OF DIAGNOSIS:

→ Confirm level of S. glucagon > **1000 pg/ml.**

→ SRI – to identify location of tumor (Tail)

→ Prognosis is bad as it is mostly malignant

→ CT/MRI abdomen

MANAGEMENT: Surgery is the only option

SOMATOSTATINOMA:

Excess of somatostatin

→ Inhibitor of other hormones

→ It is a tetra-decapeptide

→ Found in CNS (in pituitary)/GIT

[Eg: Long acting somatostatin – Lanreotide for Rx of Acromegaly]

→ Paracrine / autocrine effect

PrepLadder

CLINICAL FEATURES:

1. DM (d/t impaired glucose tolerance)
2. Secretory diarrhea
3. Gall bladder disease ≡ incidence of gallstones increases
4. Steatorrhea

Dx: SRI

VIPOMA

→ Excess production of vasoactive intestinal polypeptide.
→ It is series of 28 AA.
→ Present in GIT/CNS
→ Functions as Neurotransmitter– It causes opening of water channel in gut – causing secretory diarrhea
→ VIPoma is a tumor related to cells in Pancreas [F cells – produce VIP]
→ Consisting of stool is just like stools in cholera. Therefore, also known as **Pancreatic cholera.**
→ Large volume depletion therefore, will cause Hypokalemia, **dehydration**, achlorhydria

↓

If severe → M. Acidosis

Q. Watery diarrhea, achlorhydria / WDHA
DX VIPOMA

SECRETORY DIARRHEA

→ Osmolar gap test: To differentiate b/t secretory and osmotic diarrhea.
→ **Formula**: [290 – 2 (stool Na^+) + (Stool K^+)]
If stool osmolar gap: > 100 = osmotic diarrhea
< 50 = secretory diarrhea

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❖ **EXTRA MILE:**

Secretory Diarrhea can be seen in following conditions:

- Zollinger Ellison syndrome
- Glucagonoma
- VIPOMA
- Cholera

- **P. NET** → Primitive Neuroectodermal Tumors

- **pPNET** → Peripheral primitive Neuroectodermal tumor.

- PNET & Ppnet→They are tumor which originated from CNS/ soft tissues or from bone

  - CNS tumor → **Medulloblastoma -Classical PNET**
  - Soft Tissues → Askin tumor
  - BONE Tumor → Ewing's sarcoma→ small round blue cell tumor

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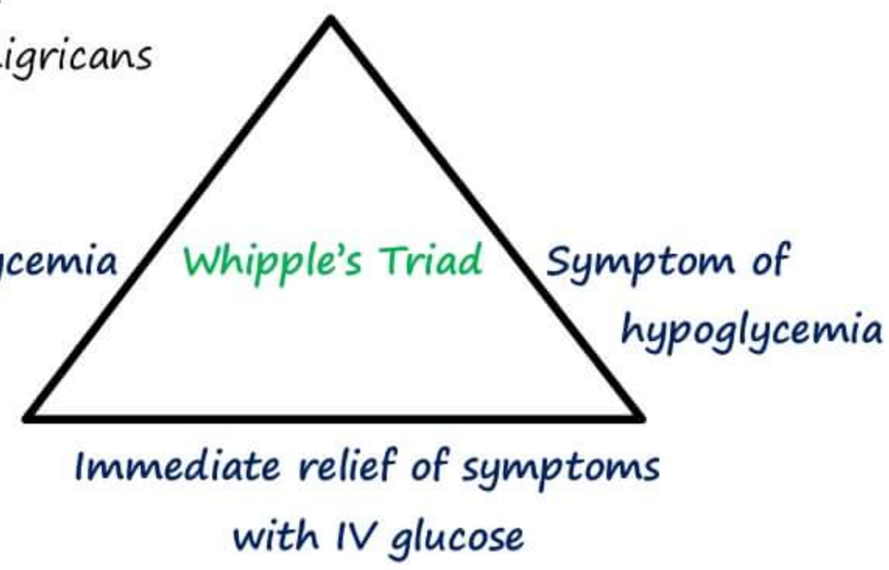
ASKIN TUMOR

C/F

→ Malnutrition

→ Acanthosis nigricans



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DIABETES MELLITUS

CLASSICAL SYMPTOMS

- Polyphagia
- Polydipsia
- Polyuria
- Weight loss

Q. NOT A CLASSIC SYMPTOM → POLYPHAGIA [As it is not measurable]

DIAGNOSIS OF DIABETES:

- CLASSIC SYMPTOMS + RBS ≥ 200mg%
- ASYMPTOMATIC → FBS > 126mg%

  After Giving 75gm glucose → 2hr value > 200mg%
- ASYMPTOMATIC PATIENT → HbA1C [glycosylated Hb] ≥ 6.5% [best answer]
- Postprandial values are **not** useful for diagnosing DM. It is useful for follow up & monitoring

HbA1C test:

- It is retrospective test
- This is not one-time value. It gives average value of blood sugar level of last 3 months
- Not effected by exercise and fasting
- If we multiply HbA1C value by **25**, it gives average blood sugar value

  Eg: HbA1C=10% ; Average blood sugar= 250mg%

*TARGET HbA1C < 7% → Good sugar control.

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COMPLICATIONS:

→ MICROVASCULAR COMPLICATIONS:

- It is directly proportional to HbA1C levels
- So, we can reduce the incidence of these complications with HbA1C CONTROL
- **Retinopathy** – 25 times Increase incidence of blindness
- **Neuropathy** – Increase Incidence of Silent MI
- **Nephropathy** – MC cause of CKD in India / USA

→ MACROVASCULAR COMPLICATIONS: Strict BP control

- Coronary Artery Disease [M.I, Unstable angina, prinzmetal angina etc] → **3-5 times** increase in risk
- Peripheral Artery Disease – **100 times**Q increase in risk [increase incidence of gangrene]
- Stroke → Due to accelerated Atherosclerosis.

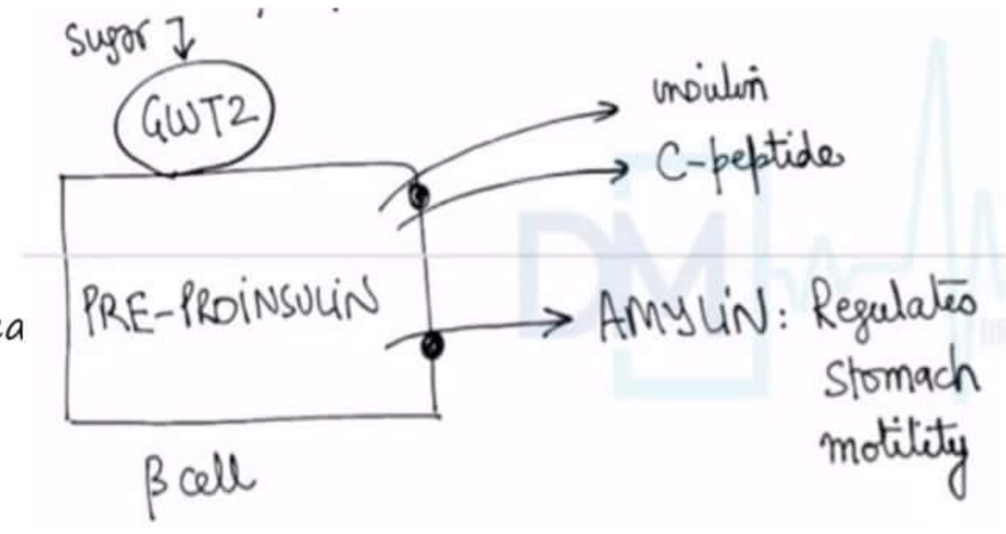
MANAGEMENT:

- Depends upon type of Diabetes

TYPES OF DIABETES:

Type I DM:

- Beta cells are damaged.
- If >80% β-cell mass is damaged, clinical features appea



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- Beta-cells are damage →decrease production of insulin → resulting in **INSULINOPENIA**
- Insulin and C-peptide are released at ratio of **1:1**
  - **Insulinoma → both insulin & c-peptide values increases**
  - **DM → both values decreases**
- Apart from insulin, hormone released by β-Cell is **AMYLIN.**
  - It regulates stomach motility
  - Regulates entry of osmotic contents into small intestine
- **GLUT-2 is sensor that continuously monitors blood sugar**
- If Glucose level is **< 70 mg%,**
  - Insulin production stops
  - Glucagon production starts
- Cut off of Diagnosis of hypoglycemia → **<55 mg% [Pediatric → 45mg%**

- **K+ channel** helps in release of insulin in circulation

CAUSES:

1. **AUTOIMMUNITY → Most Common cause**
   - HLA DQ_2, DR 3, DR 4 genes are involved
2. **VIRAL CAUSES** → Coxsackie B [MC viral cause, Can also cause viral myocarditis], Mumps, Rubella (Fulminant Diabetes → DM developing with in 8-12 weeks period]
3. **BRONZE DIABETES**: Caused d/t **Iron toxicity**

- **FEATURES:**

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  - Bronzing / Hyperpigmentation of skin
  - Cirrhosis
  - Beta cell mass decrease: Insulinopenia OR Type-I DM

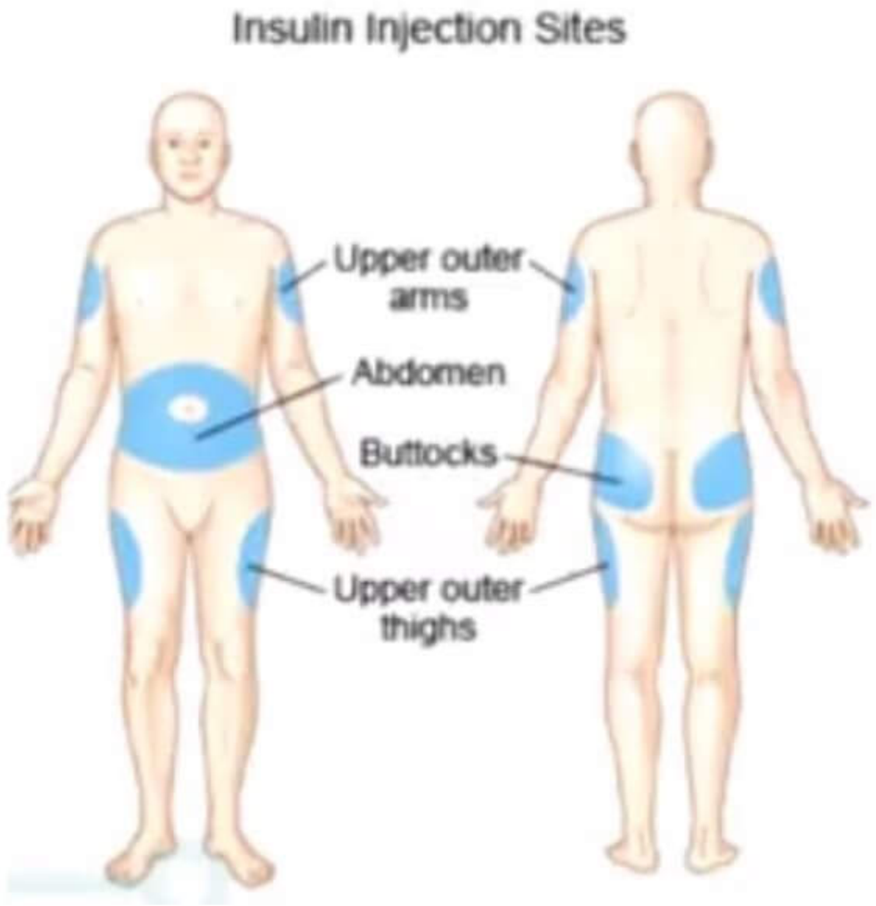
  } **TRIAD OF BRONZE DM**

  - Fasting insulin level ↓ by radio immune assay (RIA)

TREATMENT:

- **Carbohydrate counting**- Regulate the amount of carbohydrate intake & give insulin proportionate to it.
- **Insulin supplementation:**
  - Mc route of administration → Subcutaneous
- **Sites of insulin injection:**
  - Anterior abdominal wall [2cms away from umbilicus in the form of round circular band]
  - Arm
  - Anterolateral aspect of thigh
  - Buttock

- Never given in **Dorsum of Hand**



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INSULIN DELIVERY:

(A) Insulin Pump:

- → Best method → mimics artificial pancreas.
- → Microprocessor device.
- → continuously Releases Basal Insulin into body
- → Bolus insulin delivery at Meal times is also programmed proportionate to carbohydrate intake
- → It is very expensive

(B) **Insulin Pen**: (31 G) → Painless and Bloodless delivery of insulin

(C) **Inhaled Insulin** → Afreeza / Exubera

(D) **Multidose vial + 1ml syringe**

COMPLICATIONS OF INSULIN:

1. **SOMOGYI PHENOMENON**:
   - Early morning hypoglycemia d/t intake of overdose of insulin at bedtime
   - At 4A.M → Person wakes up with sympathetic symptoms like Palpitations, Tremors, Diaphoresis etc
   - At 7A.M → Glucagon⬆ in circulation → glycogenolysis⬆ → Blood sugar value⬆ → pre-breakfast hyperglycemia

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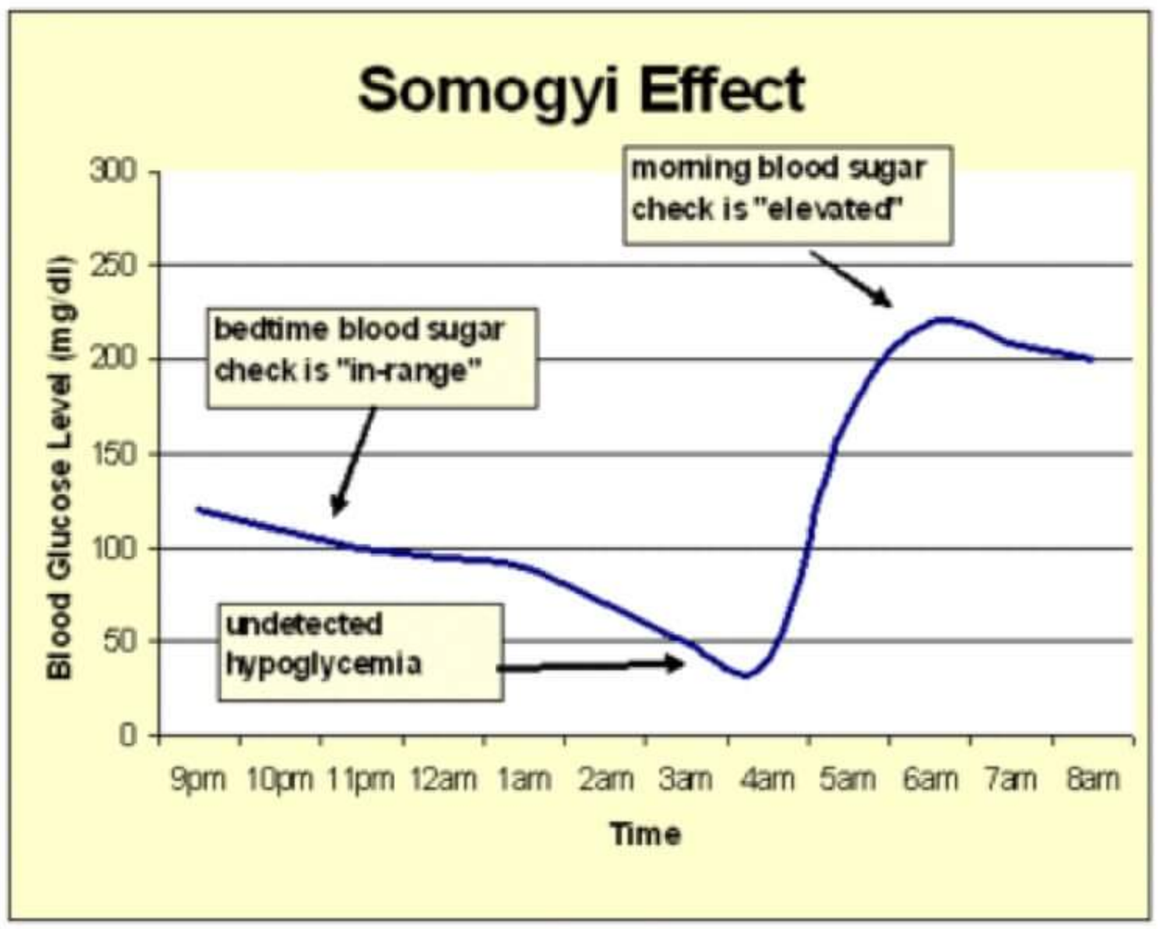
   - Thus, main manifestation of somogyi phenomenon is EARLY MORNING HYPOGLYCEMIA.



2. **DAWN PHENOMENON**:
   - 4 AM: EARLY MORNING HYPERGLYCEMIA → D/t downregulation of GLUT-4 receptors in muscle
   - 7 AM: Pre-breakfast hyperglycemia
3. Weight gain

PrepLadder

Type 1.5 Diabetes Mellitus:

- Aka LADA → Latent autoimmune Diabetes in Adults
- Variant of Type-I D.M presenting in adults. [shares etiology with Type-1 DM]
- Anti-GAD, Anti-Glutamic acid decarboxylase antibody [main Ab]
- Anti-islet cell Antibody (ICA) → 2nd Ab
- Anti-GAD- also present in paraneoplastic manifestation of **oat cell Ca of lung** K/A **stiff Person Syndrome**
- Insulinopenia is seen

TREATMENT:

1. Can start initially with Glipizide/ sulfonylureas
2. Insulin [synthesized by DNA Recombinant Tech (Human)]

- Beef/ Pork insulin [S/E : lipodystrophy, Resistance]
- Route – subcutaneous route, in abdominal wall & insulin pump is preferred
- Rapid acting insulin – Lispro/ Aspart/ Glulisine → Given in S.C route– 15-25 minute before meal → Mc recommended
- Long acting insulin – Glargine (~ 42 hrs), Degludec (~ 42 hr) [Regular insulin→ short acting]
- **Pramlintide** [best answer] – Used for both Type 1 & Type 2
- Acarbose can also be used [off label] for both Type 1 & 2, as it inhibits absorption of sugar from G.I.T

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- **Insulin (SC) Uses:**
  - Type 1 DM → Insulinopenia
  - Type 2 DM → refractory to oral hypoglycemic drugs
  - Type 1.5 DM
- **Regular insulin I.V uses:**
  - Hyperkalemia
  - DKA **(Type 1)**
  - Non- Ketotic Hyperosmolar Coma **(Type II)**
- Regular insulin can be given in both I.V & S.C routes.

Type 2 DM:

- Polygenetic [Doesn't follow mendelian law of inheritance]
- Insulin resistance is d/t
  - Resistin
  - High levels of **Adipokines**Q → promote weight gain
  - Decreased levels of **Adiponectin**Q which is **guardian against obesity**

TREATMENT:

1. **Diet control** [1st line intervention in T2DM]
   - Carbohydrate intake is strictly regulated.
2. **Exercise:** Increases **GLUT$_4$** (Promotes sugar entry into muscle resulting in decreased blood sugar level) 'Jogging'– 30 min X 5 DAYS / week is recommended
3. **Oral Hypoglycemic Drugs** → causes HbA1C control

PrepLadder

- **BIGUANIDES** → inhibit Hepatic gluconeogenesis
  - HbA1C is decreased by **1.5-2%** over a period of 3-6months [slow acting]
  - Metformin (Excreted via kidney) → so avoided in kidney damage

Q: DOC for obese T_2DM pt → Metformin

Q: DOC obese T_2DM + nephropathy → **L**inagliptin / **G**lipizide / To**l**butamide → metabolized by liver

→ Metformin is contraindicated in nephropathy. If prescribed, pt develops **LACTIC ACIDOSIS**

SIDE EFFECTS OF METFORMIN:

- Nausea / vomiting
- Lactic acidosis: if there is Concomitant renal failure
- B_{12} deficiency

PHENFORMIN:

- Not given nowadays as it causes lactic acidosis (Drug induced lactic acidosis → Type B LA)
- If Biguanides are not successful, give sulfonylureas.

- **SULFONYLUREAS:**
  - Decrease HbA1C by **1.5%**
  - S/E - Hypoglycemia attack

- **THIAZOLIDINEDIONES:**
  - Major side effects are reported in phase-4 clinical trial [post marketing surveillance]
    - Pioglitazone [bladder cancer], Rosiglitazone [CHF]
  - Decrease HbA1C by **1%**

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- **ALPHA-GLUCOSIDASE INHIBITORS:**
  - DRUGS: Acarbose, Voglibose
  - These are taken with meals. They act by inhibiting sugar absorption from GIT.
  - Decreases HbA1C by **0.5%**
  - Control P.P spikes
  - S/E – Osmotic diarrhea

- **MEGLINITIDE:**
  - Drug → Repaglinide.
  - Behave like sulfonylureas.
  - Insulinogenic action → causes burst of insulin into circulation
  - Also improves sensitivity of receptor
  - But have short half-life [$T^{1/2}$]
  - S/E - Hypoglycemia

- **DPP-4 INHIBITORS:**
  - Inhibits degradation of GLP-1. Thus, increases duration of action of GLP-I
  - Drugs: **L**inagliptin [metabolized by **L**iver]; Sitagliptin [metabolized by kidney]

PrepLadder

- **INCRETINS**:

  Terminal ileum has 'L' cells

  ↓

  produce a hormone which Behaves like insulin

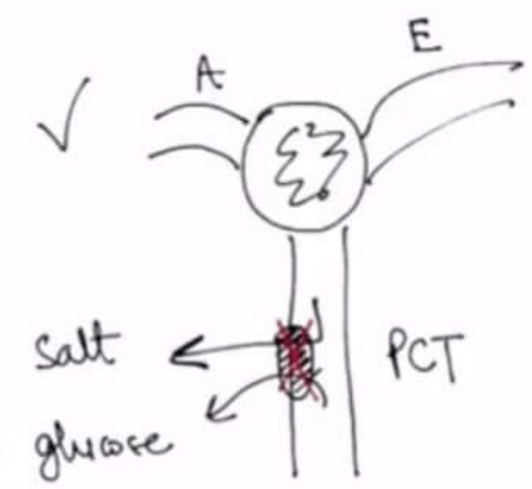
  ↓

  ↑ GLP - 1

  - Drugs: Exenatide → injection once a week
    Liraglutide
    (Exenatide brand name: ByeTTA)

    } expensive

- **SGLT – 2 INHIBITORS**:
  - Promotes urinary loss of sugar resulting in decrease of blood sugar level
  - S/E → Incidence of UTI increases.
  - Drugs: Canagliflozin



HbAIC ↓	P.P spikes
- Metformin - Glipizide - Pioglitazone	- Acarbose - Repaglinide - Sitagliptin* - Exenatide - Canagliflozin

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- In newly diagnosed pt of TYPE-2 DM, we can start with combination of Metformin [decrease HbA1C] & Acarbose [prevent P.P spikes] → decreases overall comorbidity
- Initially in Type-2 DM → Insulin levels **INCREASES**
- But later, d/t Beta cell exhaustion → insulin levels fall → hence insulin injections are useful.

MODY (MATURITY ONSET DIABETES IN YOUNG)

- AD (Autosomal Dominant- 75% chance of expression of disease in next generation)
- TYPES – 6types → MODY 1-6
- MC type in India/ USA – **MODY 3**
- Gene involved in MODY 3: **HNF 1 Alpha**
- Chromosome involved in MODY-3 : **Chromosome-12**
- Insulin secretion defective d/t defective genes
- 25 yr. Asymptomatic; FBS > 250 mg%
  Father DM ⊕
  Grandfather DM +

  } MODY, AD [expressed in every generation]

  - Radio Immune Assay of insulin → normal/low
- Grandson -40yrs DM +
  Father – Normal
  Grandfather – ⊕

  } **Type II DM**
  RiA insulin levels increases

PrepLadder

→ GENE INVOLVED IN INSULIN PRODUCTION → CTL-4A → its defect leads to insulinopenia

TREATMENT FOR MODY:

- Initiation of treatment by Sulfonylureas → stimulate β-cells to produce more insulin.
- Diet control
- Exercise

		Why?	Rx
T_1DM	Insuline ↓	Autoimmune, Pediatric onset	Insulin S.C
T_2DM	insulin ↑	resistin, adipokines ↑, adiponectin ↓	Metformin
$T_{1.5}DM$	insulin ↓	anti-GAD, Adult onset	Sulfonylureas / insulin
MODY	insulin ↓/ N	AD, Ch12 defect – in MODY-3	Sulfonylureas

→ MC type of DM → Type-2 DM

→ Rarest type → MODY

→ Most Acidic ketone body – Beta hydroxyl Butyrate → **IOC for DKA**

- High levels of beta hydroxyl butyrate with elevated blood sugar is the best way to diagnose DKA
- Urine dipstick → low sensitivity & specificity

LONG TERM COMPLICATIONS IN DIABETES:

1. **DIABETIC RETINOPATHY:**

➢ Severity α Duration of DM

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HbA1C > 7% [poor sugar control]

DM ⟶ D. Retinopathy

T_1DM = 5 yr

T_2DM= 20 yr

➢ **PROGRESSION OF RETINOPATHY IS MONITORED BY FOLLOWING:**

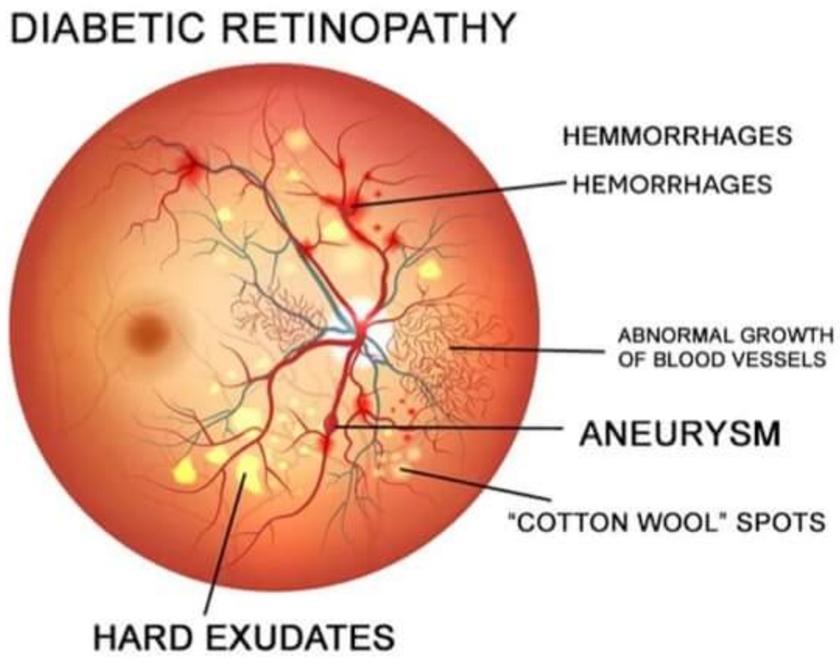
- **Raise in Serum Homocysteine levels** → BEST METHOD

FEATURES:

- Autosomal Recessive
- Premature atherosclerosis → increase incidence of STROKE, MI
- Alzheimer's progression
- Retinopathy progression

TREATMENT:

- Vit. B 6 [best answer] /Vit B9/Vit B12
  - **Raise in serum creatinine**
- Raises after 60% of kidney is damaged
  - **Fundus Examination:**
- Microaneurysm → Earliest seen in **Inner nuclear layer**



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→ NON-PROLIFERATIVE RETINOPATHY:

- Macular edema → leads to visual loss

→ PROLIFERATIVE RETINOPATHY:

FEATURES:

- Neovascularization
- Vitreous hemorrhage
- Tractional Retinal Detachment

TREATMENT:

Pan Retinal photocoagulation by ND : YAG → destroys pre-existing Blood vessels

+

Bevacizumab (ANTI-VEGF) → Intravitreal injection → prevents formation of new B.V

→ CAUSE OF VISUAL LOSS → MACULAR EDEMA Q

→ CAUSE OF BLINDNESS → TRACTIONAL RETINAL DETACHMENT Q

→ PRIMARY PREVENTION OF BLINDNESS IN DIABETIC:

- By controlling levels of HbA1C < 7% → Best method [even if HbA1C <7%, leakage of dye on fundus fluorescent angiography can't be prevented]; Normal value of HbA1C= < 5.6%
- Pan Retinal Photocoagulation
- Bevacizumab Injection.

2. DIABETIC NEUROPATHY:

- Irreversible process
- Sequence of involvement → Sensory > Motor > Autonomic

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- SENSORY INVOLVEMENT:
  - Vibration sense → First affected → tested by tuning fork of 128 Hz
  - Small unmyelinated C-fibers are involved → Hence DM is called → Small fiber neuropathy
    - Clinical feature: pain in soles of feet [nocturnal pain]
    - Another cause of small fiber neuropathy → HIV
  - TREATMENT:
    - Duloxetine
    - Pregabalin
    - Amitriptyline

❖ EXTRA MILE:

- In DM → the combination of following factors explains development of NON-HEALING ULCER [Neuropathic ulcer] in heel & metatarsal heads
  - Decreased pain sensation
  - Angiopathy→ decreased healing
  - Increased sugar in local tissues

❖ NOTE:

- **Non-healing ulcer in sole of feet → think of DM**
- **Non- Healing ulcer in hands → think of Syringomyelia** [Malformation of spinal cord]

- MOTOR INVOLVEMENT:
  - Cranial Nerve involvement: MC cranial nerve involved → 3rd Cranial Nerve
  - 3rd nerve palsy with pupillary sparing is seen.

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❖ **EXTRA MILE:**

CONDITIONS IN WHICH 3RD CRANIAL NERVE PALSY IS SEEN

- Ruptured & unruptured Berry aneurysm
- Weber syndrome [d/t midbrain stroke]
- Miller Fisher syndrome [variant of GBS having descending paralysis]
- Diabetes mellitus

▪ **AUTONOMIC INVOLVEMENT:**

- **Silent MI** Q → Leading cause of sudden death
- Hypoglycemic unawareness
- Postural hypotension → SBP ↓ > 20 mm of Hg, DBP ↓ > 10 mm of Hg } on changing position from supine to standing
  - Calculate B.P change from supine to standing position in a time lag of 3mins
  - **Midodrine** – DOC for postural hypotension
- Constipation [sympathetic action dominating]/ Diarrhea [vagal action dominating]

❖ **EXTRA MILE:**

➢ **6TH NERVE PALSY:**

Seen in:

- **Raised ICP** as 6th nerve has **longest intradural course**. It is **false localizing sign** because disease is **not present** in 6th nerve
- Millard gubler syndrome → d/t pontine stroke [7th nerve is also involved]
- Wernicke's encephalopathy → feature of Dry Beri Beri (d/t involvement of thalamus)

➢ **7TH NERVE PALSY:**

- Unilateral 7th nerve palsy → Bell's palsy
- B/L LMN palsy of 7th nerve → feature of **Facial diplegia**. Seen in
  - G.B.S
  - Sarcoidosis
  - Melkersson-rosenthal syndrome

3. INFECTIONS IN DM:

Q: 60 yr ♂ T_2DM, H/O aggressiveness, antisocial behavior, black nasal discharge

O/E: Nasal speculum; Black fungal mass seen in both nostrils

MRI head → shows fungal mass at cribriform plate [roof of nose]

➢ **DIAGNOSIS:**

- **RHINOCEREBRAL MUCORMYCOSIS**
- Anti-social behavior is d/t extension of fungal mass from roof of nose to frontal lobe of brain

➢ **TREATMENT:** IV. Amphotericin B

→ **OTHER INFECTIONS:**

➢ **Aspergillus Niger** → Angio-invasive [i.e invasive aspergilloma] → causes Hemoptysis

- **CT chest**: shows Cavity with fungal Ball
- **Treatment**: I.V voriconazole

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4. DIABETIC DERMOPATHY:

- **Non-healing ulcer** → MC dermopathy in DM
- **Acanthosis nigricans** → Type 2 DM + hyperpigmentation (at extensor aspects like back of neck etc). Also seen in
  - PCOD
  - Ca Pancreas/ colon
- Necrobiosis Lipoidica Diabeticorum:
  - Ulcer seen in shin of patient
  - Differential Diagnosis: Martorell ulcer: seen in shin d/t atherosclerosis

5. DIABETIC NEPHROPATHY: DISCUSSED IN KIDNEY SECTION

ACUTE COMPLICATIONS IN DM [Case based discussion]:

Q: Unconscious, unresponsive known case of (T_2DM) pt is brought to hospital. Vitals are secured. First investigation to be done is:

- Consider hypoglycemia & perform capillary blood sugar values by → DEXTROSTIX
  - If value is **20-40mg%,** treat the pt by giving **25-50% Dextrose I.V**
- If the pt presents with Hypoglycemic seizures & failed IV access, give **Injection** of **Glucagon/ adrenaline** by **Subcutaneous route**
- However, if blood sugar is elevated, in Dextrostix [400-600mg%], following differentials are to be considered:

	LACTIC ACIDOSIS [Type – A]	D.KETO ACIDOSIS	NON-KETOTIC HYPEROSMOLAR COMA
URINE KETONES	–	+	–
pH [arterial blood gas analysis]	< 7.35	< 7.35	7.40
HCO_3^- [22-26 meq]	< 22	< 22	24meq
BLOOD SUGAR	350mg%	400mg%	650mg%

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→ In NON-KETOTIC HYPEROSMOLAR COMA

↓

Sugar crosses Blood Brain Barrier

↓

Water follows sugar

↓ Leading to

CEREBRAL EDEMA

- It presents with **Hemiballismus** → sudden, violent jerky movements in proximal & distal parts of the body d/t involvement of **subthalamic nucleus**
- TREATMENT:
  - **Fluid of choice**: **Normal saline** along with regular insulin infusion [10L in 48hrs to treat intracellular dehydration]
  - For every **100mg% increase** in value of sugar, Na^{+2} decreases by **3meq**

    Reason: sugar draws water resulting in **DILUTIONAL HYPONATREMIA**

❖ EXTRA MILE:

- Glucose level [< 30-45mg%] → NEUROGLUCOPENIA → causes hypoglycemic seizures/ stupor & coma
- Blood glucose level <70mg% → insulin production stops
- Hypoglycemia cutoff → 55mg%

→ In DM, usually Lactic Acidosis is triggered by intercurrent infections [Eg- pneumonia, UTI etc]/ stroke/ MI → It is **TYPE A Lactic Acidosis**

→ **EMERGENCY USE OF REGULAR INSULIN IN:**

- Acute hyperkalemia
- DKA
- Non-Ketotic Hyperosmolar Coma

} fluid of choice → NORMAL SALINE

→ **INDICATIONS OF NORMAL SALINE:**

- Decompensated Shock: very low SBP [unrecordable B.P]
- Metabolic alkalosis
- DKA
- Non-ketotic Hyperosmolar coma

→ **INDICATIONS OF RINGER LACTATE SOLUTION:**

- Burns
- Cholera
- Shock [but in crushing pt with unrecordable B.P → use Normal saline]

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Diabetic Ketoacidosis

- Complication more Common in type I DM > type II DM.

- Basic Trigger is common Insulinopenia (due to which sugar cannot enter muscle)

↓

For cells to get energy, they will be burning fats, fats will generate FFA

↓

FFA breaks into ketones (highly acidic)

↓

Can damage BBB, cause encephalopathy etc.

- Mortality Rate depend upon the age group of the patient.

> 40 yr = 20% Mortality

< 40 yr = 5% Mortality

TRIGGER: -

- Insulin Pump Malfunction
- Poor Compliance
- Infection - (energy requirement of body increase)

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Following Hormones increase in diabetic ketoacidosis - Growth hormone, Cortisol, Catecholamine

↓

Higher these hormones -- more is blood sugar levels--leading to osmotic diuresis

↓

Dehydration

Triggers (infection etc.) lead to-

1. **Counter hormone increase**
2. **Blood sugar increase**
3. **Ketolysis decrease**

TRIGGER

Infection, Surgery, Myocardial infarction, Cerebro Vascular accident

↓

Energy requirement is more (sugar and insulin required)

↓

In DKA- blood sugar increases- counter hormone more- ketolysis - more ketone)

↓

Deterioration of patient

- As Blood sugar increases, Osmolality of blood increases

↓

leading to fluid shift across brain causing hyperosmolality

↓

leading to CNS MANIFESTATION - stupor and coma.

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Clinical Features: -

1. Nausea and severe vomiting (ketonemia which trigger vomiting center- CTZ)
2. Abdominal pain
3. Stupor
4. Coma

On Examination: -

- Tachycardia - HR ↑
- Orthostatic hypotension -Low BP
- Dry Oral Mucosa
- Urine Output initially increases

↓

As dehydration occur- Urine Output ↓ (kidney function deranged)

- RR increases (Kussmual breathing-- acidotic hyperventilation-- washout of Co2)

$$2H^+ + HCO_{3^-} \rightarrow H_2CO_3 \rightarrow H_2O + CO_2$$
$$(\uparrow) \qquad (\uparrow) \qquad (\uparrow)$$

→ H2Co3 reduced less than 15meq (as they are consumed more)

↓

more Co2 formed - trigger Respiratory center-

↓

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leading to washout of Co2- Leading to more proton consumption

↓

Proton is responsible for damaging BBB, Encephalopathy etc.

↓

Kussmual Breathing is a compensatory Mechanism (Fruity breath)

↓

Fruity breath is due to acetone (Ketone bodies are -acetone, acetoacetate, and beta hydroxybutyrate.

Work up-

-Urine Ketostix → Measures Acetoacetate

> **NOTE:** Acetoacetate breakdown into acetone- level of acetoacetate is falsely normal in DKA. urine ketostix is not best the way to diagnose DKA.

→ Ideal way to diagnose DKA is checking plasma beta hydroxybutyrate values.

- Blood Glucose → 350 mg% (substantially high)

- **Electrolyte values**

1. Sodium → Decrease-- Because high Glucose draws water--H2O will dilute Na value

In clinical study-- Glucose $\propto \frac{1}{Sodium}$ -- Hypertonic Hyponatremia

2. Potassium - **Elevated** (acidosis causes k+ efflux (out from cell) -leading to compartment shift)

NOTE: Total Body potassium is Reduced –

1. Vomiting
2. Osmotic diuresis
3. Blood sugar increases– polyuria – loss of electrolyte

But in blood– potassium levels are **increased**

While treating patient with DKA-- gradual correction of potassium is done as hypokalemia can lead to **Torsade's de pointes**.

↓

Thus, while treating patient with DKA, in correction fluid KCL is added in small amount to keep potassium in range of 3.5.

– Phosphate → Increases

– ABG Analysis / VBG analysis: –

pH	Pco2	HCO3–
(↓)	(↓)	(↓)

NOTE: Thus, above condition is METABOLIC ACIDOSIS._

↓

If CO2 is low – hyperventilation. It is PARTIALLY COMPENSATED METABOLIC ACIDOSIS.

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↓

If CO2 is_normal – UNCOMPENSATED METABOLIC ACIDOSIS

– Plasma β Hydroxy Butyrate **(MAIN INVESTIGATION)** → Increases

– S. Amylase / lipase → N / slightly Increases (To Rule Out Acute Pancreatitis)

– TLC → Increase (if Trigger is infection)

– KFT → Increase (due to dehydration– urea, creatinine is highly increased)

– Anion GAP = $Na^+ - (Cl^- + HCO_3^-)$ -- Anion gap is high

High anion Gap Metabolic acidosis (HAGMA)-- as positive charges are high

TREATMENT: –

Grading of severity of disease: –

Ph	β Hydroxy Butyrate (mmol/l)	Grade
7.25 – 7.30	< 4	Mild (alert)
7.00 – 7.25	4 – 8	Moderate (drowsy)
< 7	> 8	Severe (Stupor)

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A. FIRST LINE OF MANAGEMENT –

1. Fluid Resuscitation

-NS 0.9% (fluid of choice)

- **NOTE-** RL is not given because it is rich in potassium and in DKA potassium is already raised--IF raised further will lead to diastole arrest.

-5L of NS is given (in next 8 hours)

1L/Hr. x in first 2 hours
↓ after 2 hours
400 ml NS / hour

-On treatment in DKA -- fluids given--sugar will be diluted-- sodium level rises

$$Glucose \propto \frac{1}{Sodium}$$

↓

(Na^+ > 150 meq)

Then, 0.45% N/2 is Given

2. Insulin administration

a. Regular Insulin (can be administer by any route I/M, I/V, S/C) is given
b. Bolus is given initially 0.1 U/Kg to Prime Insulin receptor
c. Infusion later on (0.1 U/kg/hr.)

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↓

Blood Sugar level falls 10% initially in first Hour
Subsequently 50 mg% decreases / hour

- Fast correction can lead to Death-- most common cause of fast correction (in Pediatrics) in treating DKA is Cerebral Edema.

- When Blood sugar level falls to 250 mg%, change the fluid to 5% Dextrose.

3. Treat Hyperkalemia

- On treatment as acidosis resolve- hypokalemia occurs - can lead to Torsade's de pointes, muscle paralysis

↓

Monitor K^+ levels. Give KCL to the patient, add to IV fluids (10-30 mEq / hr. infusion)

4. Acidosis

- Give Soda Bicarbonate Only if pH < 7.0 **(in severe DKA ONLY)**

↓

If excess of HCO3 given to person - HCO3 will trigger Metabolic alkalosis

↓

K^+ influx into cell- hypokalemia - can lead to arrythmia.

PrepLadder

5. Infection control

6. Switch over to subcutaneous insulin

Hyperglycemic Hyperosmolar Coma: -

- More Common in type II DM/Occult DM.
- Mortality Rate = 10 times higher than DKA
- Middle age person is more affected.

FEATURES-

- Blood Sugar level = 600 mg%
- pH = Normal
- HCO_3 = Normal
- pCO_2 = Normal
- Urine Ketostix = Negative
- Insidious in Onset

Triggers for hyperglycemic hyperosmolar coma: -

1. Myocardial Infarction
2. CVA (Cerebrovascular accident)
3. Pneumonia

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Treatment: -

1. Normal Saline = 10 L/ 24hr
2. No need of Insulin Bolus
3. Insulin Drip Infusion (0.05 U/Kg / hr)

NOTE: -

Blood Sugar	350 mg%	350 mg%	600 mg%
pH	7.2	7.2	Normal
HCO_3^-	15	15	Normal
Urine dipstick	- Ve	+	- Ve
B hydroxy butyrate	Normal	↑	Normal
Condition	Lactic Acidosis Rx → Soda bicarbonate	DKA Seen in .Child .Poor compliance pt	Hyperglycemic Hyperosmolar State (Seen in case of Occult DM)

DISORDERS OF PARATHYROID GLAND

PARATHYROID HORMONE (PTH):

FUNCTIONS:

- Causes Bone resorption: ↑ **Ca++**
- Acts on PCT kidney → PO_4 WASTING → Po_4 ↓
- It increases Bone turnover: **SERUM ALKALINE PHOSPHATASE ↑ →Best marker for bone turn over ***
  OSTEOCLASTS→ Bone destroying action
  OSTEOBLASTS → Bone-forming action → FORMS **SERUM ALKALINE PHOSPHATASE [SAP]**
  - In bone resorption → osteoclastic activity increases → resulting in secondary increase in osteoblastic activity → which increases SAP

➔ **MUST KNOW POINTS IN SAP FLUCTUATIONS:**

SAP ↑ - RICKETS (in children), OSTEOMALACIA (in adults)
HYPERPARATHYROIDISM
SAP ↓ - HYPOPHOSPHATASIA
DISPROPORTIONATE ↑↑ in SAP - PAGET'S DISEASE
SAP normal - HYPOPARATHYROIDISM, MULTIPLE MYELOMA, OSTEOPOROSIS

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PRIMARY HYPERPARATHYROIDISM:

➔ Leading cause → **Parathyroid Adenoma**

➔ **Tumor in any of the parathyroid glands → ↑ PTH → BONE RESORPTION ↑ → Ca^{+2} ↑**

➔ Normal calcium level: 9-11 mg%

➔ **RAISE OF CALCIUM & ITS MANIFESTATIONS:**

1. **11-12 mg%** → - Nephrocalcinosis
   - Renal Colic:
     - presents as flank pain going towards umbilicus
     - A/W multiple hospitalizations d/t recurrent vomiting episodes caused by pylorospasm [as a result of Renogastric Reflex]
   - Constipation → d/t spasm of sphincters of gut → may present with abdominal pain
   - Calcinosis cutis [Ca^{+2} deposited in skin of the pt]
   - Pseudo-hypertension [HTN d/t hardening of blood vessels]
   - Psychosis **(Moaning & groaning)**
2. **12-13 mg%** → 2° Parkinsonism [d/t calcification of basal ganglia]
   Bradykinesia / Rigidity
3. **13-14 mg%** → Systolic arrest

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WORK-UP:

1. S. CALCIUM - ↑

   S. PO4 - ↓

   SAP - ↑

2. S. PTH ASSAY : ↑↑
3. Tumor Localization is done by : **SESTAMIBI SCAN (Tc 99)**

TREATMENT:

➔ Medical Stabilization of hypercalcemia component of the pt

1. Normal saline (dilution effect) : Hydration
2. Furosemide Drip (causes **Ca^{++} loss in urine**)
3. IV Ibandronate → **DOC**
4. Calcitonin Nasal spray → Antagonist of PTH → sends Ca+2 into bones

➔ After stabilization get preanesthetic checkup & fitness certificate for surgery

Treatment of Choice: Surgery → Resection of adenoma

HYPOPARATHYROIDISM

CAUSES:

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1. Autoimmunity → leading cause
2. Thyroid Surgery (inadvertent parathyroid resection)
3. **DIGEORGE SYNDROME** → Defect in **chromosome 22**

Thymus Hypoplasia		**Parathyroid Hypoplasia**
CMI ↓	+	↓ PTH → ↓Ca^{+2}
Risk of infections ↑		**Rickets like illness**

ACUTE HYPOCALCEMIA/ Tetany

→ Post Thyroid Surgery

> 72 hr → S. CALCIUM < 7 mg % → **TETANY**

MANIFESTATIONS:

1. **Perioral & Periungual Paresthesia**
2. **TROUSSEAU SIGN**: Apply BP Cuff & inflate it → results in Carpopedal Spasm (Obstetrician hands)
3. **CHVOSTEK SIGN**: Tap on anterior border of Parotid gland → results in contraction of muscles of one side of face → Facial Grimace
4. Stridor : Laryngospasm

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MANAGEMENT:

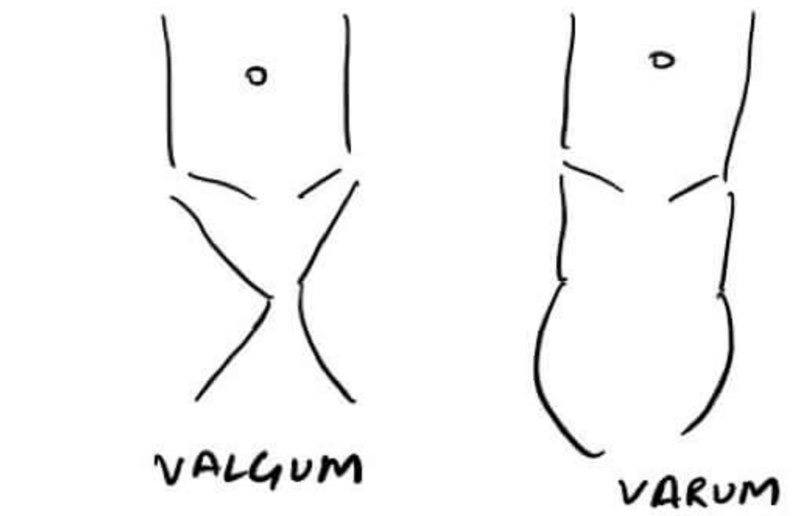
- IV Calcium gluconate
- Drug of choice for **Surgically induced hypoparathyroidism**: TERIPARATIDE INJECTIONS

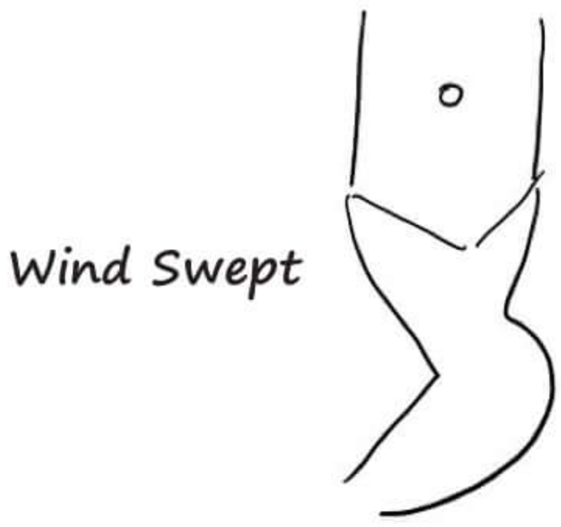
CHRONIC HYPOCALCEMIA:

➔ Rickets **like** illness

➔ FEATURES:

1. CRANIOTABES → Skull is soft & easily deformable
2. Widening of wrist joint
3. Disproportionate Short stature
4. Wide open Anterior Fontanelle
5. Delayed dentition [no teeth beyond age of 13 months]
6. Skeleton abnormalities: Knock knees, bow legs





INVESTIGATIONS:

1. **Calcium** – ↓
2. **PO_4** – ↑
3. **SAP** – Normal
4. **S. PTH Assay** – ↓↓
5. **Tc99 scan / SESTAMIBI Scan** – ↓/ absent uptake by gland

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MANAGEMENT:

- Calcium & Vit D supplements

PSEUDO HYPOPARATHYROIDISM:

- PTH values: ↑↑
- Receptors: **Resistance** to PTH, because of defect in GNAS gene

CLINICAL FEATURES:

- Similar to Hypoparathyroidism/ Rickets like illness with Archibald sign. Make a fist of the patient and compare with your own fist. Patient will be having short 4^{th} and 5^{th} metacarpal bones leading to Knuckle-Knuckle- dimple–dimple sign/ Archibald sign. This is also called as Albright Hereditary Osteodystrophy.

INVESTIGATIONS:

- Calcium – ↓
- PO_4 – ↑
- SAP – Normal

PrepLadder

- Pseudo-hypoparathyroidism is differentiated from Hypoparathyroidism based on the levels of PTH
    - PTH ↑ in pseudo-hypoparathyroidism and reduced in hypoparathyroidism:

MANAGEMENT:

No definite treatment

PSEUDO PSEUDO HYPOPARATHYROIDISM:

➔ Etiology: **D/t GENOMIC IMPRINTING from paternal side**

* Action of PTH on bones is defective → Have AHO (Clinical features)

* Action on Kidney → Normal → PO4 normal

* PTH level → Normal

Hypoparathyroidism → Albright hereditary osteodystrophy

Pseudo Hypoparathyroidism → Albright hereditary osteodystrophy

Pseudo. Pseudo Hypoparathyroidism → Albright hereditary osteodystrophy

Can differentiate from Phosphate & PTH values:

DISEASE	PO_4^-	PTH	CAUSE
Hypoparathyroidism	↑	↓	Autoimmunity
Pseudohypoparathyroidism	↑	↑	Receptor resistance
Pseudo pseudo hypoparathyroidism	NORMAL	NORMAL	Action on bones - Defective

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➔ Pseudohypoparathyroidism & pseudo pseudohypoparathyroidism are differentiated by phosphate levels

EXTRA EDGE:

- Tertiary hyperparathyroidism is seen in cases of untreated secondary hyperparathyroidism / C.K.D where transplantation/ medical management was not done
- Hence continuous stimulation of parathyroid glands leads to the gland becoming autonomous

→ **2° HYPERPARATHYROIDISM:**

MCC : Renal failure (chronic)

↓

Vitamin D3 synthesis ↓

↓

Hypocalcemia

↓

Calcium sensitive receptors are stimulated → PTH ↑

PrepLadder

MANIFESTATIONS:

	1° PTH ↑	2° PTH ↑	HP	PHP
	Adenoma	Chronic kidney Disease Vit. D_3↓	Autoimmune PTH ↓	Defective GNAS Gene PTH ↑
Ca^{+2}	↑	↓	↓	↓
PO_4	↓	↑	↑	↑
SAP	↑	↑	N	N

HP : Autoimmune destruction of gland : PTH ↓

PHP : # Receptor, GNAS gene : PTH ↑

PPHP: Genomic imprinting : PTH -Normal

- Features of AHO + PO_4 ↑ → HP, PHP

NUTRITIONAL RICKETS

Vitamin D_3 ↓

↓

Calcium ↓

↓

PTH ↑

↓

PO_4 Wasting

[urinary loss]

↓

P04 ↓

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TREATMENT:

➔ 6 Lakh international units of Vit D → Given in single dose-I.M / in sachets

Note: Phosphate is increased in CKD due to low GFR. Though PTH is high, it is not able to kick out phosphate, since filtration of PO_4 itself is defective.

PrepLadder

DISORDERS OF ADRENAL GLAND

ADRENAL GLAND:

Functioning depends on:

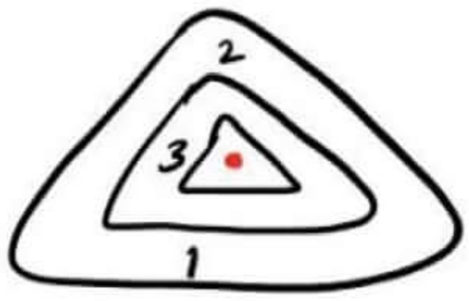
CRH [from hypothalamus]

↓

ACTH [from anterior pituitary]

↓ acts on

Adrenal glands



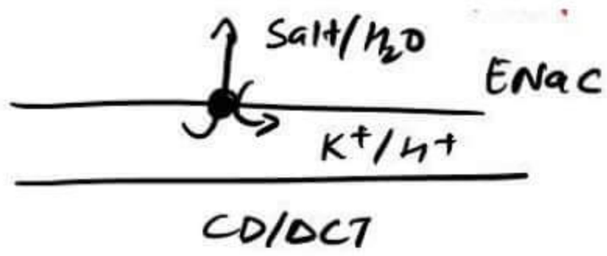
pyramidal shape

semilunar shape

LAYERS OF ADRENAL GLAND:

1. ZONA GLOMERULOSA:

- Produce Aldosterone (under control of RAAS)
- Aldosterone
  - Receptors are in kidney (K/A Epithelial Na^{+2} channels)
  - Acts on Collecting duct [1st answer]/DCT



- **FUNCTIONS OF ALDOSTERONE:**
  - Absorption of salt & water
  - Excretion of potassium & hydrogen
  - **MAIN FUNCTION: Postural adjustment of Blood pressure**

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2. ZONA FASCICULATA:

- Produce cortisol.
- Cortisol is a **stress hormone** which regulates **Blood Sugar Levels**
- Cortisol ↑ → ↑ Blood Sugar → Impaired Glucose tolerance

3. ZONA RETICULARIS:

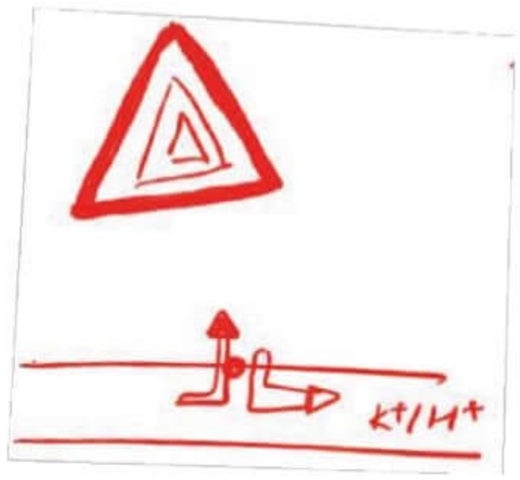
- Releases sex steroids like **DHEAS** [**D**i **H**ydro **E**pi **A**ndrosterone **S**ulfate]
- Responsible for **2° sexual characteristics**

4. MEDULLA:

- Synthesize & release catecholamines [Epinephrine, Norepinephrine, Dopamine]
  - Major catecholamine– Epinephrine (60%)
  - Most of pheochromocytomas → produce Norepinephrine → have Shortest ½ life
- A.A involved in synthesis of catecholamines → **Tyrosine**
- Epinephrine & Norepinephrine → after metabolism, forms→ **VANILLYLMANDELIC ACID**
- Dopamine → after metabolism forms → **HOMOVANILLIC ACID**
- Function of Epinephrine/Norepinephrine → **FIGHT OR FLIGHT PHENOMENON**

PrepLadder

1° HYPERALDOSTERONISM:



→ **Excess production of aldosterone d/t**

- B/L Adrenal Hyperplasia → Most common cause [90%]
- Adrenal Adenoma (tumor in the 1st layer of cortex] →CONN'S SYNDROME
- **Features:** ↑Aldosterone → (+) E NaC resulting in
  - Increase sodium & water absorption resulting in expansion of plasma volume
  - Contralateral urinary loss of K^+ & Na^{+2}

CLINICAL FEATURES:

1. Headaches – due to Hypertensions

2. Urinary loss of potassium→ Hypokalemia → resulting in Muscle cramps (weakness)

3. Metabolic Alkalosis → d/t loss of hydrogen ions

4. Gain of H_2O → Expansion of plasma volume → ↑Venous Return
   ↓
   ANF release
   ↓
   Natriuresis (Loss of H_2O)
   - ❖ Gain of H_2O = Loss of H_2O → So, no Pedal edema

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→ Polyuria [d/t ANF]

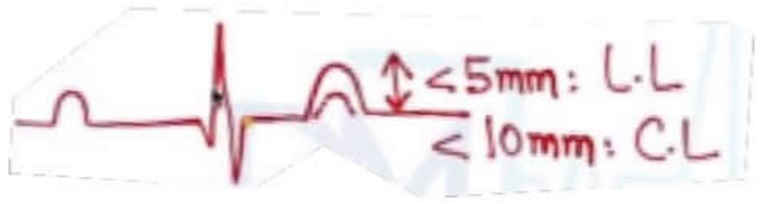
→ Polydipsia

INVESTIGATIONS:

→ **Na^{+2} levels** increases
  - Serum sodium values may be normal d/t simultaneous excess of water. But, total body salt is more

→ **K^+ levels** decreases
  - In the presence of Aldosterone → Na α 1/K

→ **ECG:**
  - Normal T-wave → <5mm in limb leads;
    <10mm in chest leads



  - In these pts → **T-wave smaller / absent / Inverted T-wave**
  - ST-depression can be seen

→ **CT Abdomen:**
  - Shows **B/L Adrenal Hyperplasia** or **Tumor**

→ **Plasma Renin : Plasma Aldosterone Ratio:**
  - Best screening test
  - Autonomous tumor – ↑Aldosterone → (-) RAAS → Decrease Renin levels →thus, renin : Aldosterone ratio decreases
  - Results in **Low renin HTN**

→ **IOC – Saline infusion test / Salt loading test**

PrepLadder

TREATMENT:

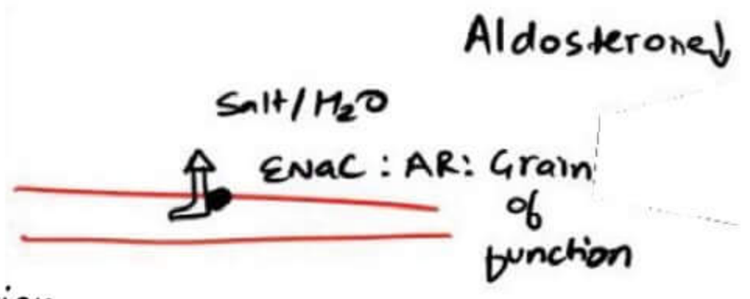
→ **CONN'S SYNDROME:**

- Initially give Spironolactone for 4-6 weeks
  - It is K+ sparing diuretic so manages both hypertension & hypokalemia
- Then get PAC fitness → do **Surgery**: U/L Laproscopic Adrenalectomy → definitive treatment.

→ **B/L ADRENAL HYPERPLASIA:**

- **DOC** → life-long treatment with **SPIRONOLACTONE**
  - S/E → Gynecomastia in males
  - So, Alternate drug- **EPLERENONE** for ♂

→ D/D of CONN'S → **LIDDLE Syndrome**



→ **LIDDLE SYNDROME:**

- AUTOSOMAL DOMINANT
- Epithelial Na-Channel defect → exhibits gain of function mutation.
- Causes HTN → (-) RAAS system → Renin decreases → Aldosterone decreases
  - By this feedback mechanism Aldosterone levels are decreased but hypertension occurs d/t excess salt & water in the body secondary to excessive activity of epithelial sodium channel.
- **Imaging** → shows (N) Adrenal gland
- **DOC → AMILORIDE** → Inhibit function of Epithelial Na^{+2} channel

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Conditions with [HTN + Hypokalemic alkalosis + Low Renin]:

1 CONN – Tumor producing excess Aldosterone → R_x: Spironolactone/Eplerenone -f/b surgery

2 Liddle – Gain of function of epithelial Na channel → Aldosterone ↓→ R_X- Amiloride

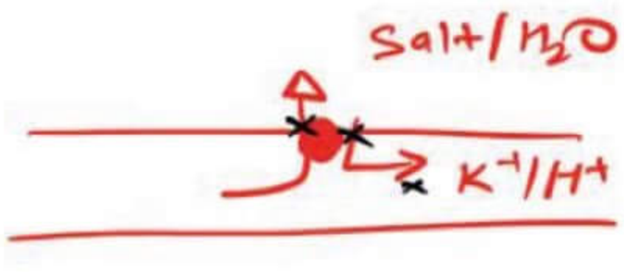
ADDISON'S DISEASE:

- **Leading cause → Autoimmune destruction**
- **MCC in India → Tuberculosis of Adrenals**
- **Harrison 20th edition mentions HIV/ AIDS as → Leading infectious cause globally**

→ Causes ↓ Aldosterone, ↓ Cortisol, ↓ DHEAS

CLINICAL FEATURES:

1. Aldosterone ↓ resulting in:
   - Salt wasting, craving for salty foods
   - Polyuria [urine output >3L/day]
   - Postural Hypotension
   - K↑
   - Metabolic Acidosis



2. **Cortisol ↓ → Sugar↓ → Palpitations, Tremors, Diaphoresis, RAGE attack, emotional fragility**
3. ACTH↑↑ → have Partial Melanocyte Stimulating Hormone like action resulting in

Hyperpigmentation at

- Palmar/ sole creases
- Scars / Areola / axilla / cubital fossa
- Groin area
- Oral Mucosa } very characteristic for Addison's disease.
- Nails }

4. ↓**DHEAS** resulting in → ↓Libido, erectile dysfunction

INVESTIGATIONS:

- $Na^+\downarrow, K^+\uparrow$
  - Rule out Sampling errors as usage of thin bore needle may result in Factitious Hyperkalemia
- CT Abdomen:
  - Shows damaged adrenals
- IOC → **ACTH Stimulation test / Cosyntropin test**
  - Normally ACTH → Cortisol↑ → Blood Sugar↑
  - In this disease, there is **No** raise of blood sugar levels

TREATMENT:

- **DOC → HYDROCORTISONE**
- Low BP is managed by giving → Fludrocortisone } give initially, observe response
- Decreased Sugar levels is managed by– Dexamethasone } then go for D.O.C
- **ADDISONIAN CRISIS** – I.V Hydrocortisone

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WATERHOUSE-FRIDERICHSEN SYNDROME

- Complication of infections like **N. Meningitidis / Pseudomonas**
- Leads to
  - Sepsis
  - DIC → Adrenal Hemorrhage → leading to ADDISONIAN CRISIS
- TREATMENT: **I.V Hydrocortisone + Antibiotics + fluid replacement**

SHEEHAN SYNDROME:

- Postpartum hemorrhage → causes Pituitary damage →results in secondary Addison's disease
- Results in ↓ ACTH → ↓ CORTISOL → Hypoglycemia.
- B.P is normal as aldosterone is not affected
- No hyperpigmentation as ACTH levels are low
- TREATMENT: DEXAMETHASONE

HYPOTHALAMUS DAMAGE:

- Caused d/t → Trauma / rupture of AV aneurysm / metastasis etc
- **Results in → CRH↓ → ACTH↓ → Cortisol↓**
- Aka **Tertiary Addison's Disease**
- No hyperpigmentation & B.P is normal
- TREATMENT: **Dexamethasone (DOC)**

PrepLadder

ADDISON'S DISEASE:

1° – Autoimmune

2° – Pituitary damage (SHEEHAN / SIMMONDS ds [non-obstetric cause])

3° – Hypothalamus damage

Crisis –Waterhouse-Friderichsen Syndrome/ Sudden stoppage of Steroids

	ACTH	Hyperpigmentation	DOC
1°	↑	+	Hydrocortisone
2°	↓	–	Dexamethasone
3°	↓	–	Dexamethasone
Crisis	(N)	–	I.V. Hydrocortisone

↑ Aldosterone CONN		↓ Aldosterone Addison
Cause	-Tumor	-Autoimmune destruction of adrenals
BP	-Increased	↓
K^+	-Decreased	↑
H^+	-Decreased	↑
Special	-Pedal edema is absent	Hyper Pigmentation
IOC	- saline infusion Test/ salt loading test	- ACTH stimulation test or COSYNTROPIN Test
RX:	-SPIRONOLACTONE	- HYDROCORTISONE

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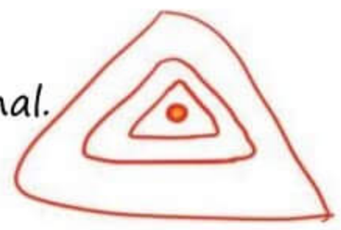
PrepLadder

PHEOCROMOCYTOMA:

- **Tumor of adrenal medulla**
- Aka chromaffin-oma
- Chromaffin cells are found in:
  - Adrenal medulla
  - Sympathetic ganglia [paravertebrally located]
- Produce **NE 80%> Epi 20%>>> Dopamine**
- 10% pheochromocytomas → Malignant
- Benign vs Malignant differentiation:
  - MRI Abdomen is indicated
  - **FNAC → contraindicated→ as it may result in damage to normal layers of gland.**
- 15% tumors → Extra- Adrenal
  - Tumor could be deep seated in medulla (85%) → MIBG scan can be done.
  - Tumor could be inside sympathetic chain (15%) → ORGAN OF ZUCKER KANDL
- **IMAGING MODALITY:**
  - MIBG scan → for Adrenal Pheochromocytoma if MRI abdomen is normal.
  - P.E.T Dopa → for Extra Adrenal tumors if MRI abdomen is normal.



  - **EXTRA MILE: Imaging modality of choice in pheochromocytoma is MRI abdomen**

If incase tumor is < 1.5 cm, we have to perform the scans mentioned above.

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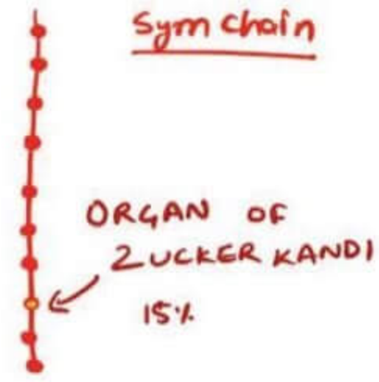
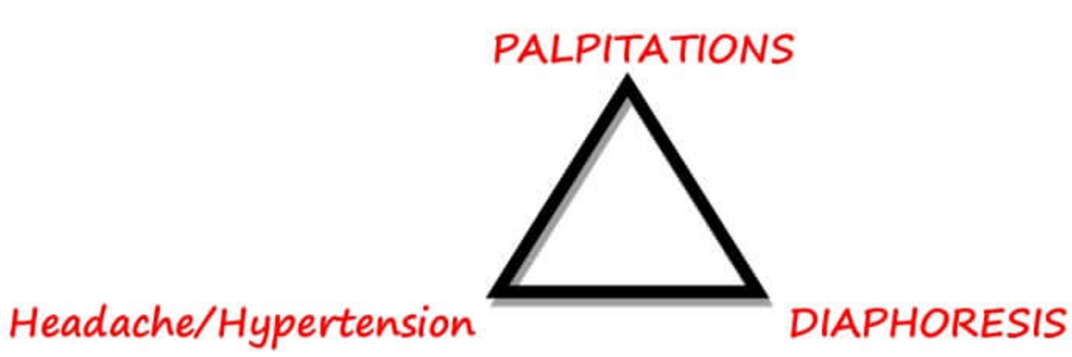


- Pheochromocytomas are associated with other endocrine malignancies
  - MEN-2A- Multiple endocrine Neoplasia (SIPPLE SYNDROME)
    - **PPM** [mnemonic]
      - → **P**heochromocytoma - 20 years
      - → **P**arathyroid Adenoma - 40 years
      - → **M**edullary Ca thyroid - 60 years
- D/t **Ret proto-oncogene**, defect in **chromosome 10**
- 10-15% tumors are B/L

CLINICAL FEATURES:



1. **IF we see this triad of symptoms in young pt → suspect pheochromocytoma**
2. HTN – episodic / Paroxysmal
   - Catecholamines have a short duration of action and hence BP can be increased for only few hours / minutes initially.
   - Later excess of catecholamines will lead to exaggerated **vasoconstriction**
   - This reduces intravascular volume → leading to **postural hypotension** in the same patient later

3. β1 (+) → increased HR, palpitations
4. β2 (+) → Fine tremors [in fingers]
5. Diaphoresis (+) → Sweaty palms / soles

} Misdiagnosed as **Anxiety neurosis**

6. Fasting Blood sugar → 100-125 mg; 2 hr BS – 140-199 mg → Impaired Glucose Tolerance
7. Weight loss
8. Falsely **Increased calcium** ↑, **Increased Hematocrit** ↑ →d/t volume contracted state

INVESTIGATIONS:

1. 24 hr Urinary metanephrine levels → for screening [best answer]
2. 24 hr urinary catecholamines
3. **IOC** – Plasma fractionated Metanephrine levels.

TUMOR LOCALIZATION

- MRI Abdomen→ Overall best modality
- MIBG scan → if Adrenal pheochromocytoma < 1.5cm [missed by MRI]
- P.E.T dopa scan → useful for extra-adrenal pheochromocytoma < 1.5cm

TREATMENT:

- Benign Pheochromocytoma → medically stabilize the pt & then do surgery [TOC]
- Oral Phenoxybenzamine → Best drug for Pre-operative Hypertension management

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- β1 – palpitations & β2 – fine tremors → use propranolol
- Vasoconstriction is max in early morning hrs. so, for symptomatic management give
  - α – blocker → oral phenoxybenzamine [controls B.P] → in early morning
  - β – blocker → oral propranolol [control palpitations & tremors] → post breakfast
  - α – blocker should be always given before β- blocker [i.e α + β]
  - if we give β – blocker prior to α-blocker, vasodilation is blocked → unopposed α - stimulation → vasoconstriction → resulting in severe hypertension [may result in brain damage/ hypertensive encephalopathy]

    Thus, [β + α] → contraindicated
- INTRA-OPERATIVE HTN IN PHEOCHROMOCYTOMA:
  - Tumor manipulation causes spikes in levels of catecholamines
  - Controlled by I.V phentolamine drip
- INTRA-OPERATIVE HTN crisis:
  - Treatment: IV NTG drip
  - Surgery is **contraindicated** in **Malignant pheochromocytoma. Chemotherapy and 1-131 loaded MiBG scan can be used in case of metastatic Tumor.**

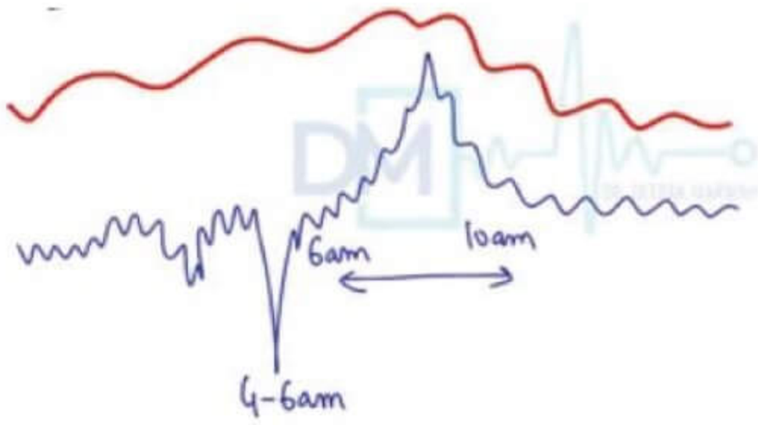
PrepLadder

CUSHING SYNDROME

CAUSES:

1. Iatrogenic steroids (exogenous) → **MCC** → Cortisol ↑ → by feedback ACTH ↓
2. Carcinoid tumor } ectopic ACTH ↑
3. Oat cell CA lung } Cortisol ↑
4. Pituitary Adenoma → Aka cushing's disease (endogenous) → ACTH ↑ → Cortisol ↑
5. Adrenal adenoma involving zona Fasciculata → Cortisol ↑ → ACTH ↓

- **Earliest manifestation of cushing's syndrome** → loss of diurnal variation of cortisol production

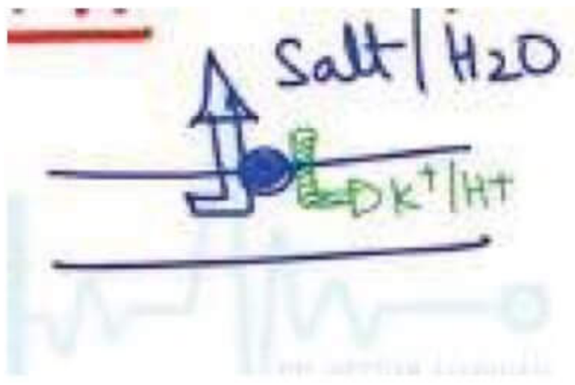


CLINICAL PRESENTATION:

1. Moon facies
2. Centripetal Obesity
3. Proximal myopathy
4. Violet/ purple Striae, Thin skin, Purpura
5. Buffalo hump

> ❖ **EXTRA MILE**: Pregnancy → pink striae are seen

6. Weight gain / Lemon on sticks description Term for Point 1–5
7. ↑ Peripheral resistance → HTN
8. Insulin resistance → sugar } FBS > 126 mg% } SECONDARY DIABETES
   Cortisol ↑ → sugar ↑ } 2hr > 200 mg% } MELLITUS
   R_x: Metformin
9. Cortisol ↑ → Activates ENaC → causes salt & water retention & **Hypokalemic alkalosis**
10. Cortisol ↑ → Activates Sex steroid receptors
    - Female - Hirsutism, weight gain, oligomenorrhea, infertility → **PCOD >> Cushing Syndrome**
11. Hyperpigmentation: (±)
    - Ectopic ACTH → (+)
    - Exogenous cause → (-)



WORK UP:

- Screening test:
  - 24 hr urinary cortisol ↑↑
  - Spot Salivary cortisol ↑
  - Overnight dexamethasone suppression test
- **IOC** : **Low dose dexamethasone suppression test**
  - Do not answer high dose dexamethasone suppression test which is used for **etiological diagnosis.** It Helps to Pin point the cause of disease and not disease per se.
- Imaging:

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- MRI Head [pituitary adenoma]
- HRCT Chest [lung cancer]
- CT Abdomen [Adrenal causes]

➢ ACTH levels ↑ / ↓
- Can be Suppressed in pituitary adenoma. Also referred as ACTH dependent cause
- Not suppressed in ectopic causes

TREATMENT:

➢ **Iatrogenic steroids:**
- Taper steroids
- Start alternate immunosuppressive drugs like **Azathioprine**

➢ **Oat cell lung cancer**:
- Chemotherapy → with Cisplatin + Irinotecan

➢ **Pituitary adenoma/cushing disease** → Trans-sphenoidal Sx

➢ **Adrenal adenoma**:
- Medical Adrenalectomy using
  - Ketoconazole [oral] → preferred
  - Aminoglutethimide (IV)
  - Mitotane IV

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NELSON SYNDROME:

➢ Caused due to **B/L Adrenalectomy** performed to treat bilateral adrenal adenoma producing a mass effect.

➢ During Surgery to prevent Addisonian crisis → IV Hydrocortisone drip can be given

➢ Post op → Life-long Hydrocortisone supplementation

➢ Follow up → D/t static levels of steroids, no feed-back inhibition on ACTH → ACTH ↑↑↑ → resulting in **Hyperpigmentation ++**

❖ **EXTRA MILE:**

➢ ACTH Dependent Cushing Syndrome: Pituitary Tumor and ectopic Tumors producing ACTH

➢ ACTH independent Cushing Syndrome: Adrenal adenoma

➢ High dose dexamethasone suppression Test is used to differentiate between these causes.

PrepLadder

DISEASES OF THYROID

THYROID STORM:

→ It is intra-operative complication of thyroid surgery

→ If a patient is operated without adequate pre-operative preparation, massive release of thyroid hormones into the circulation occurs → resulting in Thyroid storm

→ It can be prevented by giving saturated solution of potassium iodide/ Lugol iodine pre-operatively.

- **SSKI x 4 weeks** → causes shrinking of gland → I_2 TRAPPING ↓ → T4 ↓ → T3 ↓
- Occurs by **Wolf chaikoff effect** → **Downgrade process of iodine trapping which decreases T_3 & T_4**

→ **This massive release of thyroid hormones into circulation resulting in:**

- T4 ↑, T3 ↑ → persistent Sympathetic stimulation
- HR ↑↑ :- High out CCF : Pulmonary edema
- B.P starts falling + SpO_2 ↓
- Body Temp ↑↑ > 41^0 C [d/t calorigenesis] → results in further increase in H.R → leading to heart failure [for every 1^0 raise in temp, H.R increases by 10beats/min]

TREATMENT:

1. Switch off Intra Vascular Fluids / Blood Transfusions in case of pulmonary edema
2. DOC: Propylthiouracil → by NG Tube → It inhibits conversion of T4 to T3.
3. ICE packs / Soda Bicarbonate [to treat metabolic acidosis]
4. IV propranolol → prevents further increase of Heart Rate

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SUMMARY OF THYROID STORM

- Reason → Inadequate preparation of Pt. [i.e lugol's iodine was not given]
- Cause of death → CCF (congestive Cardiac Failure)
- Prevent Death → by giving S.S.K.I which acts by → by Wolf chaikoff effect and decrease production of Thyroid hormones.
- Rx - PTU → inhibit T4→ T3 conversion

JOD BASEDOW EFFECT:

- Opposite of wolf chaikoff effect
- Seen with intake of iodized salt for long duration in iodine Replete population
- Has upgrade of I_2 Trapping leading to increased production of T4/T3

THYROTOXICOSIS FACTITIA:

- It is Thyrotoxicosis occurring d/t any other cause other than high salt intake.
- Examples:
  - Seen in patient consuming poor quality beef containing thyroid gland of animal.
  - Consumption of Ayurvedic / Homeopathic medicine containing Levothyroxine. Lot of these are marketed as weight loss medication

PrepLadder

HYPERTHYROIDISM:

CAUSES:

1. PRIMARY HYPERTHYROIDISM:

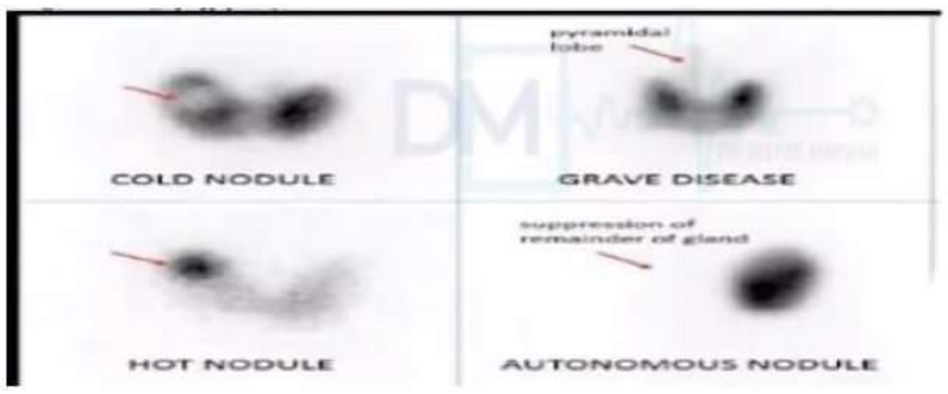
- MCC of PRIMARY HYPERTHYROIDISM → GRAVE'S DISEASE
- Grave's disease → have L.A.T.S - Ab (long acting Thyroid stimulating Antibody) → identical to TSH → resulting in T4 ↑ T3 ↑; TSH ↓↓

2. SECONDARY HYPERTHYROIDISM:

- D/t Pituitary adenoma → TSH ↑ → T4 ↑ T3 ↑

3. TOXIC NODULAR GOITER: Frequent in Areas of Iodine deficiency

- Diagnosed by Thyroid scan using I-123 / I-132 [$T_{1/2=}$ 2.3hrs]. I-131 is for ablation
  - WARm nodule → Normal Uptake
  - Cold nodule → Suggestive of Malignancy
  - Hot nodule - over active tissue



4. JOD BASEDOW EFFECT

5. THYROTOXICOSIS FACTITIA

6. STRUMA OVARI [Ovarian tumor synthesizing hormones]

7. GESTATIONAL TROPHOBLASTIC NEOPLASIA (HCG α TSH. Thus, HCG can bind to TSH receptors & stimulate them)

CLINICAL FEATURES:

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1. Sympathomimetic + :
   - Palpitations → Beta1 (+)
   - Fine Tremors → Beta2 (+)
   - Sweaty Palms/soles
   - HTN → Alpha1 (+)
2. BMR ↑ → resulting in weight loss
3. Calorigenesis ↑ → causes heat intolerance
4. ♀ → oligomenorrhea / infertility
5. Proptosis [d/t retrobulbar fat deposition & swelling of EOM] → Blinking action is inadequate → results in drying of cornea → **Exposure Keratitis** → causes grittiness / sand like sensation in eyes

O/E:

1. Sleeping Pulse Rate ↑ → **Most reliable sign** to diagnose thyrotoxicosis
2. Resting Tachycardia
3. Fine Tremors
4. CVS → loud S_1, MEANS LERMAN SCRATCH [d/t hyperdynamic circulation]
5. Proptosis, Stare sign, Stell wag sign, Von Graef sign (described Later)
6. Pretibial Myxedema [myxedema → seen in both hyper & hypothyroidism]
7. **Pemberton Sign**: On Raising arms, there will be Facial congestion d/t compression of SVC by retrosternal goiter.

Work-UP:

- **Thyroid Function Tests** → Total T4 & T3 - ↑ , Free T4, T3 -↑
- **TSH:**

→ If low → Primary hyperthyroidism [MC Grave's] → further investigations are

  - LATS titer
  - Thyroid scan
  - USG Abdomen [especially female pt to rule out ovarian/ uterine tumor]

→ If high → Secondary hyperthyroidism → pituitary adenoma → **Dx MRI head.**

TREATMENT OF GRAVE'S DISEASE:

1. Anti Thyroid Drugs
   - PTU (Propylthiouracil) → safe in pregnancy [T1] / breastfeeding → as it has high protein binding
   - Carbimazole → T2 pregnancy → Dose limiting S/E = agranulocytosis
   - Total Thyroidectomy in case of Poor response to medical Therapy
   - Propranolol → for symptomatic management
2. Ablation of thyroid gland using **Radioiodine 1-131** [t½ = 8 days]

SUMMARY OF MANAGEMENT OF GRAVE'S

Treatment of choice: Radio-iodine
Surgery of Choice: Total Thyroidectomy
Drug of choice: Carbimazole
Drug of Choice in T_1: Propylthiouracil

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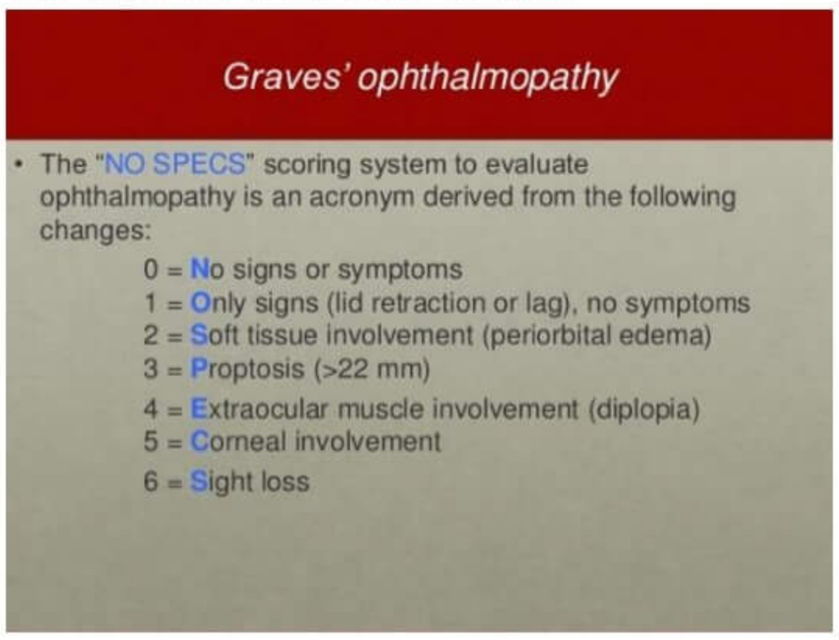
2^0 HYPERTHYROIDISM → D/t pituitary adenoma → R_x Trans-sphenoidal Sx

GRAVE'S OPHTHALMOPATHY:



- **Lid retraction → is d/t contraction of Muller's muscle [sympathetic overactivity]**
- **Lid-lag sign/ stare sign → inability of upper eyelid to follow the object from top to bottom**
- **Unilateral/ Bilateral / Asymmetrical proptosis is seen**
- " **Inferior Rectus**" is most common extra ocular muscle involved
- Corneal involvement is d/t "inadequate blinking"
- Cause of blindness → **Retrobulbar neuritis [d/t pressure on optic nerve**

PrepLadder

HYPOTHYROIDISM:

PRIMARY HYPOTHYROIDISM	SECONDARY HYPOTHYROIDISM
➢ Thyroid Gland is involved	➢ Pituitary Gland is involved
➢ T4 ↓ T3 ↓, TSH ↑	➢ T4 ↓, T3 ↓, TSH ↓
➢ CAUSES: 1. INDIA MCC →**Hashimoto thyroiditis** 2. GLOBALLY→ **Endemic goiter** 3. **ENDEMIC CRETINISM** → Baby with hypothyroidism since birth 4. Food Goitrogen→ Cabbage, Turnip 5. Drug induced hypothyroidism Amiodarone	→ CAUSES: 1. Sheehan syndrome → PPH L/t pituitary infarction 2. Non obstetric cause of pituitary damage called as Simmond's disease→ Occurs due to AVM Rupture, HTN, Trauma and sickle cell anemia 3. Cranial Radiation / Sarcoidosis 4. Empty sella syndrome / CSF leak syndrome

CLINICAL FEATURES:

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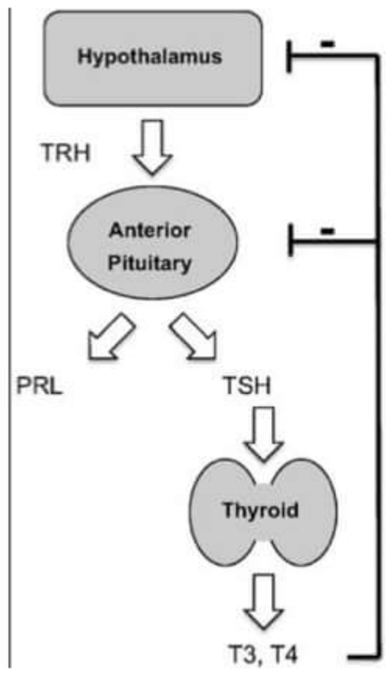
1. Cold intolerance
2. Myxedema:
    - Involve scalp – Cause alopecia
    - Involve face – Puffy face
    - Vocal cords – Hoarseness voice
    - Body – Thick Coarse skin [**Extra edge**: Leather like skin → scleroderma]
    - Gut – Constipation
3. Menorrhagia & infertility
4. Headache
5. Galactorrhea:
    - TRH stimulate Ant pituitary to produce TSH & Prolactin
    - In Endemic goiter pt → T3 & T4 are less → by feedback TRH Increases resulting in increase of both TSH & PROLACTIN → causes Galactorrhea
    - Never seen in secondary hypothyroidism [as pituitary is damaged].
      Eg: Sheehan syndrome which leads to lactation failure



O/E :-

- Bradycardia
- Pale yellow skin → occurs due to β Carotenemia. sclera is normal [jaundice sclera becomes yellow]
    - Conversion of β-carotene to Vit A in liver require T_3 & T_4
    - Thus, if thyroid levels decreases, β-carotene accumulates resulting in yellow skin.
- Hypertension → **Isolated diastolic Hypertension** → (120/90)

PrepLadder

- Coarse / Dry Skin
- **Hung up ankle jerk**-**Most reliable sign**
    - It occurs due to myxedema to achilles Tendon leading to delayed Relaxation.

> ❖ **EXTRA MILE:**
>
> - Hung up reflex → Chorea
> - Pendular knee jerk → Cerebellum damage

WORK-UP:

- TFT - **Total** T_4, T_3- ↓ ; Free T_4, T_3- ↓

PRIMARY HYPOTHYROIDISM	SECONDARY HYPOTHYROIDISM
➢ TSH is high	➢ TSH is low
➢ Defect is in thyroid gland	➢ Pituitary defect [obstetric/ non-obstetric]
➢ Next best investigation: Anti-TPO [thyroid peroxidase] Ab	➢ MRI head

Rx: Levothyroxine: 25 µg / 50 µg / 88 µg / 100 µg

→ If dose is >100µg, it increases O2 consumption → resulting in Angina [so, a very careful Titration of dose increments should be done.

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COMPLICATIONS OF HYPOTHYROIDISM:

- Elderly hypothyroidism pt not taking thyroid medications, non-compliant, suffers from UTI/Pneumonia/MI/STROKE. She is found Unconscious, unresponsive, hypothermia [Core temp. ↓]- (Measured at lower esophagus) ECG - Osbourne wave
    - → Diagnosis: "**MYXEDEMA COMA**". The **Trigger is an intercurrent illness**
    - → **Rx:**
        - IV Levo-thyronine [Active T_3 derivative]
        - Levothyroxine
        - Space blanket [Active rewarming]
- Myxedema madness → Development of Psychosis
- Myxedema heart / Serous cavity effusion:

  Pt. have massive pericardial effusion / Pleural effusion→ it is ultra-slow process → So, Pulsus paradoxus is **Absent.**
- Macrocytic anemia

> EXTRA MILE:
>
> OTHER CAUSES OF MACROCYTIC ANEMIA:
>
> → CLD (chronic liver disease)
>
> → Aplastic anemia
>
> → Hypothyroidism
>
> → B12 and Folic acid deficiency

- Accelerated Atherosclerosis: give statins like Atorvastatin [based on LDL levels]

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EXTRA MILE:

Conditions that lead to Accelerated Atherosclerosis:

- SLE
- Syndrome X
- CRF (Chronic Renal Failure)
- DM
- Hypothyroidism
- Nephrotic syndrome

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DISEASES OF ANTERIOR PITUITARY

ACROMEGALY:

- Occurs d/t excess GH **after puberty**
- Somatotrophs are abundant cells in pituitary
- **Somatotroph adenoma** is **MCC** of developing Acromegaly
- **Mammosomatotroph adenoma**
  - GH & Prolactin increases
  - C/F → **Galactorrhea**
- Leading cause of extra pituitary source of excess GH++ → Pancreatic adenoma (islet cells tumor)
- Leading cause of excessive GHRH production → **CARCINOID TUMOR**

❖ **EXTRA MILE:**

Hypothalamic Hamartoma presents with:

- Gelastic seizures → pt have uncontrolled laughing
- Precocious puberty
- SIADH

CLINICAL FEATURES:

- **ACRAL ENLARGEMENT:**
  - Increase in size of Hand /Feet
  - Increase in Finger thickness leading to **spade like hands**
  - Lower Jaw Prominence called as Prognathism.

spade like hands

- Frontal Bossing
- **Heel pad thickness > 21 mm** → used for monitoring growth in these pts
- Coarse Facies/ deep Hollow voice, Hyperhidrosis (excessive sweating), sebum ↑ (increase incidence of acne), acanthosis nigricans., skin tags.

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❖ **EXTRA MILE:**

ACANTHOSIS NIGRICANS can be seen in:

- DM
- PCOD
- Ca Pancreas
- Ca Stomach
- Acromegaly

- Premature Osteoarthritis → in bilateral limbs → d/t weight gain
- Weakness, fatigue
- ↑ Peripheral resistance → resulting in HTN [explains daily headaches]
- Increased GH results in **Impaired Glucose Tolerance**

  FBS = 100-125 mg%

  2hrs = 140-199 mg%
- Obstructive sleep Apnea d/t growth of tongue
- Colonic polyps.
- Galactorrhea
- visual deficit [Bitemporal Hemianopia]

GIGANTISM:

- Occurs d/t increase in GH **before puberty** [rare condition]
- Height of the pt increases → used to monitor growth
- Visceromegaly is seen
- Cause of death: **High output cardiac failure**

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WORKUP FOR ACROMEGALY:

- **Screening:** IGF-1 level ↑ [Insulin like Growth Factor-1]
- **IOC:** Failure to suppress GH levels with oral glucose load
- Serum Prolactin levels increases
- **MRI** Head- Size of Tumor> 10mm
- X-ray of lateral aspect of Foot is done to see **Heel Pad Thickness**

Heel pad thickness

TREATMENT:

- Trans-sphenoidal surgery. After surgery,
  - 1st to improve is → soft tissue swelling
  - After (1-2hrs) → GH levels decreases
  - After (3-4hrs) → IGF-1 levels decreases
- Prior to the surgery, shrink the size of the tumor using drugs→ Somatostatin analogues
  - Octreotide
  - Lanreotide
  - Pasireotide

  } acts on SSTR 2 Receptors → GH decreases; SSTR 5
- PEGVISOMANT → GH Receptor antagonist → hence, GH levels ↑ due to feedback

  ↓

  Used in case of recurrence of tumor
- Radiation

SHEEHAN SYNDROME:

- **SHEEHAN** → Pan- hypopituitarism
- Growth Hormone → 1st to fall
  - Results in **hypoglycemic attacks** → Earliest manifestation
- Prolactin levels fall → resulting in **LACTATION FAILURE**
- LH, FSH ↓ → resulting in Secondary **Amenorrhea**
- ACTH ↓ → Cortisol ↓ → Blood sugar levels ↓
- TSH ↓: T4 ↓, T3 ↓→ resulting in secondary hypothyroidism → wt. gain, cold intolerance etc

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Q.Non-obstetric cause to pituitary damage?

Ans: SIMMOND DISEASE

- HTN, AVM Rupture, Sickle cell anemia, Trauma etc

TREATMENT:

- DEXAMETHASONE →1st to be supplemented → Stabilize blood sugar levels
- Life-long LEVOTHYROXINE
- O.C.P/ C.O.C

→ Pan Hypopituitarism → Decrease of all the 6 Hormones produced by anterior pituitary

→ HYPOPITUITARISM: Implies only GH deficiency. Seen in pediatric population may be d/t pituitary dysplasia

FEATURES:

- Short stature
- Squeaky high Pitched Voice
- Doll like Facies
- Bone age delayed

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INVESTIGATIONS:

- Screening test: Decreases IGF-1 levels
- IOC: Insulin challenge test / Arginine challenge test

TREATMENT:

- GH injection (DNA Recombinant tech) till Puberty.

SUMMARY:

ENDOCRINE DISORDER	TEST
Acromegaly	Glucose challenge Test
CONN	Saline infusion test / Salt Loading test
ADDISON	ACTH ⊕ Test / cosyntropin test
DI	Water deprivation test
SIADH	Water loading test
Hypopituitarism	Arginine Challenge Test
Cushing	Low dose dexamethasone suppression test
Pheochromocytoma	Serum Fractionated metanephrine levels

- Please note posterior pituitary diseases like SIADH and DI have been covered in kidney section with Barter Syndrome and gitelman syndrome

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ELECTROLYTE IMBALANCE

1) Hyponatremia

→ **M/c electrolyte imbalance abnormality in hospitalized pts.**

→ Affects plasma osmolality

→ Changes in plasma Na^+ levels will affect plasma osmolality that will cause fluid shift across brain cells and can cause life threatening seizures.

Plasma Osmolality → $2(Na^+ + K^+) + \frac{BUN}{2.8} + \frac{Glucose}{18}$

- Normal → 285-295 mOsm/L
- Urine osmolality → 100-900 mOsm/L, it usually fluctuates a lot and helps to maintain plasma osmolality in a narrow range of 10 mOsm/L.

Normal Na^+ → 135-145 meq

Mild Hypo Na^+ → 130 – 135 meq

Moderate Hypo Na^+ → 125-130 meq

Severe Hypo Na^+ → < 125 meq – High risk of causing the fluid shift across the brain predisposing - Life threatening seizures

Hypotonic hyponatremia - Abnormal plasma osmolality → < 285 mOsm/L. Subsequent types of Hyponatremia depends on volume status of patient.

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→ **In Diarrhoea/ Vomiting** → **TBW ↓ and TBS ↓ = Hypovolemic Hyponatremia. Rx - fluids**

→ **In SIADH** → ADH ↑↑ → Acts on V2 receptor and causes more reabsorption of H_2O → **TBW ↑** and **TBS** is normal = **Dilutional Hyponatremia (Euvolemic hyponatremia)**

Note: - SIADH can be caused by cerebral toxoplasmosis/Meningitis/ Encephalitis / Brain abscess/Oat cell Ca lung and Carcinoid syndrome. CNS infections and Ectopic production of ADH can reset the Osmostat at higher levels so, maintaining the osmolality of plasma is hampered

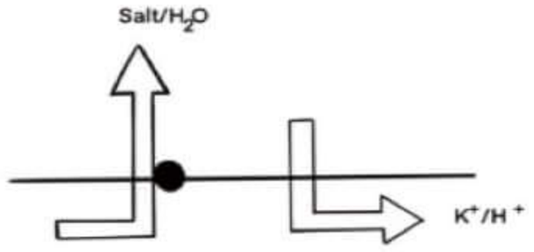
Clinical scenario: - Patient with Massive ascites→ ↓↓ Circulating fluid volume → GFR ↓

Activates

⊕ RAAS causing 2° Hyperaldosteronism

↓

causing activation ⊕ENac channels



→ **Resulting in TBW ↑↑ and TBS ↑ causing Hypervolemic Hyponatremia**

Clinical scenario: - In Patients of SAH (Worst headache of life, thunderclap headache), (After rupture of Berry Aneurysm or trauma) there is a release of **B.N.P** causing Natriuresis

→ Resulting in **TBW ↓** and **TBS ↓** causing **Hypovolemic Hyponatremia** (**Cerebral salt wasting syndrome**)

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Summary of different types of Hyponatremia

Hypovolemic (TBW↓ and TBS↓)	Euvolemic (TBW ↑ and TBS normal)	Hypervolemic (TBW ↑ and TBS ↑)
GI causes: (U. Na^+ ↓) → Diarrhoea → Vomiting **Rx:** ORS, RL **Renal causes: (U. Na^+ ↑)** → Cerebral salt wasting syndrome → Duretic excess → Addison disease	1. SIADH → T/t: vaptans 2. Post-operative → Nausea/Vomiting d/t anaesthetic drugs stimulates release of ADH ↑ 3. Endurance sports 4. Psychogenic polydipsia 5. Beer Potomania 6. Hypothyroidism **Rx:** Fluid restriction Vaptans : V_2 blockers	1. CHF 2. Cirrhosis 3. Nephrotic 4. CKD **Rx:** Diuretics

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Hypertonic hyponatremia: - ↑↑ in Osmolality of plasma > 295 mOsm/L

Examples:-

- **In patients with DM-II, having high blood sugar values** → Hyperosmolar coma

↓

↑↑ Plasma Osmolality = Osmotic load → Draw in H_2O and ↓ Na+ levels.

Note:- if blood sugar ↑↑ by 100 mg% → Na^+ ↓↓ by 1.6 meq, **Therefore, inverse relation b/w sugar & Na^+ is there.**

- **Mannitol**
- **Radiocontrast**

Isotonic hyponatremia (Pseudo hyponatremia - because Na^+ is normal but values are low)

- Hyperlipidemia
- Hyperproteinemia (Multiple myeloma)

} Interfere with measurement of Na^+, so false values of Na comes.

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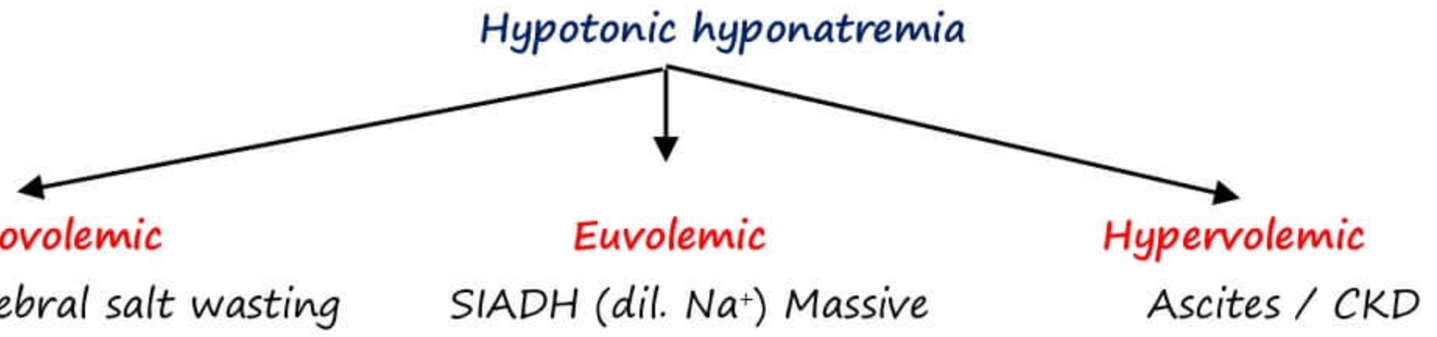
Summary of Hyponatremia



- **Isotonic** (Caused by Laboratory error as explained above)
- **Hypertonic** → Ex- Hyperosmolar coma

Note: - Whenever the Na^+ < 125 mEq in blood, there could be development of Seizures

Rx-

→ **Acute hyponatremia**

- Administering the 3% saline,
- correction of Hyponatremia → 4-8 meq/ day (Gradual rise is better),
- If fast correction is done → **Central pontine myelinosis** or **Osmotic demyelination syndrome** occurs → **Stroke like manifestation- Quadriplegia + Babinski sign +ve**

Na deficit = **wt. x** 0.6 (male) or 0.5 (female) **x** (Desired Na value − Actual Na value)

TBW = wt. x 0.5(male) / 0.6(female)

Na deficit = TBW x (Desired Na value − Actual Na value)

Clinical Scenario:- 60 kg female athlete, marathon runner, collapsed before finishing the race. On examination Na^+ → 120 mEq. Calculate Na^+ correction over the next 24 hours.

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Solution: Na deficit = 60 x 0.5 x (128 - 120)

- 240 mEq over 24 hrs via infusion pump

→ 1000ml of 3% saline = 514 mEq of Na^+

So for 250 mEq we need to give 500ml of 3% saline (Approx) given over 24 hrs

→ so 500/24 = 20.83 ml/hr 3% saline need to be given

→ In case of 0.9% normal saline = 154 mEq of Na and Cl^- in 1000 ml

→ 1 ml N.S. =154/1000 = 0.15 mEq Na^+

→ 1 ml 3% saline = 514/1000 = 0.5 mEq Na^+

Correction formula for hyponatremia

→ **Na deficit = wt. x 0.5/0.6 x** (Desired Na value − Actual Na value)

→ **Desired value is always 8 more than actual value**

→ **So Na deficit = TBW x 8** in 24 hours

2) Hypernatremia

Dangerous Hyper Na+ > 158 mEq/L: leads to development of seizures in a patient.

Rx: Diluted fluids (5% dextrose or N/2 in 5% dextrose)

Cause → Loss of water from body like in extremely debilitated old patients having extreme thirst

→ Lactulose: Osmotic diarrhea

→ Mannitol (Excess doses)

→ DI with loss of water

PrepLadder

Investigation→ Urine osmolality

- If osmolality is < 250 mOsm/L in case of DI with polydipsia and no access to water. Se here water loss in body occurs.
- If osmolality is > 400 mOsm/L in case of extreme sweating

→ In asymptomatic hypernatremia: Liberal H_2O intake

→ Volume of fluid correction in case of Na↑ - 160 mEq

$$= TBw \times \frac{Na+\ actual-140}{140}$$

Q 60 kg female, Na^+ = 160 mEq

$$= 60 \times 0.5 \times \frac{160-140}{140}$$

$$= 30 \times \frac{20}{140}$$

≡ 4 l/day

→ DKA: Sugar ↑: Solvent drag (Water comes out of cell) → K^+ ↑ (Solvent drag)

- K^+ efflux
- $pH\ \alpha\ \frac{1}{K+}$
- K↑ = Negative tubular exertion of NH_3^+ ions → H+ ↑
  → M. Acidosis

→ K ↑ by 0.7 mEq/l for every 0.1 ↓ in pH

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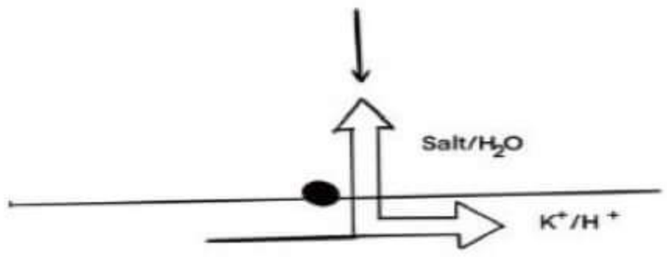
Hypokalemia

→ Death can occur due to respiratory muscle paralysis

Causes

1. Decreased intake
2. Alkalosis: Potassium shift into cells
3. Sympathomimetic stimulation: Trauma, Thyrotoxic periodic paralysis, β2 agonist toxicity (Salbutamol)
4. Renal loss
   - ↑ aldosterone = Conn's syndrome, Bilateral adrenal hyperplasia, ascites, CHF
   - Barter's, Gitelman syndrome
   - Salt wasting nephropathy
   - RTA type 1and 2
5. Vomiting, diarrhea



C/F:

1. Cramp/ weakness **(Earliest)**
2. Ileus
3. Flaccid paralysis
4. Hypercapnia: CO_2 narcosis

Work up:

→ Serum K^+ (Best test)

→ TTKG – Trans tubular K^+ gradient
If > 4 = renal wasting of K^+

PrepLadder

→ ECG: a) T wave – ↓ / absent/ inverted

↓

D/D: Unstable angina

NSTEMI

K↓

b) ST ↓ ⟶

c) Pseudo P-pulmonale ⟶

p wave > 2.5mm in

absence of PAH

d) Prolongation of PR interval

e) Prominent U waves

f) Prolonged QU interval

Complication: Hypo K^+

↓

Arrhythmia

↓

Torsades De Pointes (Hypomagnesemia also causes this)

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Rx: if K+ b/w 3.0 – 3.5 mEq/l → Oral KCL (POTCHLOR)

If < 3 mEq (Can't take orally) → i.v KCl (infusion)

Note – for 1 mEq/l ↑ rise in blood: give 200 mEq of KCl (slow i.v)

Q- Pt. on amphotericin B, K^+ = 2.3 mEq? Calculate correction?

Solution:

- 2.3 mEq → 3.0 mEq: ↑ 0.7 mEq
- 0.7 mEq x 200 → 140 mEq of KCl/24 hrs fluid

→ Central line (Conc of K+ delivered) = 20 mEq/l

→ Peripheral line (Conc of K+ delivered) = 40 mEq/l

Hyperkalemia

→ K+ > 8.0 mEq

→ Causes **diastolic arrest** (Systolic arrest seen when Ca > 13 mg %)

Causes

1. Pseudo hyperkalemia: Fist clenching, narrow bore needle, cooling of sample, TLC ↑. Platelet ↑, RBC↑
2. Acidosis: Trans-cellular shift
3. CKD/AKI
4. Aldosterone ↓ → Addison disease, histoplasmosis, HIV, Waterhouse Frederickson syndrome
5. Gordon syndrome – + gain of fn of NaCl cotransport

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Work-up

→ K↑

→ ECG –

- Tall tented T wave
- ST ↑
- P wave ↓ / (–)if K+ is 7 mEq
- QRS broad
- If > 8.0 mEq : SINE WAVE PATTERN

Rx:

- Antagonism → Ca gluconate (Usually used)
  → Ca chloride (Best)
- **Redistribution** → Insulin drip with 50% dextrose
  → Salbutamol nebulization
  (Dose 4x than asthma)
  ↓
  Symptoms ⊕
- **Removal of K^+** → Furosemide, Resin sodium polystyrene sulphonate, PATIROMER [K^+ binding agent], ZS – 9 (Na zirconium cyclosilicate)

Soda bicarbonate is not routinely used for Mx of metabolic acidosis

Calcium ↓	Calcium ↑
→ Tetany (Death due to Laryngospasm) Rx: I.V 10% Ca gluconate (DOC)	Acute hypercalcemia crisis (Death due to systolic arrest) Rx: 1. Normal Saline 2. Furosemide drip→ Calciuria loss in urine 3. I.V. bisphonate 4. Calcitonin nasal spray 5. I.V. hydrocortisone (in sarcoidosis vit, D_3 intoxication)

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* Hypocalcemia increases neuronal excitability by decreasing threshold potential needed to activate sodium channel.

HYPOMAGNESEMIA

Normal Mg range = 1.3 – 2.1 mEq/l

Causes

1. Diarrohea, alcoholics
2. Thiazides → inhibits TRPM6 which causes Mg reabsorption
3. Amphotericin B
4. Aminoglycosides
5. Renal wasting: Gitelman syndrome

Pathophysiology: ↓ Mg → relaxation of blood vessels
(–) PTH release → ↓ Ca^{++} and ↑ Neuromuscular excitability

C/F:

1. Muscle cramps
2. HTN, HR ↑, arrhythmia (Torsades de pointes)
3. Tremors/ nystagmus / athetosis

PrepLadder

Work up

→ S. Mg^+

→ Urine Mg^+

→ ECG: prolonged QT → Torsades de Pointes

Rx: I.M / I.V $MgSO_4$ / Mg oxide /watch DTRs

Hypermagnesemia

Death d/t Asystole

Cause:

1. CKD
2. Eclampsia: $MgSO_4$ toxicity
3. Antacids/ Laxative abuse

Pathophysiology

→ (-) PTH release: ↓ Ca^{2+}: BV relaxation

→ Neuromuscular excitability ↓ → decreased reflexes

C/F:

1. Shock Non responsive to vasopressors and iv fluid
2. DTR ↓, Respiratory rate ↓: CO_2 ↑
3. Urinary output ↓

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Rx:→ Vigorous iv hydration

→ Ca gluconate

→ Hemodialysis

Summary

Dyselectrolytemia	Cause of death	TOC
NA^+ <125 mEq NA^+ >158 mEq	Seizures	3% saline 5% dextrose
K^+ > 8.0 mEq	Diastolic arrest	Ca gluconate
K^+ < 2.5 mEq	D. Paralysis	KCL drip
Ca^{2+} > 13 mg%	Systolic arrest	Ibandronate
Ca^{2+} < 7 mg%	Laryngospasm	Ca gluconate
Mg^+ > 10 mEq	Asystole	Ca gluconate
Mg^+ < 1.0 mEq	V. Arrhythmia	$MgSO_4$

Metabolic Acidosis

Causes (Mnemonic – **KULT**)

- **K**etoacidosis: DM/ Starvation/ Alcoholic
- **U**remia: AKI/ CKD/ RAS/ ATN
- **L**actic acidosis

PrepLadder

→ Type A: Shock, CO poisoning

→ Type B: D.M/ drugs eg Phenformin, Vancomycin

→ Type D: Short bowel syndrome, Jejunoileal bypass Sx Carb fermentation: Bacterial flora ferment & form D-lactate.

- Toxins

→ **Methyl alcohol** - ↓ Alcohol dehydrogenase **(Antidote of choice → Fomepizole)**

↓

Formaldehyde formation occurs → Retina damage - blindness

↓

Formic acid and H^+ causes damage to BBB causing the Encephalopathy

→ **Ethylene glycol** (Antifreeze agent)

- Consumption can cause precipitation of Ca oxalate crystals and cause ATN

Rx:-

1. **Fluid of choice – Ringer lactate**
2. **Sodium bicarbonate**

If pH <7.2, inspite of fluid resuscitation → give soda bicarbonate.

3. **Total correction → 0.5 x wt. x (24-actual value)**
   - ½ bolus
   - ½ with iv fluid infusion
4. **Initial correction → 0.5 x weight x (15 - Actual value)**

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Metabolic Alkalosis

❖ **In chronic vomiting,**

Loss of H_2O + HCl (Hypochloremia)

↓

Dehydration

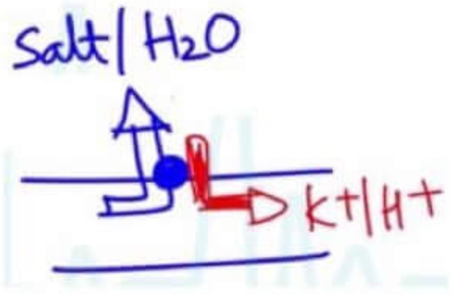
↓

GFR ↓↓ and the activation of **RAAS;**

↓

↑ Aldosterone

↓

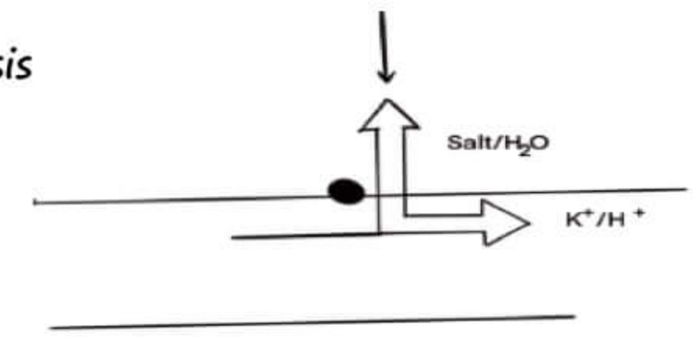


Hypokalemic hypochloremic metabolic alkalosis →

Causes: Congenital hypertrophic pyloric stenosis, Ca stomach, healed peptic ulcer disease.

Rx:- **Normal Saline (0.9%)**

So it is saline / chloride responsive metabolic alkalosis



But if still pH: > 7.55 in spite of fluids +,

➔ Give NH_4CL

DKA:- Insulinopenia: Efflux of K+ out of cell : K ↑

- **RL** (K^+ rich fluid) –so Contraindicated as it will further increases potassium values.
- **Fluid of choice = Normal Saline**
- **TOC:** Insulin drop/ I.V. regular insulin
- **So in all acidosis we give RL but in DKA we give NS**

PrepLadder

❖ In patient with Ascites (Hypokalemic metabolic alkalosis – chloride non responsive metabolic alkalosis).

- Circulating fluid volume ↓ and it affects the GFR ↓↓ and causes the activation of RAAS; and the Aldosterone is release and activation of ENaC channels.
- There occurs the loss of K^+/H^+ and retaining of salt/H_2O,
  so the RxOC → **Spironolactone (Aldosterone antag.)**

Hypokalemic metabolic alkalosis – chloride non responsive metabolic alkalosis

Causes: 1. Nephrotic syndrome
2. Protein losing enteropathy eg celiac sprue, Ménétrier's ds
3. CHF
4. Cirrhosis

Summary

Metabolic alkalosis		
Chloride / Saline Responsive	Chloride / Saline non-responsive	
1. PUD healed 2. Ca stomach 3. CHPS	Ascites → CHF → Cirrhosis → Nephrotic	↑ Aldosterone → CONN → Cushing → B/L adrenal hyperplasia
Rx: Normal saline	**Rx:** Spironolactone and restrict salt intake	

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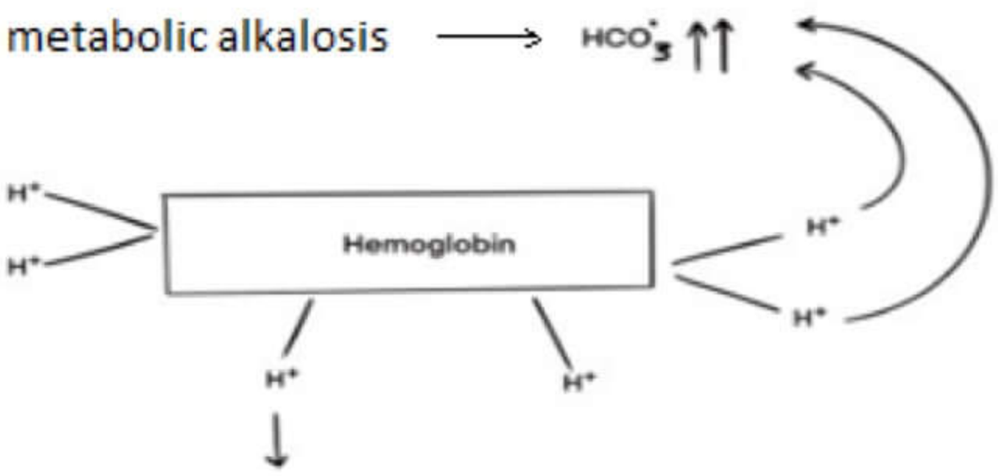
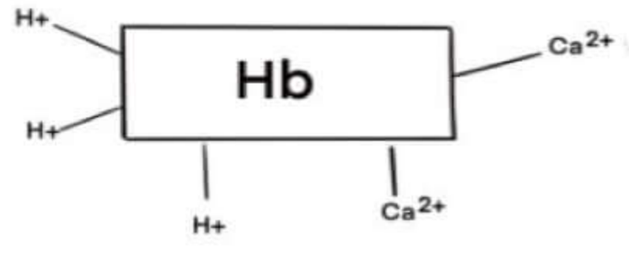


1. Mobilization of H^+ ions to neutralize excess HCO_3^-
2. Creation of vacant site on Hb
3. Vacant sites get occupied by Ionized Ca^{2+}



4. Ionized Ca^{2+} ↓↓ → Tetany (d/t Ca^{2+} re – distribution)

Metabolic alkalosis can lead to Tetany by causing redistribution of calcium.

PrepLadder

Q 3 week old boy baby with diagnosis of : CHPS scheduled for Ramstedt operation
Pre-operation / Ca^{2+}: 6.0 mg%, next best step?

a) Cancel the surgery

b) Ringer lactate → by liver → HCO_3 ↑↑ worsens metabolic alkalosis

c) Cal. Gluconate

d) Normal saline

Ans. Normal saline to correct metabolic alkalosis.

20 year female: Anxiety neurosis, fear of heights, travel by air and hyperventilates causing respiratory alkalosis develops perioral paresthesias, carpopedal spasm?

Rx: Paper bag rebreathing

R. Acidosis	R. alkalosis
$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$	
Causes: 1. Severe acute asthma 2. Flail chest 3. COPD exacerbation 4. Diaphragmatic paralysis - ↓ K^+, GBS, Transverse myelitis, Botulinism - Cervical fracture C3, C4, C5	**Causes:** 1. Hyperventilation 2. High altitude pulm. Edema 3. Pneumonia 4. Pleural effusion 5. ILD 6. Acute asthma

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Summary

M. acidosis → K.U.L.T → Rx – RL / Soda Bicarb
M. Alkalosis → G.O.O → Rx - NS
→ Ascites, endocrine aldosterone → **Rx**: Spironolactone
R. Acidosis → CO_2 ↑ → **Rx**: IPPV
R. Alkalosis → M/c is hospitalized patient
→ CO_2 ↓ → **Rx**: Paper bag rebreathing

Normal values

pH: 7.35 – 7.45 mmHg
po_2: 60-100 mmHg
pco_2: 35-45 mmHg
HCO_3: 22-26 meq (Average = 24 mEq)

CO2 narcosis → Asterixis → Flapping tremors

Cause:

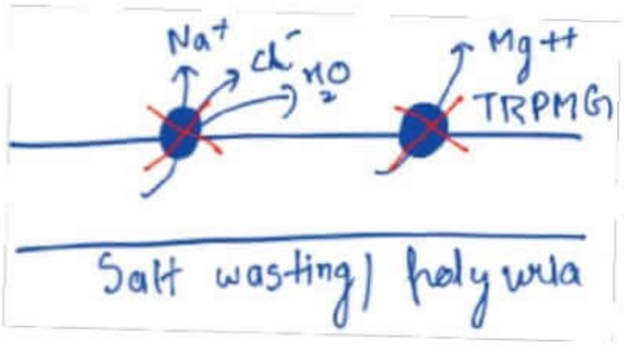
- Ammonia ↑
- BUN ↑
- CO_2 narcosis

PrepLadder

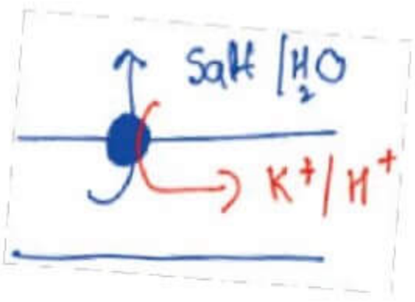
BARTTER SYNDROME, GITELMAN SYNDROME, LIDDLE & COMPARISON WITH SIADH

→ **These disorders are related to tubules of the kidney**

GITELMAN SYNDROME



- Autosomal recessive
- Defect in "**Na^+-Cl^- cotransporter and TRPM6 transporter**" in DCT
- Hallmark feature: **Salt wasting and Polyuria.**
- **Features:**
    - Antenatal H/O: Polyhydramnios
    - Failure to thrive
    - Dehydration: Sunken AF/ delayed skin pinch
    - Diaper change frequency ↑
    - GFR ↓: Renin ↑: Aldosterone ↑
    - Sluggish MORO/ Poor cry - k^+ ↓
    - Metabolic alkalosis
    - **Mg^+ wasting**: Release of PTH ↓ → hypocalcemia (tetany)



(Mg ↓) → tetany

→ WORKUP:

1. Serum Electrolyte: Na^+ ↓ K ↓
2. Urine Osmolality: Low, ↓
3. **24 hour Urinary Chloride: ↑ (IOC)**
4. Serum Mg^+: ↓ ↓

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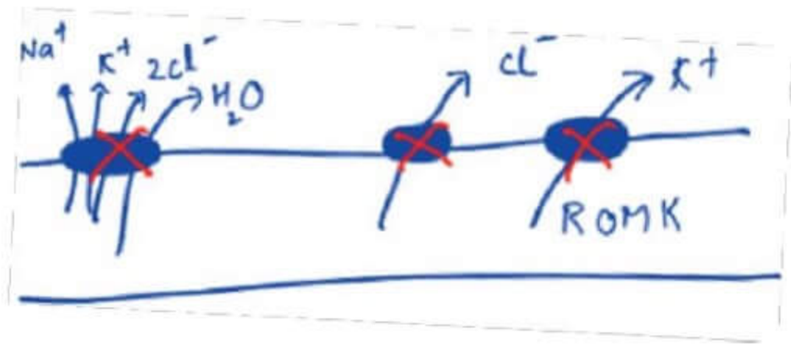
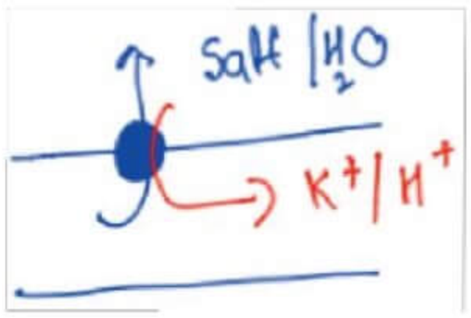
→ RX: No definitive treatment

Clinical profile of Thiazide diuretic is similar to Gitelman syndrome.

BARTTER SYNDROME

- Autosomal recessive
- Defect in "**Na-K-2Cl cotransporter, Cl channel & ROMK**" in loop of Henle
- These channels are responsible for voltage gradient which causes Ca++ reabsorption.
- Hence defect in these channels leads to Ca2+ wasting
- Cl Channel present in inner ear are also defective → SN deafness.
- Manifestations
    - **Salt wasting / polyuria**
    - Poly hydramnios
    - **SN deafness**
    - Failure of thrive
    - Dehydration: Sunken AF/ delayed skin pinch
    - Diaper change frequency ↑
    - GFR ↓: RAAS: ↑ Aldosterone → ⊕ Enac → loss of K+ & H+.
    - Hypokalemic alkalosis
    - **K^+ channel defect: Hypokalemia severity ↑ than Gitelman syndrome**
    - Voltage gradient ↓ which helps in calcium resorption.
    - Calcium wasting: **Nephrocalcinosis**
    - Renal rickets: Delayed dentition, wide open AF, short stature





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→ **WORKUP:**

1. Serum electrolyte: Na ↓, K↓
2. Urinary Osmolality: ↓
3. 24 hr. U. chloride: ↑
4. 24 hr U. calcium: ↑
5. Serum magnesium: Normal

(**Note**: Calcium loss in the patients is sufficient to cause stone formation and renal rickets but not severe enough to cause tetany)

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PrepLadder

→ Rx:

1. Indomethacin (DOC)

   Other conditions in which Indomethacin is DOC -

   - PDA (PT)
   - Acute gout
   - Acute migraine (Mild – moderate)

2. Salt supplement
3. Ca^{+} supplement

GITELMAN (DCT #)	BARTTER (LOH #)
Failure to thrive (Polyuria: ↑ diaper change frequency, dehydration)	

- TRPM6 # → Mg ↓
- Tetany:
  - Periungual Paraesthesia
  - Chvostek sign
  - Trousseau sign
	Calcium wasting:
	- Nephro-calcinosis
	- Renal rickets

Tests: 1. Na ↓, K↓ 2. 24 hour urinary Chloride ↑	
S. Mg^{+} ↓ (1.7 – 2.5 mg%)	24 hr. U. calcium
No drug of choice	Indomethacin

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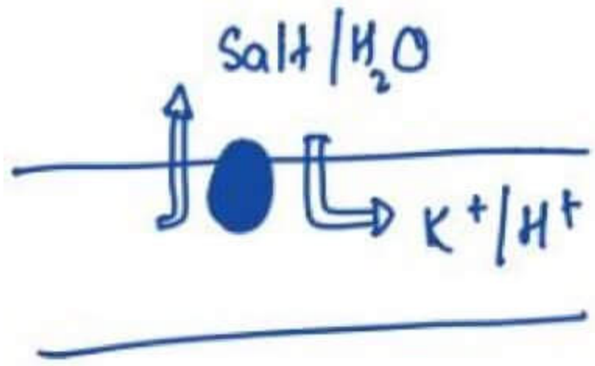
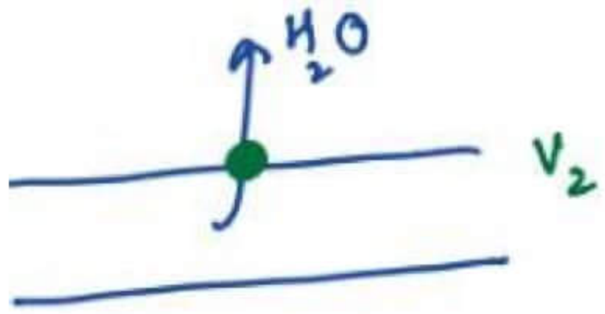
LIDDLE SYNDROME

- Gain of function of epithelial Na channel (ENaC)
- Features:
  1. Gain salt / H_2O:→ HTN
  2. Hypokalemic alkalosis
  3. HTN → feedback RAAS: ↓ Renin: ↓ Aldosterone
     (Low renin HTN)
  4. Dehydration: Absent



→ Rx: Amiloride



DIABETES INSIPIDUS VS SIADH

- ADH/ vasopressin secreted from Hypothalamus
- Acts on Collecting duct Kidney

SIADH: ADH ↑ → ⊕ V_2 → gain of H_2O (still BP normal because Aldosterone regulates BP and not ADH)

Central Diabetes Insipidus: ADH ↓ → Loss of H_2O (BP normal)

PrepLadder

SIADH CAUSES:

1. CNS: Meningitis / encephalitis
   Brain abscess HIV (+): Cerebral Toxoplasmosis
2. Ectopic source: Carcinoid tumor (Kulchitsky cell tumor)/ oat cell Ca lung
3. Vincristine
4. Hypothalamic tumor

ADH ↑ → V_2 ++ → more water reabsorption → "Scanty Urination"

- Renal & Liver parenchymal disease is ruled out as **s. creatinine & LFT is normal**
- Renal tubular disorder:
  - Urine Osmolality: ↑; Plasma osmolality: ↓; Na^+ concentration: ↓
  - **Dilutional hyponatremia**
  - **IOC→ Water loading test**

→ **Rx:**

- Water restriction
- V_2 Receptor blocker: Tolvaptans/demeclocycline.

HYPOVOLEMIC HYPONATREMIA (water ↓, Na ↓)	Diarrhea (Mx → IVF)
EUVOLEMIC HYPONATREMIA (water ↑, Na ↓)	SIADH (Mx → Vaptans)
HYPERVOLEMIC HYPONATREMIA (water ↑↑, Na ↑)	AKI (Mx → Diuretics)

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DIABETES INSIPIDUS

- Central: ADH ↓, Receptor normal
- Nephrogenic: ADH ↑, Receptor abnormal
- Polyuria, Polydipsia
  1. U. Osm: Dilute
  2. P. Osm: Conc.
  3. Na conc.: Na/water ↓ = ↑ **Relative hyponatremia**
  4. Water deprivation test – **IOC**

ADH: Plasma osm. ∝ 1/Urinary Osm.

→ **Rx:**

- **CDI: Desmopressin**
- **NDI: Thiazide diuretics** (Initially thiazide will ↑ diuresis but due forced dehydration, PCT will start reabsorbing more water → Urine output decreases)

Diagnosis of SIADH is best defined by Barter and Schwartz criteria–

1. Hyponatremia with low osmolality of plasma
2. Continued renal excretion of sodium
3. Absence of volume depletion
4. Correction of Hyponatremia by fluid restriction

PrepLadder

CILIOPATHIES / CHRONIC TUBULOINTERSTITIAL DISORDERS

CILIA in kidney located in:

i) PCT

ii) DCT

iii) Collecting Duct

But not in Loop of Henle viz. its primary function is reabsorption of water.

Motile cilia → Lungs, Embryonic Development

Affected in Kartagener syndrome

Non-motile cilia → Collecting Duct of kidney, Retinal pigmentary Epithelium (RPE)

Ciliopathy

1. ADPKD
2. ARPKD
3. Medullary sponge kidney
4. ADTKD (T → Tubulointerstitial kidney) aka MCKD (Medullary cystic kidney disease)
5. Nephronophthisis

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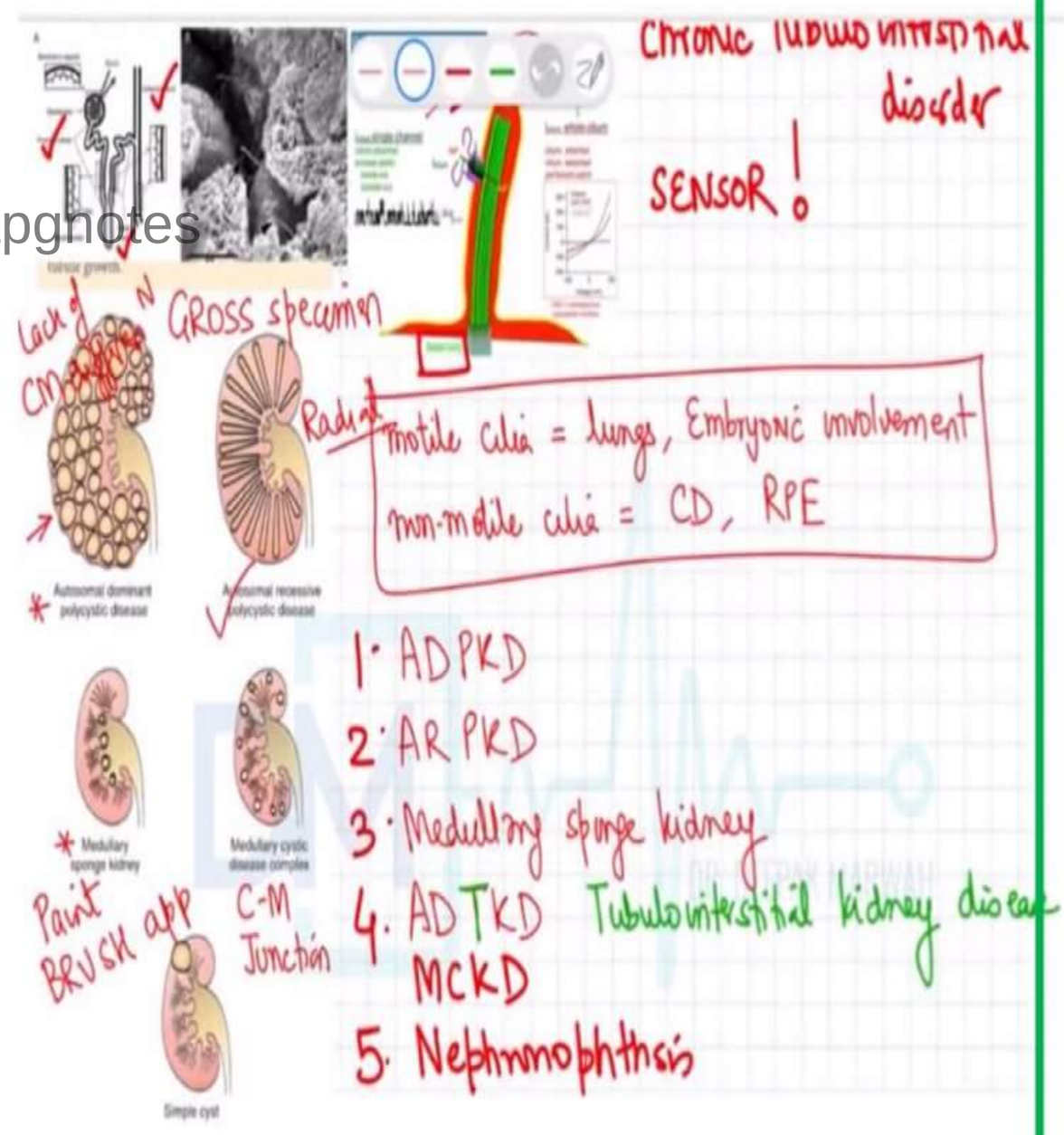
Gross specimen of kidney

1. **ADPKD** → Big cyst where whole kidney parenchyma is replaced by cyst & **complete lack of cortico medullary differentiation**

↓

ADPKD (Usually diagnosed in b/w 30-50 years)

2. **ARPKD** → Renomegaly with radial striations presents across the parenchyma of kidney.
3. **Medullary sponge kidney Disease** → Cysts present in medulla with characteristic **paint brush appearance**
4. **Medullary cystic kidney disease** → Cyst present in **cortico medullary junction** aka (ADTKD)
5. **Nephronophthisis** → Pediatric version of ADTKD



Medullary sponge kidney Disease

→ Sporadic

→ Developmental Malformation of cilia

PrepLadder

→ Cystic Dilatation of collecting Duct (CD)

→ Incidental diagnosis → 50—60 years

Clinical Presentation

1. **Renal stones** → Calcium oxalate (**Recurrent** stones)
2. **Renal UTI/ Pyelonephritis/ Tenderness** at costovertebral junction
3. **Hematuria** → Viz stone in jaggered
4. **Polyuria** → Viz. Tubules and collecting Duct are defective

↓

Reabsorption of water affected

5. **Peritubular cells** → Since peritubular cell affected

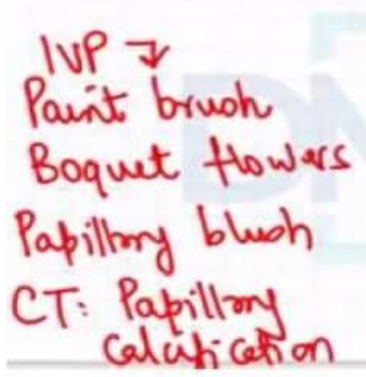
↓

Erythropoietin ↓

Therefore **Anemia (Mild to moderate)**

Anemia also seen in CKD viz Both the glomerulus & Tubules are affected

5. **RTA Type 1** → DCT affected



Investigation

1. IVP: Paint **Brush appearance**

Aka/ bouquet flowers / aka papillary blush

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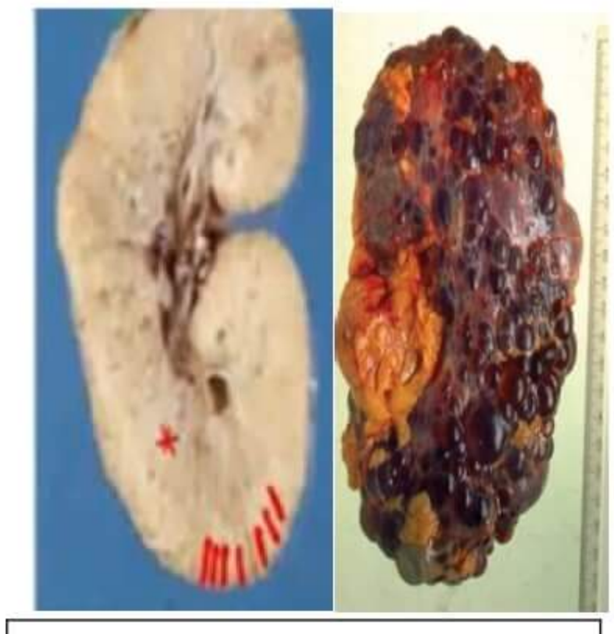
IVP has been discontinued due to risk of Anaphylaxis

2. **On CT Scan** → Papillary calcification

Note → Papillary calcification should not be confused with papillary necrosis

Papillary necrosis seen with:

1. DM
2. Analgesic Nephropathy
3. Sickle cell anemia



Loss of CM Differentiation

PrepLadder

Medullary cyst	Studded with Large Cysts
ARPKD	**ADPKD**

ARPKD

- PKHD 1 gene affected → Chr. 6
- Protein affected → Fibrocystin
  → Polyductin

→ **Distal and collecting duct cyst**

C/F

1. Can be diagnosed as early as 24week of Gestation

Antenatal USG → Echogenic Kidney/ Large Kidney

↓

Loss of CM differentiation

2. **Oligohydramnios** → Viz. Kidney is malfunctioning
3. Pulmonary Hypoplasia → Leading cause of death in neonate.

Note

→ In Barter and Gitelman syndrome → Polyhydramnios

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4. At 1 years → Renomegaly / HTN → ESRD: (HTN) → Leading cause of death in infant.

Extra Renal manifestation of Autosomal Recessive PKD:

1. **Congenital hepatic periportal fibrosis (MC)**

→ Portal HTN

→ Esophageal varices

→ Hematemesis

Note: In ADPDK → Liver cyst

2. **Biliary Dysgenesis**
3. **Caroli Cyst**: Aka Type 5 choledochal cyst

Work up

1. **USG/CT** → Echogenic kidney with loss of cortico medullary differentiation

Rx

1. **ACE Inhibitors** → For HTN

PrepLadder

2. For complications:

$K^+ \uparrow \rightarrow$ Patiromer / SPS (Resin)

3. If disease progress to ESRD, perform **allogenic kidney transplantation**

Extra Renal Manifestation of Autosomal Dominant PKD:

1. Hepatic cyst
2. Pancreatic/ Splenic/ Arachnoid cyst

But pulmonary cyst are not generally encountered

3. MVP (Mitral valve prolapse)
4. Berry Aneurysm
5. Colonic Diverticulosis

ADTKD (Autosomal Dominant Tubulointerstitial Kidney Disease)

Aka Medullary Cystic Kidney Disease

→ Gene affected:

- MCKD1 Genes → Protein affected MUCIN 1
- MCKD 2 Genes → Protein affected UMOD (Uromodulin) aka Tamm Horsfall proteins

↓

These cells are synthesis by Ascending limb of loop of Henle

↓

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Then excreted in form of cast (Hyaline cast)

→ In these condition **Tamm Horsfall proteins are not excreted**

↓

Accumulate in Tubulo-Interstitial cells

↓

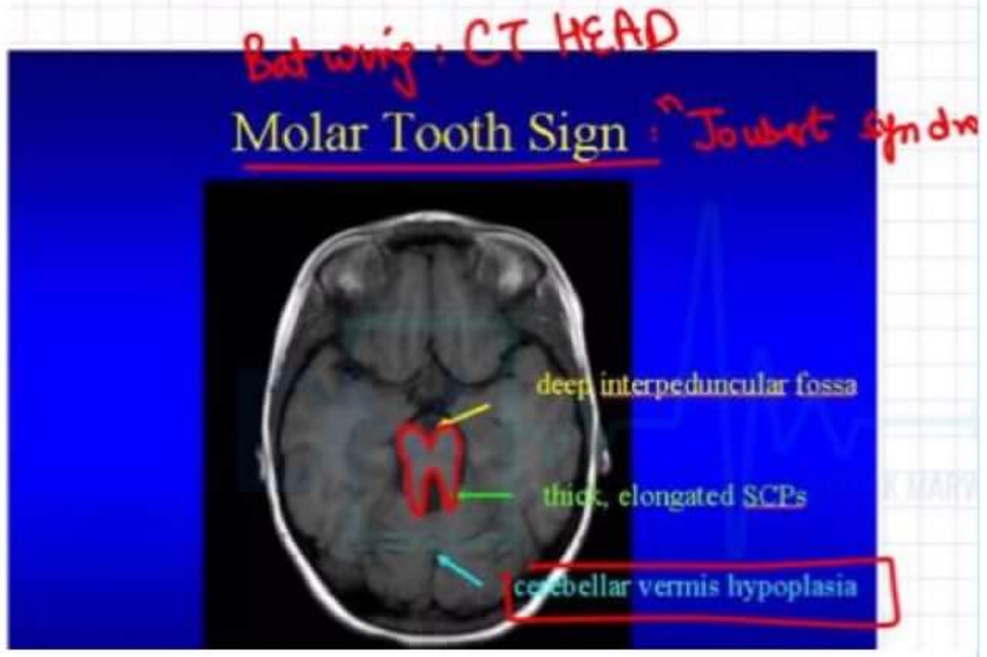
Therefore, these cells are not able to function properly

→ Note: Always have adult presentation

ADTKD	Nephronophthisis
Medullary cystic kidney disease MCKD 1 → Mucin 1 MCKD 2 → UMOD (Uromodulin aka Tamm Horsfall proteins)	NPHP 1 gene → ch – 2 NPHP 2 gene → ch – 9

Adult	Juvenile / Child
→ Salt wasting, polyuria, Anemia, Failure to thrive, Stunting	
Features not seen: → Cast → Dysmorphic R.B.C's	

PrepLadder

→ **Hematuria** – Hallmark feature of glomerular disease	
→ ↑ Uric Acid	→ Associated with **Joubert syndrome** ↓ **C/F:** Agenesis of vermis of cerebellum **Radiological Finding** 1. Molar tooth appearance 2. Cerebellar vermis Hypoplasia. Bat wing on CT Head 

Bat wing CXR : Acute Decompensated CHF

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Bat wing CT head : Joubert Syndrome

Note:

NPHS 1 Gene → Finnish variety of nephrotic syndrome (Nephrin) protein

NPHS 2 gene → Podocin protein

PrepLadder

POLYCYSTIC KIDNEY DISEASE

- **ADPKD** → 75% chances of expression in next generation.
- **ARPKD** → 25% chances of expression in next generation.

- **Chr 16 PKD1 gene defect → Polycystin 1 protein affected**
- **Chr 4 PKD2 gene defect → Polycystin 2 protein affected**

- Multiple cysts present both in medulla and cortex.
- Renomegaly and progressive development of cyst occurs.
- Development of bleeding in cyst can occur and which can cause flank pain.

→ **Clinical features:**

- Usual age of presentation = 30 – 45 yrs

1. **Flank pain** (M/C) [Can be due to stone formation, bleeding in cyst → Gerota fascia stretch]
2. **UTI incidence ↑** : Higher chance of pyelonephritis
3. **Stones incidence ↑** [M/C stone in polycystic kidney = Urate stones)
   (M/C kidney stone otherwise=Oxalate stones)
4. **Can develop RCC** : B/L multicentric

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5. **GFR ↓** because cysts are progressively developing:

Renin concentration ↑

↓

Retention of Na → HTN resulting in daily Headache

Extra renal manifestation (ADPKD):

6. → **Liver cyst** (Lined by biliary endothelium) } Usually asymptomatic
   M/C extra renal manifestation
   → **Pancreas cyst**
   → **Spleen cyst**

6. **CNS**

→ Berry aneurysm → Subarachnoid hemorrhage, warning leaks → Excruciating headache.

→ Arterial dolichoectasia → Malformation in vascular supply of brain – predisposes patient to arterial dissection and can cause Stroke manifestation.

7. **CVS** → Mitral valve prolapse – Mid systolic clicks
   Tricuspid regurgitation → Pansystolic murmur
8. **GIT** → Colonic diverticulosis (Can present as constipation)

PrepLadder

→ M/C cause of death in ADPKD → Hypertension related complications (Left ventricular hypertrophy can be present)

ADPKD → Has High Penetrance (Expressed in almost every generation) and Variable Expression.

→ **Work up of patient of ADPKD:**

1. CT abdomen / USG
2. T_2 Weighted imaging in MRI

→ Contrast study done only after kidney function test as contrast induced nephropathy can occur.

D.O.C for Contrast induced nephropathy → N- Acetyl cysteine, and supportive therapy with IV fluids

> Qs → How many cysts should be present per kidney to say that pt. has polycystic kidney?
> Ans → **> 2 cysts/kidney** [Age group 30-59 yr], and > 4 cysts/kidney after age 60yr

3. KFT: to check BUN/ Creatinine.
4. Serum electrolytes: K+ increases in stage 3 and 4 CKD
5. Genetic linkage study: To identify gene involved
6. MRA head, Echocardiography, Ba enema

→ **Treatment**

1. **Control hypertension** = ACE inhibitors/ARB's
   - Target BP to be maintained → 140/90 mm Hg in pt. of ADPKD (Target BP → 130/80 mmHg in CKD)
2. **Lipid soluble antibiotics** = Cotrimoxazole, Quinolones
   - Culture sensitivity is to be done.
3. **Analgesia** for relieving from pain, because
   (1) Colonic diverticulosis
   (2) Flank pain due to cyst expansion.
   - Abuse of narcotics is present in the patients.
   - There is no role of Gabapentin and Pregabalin.
4. **Transcutaneous electrical nerve pacing.**
5. **Kidney transplant** is recommended in stage 4 patients,
   - if donor is not available then **hemodialysis** can be done, but peritoneal dialysis is not preferred as the kidneys are very big and are occupying a lot of space in peritoneum.
6. **Pre-transplant nephrectomy**
7. **Sirolimus** (mTOR inhibitor) → Inhibits cell proliferation and can reduce progression of cyst.
8. **Tolvaptan** (V_2 ® antagonist) / **Octreotide** (Long acting) - Slows the decline of renal function.
   [ACE inhibitor - slows decline of GFR in diabetic kidney disease]

→ **Common cause of death in ADPKD** = HTN related complications

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PrepLadder

→ **Cause of constipation / abdominal pain of non specific nature** – Colonic diverticulosis (Identified by Ba enema)

→ **Identification of Berry Aneurysm**= MR -Angiography

→ **Mitral valve prolapsed/MR/TR** → Echocardiography for dx

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PrepLadder

T.T.P

Thrombotic Thrombocytopenic Purpura

ADAM TS – 13 (Metalloproteinase enzyme)

→ **Full form** →"A disintegrin and metalloproteinase with thrombospondin motif 13"

→ Disintegration of the ultra large multimers of vWF (Von Willebrand Factor)

→ Absence of ADAM TS-13 – OR Decreased ADAM TS-13

↓

Leads to Microthrombi Formation

↓

Stroke

Micro Angiopathic Hemolytic Anemia (M.A.H.A)

→ Schistocytes/ helmet cells (due to damage because of microthrombi and not antibodies)

(Also seen in A.I.H.A – due to antibodies)

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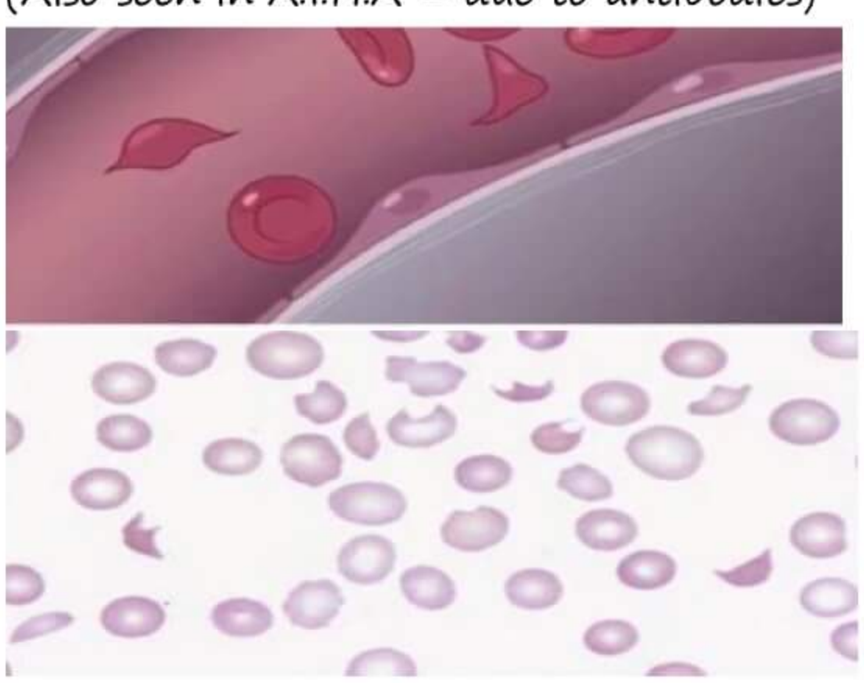


→ **Consumption of Platelets**

↓

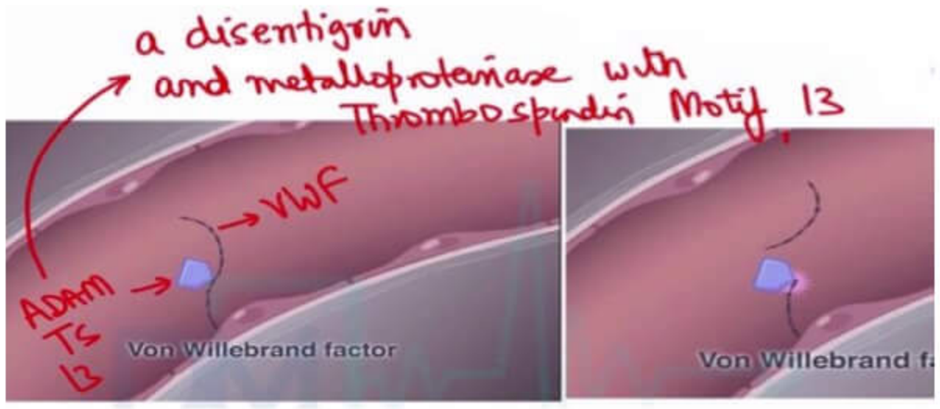
Differential Diagnosis

a) H.U.S

b) T.T.P

c) D.I.C

PrepLadder



Causes of TTP:

a) **Primary/ Idiopathic** → Antibodies which increases clearance of ADAM TS-13

b) **Secondary**

→ Mitomycin – C
→ Gemcitabine
} Anticancer

→ Cyclosporine
→ Interferons
→ Sirolimus, Everolimus
} Immunomodulator

→ Clopidogrel

→ Quinine

→ Bevacizumab – Anti VEGF

c) **Congenital Absence of ADAM TS-13**

↓

aka **Upshaw Shulman disease**

↓

Rx – Multiple Plasma infusion

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d) **Pancreatitis, Malignancy** → Neutrophils produce peptides which inhibits activity of [ADAM TS-13]

→ Clinical features:

(Mnemonic → FAT – NRI)

F – FEVER→ (never presents in H.U.S)
A – Anemia (M.A.H.A)
- Bilirubin ↑↑
- LDH ↑↑
- Reticulocyte ↑↑
- Coombs' Negative

T → Thrombus formation, Thrombocytopenia
N → Neurological features
- Acute Ischemic stroke
- Aphasia
- Hemiplegia

R → Renal failure
I → x

} PENTAD

PrepLadder

→ Work up:

1. ↑↑ PT, ↑↑ aPTT (Because clotting factors are consumed)
2. PBF – Schistocytes
3. **Fibrinogen – Normal (reduced in DIC)**
4. FDP - ↑↑ (Fibrin Degradation products)

   D – Dimer Assay →↑↑
5. Reticulocyte count ↑↑
6. Comb's Negative Hemolytic Anemia
7. ↑↑ LDH
8. NCCT → Acute Ischemic stoke

↓

Hyperdense MCA

↓

Loss of grey and white matter differentiation at **Basal ganglia**

↓

Hypodensity

→Rx

:

1. **Plasmapheresis** – Clearing of Antibodies

↓

x 5 times ~ 10 days

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2. **Upshaw Shulman disease** → Cooled Plasma Transfusions
3. **RITUXIMAB** → Anti CD-20
4. **CAPLACIZUMAB**
5. Hemodialysis → Uremia

TOC → Plasmapheresis

H.U.S (Hemolytic Uremic syndrome) [D+ HUS]

→ Etiology:

- Shiga Toxin producing E. Coli (STEC) → E. Coli O157:H7 → EHEC
- Verocytotoxin / Shiga Toxin
- It causes **complement activation → RBC damage**

→ C/F:

- **Child with Gastroenteritis like symptoms**
- Nausea

PrepLadder

- Vomiting
- Abdominal pain
- Cramping
- **Fever absent**

↓ after 7 days

→ Pallor ++ (M.A.H.A)

→ Scantly Urine output

→ CNS manifestation → Seizures, Encephalopathy, Agraphia

→ Platelets ↓↓ (Thrombocytopenia)

Note: **HSP (Henoch Schoenlein purpura) – Nonthrombocytopenic Purpura (Extensor purpura)**

→ **Pneumococcus** → Neuraminidase ⊕

→ Complements ⊕

→ M.A.H.A (Micro angiopathic hemolytic anemia)

→ A.K.I (Acute Kidney Injury)

Antibiotics should not be given in E. coli but in Pneumococcus, antibiotics should be given.

→ **Atypical H.U.S** → Complement dysregulation (Factor - H deficiency)

Rx

→ **Plasma exchange → Not effective in STEC** (Shiga toxin producing E. Coli)

→ **Stop Antibiotics**

→ **Plasma Infusion/ ECLUZIMAB**

→ Packed RBC

→ Hemodialysis ±

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H.U.S	T.T.P
Child	Adult
H/O G.I illness ↓ 7 days - MAHA (Pallor) - A.K.I - Thrombocytopenia - **Fever absent**	Headaches ↓ Weeks - MAHA - A.K.I - Thrombocytopenia - **STROKE** - **Fever present**
→ **Rx:** - Supportive care - PRBC - Hemodialysis	→ **Rx:** - Plasmapheresis

PrepLadder

ITP (Epistaxis, Petechiae)	HSP (Extensor purpura)	TTP (Headache, AIS)	DIC (Septic patient)
→ Autoimmune → BT ↑ → PT (n) → aPTT (n) → **Rx:** - Steroids and splenectomy	→ IgA + → BT (n) → PT (n) → aPTT (n)	→ ADAM TS 13 ↓ → BT ↑ → PT ↑ → aPTT ↑ → Schistocytes → Fibrinogen (n)	→ Sepsis → BT ↑ → PT ↑ → aPTT ↑ → Schistocytes → Fibrinogen Reduced

HUS (Hemolytic uremic syndrome)	R.V.T (Renal vein thrombosis)
G.I illness ↓ A.K.I → **USG:** B/L Kidney Size (n) → SCHISTOCYTES present → Decreased platelets	G.I. Illness ↓ A.K.I (Acute kidney injury) → **USG:** U/L ↑ Kidney → Painful enlarged Kidney

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URINE ANALYSIS

→ **Proteins in urine:** –

- In normal individual urinary proteins → <150mg/ day

<150 mg/ day

Glomerular	Tubules
– Albumin (<30 mg/day)	– Tamm Horsfall protein / Uromodulin (120 mg/day)

↓

Formed in Ascending LOH

- **Albumin excretion rate:** Can be expressed as
  1. **milligram per day** (mg/ day)
  2. **milligram per gram of urinary creatinine** (mg/gm of urinary creatinine)

Albumin excretion rate (AER) /Urinary albumin creatinine (UAC) ratio:

- 30–300 mg/ gm = **Moderately ↑ albuminuria** (earlier known as Microalbuminuria)
- 300 mg–3500 mg/gm = **Severely ↑ albuminuria** (earlier known as Macroalbuminuria)
- >3500 mg /gm = **Nephrotic Range proteinuria**

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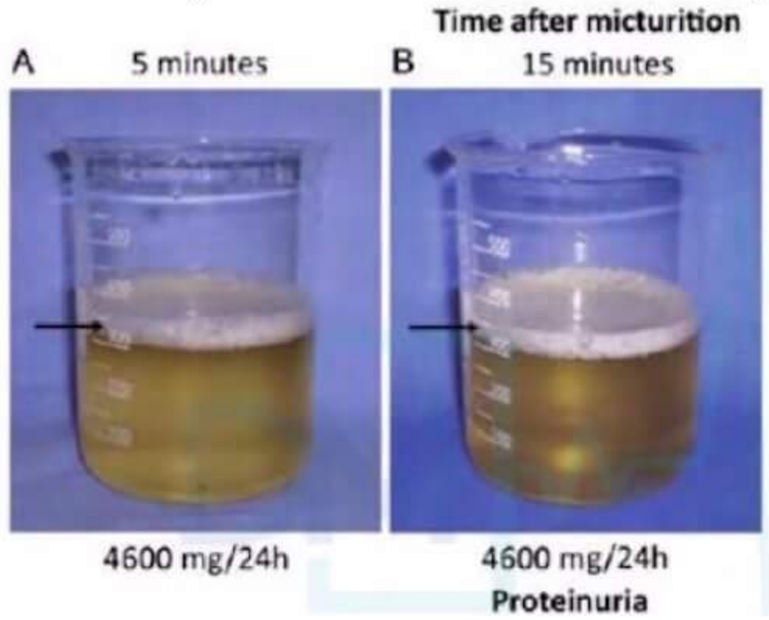
→ Overload proteinuria seen in = Multiple myeloma, Myoglobinuria, Hemoglobinuria



→ **Causes for moderate ↑ albuminuria:** –

- Diabetes Mellitus
- Hypertension
- Glomerulonephritis

- ↑sed risk for cardiovascular mortality

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→ Causes for severely ↑ albuminuria:-

- Diabetes Mellitus
- HTN
- Glomerulonephritis
- Myeloma
- Congestive Heart Failure
- Fever
- Exercise
- Postural proteinuria

→ Causes for nephrotic range proteinuria: -

- Diabetes Mellitus
- Amyloidosis
- Minimal change disease
- Focal segmental glomerulosclerosis (FSGS)
- Membrano-glomerulonephritis (MGN)

→ Dipstick test: -

- Trace → 15-30 mg/dl
- 1+ → 30-100 mg/dl
- 2+ → 100-300 mg/dl
- 3+ → 300-1000 mg/dl
- 4+ → >1000 mg/dl

→ Hematuria: -

- RBC's are also present in urine of normal person
- Significant / Persistent hematuria:
  - >3RBC/ HPF centrifuged specimen x 3 times; at an interval of 1 week

    or
  - >100 RBC /HPF in single sample

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→ Causes of gross hematuria: -

- Urological (90%) > Renal parenchymal (9%) > Hemolysis (1%)

If dipstick test ⊕ hematuria

↓

Centrifuge specimen @ 5 min 1500 rpm

Supernatant **clear** → Hematuria

Supernatant **red** → Myoglobinuria (Clear after 3 hr)/ Hemoglobinuria

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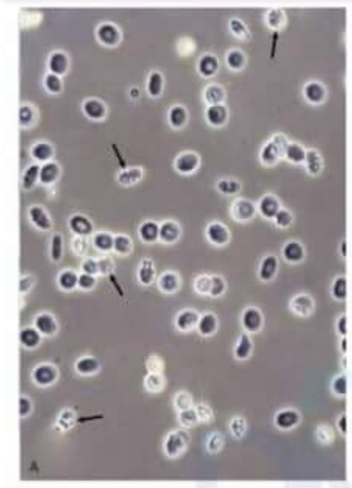
- Dysmorphic RBC's
- Suggestive of glomerular bleed



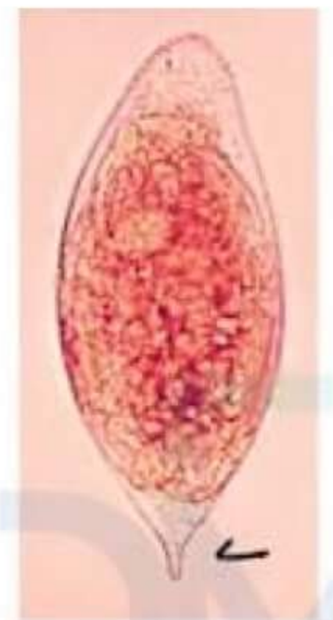
- **Dipstick only identifies albumin**
  - It can't identify para proteins
  - False +ve →If Urine pH >7.0

- Hematuria + Pyuria/ Bacteriuria = UTI
- Hematuria + RBC cast / dysmorphic RBC + Proteinuria

↓

Glomerulonephritis

- Schistosomiasis hematobium:
  - Causes hematuria & fever (known as Katayama fever)
  - Its egg has terminal spine →



→ **Eosinophiluria: -**

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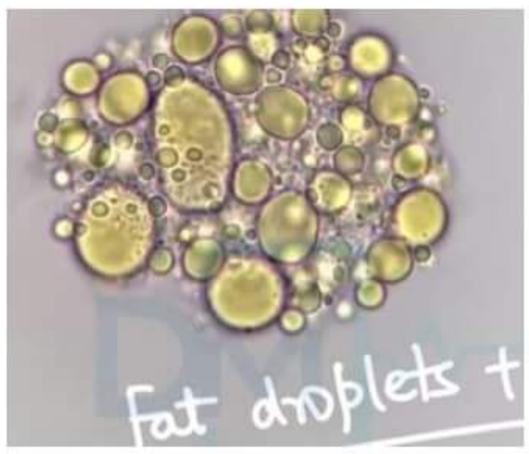
Causes:

- Atheroembolic kidney disease
- Allergic interstitial nephritis

  - **Stain used to evaluate eosinophiluria = Wright/ Hansel's stain**

→ **Fats in urine / Oval fat bodies found in:-**



  - Nephrotic syndrome
  - Fat embolism syndrome
  - Chyluria

→ **Maltese cross appearance:**

In Peripheral smear

↓

Babesia microti

↓

In urine (Polarized microscope)

↓

Fabry's disease (GLA gene involved, lysosomal storage disorder, enzyme defective is alpha Galactosidase A)

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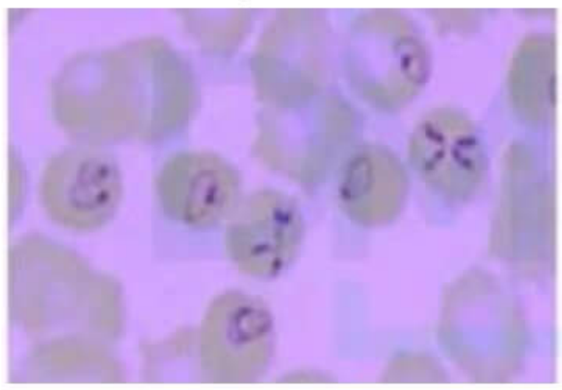
Transmitted by ticks (Ixodes)



(Peripheral smear)

(Polarized microscopy)

- Maltese cross app. In CSF = Cryptococcus neoformans

→ **Specific gravity:**

- Normal = 1.020 – 1.030
- **Isosthenuria** = Inability to concentrate the urine
  - Specific gravity of urine is equal to plasma (1.010)
  - Cause = Chronic tubulointerstitial disease
- Sp. Gravity helps in differentiating Pre-renal vs. Renal cause of AKI
- Pre-renal AKI → sp. Gravity ↑ (normal), while in Renal AKI → sp. Gravity ↓

→ **p.H**

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- Normal pH of urine: 4-4.5

If pH > 5.5

PCT

HCO^-_3 loss → **Bicarbonaturia**

(due to reabsorption defect)

↓

RTA – II

DCT

↓

Inability to excrete H^+

→ **Color:**

- **Pink** = Deferoxamine
- **Pink diaper sign** = Caused by Serratia mascarens
- **Red** = Clofazimine / Porphyria / Myoglobinuria
- **Cola colour** = Hematuria
- **Black** = Hemoglobinuria (PNH/PCH)
- **Black on air exposure** = Alkaptonuria

↓

Prevention by vitamin C

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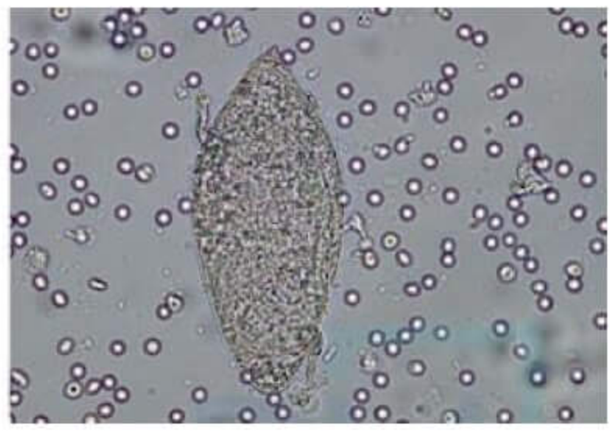
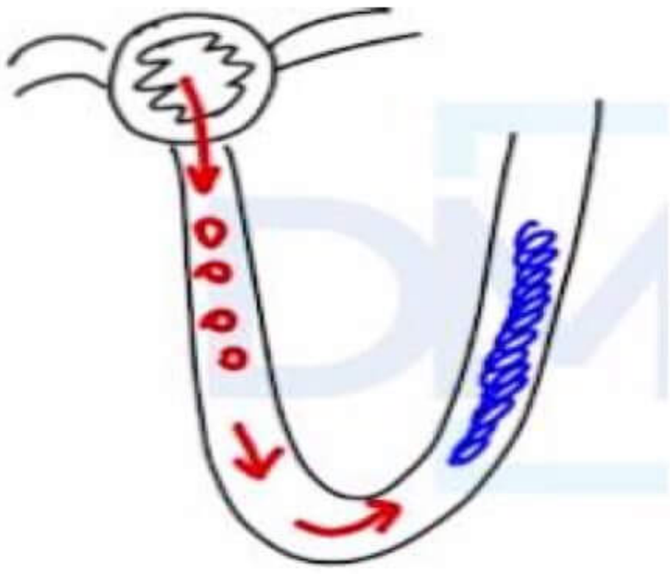
→ CASTS:

- Hyaline cast are seen normally.



  - RBC cast = Acute glomerulonephritis →
  - WBC cast =
    - Acute pyelonephritis
    - Acute interstitial nephritis
  - Broad cast = Chronic kidney disease
  - Muddy brown cast = Acute tubular necrosis



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ACUTE KIDNEY INJURY

Stages	S. Creatinine	Urine Output	Time
I	1.5 – 1.9 times of normal	<0.5 ml/kg/hr	Over 6 hr
II	2-2.9 times of normal	<0.5 ml/kg/hr	Over 12 hrs
III	> 3 times of normal or S. creatinine > 4mg %	<0.3 ml/kg/hr	Over 24 hrs

→ **Biomarkers of acute kidney injury:**

1. **NGAL** = Neutrophil gelatinase associated lipocalcin
2. **K.I.M-1** = Kidney injury molecule – 1 (BEST)
3. IL-18

   All these parameters are checked in urine

→ **ETIOLOGY OF A.K.I:**

1. **Pre- renal cause: Most common cause**
   a. Hypovolemia
   b. Congestive heart failure
   c. Ascites (massive) → circulating fluid volume decreases
      - In a cirrhotic pt. **HEPATORENAL SYNDROME** can develop.
      - It is of two types:

   - **Hepatorenal syndrome I**
     - Pt. deteriorates in as early as 2 weeks
     - ↑↑ s. creatinine >2.5 mg%
     - Normal kidney perfusion ensured by giving IV fluids and stop diuretics but creatinine still continues to rise in HRS 1
   - **Hepatorenal syndrome II** = in case of refractory ascites

   d. Drugs:
      - **NSAIDS** -as PGs are not produced and Afferent arteriolar dilatation does not occur
      - **ACE inhibitors** in B/L renal artery stenosis pt.
      - **Cyclosporine**: acts through altering intrarenal hemodynamics.

2. Renal cause
   a. Glomerulus

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b. Tubules

c. Vascular

a. **Glomerulus:**

- Acute glomerulonephritis
- Post streptococcal GN
- S.L.E
- Good pasture syndrome/ Anti Glomerular Basement Membrane Ds.
- Vasculitis related to ANCA

b. **Vascular:**

- Hemolytic Uremic Syndrome
- Thrombotic Thrombocytopenic Purpura
- Malignant HTN
- **Renal vein thrombosis**
- Athero-embolic kidney ds. → Eosinophiluria is present..

c. **Tubular cause:**

i. **Sepsis:** Toxins can cause tubular necrosis

ii. **Ischemic**

- 20% of cardiac output goes to kidney
- 10% of O_2 consumption is by kidney
- But wt. is only 0.5%
- **Outer medulla is most vulnerable**

↓

S_3 segment of PCT

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- **Post-operative renal ischemia due to prolonged anaesthesia.**
- **Post cardiac surgery**

↓

Cardiopulmonary bypass

↓

Non pulsatile blood flow to kidney → Kidney ischemia

- **Post-operative atheroembolic disease**
- **Burns & acute pancreatitis**

↓

Massive fluid resuscitation

↓

Due to leaky capillaries

↓

Massive ascites

↓

PrepLadder

Abdominal compartment syndrome (> 20 cm H_2O)

↓

Renal vein compression & ischemic damage to kidney

iii. Nephrotoxic

Renal variety of AKI

↓

Exogenous **Endogenous**

Exogenous Causes:

- Aristocholic acid (Chinese herbal medicine)

  ↓

  Balkan nephropathy

- **Aminoglycoside toxicity**

  ↓

  Non oliguric A.K.I (Urine output > 400 ml/day)

  Aminoglycoside damages V_2 receptor in collecting duct
- Amphotericin B
- Cisplatin
- **Contrast induced nephropathy**

  ↓

  Recovery occurs within 7 days

  Antidote: N acetyl cysteine

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Endogenous cause:

- Hemolysis
- Rhabdomyolysis
- Multiple myeloma
- Crystals
  - E.g. If a person consumes antifreeze agent/ ethylene glycol poisoning

    ↓

    Production of Ca-oxalate crystals

    ↓

    Blocks tubules of kidney
  - **Antidote: Fomepizole**
  - **Fomepizole** is also used in **Methyl Alcohol poisoning**

PrepLadder

- Uric acid crystals

  - Chemotherapy in Cancer →Anaplasia (↑↑ Nucleus: Cytoplasm ratio)

    ↓

    More amount of DNA

    ↓

    DNA breaks to produce uric acid

    ↓

    Uric acid crystal causes blockage of renal tubules

When chemotherapy setting is started in case of malignancy

↓

Tumor lysis syndrome

→ K^+ ↑

→ PO_4↑

→ Calcium ↓

→ DNA damage = ↑ **uric acid crystal**

↓

Renal shutdown

- **Management**

- Chemotherapy should always be started in morning hours so that monitoring of pt. can be done

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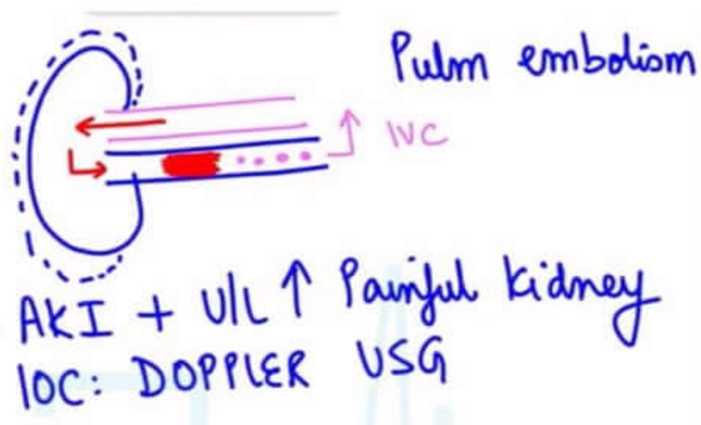
- **For prophylaxis:** Adequate hydration = N.S Drip
- **Treatment: of Tumor Lysis Syndrome:**

I.V Fluid +
Furosemide Drip +
IV allopurinol
IV Rasburicase

} 1st line treatment

- Urine alkalinization is removed from treatment

R.V.T



b. Vascular cause

i. Renal vein thrombosis:

→ AKI + U/L enlarged painful kidney (Hydronephrosis have enlarged but not painful kidney)

→ **I.O.C = Doppler USG**

→ Complication: Pulmonary embolism

Etiology:

- In child → Diarrhea or Dehydration → increased viscosity & sluggish circulation
- In adult → Membranous GN

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ii. Crush injury → Red urine (Myoglobin blocks tubules and causes renal shutdown)

Other causes of red urine
- Porphyria
- Beet root
- Crush injury
- Urological cause

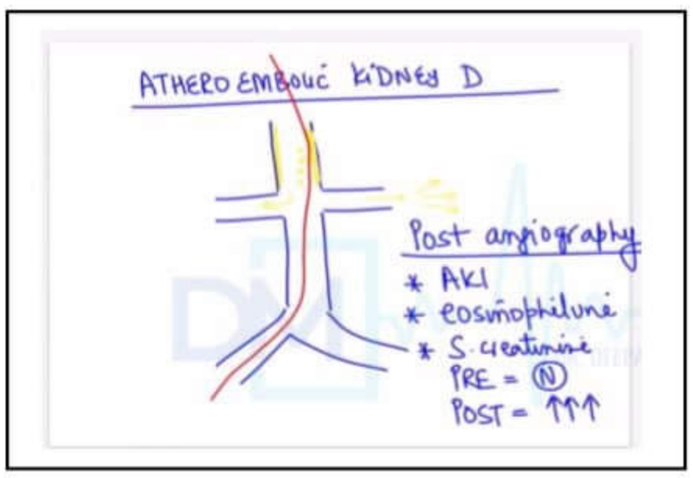
iii. P. falciparum malaria → Hemolysis: Hemoglobinuria →blocks the renal tubules

↓

Black water fever

iv. Athero-embolic kidney disease

- During angiography, guide wire can cause damage to atherosclerotic plaque and multiple small embolic fragments develop which can cause blockage of small renal vessel and cause ischemia of kidney



Post angiography Acute Kidney Injury:

- Eosinophilia
- S. creatinine levels
- Pre procedure = normal
- Post procedure = ↑↑↑
- Prognosis: bad

- Livedo reticularis → fishnet appearance of skin
- Retinal plaques

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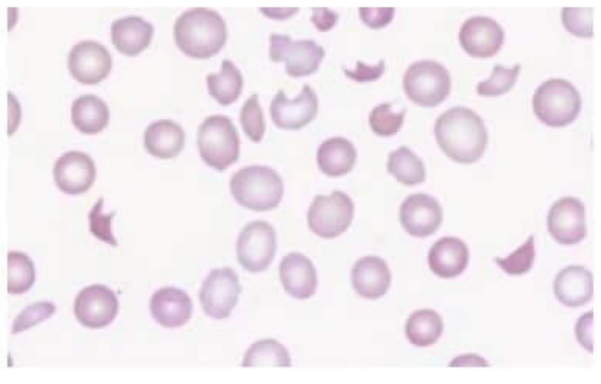
In Contrast Induced Nephropathy

S. creatinine
- Pre procedure =↑↑
- Post procedure =further increases ↑↑↑

Prognosis: Good

Hemolytic uremic syndrome (H.U.S)

- Caused by E. coli O157: H7
- Shiga toxin
- Features:
  - **Complement mediated vasculitis**
  - M.A.H.A (microangiopathic hemolytic anemia)
  - Coombs negative hemolytic anemia
  - **Uremic manifestations** like nausea, vomiting, encephalopathy or uremic pericarditis
  - P/smear: Helmet Cells / Schistocytes



Case: Pt.. had diarrhea/ slight dysentery for which he was managed conservatively, after a week pt. develops severe hemolysis

D_x: Typical HUS or D^+ HUS

→ Atypical HUS/D^- H.U.S = due to drugs

Note: Do not give antibiotics in HUS because antibiotics can worsen the ds. and increase mortality by as much as 17 times.

3. Post Renal causes:

a) B/L stones at pelvi-ureteric junction

b) **BPH**

c) Bladder outlet obstruction d/t stones or tumor

d) Blocked foley catheter

e) B/L ureteric fibrosis could be seen in **scleroderma** or with the use of **bleomycin**

→ C/F of A.K.I:

1. Urea ↑↑ – Irritation of stomach mucosa causes severe vomiting
   – Irritate diaphragm causes hiccough
2. Urea → Pericarditis – Chest pain
3. Urea → Cross Blood Brain Barrier

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↓

Draws water

↓

Cerebral edema

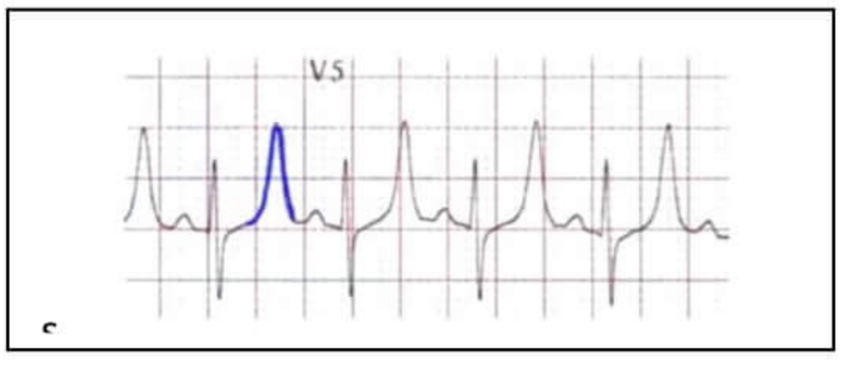
↓

Encephalopathy and develops asterixis (flapping tremors)

4. GFR ↓: Renin ↑ = Hypertensive encephalopathy
5. Volume overload = Puffy eyes
   = Pulmonary edema (dyspnea)
6. Renal shut down = Anuria → U. output < 100ml/day

→ Work up:-

1. Kidney function test: S. creatinine ↑↑
2. Electrolytes = Na^+ ↓ hypervolemic hyponatremia
   K^+ ↑
3. ECG =
   → Tall tented T waves
   → ST elevation



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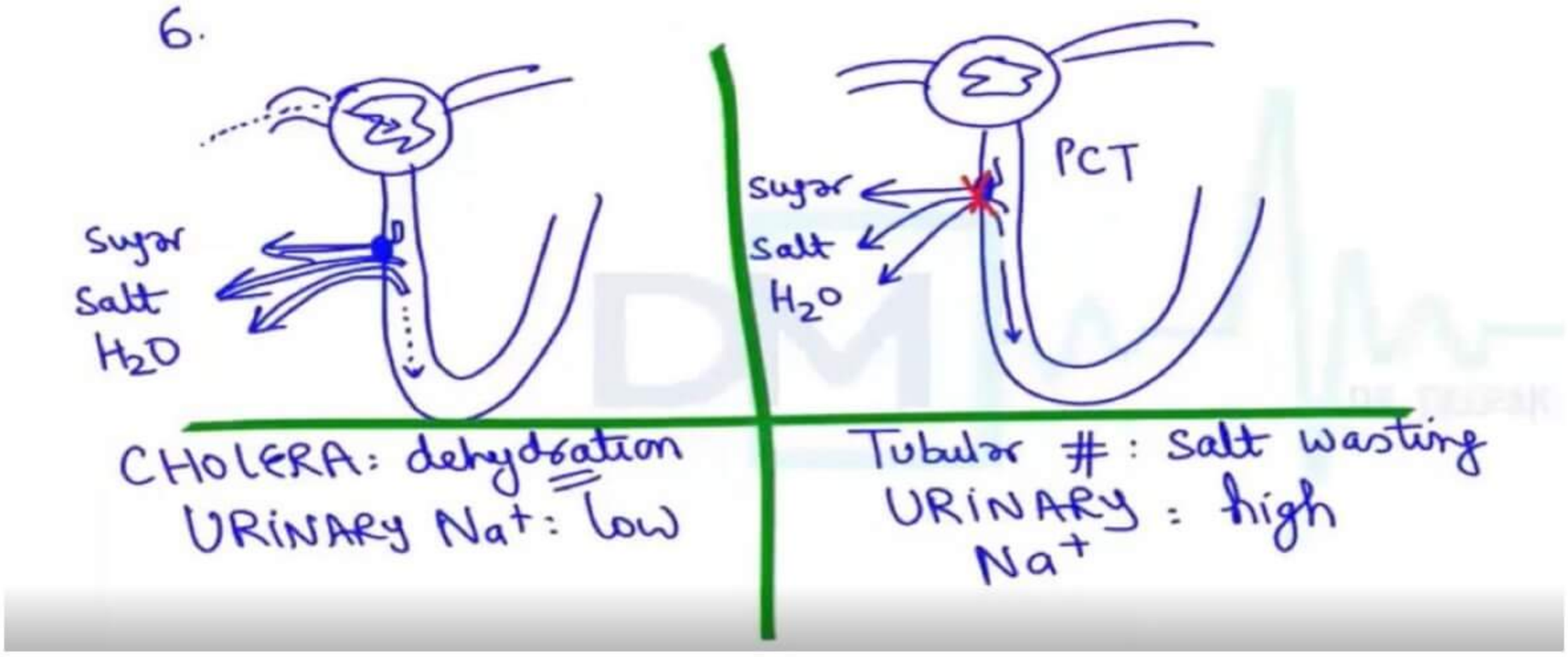
4. USG of kidney = To rule-out post renal causes
5. A.B.G = Metabolic acidosis pH < 7.35

   HCO_3^- <22
6. FeNa (Fractional excretion of Na^+) differentiate b/w Pre-renal & Renal AKI.



PRE RENAL	RENAL
Cholera = dehydration	**Tubular damage** = Salt wasting
Urinary Na^+ = low	Urinary Na^+ = High
Fe Na <1% (fractional excretion of Na^+)	Fe Na >1%
Urine osmolality = High	Urine osmolality =low
> 500 m osm	= 300 m osm

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→ Management of A.K.I:

1. Input fluids = urine output last 24 hr

   +

   Insensible losses (400 – 800 ml)

   - Water vapor during breathing
   - Stool

   - 10% dextrose is the fluid used
2. Furosemide drip
3. If Na^+ <125 meq → causes seizures

   then give 3% saline
4. If K^+ >6.5 meq → give Ca- Gluconate (antagonize K^+ effects)

- Insulin drip regular (only this causes K^+ influx into cells) - Most Effective drug
- Salbutamol nebulization
- **Hemodialysis → most effective method for acute ↑ K^+**

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5. If pH <7.2 = IV soda Bicarbonate is given
6. HTN crisis / encephalopathy

   ↓

   Give IV labetalol or

   IV fenoldopam or

   IV Nicardipine
7. Uremia: Hemodialysis is done → through Int. jugular vein or subclavian vein

Recovery phase of A.K.I characterized by:

- Polyuria
- ↑↑ Na^+
- ↓↓ K^+

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CHRONIC KIDNEY DISEASE

Definition → progressive nephron loss in a patient.

Chronic kidney disease: -

Test to determine GFR:

1. "CKD – EPI - Cystatin C" method (BEST)
2. Modification of diet in renal disease (MDRD) formula.
3. Cockcroft Gault formula
4. Creatinine clearance
5. Inulin clearance

- Cystatin – C is produced by nucleated cells
- Cockcroft gault formula:

$$\frac{(140 - \text{Age}) \text{ x wt.}}{72 \; x \; S.creatinine}$$

→ **CKD =GFR ≤ 60ml/min/1.73m² + proteinuria x 3 months**

Grading: -

- G_1 = ≥ 90 ml/min/1.73 m²
- G_2 = 60 – 89 ml/min/1.73 m² (HTN develops in this stage)
- G_3 = 30 – 59 ml/min/1.73 m² (Anemia develops in this stage)

From G2 TO G3 transition, value of PTH INCREASES thus increasing the bone turnover but despite being PTH INCREASE the phosphate levels INCREASES from G3 to G4 transition as kidneys are not working properly.

- G_4 = 15- 29 ml/min/1.73 m² (Acidosis, hyperkalemia develops in this stage)
- G_5 = < 15 ml/min/1.73 m² (URAEMIA develops)

- Spot urine sample - Ratio of Urine albumin / Urine creatinine

  - A_1 → <30 mg/g
  - A_2 → 30-300 mg/g
  - A_3 → >300 mg/g

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				Albuminuria categories		
				A1	**A2**	**A3**
				Normal to mildly increased	Moderately increased	Severely increased
				<30 mg/g <3 mg/mmol	30-299 mg/g 3-29 mg/mmol	≥300 mg/g ≥30 mg/mmol
GFR Stages	**G1**	Normal or high	≥90			
	G2	Mildly decreased	60-90			
	G3a	Mildly to moderately decreased	45-59			
	G3b	Moderately to severely decreased	30-44			
	G4	Severely decreased	15-29			
	G5	Kidney failure	<15			

→ Causes of CKD: -

1. Diabetic nephropathy (m/c)
2. Chronic glomerulonephritis
3. Ischemic nephropathy
4. ADPKD
5. Chronic tubulointerstitial disorder

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→ Treatment

a) G_1 to G_3 CKD treatment: -

Mnemonic = ABCDEK

i) Keep HbA_{1c} <7%

- Stop metformin as it is excreted by kidney.
- Metformin is contraindicated if S. creatinine >1.5 mg%
- Give insulin injection
- Dose reduction is required to avoid increase risk of hypoglycemia as insulin is not effectively excreted (80% calculated dose)

ii) BP control

- CKD pt. have high Renin Hypertension
- Target BP < 130 / 80 mm Hg
- Drug = ACE inhibitor/ ARB + CCB(calcium channel blockers)

iii) Cholesterol control

- CKD pt. have ↑ cholesterol
- Target = LDL<70 mg%
- Drugs = Statins → Atorvastatin

PrepLadder

iv) Low Vit. D_3

- Vit D_3 synthesis – occur in PCT (by 1α Hydroxylase enzyme)
- Hypocalcemia- activates Ca SR(Calcium sensing receptor)
- ↑ PTH (2° Hyperparathyroidism) (high bone turnover rate)
- Bone pain / pathological fracture of ribs
- Subperiosteal resorption of phalanges →
- PTH causes bone marrow fibrosis

↓

Osteitis cystica fibrosa (Brown tumor)

- This is known as Azotemic osteodystrophy/ high bone turnover state
- Rx → - Sevelamer (phosphate binder)
  - lanthanum Carbonate (Phosphate binder)
  - Calcium Acetate
- PTH release inhibitor = Calcimimetic drug (Cinacalcet)
- Low bone turnover rate can also be there

↓

Due to more/excess calcium supplementation + vit D3

↓

↑ Ca^{2+} leads to ↓ PTH (low bone turnover)

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- 1° PTH ↑ = Parathyroid Adenoma
- 2° PTH ↑ = CKD
- 3° PTH ↑ = Untreated 2° hyperparathyroidism leading to autonomous function of parathyroid gland.

v. Erythropoietin → low

↓

Anemia (Normocytic normochromic)

→ Causes of Anemia in CKD:

1. ↑ PTH → Cause BM fibrosis
2. Anemia of chronic disease
3. Bleeding manifestations

→ Rx of Anemia: -

- Iron parenteral
- Erythropoietin s/c or i/v
- Darbepoetin, Epoetin B

Synthesis:

- Renin = JG cells
- Vit D_3 = PCT
- Erythropoietin = Peritubular cells

S/E = Cardiovascular accident ↑
MI risk ↑

PrepLadder

vi. K^+ ↑ – Hyperkalemia

→ Rx: –

- Sodium polystyrene sulphonate (SPS resin → K^+ binders)

  S/E → Necrosis of GUT
- Patiromer
- Sodium zirconate cyclosilicate (Zs-9)

Summary: –

G_1– G_3 CKD patients: –

A = Insulin (low dose)

B = ACE – / ARB + CCB (target BP < 130/80)

C = Statins (LDL < 70 mg%)

D = PO_4 ↑ (phosphate binders-sevelamer/ lanthanum), cinacalcet

E – Erythropoietin s/c or i/v

K = Patiromer / SPS

G_4 → **Renal replacement therapy:**

1. Dialysis

2. Allogenic kidney transplantation

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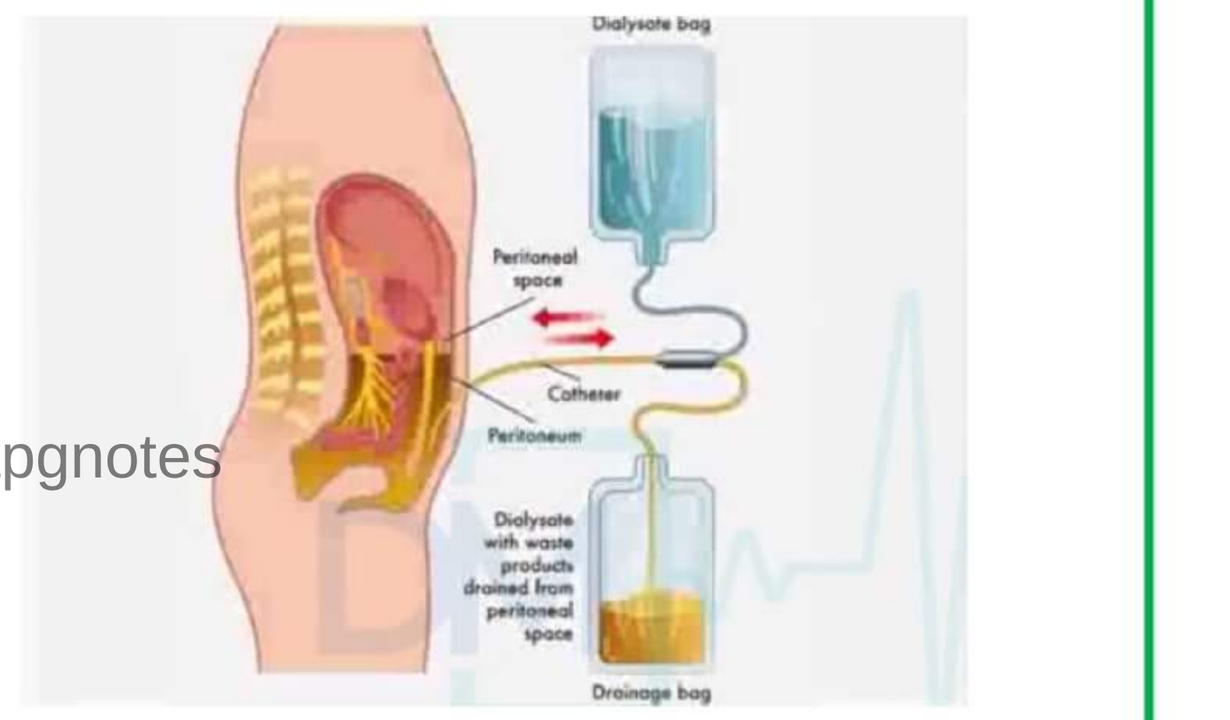

– Hemodialysis

- 3 times / week
- 1 session = 4 hour
- 12 hr per week

– Peritoneal dialysis – risk of infections.

→ Allogenic kidney transplant

- HLA matching mandatory
- Blood group matching is also required

–HLA matching not mandatory in : –

- Liver
- Cornea
- Heart

- Test for donor = HIV, CMV, Hep. B, Hep. C, Syphilis, & **Doppler (to rule out U/L Renal artery stenosis)**

→ In Donor, left kidney is removed (because of longer left iliac vein).

→ New kidney is placed in right iliac fossa because of ease of removal.

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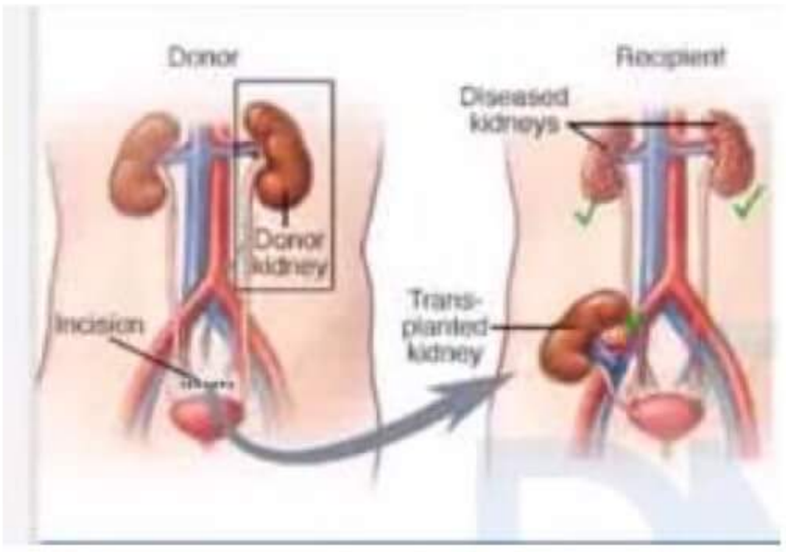
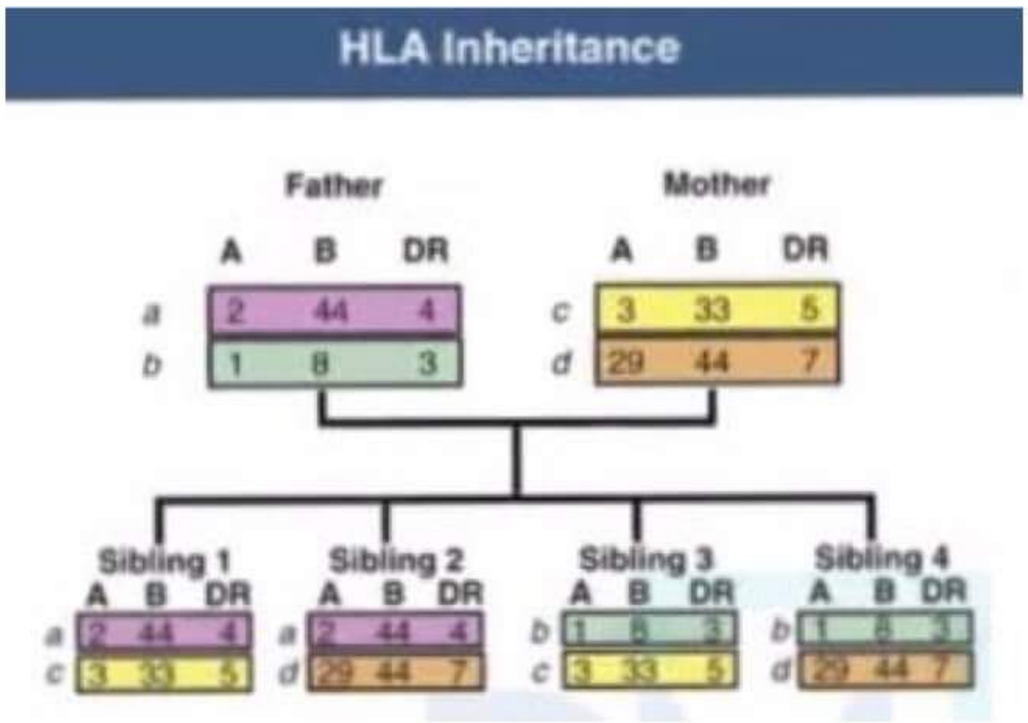


- HLA inheritance : -



- HLA A, B, C, DP, DQ, DR
- HLA matching is done for A, B, DR for kidney transplantation

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1/6 – 2/6 Match Occurs	3/6 Match Occurs	4/6 – 5/6 Match Occurs
↓	↓	↓
Induction with anti-thymocyte globulin (A.T.G)	Induction with Basiliximab (Anti CD 25)	No need for induction, only maintenance therapy

→ Rejection: -

	Hypersensitivity reaction	Time
1. Hyperacute	II	Minutes
2. Acute	IV	<6 months
3. Chronic	IV	>6 months

→ Maintenance therapy: -

- Steroid
- Tacrolimus/ cyclosporine
- Mycophenolate
- Azathioprine
- Sirolimus (non-nephrotoxic)-mTOR inhibitor

PrepLadder

→ Opportunistic infection post kidney transplantation –

• **<1 month** – Surgical site infection (SSI) with MRSA
• **1–6 months** – Pneumocystis jiroveci – **Cytomegalovirus (CMV)** – Hep B and C
• **>6 month** – Aspergillus – Nocardia – Bk virus (polyoma virus)

- CMV – m/c infection that is responsible for graft failure after kidney transplantation./ solid organ transplantation.
- CMV – m/c infection after hematopoietic stem cell transplantation
- EBV – m/c cause of post transplantation lymphoma
- M/c malignancy post kidney transplantation – skin cancer

→ **Hemodialysis:**

- CIMINO – BRESCIA FISTULA

Radial Artery – Cephalic vein is connected

↓

BRUIT/ DOPPLER used to identify patency of fistula

↓

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ARTERILIZATION OF VEIN

↓

THROMBOPHLEBITIS incidence is reduced

- Complications of hemodialysis: –
  - Hypotension (M/c)
  - Accelerated atherosclerosis (m/c in Recurrent hemodialysis)
  - Dialysis dementia (Due to $A\beta_2$ amyloid deposition)
  - Carpal tunnel syndrome
  - Dialysis disequilibrium (Cerebral oedema, seizures)
  - Peripheral neuropathy / myopathy

- Principal of hemodialysis:
  - 1. Diffusion (Main)
  - 2. Solvent drag (Ultra filtration)

PrepLadder

DIABETIC NEPHROPATHY

→ Most common causes of C.K.D (Chronic kidney disease)

→ Most common indication of Kidney Transplantation

DM $\xrightarrow{HbA_1C > 7\%}$ Nephropathy

Type-1 DM – 5 years

Type-2 DM – 20 years

→ B/L enlarged kidneys → Differential Diagnosis

a) HIV associated Nephropathy
b) Amyloidosis
c) Diabetes Mellitus
d) Polycystic kidney disease
e) Hydronephrosis

→ Painful unilateral enlarged kidney with Acute kidney Injury

↓

Renal vein Thrombosis

→ Screening

a) Albumin Excretion Rate
b) Urine Albumin creatinine Ratio

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→ Spot urine sample

- Urinary Albumin Creatinine Ratio
- Albumin (mg) / urinary creatinine (gm)

↓

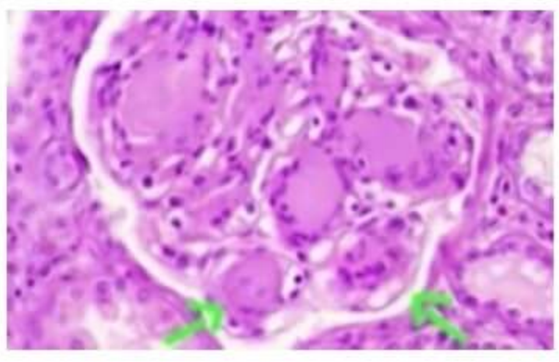
$$\text{Spot sample} = \frac{\textit{Albumin (mg)}}{\textit{Urinary creatinine (gm)}}$$

→ 30-300 mg/gm (moderately ↑ albuminuria)

→ Serum creatinine may be Normal

- Rises late (After 60% of kidney damaged)
- Most specific Kidney function test

→ Kidney Biopsy



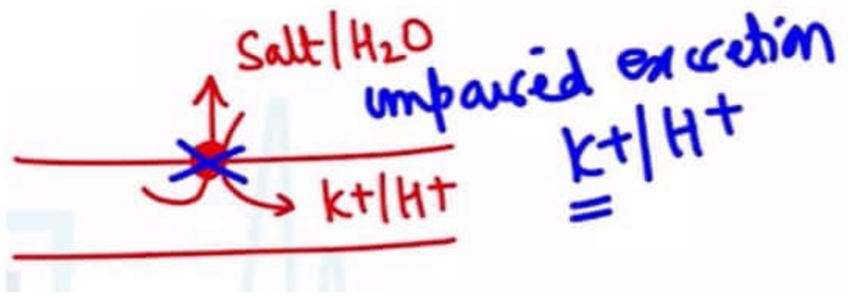
1. Nodular glomerulosclerosis → Kimmelstiel Wilson Change
   → Most specific
2. Diffuse Glomerulosclerosis
   → m/c kidney biopsy findings
3. Armani Ebstein change: PCT
4. Damage to DCT leads to development of Type – 4 RTA (Renal tubular acidosis)

PrepLadder

→ Thus ENaC (Epithelial sodium channel) become defective.

→ Resulting in aldosterone resistance:

- Impaired excretion of K+/ H+
- Use ACEI cautiously.
- ↑↑ K+ can result in cardiac arrest.



→ GFR in Diabetic Nephropathy

- Initial 0-5 years: GFR ↑↑
  - → Glomerular hyperfiltration
  - → Glomerular Hypertrophy
- 5-10 years → Albuminuria → Irreversible damage.
  - → False (+)ve albuminuria:
    - HTN
    - CHF
    - Pyelonephritis

→ Co-existing: Complications in DM at onset of Albuminuria

1. HTN
2. Non healing ulcer
3. Peripheral vaso-occlusive disease
4. Retinopathy: Blindness

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→ Treatment

1. Stop Metformin / Sulfonylurea

Glipizide
Linagliptin
} Can be given in kidney disease as they are **metabolized by liver**

2. Initiate Insulin: 80% of calculated dose
3. Target BP < 130/80 mm of Hg if Tolerated
4. ACE Inhibitor / ARB

↓

Side effect → Hyperkalemia (due to Type IV RTA)

5. **Treatment of Hyperkalemia**
   a) K^+ Binding Resins - Sodium polystyrene sulfate
   b) Patiromer

Transplant indication

→ GFR < 20 ml/min/ 1.73 m^2.

PrepLadder

KIDNEY STONES

1. Calcium Oxalate – Most common

- Leading cause: **Idiopathic hypercalciuria**
  (Defective handling of calcium)
- TEST : 24 hour urinary calcium ↑↑

→ **WORK UP**

1. Urine microscopic examination–
   - Shows "Envelope shaped" crystals
2. 24 hr urinary calcium is elevated

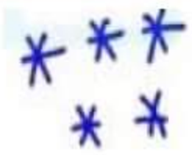
→ **TREATMENT**

- Thiazides MOA : (↓ Urinary calcium excretion)
- Normal calcium & vit. D3 and low sodium diet.

Note: Furosemide : ↑ urinary calcium excretion (Contraindicated)

EXTRA MILE– Calcium monohydrate oxalate crystals are found in individuals with ethylene glycol toxicity and have "dumbbell/picket fence" form.

2. Calcium Phosphate Stones:



- Microscopy Urine : Rosette crystals/blunt end needles
- Seen in:
  a. Hyperparathyroidism → ↑ Ca^{2+}
     [R_X – Resection parathyroid adenoma]
  b. Hypoparathyroidism (phosphate ↑)
     [R_X– Teriparatide injection]

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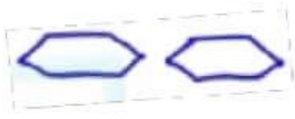
Whenever multiplication product of Calcium x PO4 > 55, the two chelate and get deposited in tissues

3. Triple Phosphate Stone:

- Magnesium ammonium phosphate ($MgNH_4PO_4$)
- Due to alkaline nature of urine
- Proteus mirabilis urease positive
  Splits urea → ammonia (alkaline media) → precipitates $MgNH_4PO_4$ stones
- Crystals – coffin lid appearance
- Very big stones
- Take shape of kidney
- STRUVITE stones and STAGHORN calculi



→ **TREATMENT:**

- Elimination of proteus (Antibiotics / Aceto-hydroxamic Acid): Irrigation of parenchyma kidney

PrepLadder

4. Urate Stone:

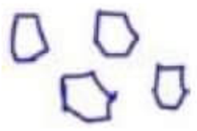
- Softest
- No particular shape of crystals
- Can be - rhomboid/ rosette/ barrel shaped
- Formed in acidic urine
- Cause: Chronic gout
- TEST: 24 hr urinary uric acid to differentiate between

Over producer (Allopurinol) Under excretor (Probenecid)

Extra Mile:

- Ammonium urate crystal appear as brown spherical bodies with irregular protrusions resembling thorn apples
- Cholesterol crystals in urine can be seen in nephrotic syndrome.

5. Cystine stone:



- Hardest stones
- M/e: "Hexagonal crystals"
- Etiology - Cystinuria d/t AR defect, there is defective proximal renal tubular reabsorption of cystine
- Sodium cyanide nitroprussiate test is the initial screening test.
- It gives an intense purple color.
- Urine may have rotten egg smell
- Rx: Cystine stone = d - penicillamine / tiopronin

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6. Xanthine Stone:

- Irregular shape
- Xanthinuria: Deficiency of xanthine oxidase.
- Rx: Xanthine stone = d - penicillamine / tiopronin

→ Clinical Features:

1. Renal colic / flank pain
   - Radiating to umbilicus or vulva or tip of penis
2. Reno gastric reflex → Vomiting
3. Hematuria gross
4. Flank pain → Umbilicus / Tip of penis / Uvula

→ IOC:

- For renal stones CT abdomen (Non contrast)

PrepLadder

- For ureteric stones: CT abdomen (Non contrast)
- KFT
- Urine microscopic examination

→ **Treatment**

- SURGICAL MANAGEMENT:
  - Renal Stone < 2 cm : Extracorporeal shock wave lithotripsy (ESWL)
    (More than once in cystine stone)
  - Renal stone > 2 cm : Percutaneous nephrolithotomy (PCNL)

→ **ESWL contraindicated in (Absolute CI):** Pregnancy, bleeding diathesis

→ **Radiolucent stones (LUX: Mnemonic)**

Lucent → Urate, Xanthine

Extra Mile:

- Stone development **independent of pH urine:** Ca Oxalate
- Secondary xanthine stone is seen in case of treatment with allopurinol of severe hyperuricemia associated with myeloproliferative disorders and Lesch nyhan syndrome.

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RENAL TUBULAR ACIDOSIS

RTA – 1

- Distal convoluted Tubule (DCT) involved.
- α Interrelated cells responsible for H^+ excretion
- β Interrelated cells responsible for HCO_3^- excretion

In RTA-1, α Interrelated cells are not working

a) Impaired H^+ excretion
b) Impaired NH_4Cl excretion
c) Salt wasting → ↑ ↑ Aldosterone

} Electro neutrality maintenance is function of kidney.

d) Hypokalemia
e) Metabolic Acidosis which impairs tubular reabsorption of Ca^{+2} leading to

↓

Nephrocalcinosis

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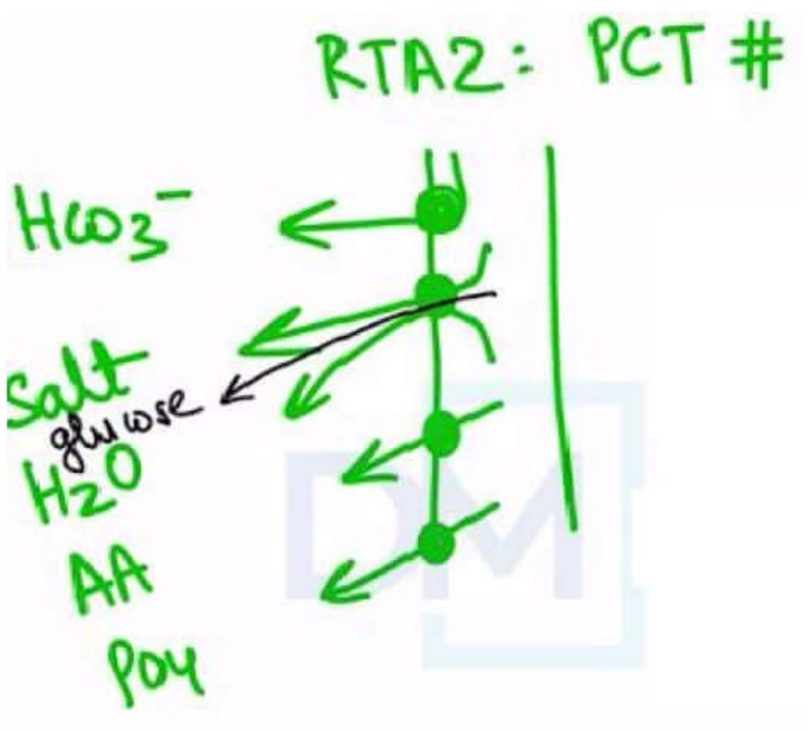
→ Causes: Multiple Myeloma
Scleroderma
Amphotericin – B

→ Treatment: Oral soda Bicarbonate

RTA -2

- PCT (Proximal convoluted Tubule) involved
- Associated with Fanconi syndrome
- Characterized by:
  - Bicarbonaturia,
  - salt wasting,
  - polyuria,
  - aminoaciduria,
  - glucosuria,
  - phosphaturia



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→ Etiology:

a) Multiple Myeloma

b) Wilsons disease

c) Expiry date Tetracycline

→ Treatment:

1. Thiazides: Cause Volume contraction → Metabolic Alkalosis
   - GFR ↓↓: RAAS activation
   - Aldosterone ↑↑ (Leads to increase H+ Excretion thus causing alkalosis and neutralizing the acidosis component).
2. Soda Bicarbonate

RTA-4 (m/c type RTA)

→ Etiology: Aldosterone is not able to function (d/t Resistance/Deficiency)

a) Diabetes Mellitus – Most common association

b) AIDS

c) Chronic Tubular Interstitial disorders

d) Hypertensive nephrosclerosis

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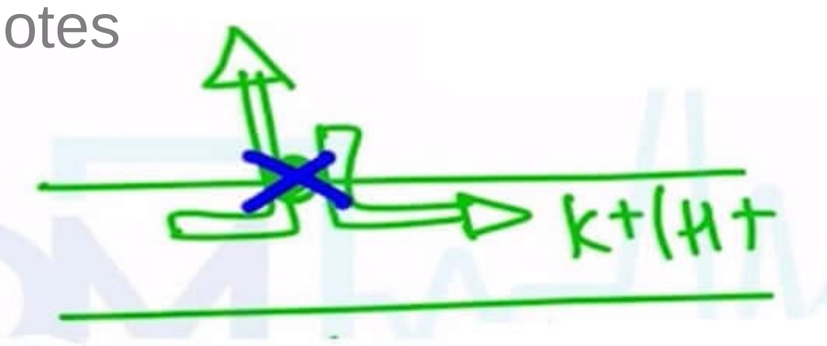

→ C/F:

1. Salt wasting/ polyuria
2. Hyperkalemia
3. Inability to excrete H^+

→ Treatment:

1. Fludrocortisone
2. Diet – K^+ Restriction
3. Furosemide
4. Soda Bicarbonate

PrepLadder

Summary of Renal Tubular Acidosis

RTA-1	RTA-2	RTA-4
- Defective α-Intercalated	- Damage to PCT	- Aldosterone Deficiency/ Resistance
- Nephrocalcinosis - K ↓	- Bicarbonaturia - Aminoaciduria - Glucosuria,	- Inability to acidify urine - K ↑

→ All types of RTA → Normal Anion Gap Metabolic Acidosis (NAGMA)

→ High Anion Gap Metabolic Acidosis (HAGMA) causes:

- K → Ketoacidosis
- U → Uraemia
- L → Lactic Acidosis
- T → Toxins – Methyl alcohol poisoning

→ Urinary Anion Gap → Positive in RTA

↓

$\{[Na^+] + [K^+] - [Cl^-]\}$

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Important points in RTA:

a) NAGMA (Normal anion gap metabolic acidosis)

b) RTA – 1 → Kidney stones

RTA – 2 → Bicarbonaturia

RTA – 4 → Hyperkalemia

c) Urinary Anion Gap → Positive (Blood anion gap is normal)

d) Oral Soda Bicarbonate is used to neutralize the acidosis

PrepLadder

NEPHROTIC AND NEPHRITIC SYNDROME

NEPHROTIC SYNDROME

1. Massive proteinuria > 3.5 g /day
2. Hypo albuminemia S. Albumin <2.5 gm% } Essential of Diagnosis
3. Oncotic pressure decreased – Oedema
4. Increased lipids–accelerated atherosclerosis – SLE /APLAS/Syndrome X/DM / Hypothyroidism
5. Lipiduria – Oral fat globules – CHYLURIA (FILARIASIS); fat embolism.
6. Loss of protein → C/S / Anti thrombin III Loss of
   Albumin / ferritin / ceruloplasmin
   Fibrinogen – (N) / increased as it is also an acute phase reactant.

- State of HYPER COAGULABILITY – VTE (Venous thrombo embolism)

Etiology:-

→ Non-selective proteinuria

- Adult – FSGS (focal segmental glomerulo sclerosis)
- Prediliction : Nephrons at cortico medullary junction
- Hence, always a possibility of diagnosis missed on kidney biopsy.

C/F:-

1. Hematuria / cola color urine
2. HTN – Headache
3. Nephrotic range proteinuria
   - Foamy urine
4. Renal In sufficiency (50% cases) in 6-8yrs

Etiology:-

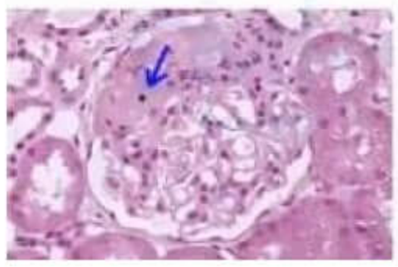
1. Idiopathic
2. Infection: HIV, HBV, Human Parvo virus
   Reflux nephropathy, Hypertensive nephropathy Heroin addiction, Pamidronate
   Alport, Sickle cell Anemia

Work-up:-

1. KFT-Serum Creatinine
2. Urine m/e : > 3RBC / HPF
   (N) Centrifuged specimen < 3 RBC / HPF
3. Biopsy Kidney LM
   image

↓

- Eosinophilic deposits
- Hyper Cellularity of Glomerulus EM –
Hyaline Deposits
  – Podocytes foot process – effacement of podocytes



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- Vacuolization
- detachment

Management

Primary - ACE inhibitors – HTN

Proteinuria: Steroids: for 4-16 weeks or until complete remission. Defined as secondary FSGS: Treat the cause.

> Proteinuria with > 85% albumin is selective proteinuria. Since albumin is negatively charged, it implies net loss of negative charges.

Membranous Glomerulopathy (MGN)

- MC in Geriatric population
  - 1^{O} :- Antibody against PLA_2 receptor
  - 2^{O} :- 1. Connective tissue disorder
    - RA / SLE / Scleroderma / MCTD
  2. Autoimmune disorders like Hashimoto thyroiditis/Graves
  3. Infection – Enterococci endocarditis
     HBV / HCV / leprosy / malaria
  4. Solid organ tumors
     Leukemia
     ↓
  5. Drugs – Penicillamine, Captopril, Mercury based compounds

> **Extra Mile**
>
> HCV leads to Membrane Proliferative Glomerulonephritis

C/F - Puffy eyes – Pedal edema
- Anasarca
- HTN

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Work up:-

1. Urine – oral fat bodies
2. Blood urea nitrogen increased, serum creatinine increased
3. ANA (+)
4. HIV / HBV / HCV
5. Work up for malignancy
6. Cryoglobulin levels
7. Kidney Bx – Hyper cellularity
   PMN cells
   C3 / IgM / IgG
   Sub epithelial deposits + spikes
8. Anti-PLA2 Ab – (+)

Rx – Low protein diet
- Furosemide
- HTN – ACEI
- Statins

Complication of MGN – RENAL VEIN THROMBOSIS
U/L enlarged painful kidney with AKI features

Neonate

CONGENITAL NEPHROTIC SYNDROME

- NPHS1-gene – Nephrin decreased zipper mechanism # defect
- NPHS2 gene – Podocin decreased (Bad Prognosis)

C / F:-

1.Non Immune Hydrops fetalis

2.Anasara

3.Foamy urine

Work up :-

- 24 hr urinary protein = Increased ↑ = > 40mg / m^2 BSA
- Serum Albumin – decreased

Rx – Daily Albumin Infusion
- Steroids
- Death – Infection

CHILDREN MCD (Minimal change Disease)

Most common cause of nephrotic syndrome in children.

2-8 yr

1. - Puffy eyes
   – Vulval edema / Scrotal edema
   – Pedal edema, with diurnal variation of edema
2. Wt gain (+)
3. Oncotic pressure decreased – Albumin decreased
   – Selective proteinuria
   – Pleural effusion B/L (Transudative) – dyspnea
   – Ascites – Abdominal girth increased, everted umbilicus

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Work up M.C.D:-

1. BUN / creatinine – (N)
2. Urine m/e – Oval fat Bodies
3. 24 hr urine protein increased
4. Urine protein electrophoresis
5. C3 levels (N) / decreased
6. Kidney Biopsy – LM (N)
   EM – Podocytes – foot process effacement

Rx – Steroids

Prednisolone X 8 weeks (Taper dose), good response and hence called as STEROID RESPONSIVE NEPHROTIC SYNDROME.

- Sudden withdrawal cause – Addisonian crisis

Case scenario of steroid dependent nephrotic syndrome where steroids have been given without supervision. Hence child has developed features of steroid toxicity.

PrepLadder

- Hirsutism
- Wt. gain
- Post sub capsular cataract
- HTN
- Psychosis

R_X :

Discontinue Steroids and Start CYCLOPHOSPHAMIDE/LEVAMISOLE

- For STEROID RESISTANT NEPHROTIC SYNDROME

↓

R_X-CYCLOSPORINE / TACROLIMUS

QUICK SUMMARY OF CAUSES OF NEPHROTIC SYNDROME

FSGS (Adult)	Non-selective proteinuria	EM Foot process detachment, Hyaline effacement, vacuolization deposits
MGN (Geriatric age)	> 65 yr – R.V.T	Subepithelial deposits +spike
MCD (Pediatric age)	2-8 yr selective proteinuria	Foot process effacement
Finnish	Neonate-hydrops fetalis	Similar to FSGS

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MGN

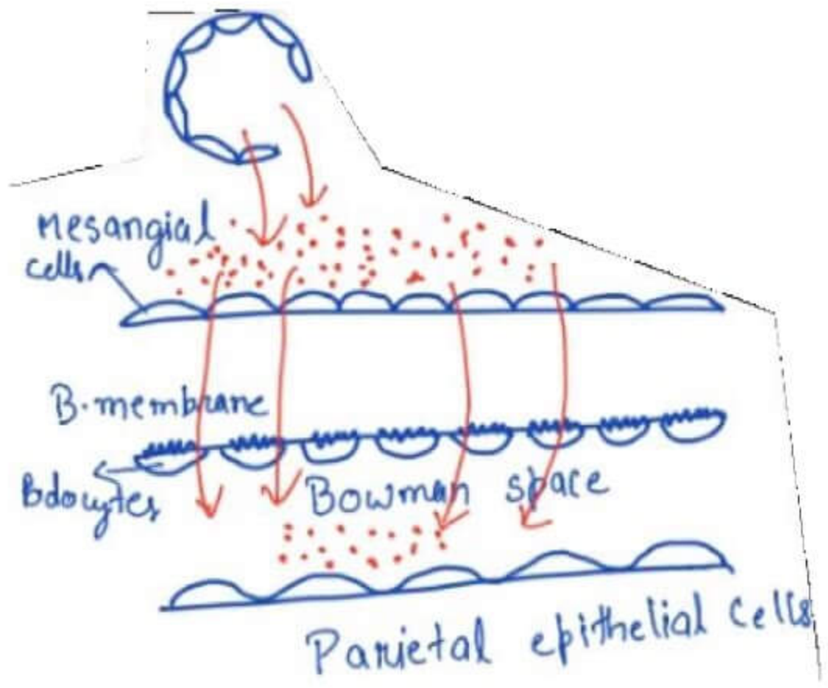
HBV
CTD
Solid Organ Tumors / Malignancy Associated

Inv :-

- 24 hr urinary protein
- Albumin decreased
- U.P.E.P- Urinary Protein Electrophoresis
- IG levels decreased – Infections – Pneumonia
- CXR – blunting of CP angle due to Transudative pleural effusion
- USG (Abdomen) – free fluid abdomen

R_X :-

2° FSGS – T/t the cause
1° FSGS – ACE (-) + steroids
1° MGN – (Alternative) steroids /
Cyclophosphamide / chlorambucil
Edema, wt. gain, Pleural effusion → t/t Spironolactone



NEPHRITIC SYNDROME

Vasculitis – GFR Decreased and Renin increased leading to

1. HTN
2. Hematuria
3. Sub Nephrotic proteinuria

Post Streptococcal Glomerulonephritis

- Type III Hypersensitivity reaction
- Immunological manifestation seen with Nephritogenic stain – Streptococcus
- Antigen – Streptococcal Pyrogenic exotoxin B (SPEP)
- Immune complex (+) – Complement mediated vasculitis
- PSGN- begin as Impetigo or Pharyngitis

Impetigo

Strains-47,49,5955,60

↓

1,2,3,4,25 2-6 week

week

Pharyngitis

Strains-

↓

1-3

Nephritic Syndrome

1. Hematuria cola colored urine
   - Smoky urine (Freshly voided sample)
2. HTN – sudden onset – LVF
   * Dyspnea – pulmonary edema (+)
3. Renal Insufficiency leading to features of uremia

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Work Up:-

1. Urine m/e - >3 RBC / HPF
   - RBC casts
   -Dysmorphic RBC: Always indicate Glomerular bleeding.

1. C3 ↓ decreased CH50 decreased C4 (n)
2. Anti DNAase increased , ↑ Anti Hyaluronidase Increased ↑
3. Kidney Bx – LM – Hyper cellularity
   - PMN infiltration
   - IgG / IgM / C3 deposits (sub epithelial cell deposits)

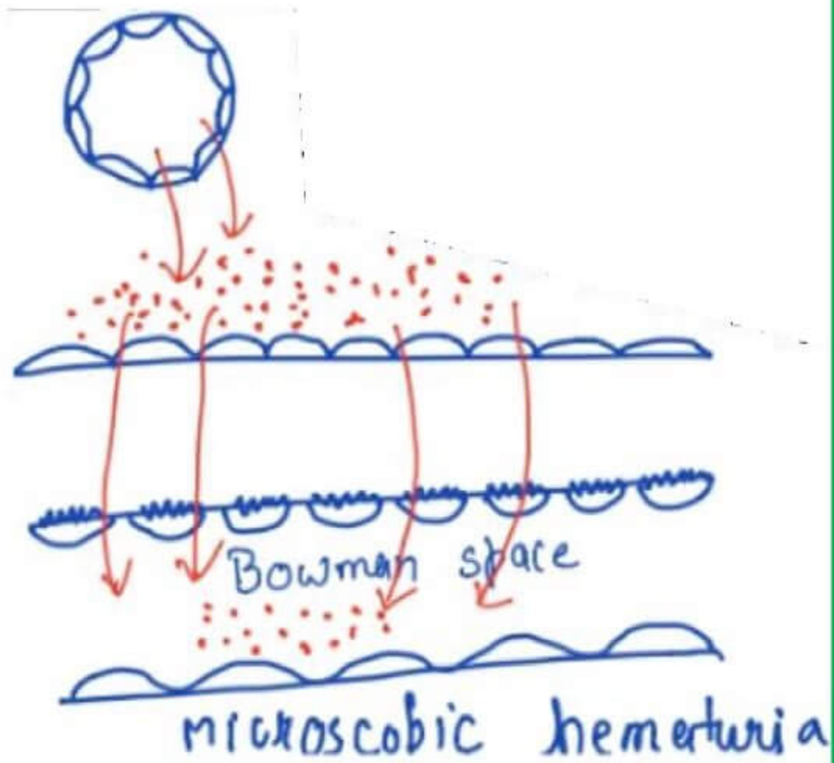
Immuno florescence study – Starry Sky appearance

Rx :-

1. Acute Pulmonary Edema – Furosemide
2. HTN crisis – IV Labetalol
   - ACEI
3. Hemodialysis

PrepLadder

BERGER'S DISEASE/IgA Nephropathy



* 1st Line of defense – Ig A (Mucosal Immunity)
* MC form of glomerulonephritis worldwide
* In Berger disease IgA ↑↑ with diffuse mesangial deposits
  - Capillaries (N)
  - GFR (N)
  - BP (N)
  - Microscopic Hematuria

If Pt develops URTI – IgA levels rise and over next 48 hrs, Microscopic Hematuria is replaced by macroscopic/Gross hematuria.

Some patients have asymptomatic microscopic Hematuria and may be picked up on annual clinical medical checkup.

O/E – BP (N), no edema is noted

Work up – >3RBC / HPF
- C_3 NORMAL in most cases

Rx – No consensus on optimal treatment

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HEMATURIA

H/O : Impetigo/ Pharyngitis (Weeks Back)
- Deranged KFT
- BP ↑↑

PSGN

H/O : URTI (for 48 hr)
- BP-N
- KFT - N

IgA Nephropathy

- MC cause of Hematuria [Microscopic] → **BERGER DISEASE**

Extra Mile

IgA increased ↑ → Henoch .Schoenlein purpura
→ Berger Disease
IgA ↓ → Ataxia Telangiectasia

PrepLadder

Mesangioproliferative glomerulonephritis	Membranoproliferative glomerulonephritis
Seen with- 1. IgA Nephropathy 2. Falciparum malaria 3. Resolving post infectious glomerulonephritis	Type1 (MC) :Hepatitis C Lupus Cryoglobulinemia Biopsy shows mesangial cell interposition between basement membrane and endothelial cell called as Tram Tracking. Type 2: Idiopathic , Dense deposit disease Type 3: Idiopathic

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PrepLadder

RENAL ARTERY STENOSIS

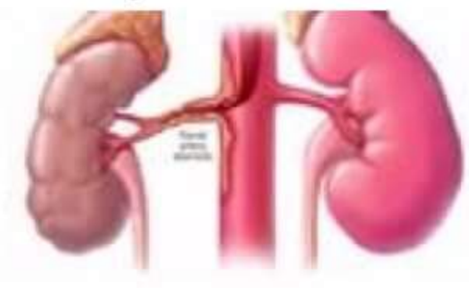
(Reno Vascular Hypertension)

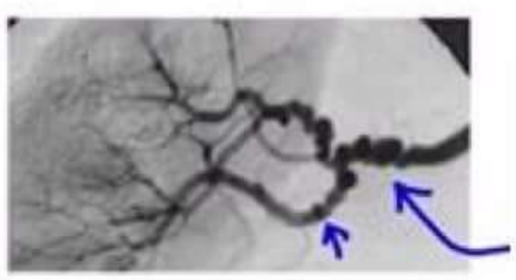
Etiology:

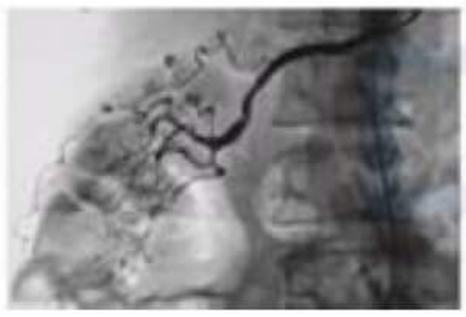
→ Most common cause – Atherosclerosis (Ostial narrowing)

→ Fibromuscular dysplasia (FMD) (Young females)

→ Takayasu arteritis – Asian population (Pulseless disease)







Renal Angiogram → Chain of beads appearance in FMD

Clinical Features:

1. Refractory HTN
2. Sudden ↑↑ BP in preexisting HTN patient
3. Flash pulmonary edema
4. Presence of Abdominal Bruit (Systole + diastole)
5. Check peripheral pulses
6. Poly Arteritis Nodosa → Not cause of Renal Artery Stenosis but can lead to Aneurysm formation

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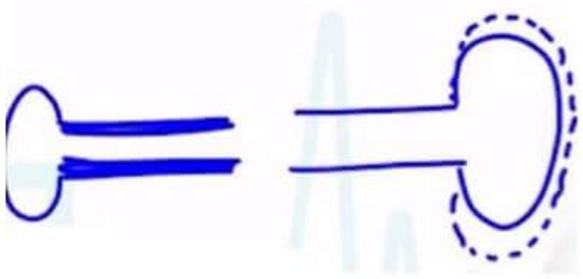
Work up:



1) USG → Asymmetric kidneys size

→ Not responding to anti hypertensive medication

2) Doppler –Best Screening test

3) CT Angiography

4) Magnetic Resonant Angiography (M-R-A)-expensive

↓

– False positive results – due to Turbulent flow

– Gadolinium → cause Nephrogenic systemic fibrosis

5) IOC → Renal Angiography (Invasive test) (Gold standard)

6) DTPA scan before and after giving ACE inhibitor (Captopril Renogram)

PrepLadder

→ Treatment

1) ACE Inhibitors:

→ Contraindicated in Bilateral RAS because it causes efferent arteriole dilatation leading to loss of filtration gradient and increasing the risk of acute kidney injury.

→ Risk of Acute kidney Injury

2) Calcium Channel Blockers

3) PTRA [Percutaneous Transluminal Renal Angioplasty]

↓

Stenting

↓

Preferred for- Fibromuscular dysplasia

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PrepLadder

BLEEDING FROM THE GUT

- Anatomical landmark to differentiate between Upper GI & Lower GI Bleeding: **Ligament of TREITZ**

Causes of Upper GI bleeding / Hematemesis:

1. Peptic ulcer disease (leading cause for hematemesis)

*Duodenal ulcer =Gastroduodenal artery

↓

(Source of bleeding)

- Managed by: - UPPER GI Endoscopy + cautery

* Gastric ulcer: - Left gastric artery

-Managed by: - UPPER GI Endoscopy +cautery

(M/C site for Gastric Ulcer is: lesser curvature)

Esophageal varices

2. Drug induced gastritis: COX -1inhibitors (like Indomethacin, ketorolac)
3. Portal hypertension (Splenomegaly will be noted)
   (Defined as pressure > 10mmHg or > 15cm of H_2O)

Extra Mile:

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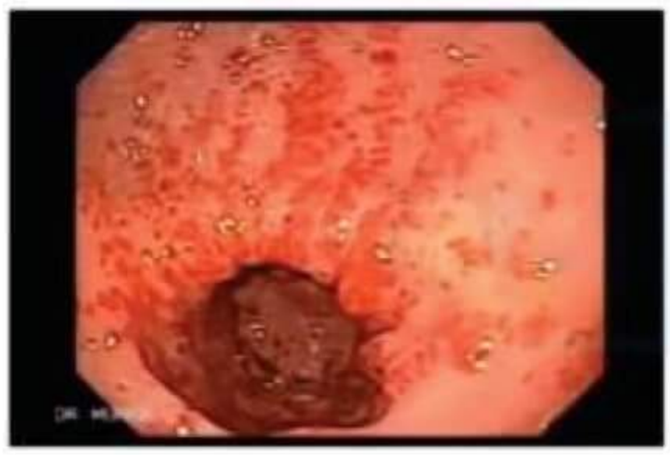
Leading cause of portal hypertension is alcoholic cirrhosis but if in the question mentioned non alcoholic with negative viral serology then the answer as Non Cirrhotic portal fibrosis.

In paediatric patient M/C cause is EHPVO (Extra Hepatic Portal Vein Obstruction)

4. Mallory Weiss syndrome: (sub mucosal tear)
   - KEY POINTS:- RETCHING episodes: Alcoholic binge drinking/ hyperemesis gravidarum

* Primary site of tear = Lower esophageal sphincter and starts from cardia.
* Source of bleeding = Left gastric artery



(watermelon stomach)

5. Dieulafoy's lesion: Aberrant sub mucosal artery bleed

6. GAVE: gastric antral vascular ectasia (Water melon stomach)

↓

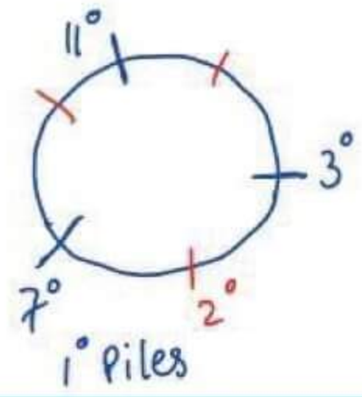
(Least common cause)

PrepLadder

Lower GI bleeding:

Hematochezia: fresh blood in stool

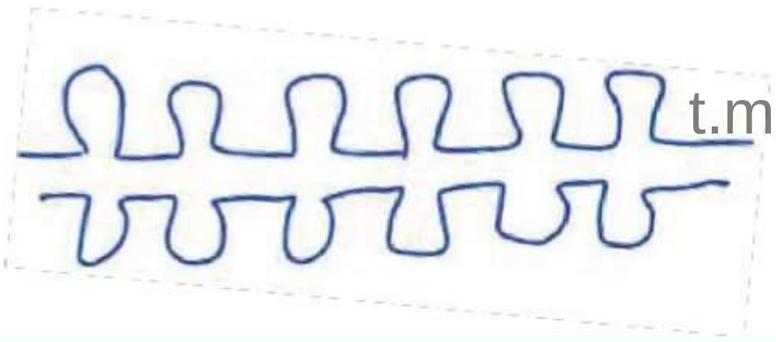
1. Piles/ Internal hemorrhoids: "flash in the pan" painless bleed, post defecation and present with anemia



- IOC= proctoscopy

2. Diverticulitis ↓ Inflammation of the wall of diverticulosis For diverticulitis to occur, diverticulosis must be present before / preexisting result in rectal bleeding.	Leading site of diverticulosis ↓ **Sigmoid colon** (Narrowest part of colon) Forces within the lumen of diverticulum leads to segmental weakening of Vasa rectum Rupture of these Vessels into the lumen.

For Dx of diverticulosis → Use Ba enema or colonoscopy



(Saw tooth pattern)

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Key points:

* Case will describe a geriatric patient with long standing constipation

And 'sudden onset crampy L.I.F pain + hematochezia'

DIVERTICULOSIS

Investigation of choice for diverticulitis: - CT abdomen

Rx - Hinchey classification

1) Localized abscess: Liquid diet + Antibiotics oral x 10day
2) Walled up abscess: IV Antibiotics
3) Purulent peritonitis: Surgical Exploratory Laparotomy
4) Gross fecal contamination

Extra Mile:

1. SAW Tooth Ba enema: Diverticulosis
2. SAW TOOTH ECG: Atrial flutter
3. SAW TOOTH EEG: REM

PrepLadder

3. **Inflammatory bowel disease**-

Ulcerative colitis: Painless bloody diarrhea 10-15 times/ day

Crohn's disease: Colicky pain + hematochezia

- Screening Test for UC: **p-ANCA**

- Screening Test for CD: **A.S.C.A** (Anti saccharomyces cerevisiae antibody)

4. **Malignancy colon**-

Ca caecum = **Bleeding +**

Ca rectum = **Napkin ring stricture**

Key points: Progressive constipation and intestinal obstruction

Investigation-Rectal biopsy followed by **DUKE Staging**

DUKE CRITERIA = **IE (Infective Endocarditis)**

DUKE SCORE = **Severity of chronic stable angina**

5. **Angiodysplasia of colon** (Vascular malformation of colon):

KEY POINTS - Pin point bleeds and may not bleed on the day colonoscopy was done.
Hence high probability of missing the lesion

IOC: **Angiography**

CASE SCENARIO:

- In a patient of 70 years of age 2 colonoscopies are done in last 1 year, both reports are normal but hematochezia is persisting off & on (+), diagnosis will be **angiodysplasia colon.**

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Melena-

Presentation: **60ml blood**, 6-8hours in the gut to results in **Black tarry stool.**

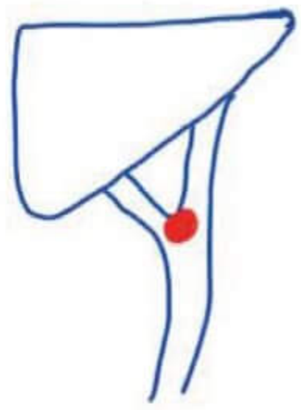
Cause-

1) P. U.D (Peptic ulcer disease)
2) Erosive gastritis
3) Portal HTN
4) Mallory Weiss

Investigation of choice: - **Upper GI Endoscopy**

PrepLadder

Hemobilia-(Upper GI Bleeding)

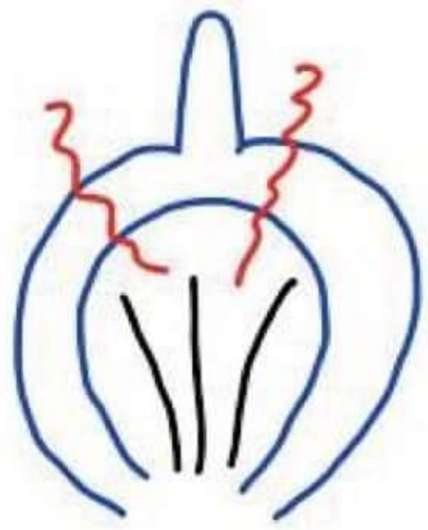


1) Trauma – Lap cholecystectomy
2) Instrumentation: (like ERCP)
3) Cholangiocarcinoma
4) Klatskin tumor (also a type of cholangiocarcinoma)
5) Parasites

Investigation of choice: -**Angiography**

Rx - **Gel embolization of bleeder**

Causes of Hematochezia in Pediatric: Rectal polyp> Meckel's diverticulum



Rule Of 2
- 2% population
- 2 inches size
- 2 feet from ileocaecal junction
- 2 mucosa :stomach |pancreatic

* Remnant of vitello intestinal duct and occurs on anti – Mesenteric Border.
* Asymptomatic: > 90%
* IOC: - TC^{99} pertechnate scan

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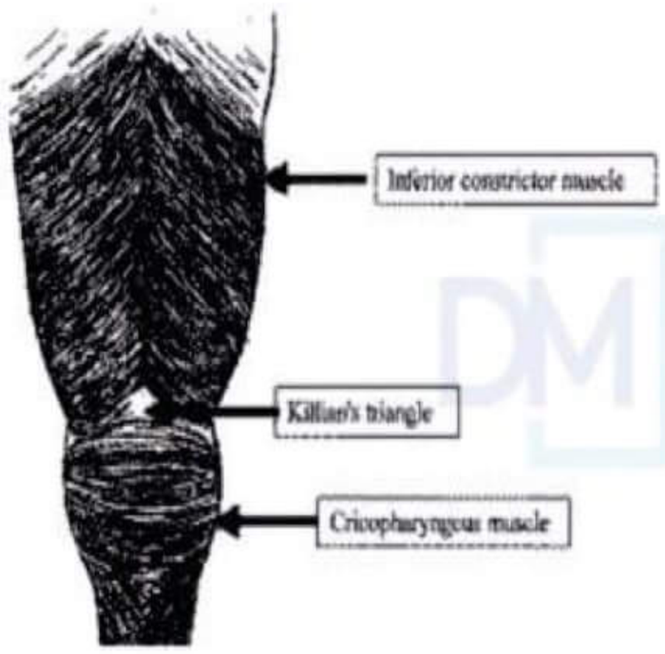
Rx:- Resection and end to end anastomosis

ESOPHAGEAL DISORDERS:-

1) Zenker diverticulum: (Location: Killian Δ > Lavemir Δ)
   1. Non- progressive dysphagia
   2. Halitosis
   3. Regurgitation of yesterday food items

Investigation of choice: -**Ba swallow**

Rx:- **Surgery**



2) Diffuse esophageal spasm-

M/c cause: Idiopathic

PrepLadder

Clinical Features:-

1. Intermittent Chest pain at rest (Symptoms of CHF are absent). Must differentiate from chest pain of coronary etiology
2. Esophageal angina
3. Intermittent chest pain
4. Dysphagia non- progressive

Ba Swallow: Cork Screw appearance / Rosary Bead appearance

Investigation of choice: - Esophageal Manometry

- Luminal pressure ≥ 120mm Hg for > 3sec

Nut cracker esophagus- If pressure > 180mm Hg > 6.5 sec

Rx- 1. Anxiolytics
2. Nitrates → Isosorbide mononitrate (long acting)
3. Calcium channel blocker →Amlodipine

Ba swallow → irregular shaggy appearance esophagus → (esophageal candida infections)

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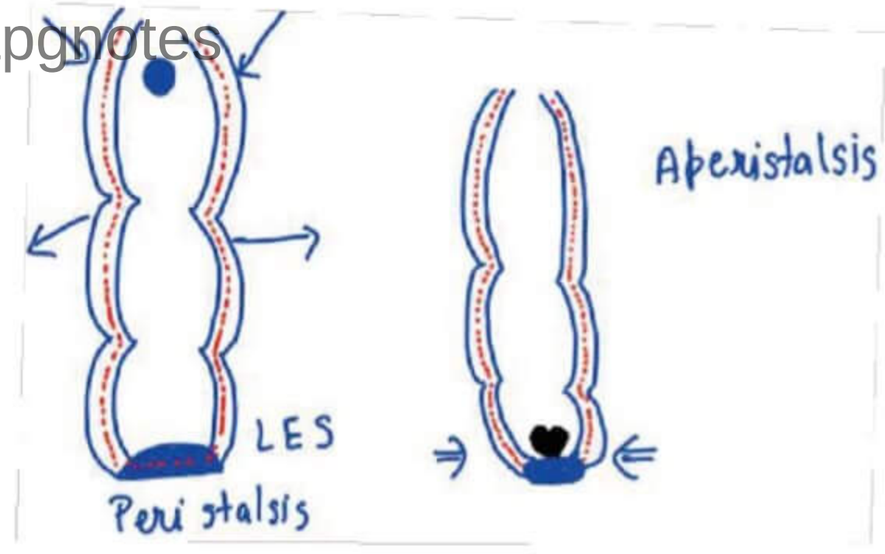
ACHALASIA CARDIA

Causes-

1) Idiopathic(M/C)
2) Oat cell Ca lung
3) Chagas disease (Reduviid bug)
- Loss of (Inhibitory) ganglia



Pathophysiology of Achlasia: Aperistalsis and increased Tone of LES due to loss of inhibitory control.

Clinical Features-

- Female: 25-year **progressive dysphagia**
- **Liquids > solid (Dysphagia)**
- Food sticks behind sternum
- Halitosis
- Regurgitation of previous day food items

PrepLadder

IOC-Esophageal manometry: (LES tone increase)

Ba swallow: Bird beak appearance

Ba enema: Bird beak → Sigmoid volvulus Q***

Rx-

Laparoscopic Heller's myotomy + Nissen fundoplication

Botulinum toxin + balloon dilatation

+CCB

Case scenario: 25yr old female presents with progressive dysphagia(oropharyngeal dysphagia)

but LES tone: **decreased**

↓

Then Dx is **Scleroderma** **and not Achalasia cardia where LES tone is increased.**

Case Scenario: 30 years alcoholic, binge drinking, retching chest pain, syncope O/E:

HR= 120/mm

BR = 90/60 mm Hg

Probable diagnosis?

Ans-Boerhaave syndrome

- Oesophageal tear: Lower 1/3 of esophagus is involved (post lateral)
- Chemical mediastinitis explosive chest pain
- Pneumomediastinum: Kinking SUC/IVC venous return decrease BP decrease Vasovagal component
- Mackler's triad = Chest pain + Vomiting + SC emphysema (l/t crepitus +)

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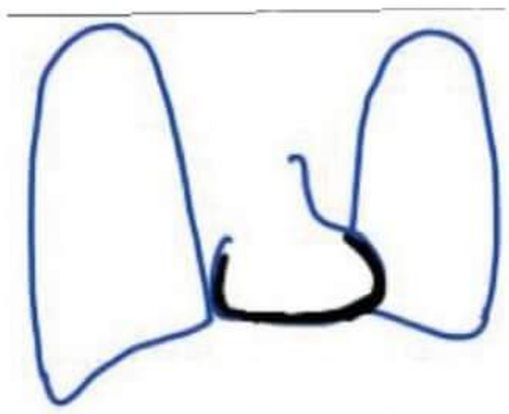
Investigation -

1. Chest X-Ray

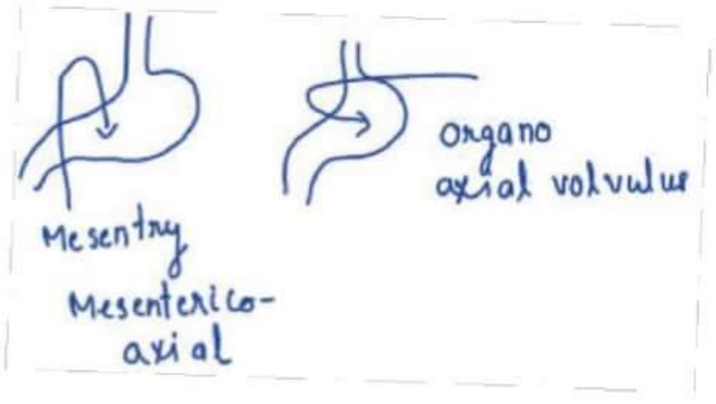
2. IOC - CT chest + contrast (Water soluble)

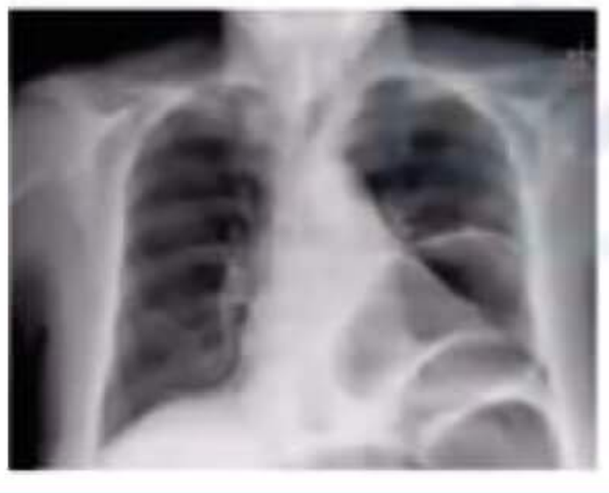
Rx: - Surgical repair



Case Scenario: 30 years alcoholic presents with **epigastric pain, trying to** vomit but no vomiting yet, failure to pass NG tube probable diagnosis?

Ans: - **Stomach Volvulus**





Investigation: - 1. Chest X-Ray
2. CT abdomen: IOC

Rx: Surgical exploration

NG Tube should be put in conscious patient in sitting position with neck partially flexed to protect the airway

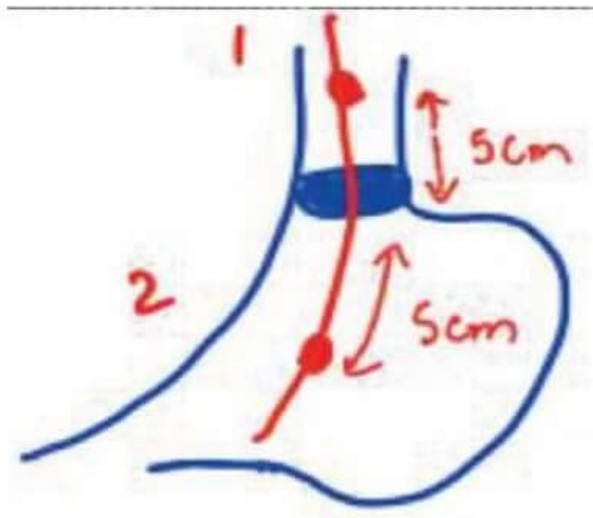
GERD | Non ulcer dyspepsia (NUD):

Clinical features:

1. Chest pain/heart burn/LES tone decrease/retrosternal pain
2. Sore throat (multiple episodes)
3. Nocturnal cough (chemical tracheitis) - seen in asthma/ post nasal drip/GERD
4. Sour brash
5. Dental enamel damage (enamel hypoplasia)

Investigation of choice: - 24 hr pH monitoring

Esophageal pH: < 4.0 for > 4hrs/day



Rx-DOC is PPI + Prokinetic agents (like Mosapride / Itopride) improve symptoms faster.

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Barrett Esophagus:

* Metaplasia: Squamous to columnar
* Dysphagia
* Carcinoma in situ
* Cancer

Investigation:-Upper GI Endoscopy and Punch biopsy (Goblet cells+)

Extra Mile: M/C type of metaplasia-

- Columnar to squamous due to effects of smoking.

PrepLadder

PEPTIC ULCER DISEASE

Type B gastritis:

- **Helicobacter pylori** (MC)
  - * Gram negative coccobacilli
  - * Microaerophilic
  - * Feco-oral route
  - * Non-Spore forming: eradication possible
  - * Extra Cellular Bacteria
  - * Urease

Urea —urease→ Ammonia (Alkaline media)
↓
Irritation of G cells& parietal cell
↓
Excessive acid production (Hyper chlorhydria)
↓
Ulcer
Duodenal ulcer>Gastric ulcer

WORK UP

1. Screening test/eradication → **Breath urea test (Non-invasive)**
2. Urease test (Invasive) (CLO TEST- commercial name) → **scraping wall of stomach endoscopy**
3. Biopsy: **Warthin starry stain**

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Treatment: - Antibiotics

1. Pantoprazole (PPI)
2. Clarithromycin
3. Amoxicillin/clavulanic acid (Resistant cases) -2weeks

} **Triple theraphy**

Quadruple therapy: BISMUTH
TETRACYCLINE
Metronidazole
Pantoprazole

- **(Erythromycin Not used for Rx)**

Type A gastritis: (4 A)

- **A**utoimmune disorders, premalignant condition
- **Anti-parietal cell antibodies**
- **A**chlorhydria → gastric ulcer
- Intrinsic factor ↓, B_{12} ↓ (**Macrocytic anemia**)

Gastric ulcer	Duodenalulcer "Do"
Blood group: A	O
Site: Type 1: lesser curvature (MC site) near incisura Angularis	Duodenal Cap
Pain: Epigastric pain (Immediately after food Intake) weight loss	Epigastric pain "hunger pain" Snacking by patient leads to weight gain

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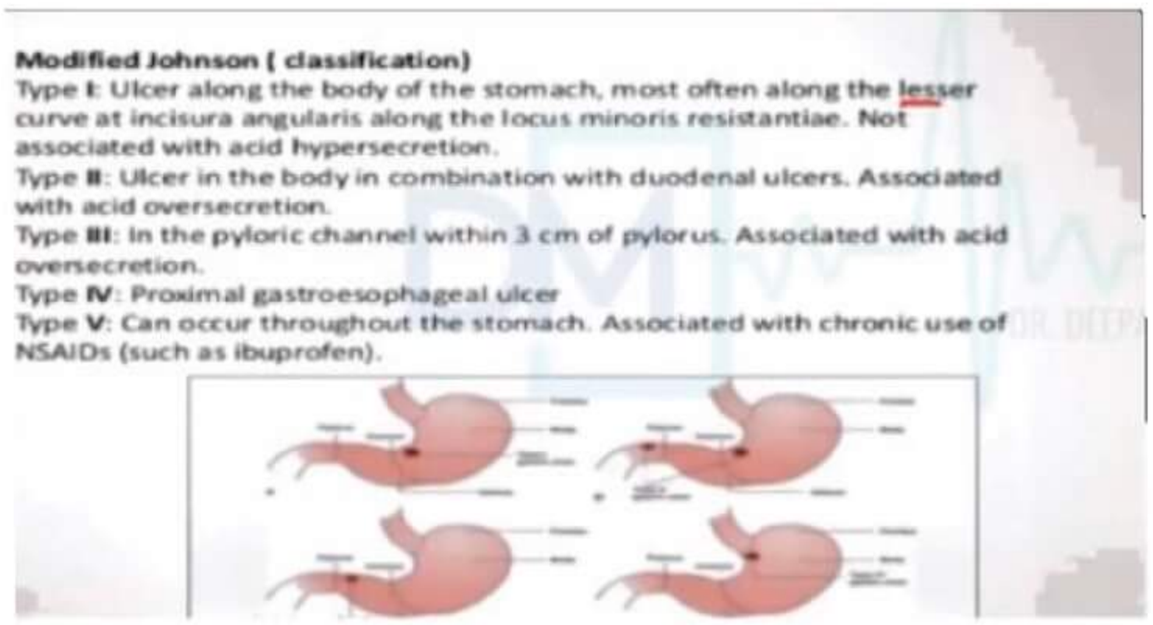
Extra Mile:

H. Pylori is an Extracellular bacteria while Tropheryma whippelii leading to Whipple's disease is intracellular bacteria found inside macrophages of intestine.

Johnson classification:



IOC for PUD: – Upper GI endoscopy (UGIE) + Biopsy

Complications in gastric ulcer:

1. **Bleeding**: Left gastric Artery

   Upper GI Endoscopy

   +Cautery

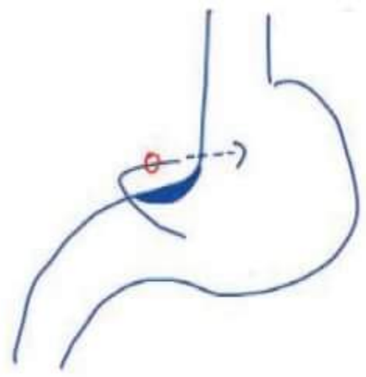
   ↓ fails

   Massive transfusion protocol [6 packed RBC, 6 FFP, 6 platelet rich plasma]

   ↓

   Exploratory laparotomy ligation of bleeder

2. **Perforation**: Lesser sac



3. **Penetration**:

   Slow, posterior by,

   - Pseudo pancreatic cyst
   - Necrotizing pancreatitis

4. Malignancy
5. Hour glass stomach

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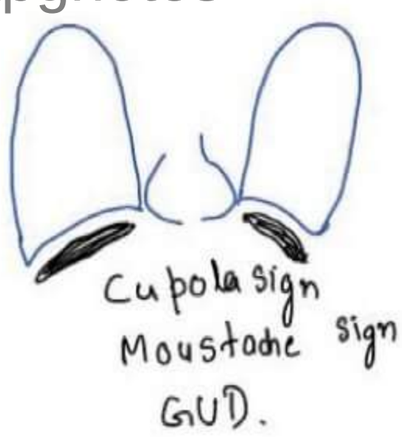
In duodenal ulcer:

1. **Perforation** : Anterior > posterior (Most common)
   - Cupola sign
   - Moustache sign
   - Gas under diaphragm



2. **Bleeding**: Posterior > Anterior

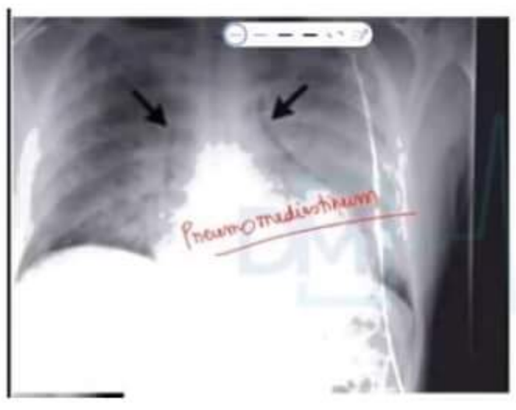
   Source - Gastroduodenal artery

   Mx: - Adrenaline at base of ulcer

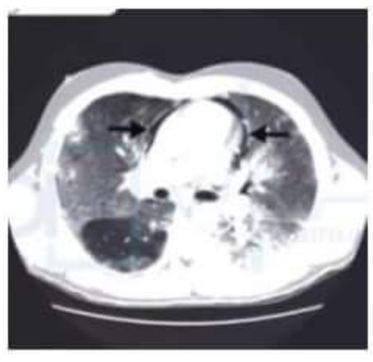
   - Cautery, ligation, exploratory laparotomy

Gas under diaphragm:

Pneumoperitoneum



Pneumomediastinum



Coffee been appearance:

Sigmoid volvulus

PrepLadder

Sigmoid volvulus :

Large Bowel Obstruction :

1. Sudden onset Left iliac fossa crampy pain
2. Obstipation (Can't pass flatus)
   * Anti clockwise direction
     - X- Ray abdomen: Coffee bean app.
     - Barium enema: Bird BEAK app

Treatment :

1. Intravenous Fluids
2. Flatus tube
3. Colonoscopic detorsion

PRE- MALIGNANT CONDITIONS OF GUT

1. Oral cavity ;

→ **Leukoplakia** : More common

→ **Erythroplakia** : More malignant

2. Esophagus :

* **Tylosis palmaris**: Hyperkeratosis in palms and soles (SCC risk↑)
* Plummer Vinson syndrome : Esophageal web +IDA (Iron deficiency anemia)+ Koilonychia
* Barrett's esophagus
* Achalasia cardia

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3. STOMACH

* Type A Gastritis
* Gastric ulcer
* Ménétrier's disease

4. Small Intestine

* Crohn's disease
* Cronkhite Canada Syndrome : Polyps in duodenum

5. Large Intestine

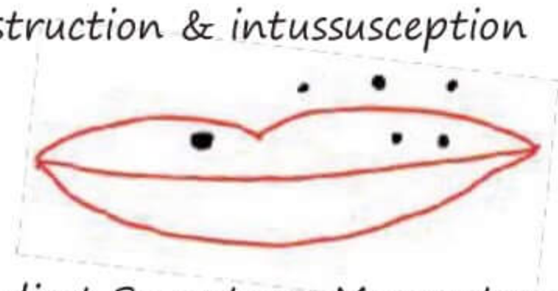
* Familial adenomatous polyposis(FAP)
  - APC gene
  - Chromosome 5 #
  - >100 polyps / colon
  - Primary colectomy
* Inflammatory bowel disease
  - Malignancy Incidence is equal in both UC = CD

Condition where polyps themselves are not premalignant but a definite association between gut malignancy is seen:

PrepLadder

PEUTZ JEHGER SYNDROME :

- Hamartomatous polyps in jejunum that lead to bleeding, obstruction & intussusception
- **STK II gene, AD**



Earliest Symptom: Mucocutaneous pigmentation in first year of life

- **Mc site**: Jejunum
- Mucosal melanosis lips/anus
- Increased incidence of Ca breast, stomach, Pancreas and large gut cancer.
- Polyps themselves are not premalignant but a definitive association with both intestinal, hepatobiliary and extra intestinal malignancy.

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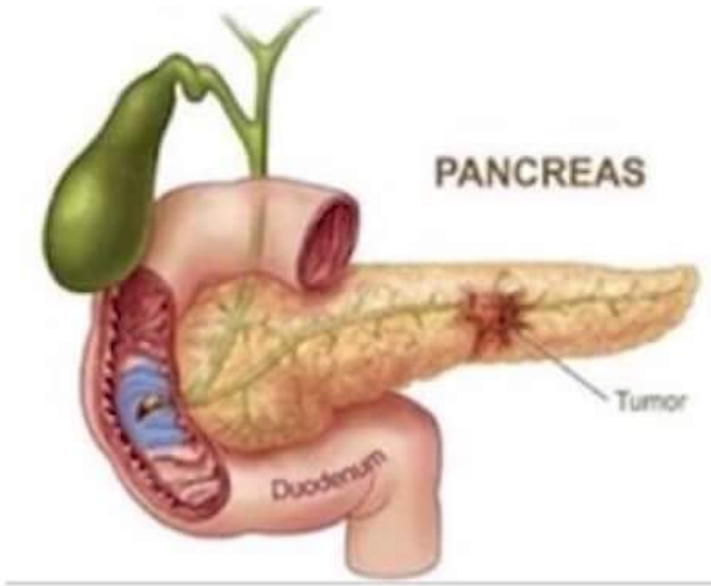
PrepLadder

Zollinger Ellison Syndrome / Gastrinoma



- Tumor of G cells
- M/C site of G cells is stomach but Gastrinoma does not arise M/C in stomach. M/C site of Gastrinoma- **Duodenum > Pancreas > Stomach**. Also can present in rare site as ovary, testis, heart.

- Tumor lead to → Gastrin +++ → Continuous stimulus → increase in number of parietal cells

  |

  Characterized by hypergastrinemia & hyperchlorhydria (Causing recurrent peptic ulcer)

  |

  Duodenal ulcer is Giant ulcer in 2nd part duodenum

- 25% cases have association with **MEN I** → Can be pituitary adenoma, parathyroid adenoma, pancreatic adenoma (Zollinger Ellison syndrome) in patient.
- **Overall MC pancreatic adenoma functional** –Insulinoma
- M/C **MEN I** overall pancreatic adenoma functional– Zollinger Ellison syndrome

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Usual age of presentation: 30-50 years of age(female > male)

C/F:

1. **Abdominal pain (Epigastric)** - Hunger pain present
2. **Diarrhea** (D/T excess acid produced causes inactivation of pancreatic enzyme & Acid also contribute to mucosal Injury.)
3. **GERD** (Cause reflux esophagitis, retrosternal pain)
4. **Past medical history**: Kidney stone.

Note:

- Very Important to confirm Dx
- Patient on PPI can also has ↑ gastrin level in blood
- So alone ↑ gastrin level can't make the Dx ZES

- Association with MEN I – has favorable prognosis (As person becomes symptomatic earlier)

Work up:

- Upper GI Endoscopy: Multiple DU/Giant DU
- Breath urea test: → Negative
  Urease test: → Negative
  } Rules out H. pylori
- Ca^{2+}/ PTH/ PRL / Pancreatic polypeptide levels tested to see association with MEN I: **chr 11q13**;

PrepLadder

3P's

1. Pituitary adenoma
2. Parathyroid adenoma
3. Pancreatic adenoma

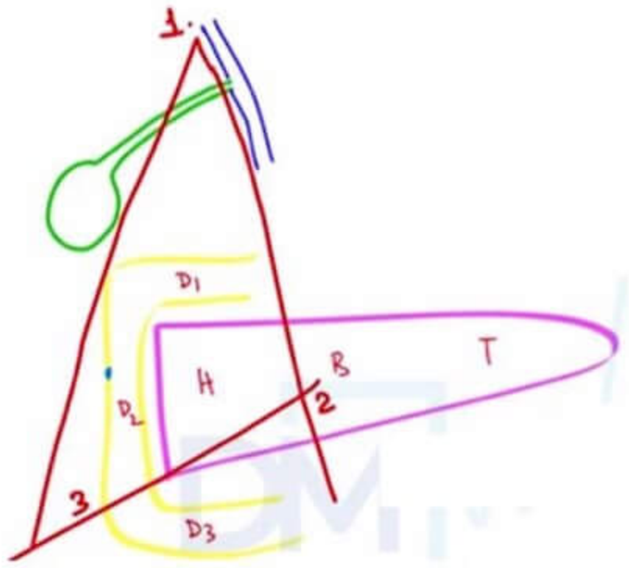
1. IOC: Secretin study
   - Check for **fasting gastrin level** > 1000 pg/ml (x10)
   - **Blood acid output** >15 meq/hr
   - **BAO/MAO** (Basal area output/maximal acid output) > 0.6

False positive: gastrin d/t H. pylori, gastric outlet obstruction injudicious use of PPI

2. Tumor localization

Tumor can be present in hypothetical **Gastrinoma triangle*****.

1. Confluence/junction of common hepatic duct & common bile duct
2. Head & body of pancreas dissected
3. Between D2 & D3



Gastrinoma Triangle

- **Main investigation**: Endoscopic U.S.G (To locate the tumor)
- **MC site**: Duodenum > Pancreas > Stomach > mesentery >>> **Ovaries, heart*****
- **Best imaging modality** = Endoscopic ultrasound
- **Best imaging modality** (For **metastatic Gastrinoma**) = Somatostatin scintigraphy

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RX:

1. DOC : PPI (Will not control diarrhea component)
2. Somatostatin analog - Lanreotide
3. Sx resection: If tumor >1.5 – 2 cm (On CT/MRI)
4. ↑ calcium: Lead to ++ Acid ↑ from stomach

|

Parathyroid adenoma worsen acid component of patient

|

Parathyroid adenoma-- TC -99/ sestamibi scan

→ Sx resection

5. Metastasis liver: Hepatic resection.

PrepLadder

MALABSORPTION SYNDROME

Sites of Absorption

Iron - Duodenum	# **S.ferritin levels**
Folic Acid - Jejunum	# **FIGLU Test**
B_{12} - T. Ileum	# **Serum B_{12} Level**

- Serum Homocysteine Level
- Methylmalonic acid
- Schilling Test (usually not done)

Carbohydrate Malabsorption work up:

1. D-xylose Absorption Test
2. Breath H_2 Test
3. Stool for Reducing substances

Overall best investigation is small intestinal mucosal biopsy.

Fat Malabsorption work up:

1. 24 hour fecal fat estimation
2. Breath 14C-Triolein test

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Gluten sensitive Enteropathy /Celiac Sprue:

≤ 6 months = Exclusive breastfeeding

> 6 months = Complimentary feeding

- Cereals (Barley, Rye, Oats, Wheat): Mnemonic BROW
- Gluten +

Since child → Allergic to gluten/Gliadin in cereals → Antibody induced damage to microvilli in gut → Reduced absorptive area → Sugar remain unabsorbed → Osmotic diarrhea

Pathogenesis

Clinical Features:

> 6 months → Failure to thrive

Loose motion (Osmotic diarrhea)

Damage → Duodenum >Jejunum >Ileum

Deficiency → Iron > Folic acid>B_{12}

Delayed milestones

Diagnosis

Screening Test:

1. **Anti-Tissue transglutaminase Antibody**
2. **Anti Endomysial Antibody**
3. **Anti-Gliadin Antibody**

IOC :

Biopsy of small intestine → **Flat Villi**

Strict diet restrictions for **4 weeks**

Repeat biopsy of small intestine → **Regeneration of Villi**

PrepLadder

Treatment :

Stop wheat/oat/rye/barley

Start Quinoa Maize, rice(small amounts Gluten +)

Iron, FA,

↓ ↓

For For

Microcytic Macrocytic

Anemia

Strict dietary restriction for < 10 yrs of life leads to reduction is disease severity.

Follow Up

1. **Dermatitis Herpetiformis**

- Pruritic vesicular eruptions (Elbows)

Anti epidermal transglutaminase antibody – (Imp)

On Biopsy: D/F study

Dermatitis Herpetiformis

Rx → Dapsone

2. **Type 1DM**

3. **Lymphoma (HL)**

Most common cause of death in celiac sprue → **Cancer of gut**

Tropical Sprue

Cause → Giardia/E. coli , recurrent acute attacks lead to mucosal injury.

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Clinical Features

1. Osmotic Diarrhea
2. Steatorrhea, bulky stool, foul smelling
3. Weight loss
4. Muscle wasting
5. Deficiency of fat soluble vitamins (Vit. A, D, E, K)

Vit A deficiency → Nyctalopia

Vit D deficiency → Bone pain

Vit K deficiency → Bleed, Purpura

Vit E deficiency → Ataxia, Acanthocytes

IOC – Biopsy shows flattening of villi

Treatment- Tetracycline + folic acid

Whipple Disease

Tropheryma Whippelii (Intracellular Gram positive Intracellular bacteria found in macrophages of lamina propria of gut)

Clinical Features :

1) Diarrhea, weight loss, abdominal distention
2) Steatorrhea
3) **Dementia (reversible) → (D/T) Niacin deficiency**
4) **CVS → Aortic valve involvement leading to stenosis.**
5) Joint Pain

PrepLadder

Diagnosis:

Biopsy of small bowel → PAS positive bacteria is found in macrophages of gut or real time PCR

Treatment:

- IV Ceftriaxone x 2 weeks
- Cotrimoxazole (Oral) X 1 year

Extra Mile:

Whipple Triad

→ For diagnosis of **Insulinoma**. [Covered in Endocrinology section as PNET]

→ IOC → **72-hour prolonged fasting sugar levels**

Whipple operation: For cancer of head of Pancreas

Bacterial Overgrowth Syndrome:

Normally Anaerobes are not found in jejunum of health people.

Count in ileum is 10^8 organisms/ mL. and Count in Large bowel is a huge 10^{11} organism/ mL

Symptoms:

1. Osmotic diarrhea
2. B_{12} deficiency
3. ↑ Folic acid due to production of Folate compounds by bacteria
4. Bile acid malabsorption which damages enterocytes and induces water secretion by colonic mucosa

IOC - **Jejunal aspirate + culture : positive.**

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Treatment–Antibiotics

For absorption of B_{12} we require

1) Intrinsic factor (From parietal cells)
2) Pancreatic enzymes
3) Terminal Ileum Mucosa

If -**Parietal cell damage** (Type A gastritis) → B_{12}↓

- Terminal Ileum Mucosa damage (Crohn's Disease) → B_{12}↓
- Bacterial overgrowth syndrome → B_{12}↓
- Celiac sprue → B_{12}↓
- **Abnormal Schilling Test:**

1. **On antibiotic administration** -Normal Schilling test → **BOS**
2. **Pancreatic enzyme supplement** -Normal Schilling test → **Chronic Pancreatitis**
3. **Intrinsic factor supplement** -Normal Schilling test → **Type A Gastritis**

PrepLadder

SUMMARY :

	D-xylose Test	Schilling test	Duodenal Mucosal Biopsy
Chronic Pancreatitis	Normal	Abnormal Normalize with pancreatic enzyme.	Normal
Bacterial overgrowth syndrome	Normal or modesty abnormal	Abnormal Normalize with Antibiotics	Normal
Celiac sprue	Decreased	Usually normal as proximal damage is seen	Flattening of villi
Intestinal lymphangiectasia	Normal	Normal	Abnormal dilated lymphatics

Imp→Normal schilling test → Type A gastritis

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PrepLadder

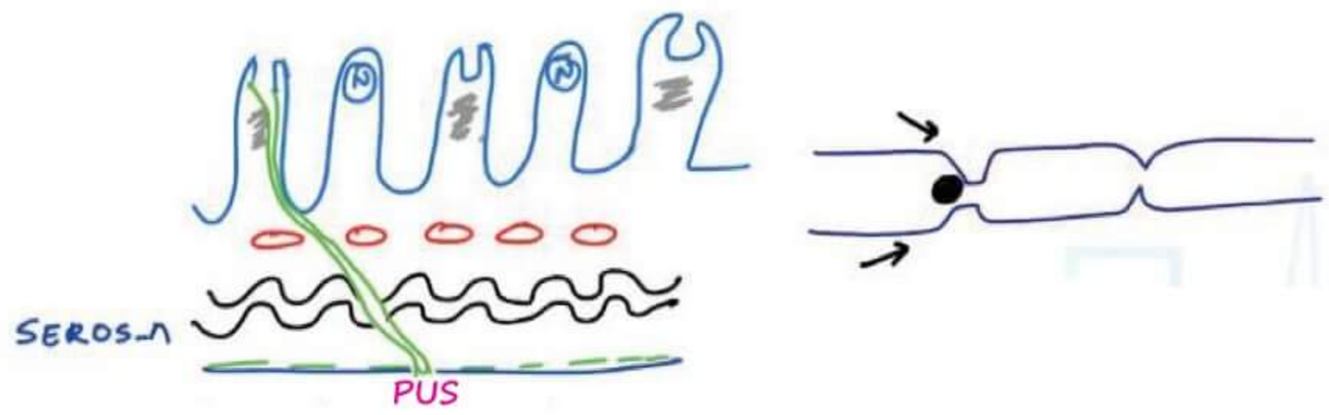
INFLAMMATORY BOWEL SYNDROME

CROHN'S DISEASE

MC Site- Terminal Ileum

Sparing- Rectum

Earliest presentation :- Aphthous Ulcer



C/F:

1. Colicky pain
2. Hematochezia
3. Toxic Megacolon (Transverse colon)
4. I/A abscess : fever / chills, rigor
5. (Adhesions) ♀: Infertility
6. Peri anal hygiene → Poor → (L/T) formation of fistula

COBBLE STONE MUCOSA

SUBMUCOSAL FIBROSIS

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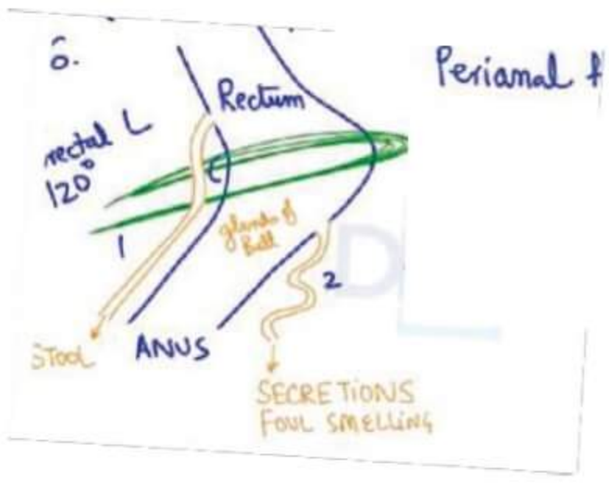
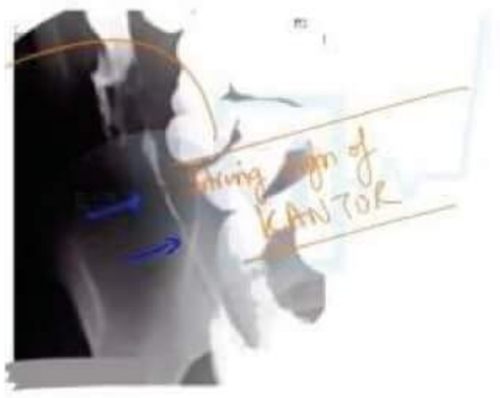
Perianal Fistula - Clinical Hallmark of Crohn's disease



Work Up:

1. ASCA - **Anti saccharomyces cerevisiae antibody**
2. IOC: **Upper GI endoscopy / colonoscopy + biopsy**
   → Granulomas +ve rule out malignancy



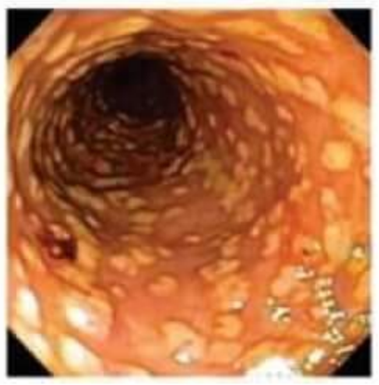
3. Ba MFT: **String of KANTOR** due to stricture formation

Rx : **DOC** - CROHN : STEROIDS

- Azathioprine, Mesalamine- Mycophenolate
- **Infliximab** (TNF Antagonist)

PrepLadder

PSEUDOMEMBRANOUS COLITIS:

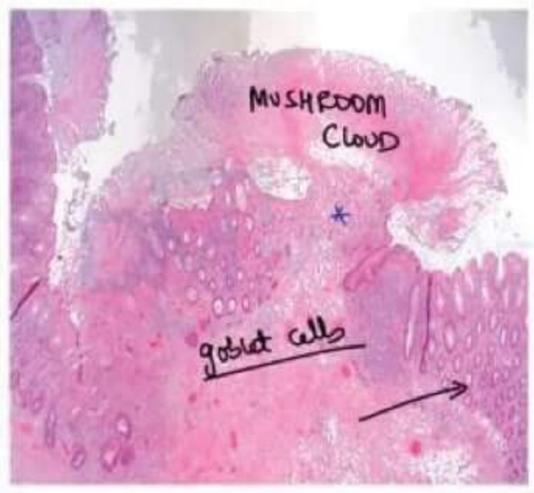


→ Suspected if the patient has received antibiotics in previous 3months
→ Diarrhea
→ Hospitalized pt. Developed diarrhea > 48 hours of admission

Reason: -Cephalosporins > Clindamycin

C/F→ Explosive watery diarrhea(rarely bloody)Cramps/abdominal pain

Cl. difficile toxin, A/B is responsible for PMC



Work Up:-

1. STOOL CULTURE: - Report delayed
2. EIA-glutamate dehydrogenase
3. EIA-Toxin A&B
4. PCR for Cl. difficile gene **(Ideal)**
5. Histopathological examination

Rx:- Vancomycin ORAL
Toc: fecal transplantation.

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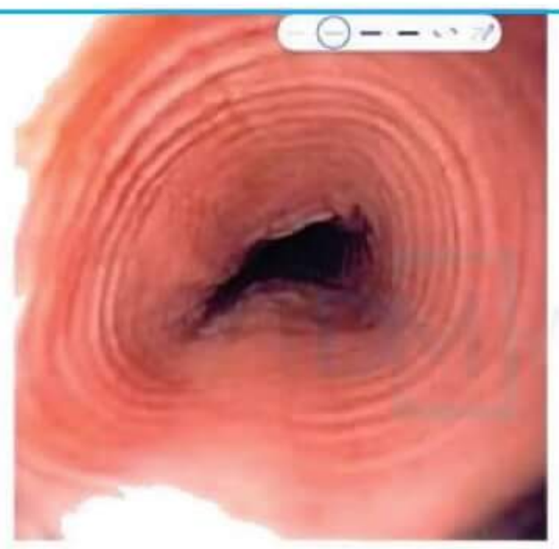
Extra Miles:



This endoscopic image is of **feline esophagus**

↓

Concentric rings luminal narrowing

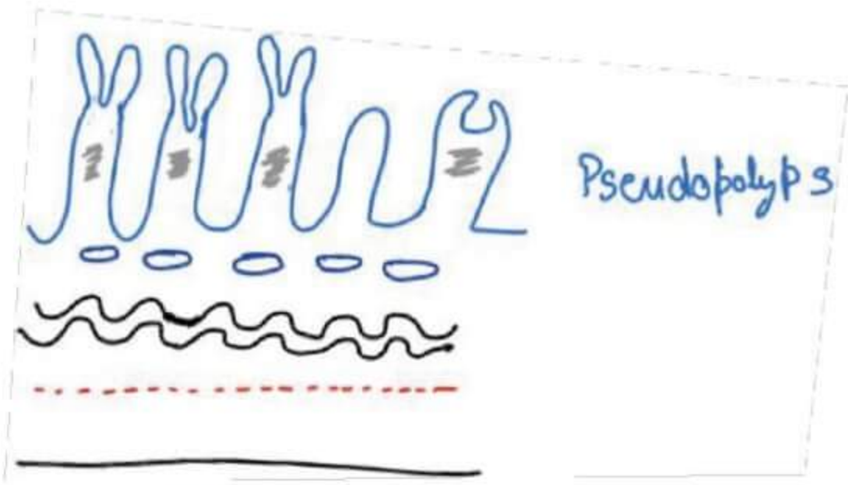
↓

Eosinophilic esophagitis→**10-15 eosinophills**

(It is associated with Gerd and Atopy)

→ **HPE in Bx**

Ulcerative Colitis:



MC site-Rectum
Pseudopolyps formation

C/F:

1. Painless bloody diarrhea - **10-15times/day**
2. Anemia
3. Hypoproteinemia -**Puffy eyes**
   Pedal edema
4. Toxic megacolon : **UC > CD**
5. Malignancy : **UC =CD**

Fistula-
Stricture ±
Abscess -

PrepLadder

Investigations:

1. p -ANCA
2. **FECAL CALPROTECTIN**, is a biomarker of bowel inflammation and help in differentiating from irritable bowel syndrome.
3. **Colonoscopy + Bx**- Granulomas are absent
   r/o malignancy
4. **X Ray abdomen**

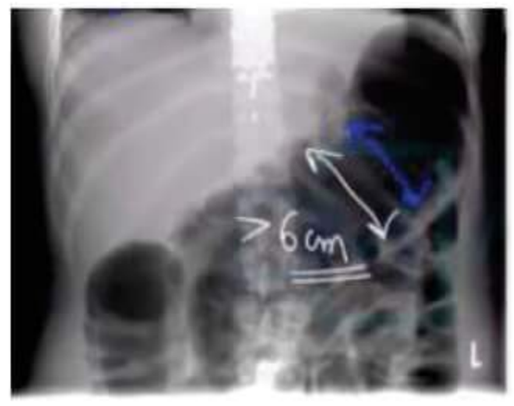
Toxic megacolon

* Transverse colon
* > 6 cm

5. **Ba enema**

↓

* Loss of Mucosal granularity appearance (Earliest feature)
* Loss of haustrations
* Lead pipe colon



Treatment:

→ **SULPHASALAZINE** (Pro drug) → **5 ASA**: Local auto inflammatory aminosalicylic acid (Active)

LARGE BOWEL ▷

→ In acute exacerbation→ Budesonide enema
Sulfasalazine
Azathioprine
Infliximab

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If Medical therapy fail → **PROCTOCOLECTOMY** with ileo-anal pouch anastomosis

Extra Intestinal manifestations of Inflammatory Bowel Disease (CD >UC)

*Arthritis (MC): **Sacroiliac joint / Peripheral arthritis**
involved: HLA B_{27}+

- Psoriatic arthritis
- JRA
- REITER'S SYNDROME
- Ankylosing Spondylitis
- IBD

1. Dermatological Features
   * Erythema Nodosum *ULCER SHIN - PYODERMA GANGRENOSUM
2. Clubbing
3. Osteoporosis
4. Primary Sclerosing Cholangitis (UC >CD)

	UC > CD	CD > UC	CD = UC
1.	Toxic megacolon	Arthritis	Incidence of Cancer
2.	PSC		

PrepLadder

STRICTURE – OJ (Obstructive jaundice/ ICTERUS) } PSC
Cholestasis

STENTING: Rx

Can relieve cholestasis: Definitive management is Orthoptic Liver Transplantation.

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PrepLadder

CHRONIC LYMPHOCYTIC LEUKEMIA

- MC leukemia in adults – CLL chronic lymphocytic leukemia
- MC leukemia in children – ALL acute lymphoblastic leukemia
- Acute megakaryocytic leukemia (M7) associated with Down syndrome → Trisomy 21
- CML → Philadelphia t (9:22)

CHRONIC LYMPHOCYTIC LEUKEMIA

- Abnormal proliferation of Immuno-incompetent B cells in mantle zone lymph node
- Characterized by:
  - Auto immune hemolytic anemia
  - Auto immune thrombocytopenia

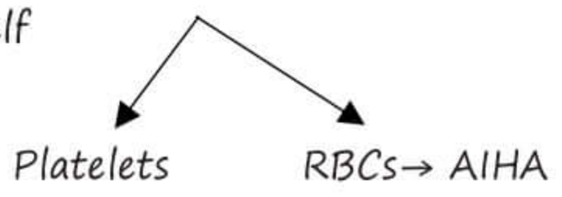
→ **CAUSES**

1. Deletion 13q
2. Trisomy 12
3. Deletion short arm chromosome 17
4. Over expression of BCL – 2 (anti-apoptosis)
5. Over expression of ZAP-70 (anti-apoptosis) Zeta associated protein

→ **C/F:**

Median age of presentation: 72 years

1. Progressive cervical lymphadenopathy, night sweats
2. Infections: Recurrent Pneumonia, Herpes labialis, Herpes zoster
3. Antibodies against self



6. Petechiae
   Non blanching
   @ Ankles
7. Purpura
8. Epistaxis
9. Hepatosplenomegaly

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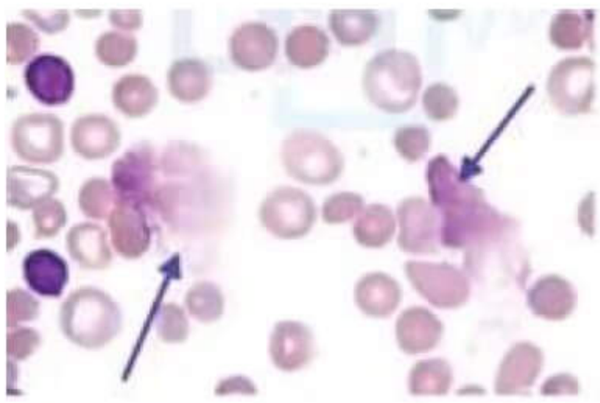
→ **Work up:**

1. **TLC ↑** (4k – 11k) → B cell lymphocytosis > 5000 / μ L x 3 months
2. **On Peripheral Smear** – SMUDGE Cells fragile, immune incompetent B cell which breaks down by pressure of glass slide.
3. **IOC→** Flow cytometry CLL→ CD19, CD20 (dim), CD21, CD23, CD5
   – B cell presents with T cell marker.



SMUDGE CELLS

If the case presents Peripheral blood (MCL): CD19 CD20 (bright) CD21, CD5 FMC-7
With enlarged lymph node and CD 23 is missing → **Mantle cell lymphoma**

PrepLadder

4. **LN biopsy**: if there is Fast progressive increase of LN size with pain, fever → all these presentations are the signs of high grade transformation called as RITCHER SYNDROME where CLL transform in to high grade lymphoma

➢ **RAI – SAWITSKY STAGING:**

- Low risk (25%) – lymphocytosis (>5000 cells) cu mm
- Intermediate risk: MC 50% – Lymphocytosis + LN
- High risk (25%)– Lymphocytosis + LN + AIHA / thrombocytopenia

➢ **Binet classification:**

A: < 3 Areas of lymphadenopathy with no anemias or thrombocytopenia

B: <3 Areas of lymphadenopathy with no anemias or thrombocytopenia

C: Hb < 10gm% and /or platelets < 100 x 10^9 /L

Treatment:

Low risk, stage A: 75 year old → CONSERVATIVE MANAGEMENT

High risk: Fludarabine, Cyclophosphamide, Rituximab (FCR) or
Pentostatin, Cyclophosphamide, Rituximab (PCR)

DOC: Fludarabine

TOC: Allogenic Bone Marrow Transplantation

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CHRONIC MYELOID LEUKEMIA

Genetics: Chromosomes involved → t (9:22) (PHILADALPHIA CHROMOSOME)

(Between both long arms)

i.e. long: long swap.

→ It is a balanced translocation because there is no loss of genetic material.

→ This leads to creation of a hybrid oncogene known as **BCR-ABL1 gene** which leads to **activation of tyrosine kinase enzyme** that will provide unlimited energy to the cells leading to increased mitosis and thus leading to cancer.

Note:

Bcr → Break Point cluster

Abl → Abelson leukemia

This oncogene abl:bcr is in turn responsible for production of a NOVEL ONCOPROTEIN Known as:

P- 210$^{BCR-ABL1}$

↓

It is called so because of the molecular weight i.e. 210 Kilo Dalton.

Problem with **P- 210** $^{BCR-ABL1}$:

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(i) ⊕ **of tyrosine kinase enzyme**: which provides unlimited energy to the cells leading to uncontrolled mitosis.

(ii) **Θ apoptosis**: neutrophils will not die and will lose their ability to fight bacteria. They will not die at their usual time i.e. $t^{1/2}$ → 6 hrs but in CML, they are living longer.

Hence **Neutrophil Alkaline phosphatase (NAP) score is lesser** which is responsible for neutrophils to fight infections.

↓

Hence infection like pneumonia are seen in CML patients and that is the reason we use **tyrosine kinase inhibitors** in these patients.

Advantage with **TKI**→ 10 Year survival rate has increased up to 85%.

Important Points :

- P- 190 $^{BCR-ABL1}$ → Worse outcome
- P- 240 $^{BCR-ABL1}$ → Indolent Course

Extra miles :

Why the survival rate (10 Year) has increased with the use of Tyrosine Kinase inhibitors ?

↓

Before TKIs were available, the 10 year survival rate was only 30%.

After TKIs → 10 year survival rate → 85%.

Hence treatment of choice for CML is tyrosine kinase inhibitors.

PrepLadder

C/F:

Most patients of CML have a triphasic course i.e.

1. **Chronic phase**
2. **Accelerated phase**
3. **Blast crisis**

❖ **Age**: 55-65 years (usual age of presentation)

↓

1. **Nonspecific symptoms** → Fever, involuntary wt loss, fatigue, sweating (due to hypermetabolism) due to large no. of cancer cells.
   - Weight loss is unintentional / involuntary → defined as **>5% over 6-12 months**.

Extra miles: If mentioned in ques. **category B symptoms** in Hodgkin's lymphoma → then it is > 10% over 6-12 months.

2. Extensive pruritis present → Because basophil count ↑↑
   i. Leading to release of histamine
   ii. Leading to itching, flushing, episodes, peptic ulcers,
   iii. Secretory diarrhea.
3. Early satiety
4. On per abdomen Examination → Massive splenomegaly

5. Constipation can also develop in contrast to secretory diarrhea due to spleen pressing upon the transverse colon and early satiety due to spleen pressing on stomach.

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EXTRA MILES: D/D of Massive Splenomegaly

↓

→ Kala Azar
→ Gaucher's disease
→ CML

6. Fullness in the left upper quadrant of abdomen.
7. Lymphadenopathy can be seen as the disease progresses.
8. Hepatomegaly, LN (+)
9. Thrombotic events can also be seen.
   - Reason for thrombotic events: TLC ↑↑ (Accelerated Blast crisis phase)

↓

If TLC > 1 Lac/mm^3 aka Hyper leukocytosis

↓

Leads to Sluggish circulation

→ Also, in CML initially platelet counts are also elevated
→ Leukostasis (brain and lung parenchyma are affected)

PrepLadder

Sluggish Brain circulation	Sluggish Lung circulation
Confusion	Severe respiratory distress
Encephalopathy	dyspnoea
Stroke/CVA	

→ Priapism → cut off is 4 hrs. (if painful erection lasts for > 4hrs)

→ Blindness → (involvement of retinal vasculature)

→ MI (Coronary circulation involvement)

→ DVT

→ Confusion

→ Respiratory distress

❖ As the disease progresses towards blast crisis: platelets ↓ leading to bleeding manifestations, petechiae, purpura.

Workup:

1. **Hb:** (N) / ↓
2. **TLC** ↑↑↑↑ (leukostasis→ Highest incidence is seen with AML) and Organs involved are primarily Brain & Lungs.
3. **DLC**: Basophilia

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In CML, there is no maturation arrest.

↓

Leading to shift to left (myeloblast series coming to circulation)

In PBF → myelocytes can also be seen

4. NAP score ↓↓↓
5. S. vitamin B12 ↑↑↑
6. **IOC**: Cytogenetics and molecular evaluation

↓ ↓

F.I.S.H **PCR** → bcr-abl 1 transcript

7. Bone Marrow Aspiration: **Myeloid: Erythroid → 15-20:1**

(↑ Reticulin content of BM– dry tap might seen)

↓

(Earlier silver staining was done)

PrepLadder

❖ **Accelerated phase of CML:**

I. PB > 15 % blasts
II. PB > 30 % blasts + promyelocytes
III. PB > 20 % basophils
IV. Platelet count ↓ < 1 lac / mm^3

❖ **<u>Blast Crisis in CML:</u>**

→ >30% peripheral or marrow blasts

→ Extramedullary (LN, Liver, spleen) blast proliferation

CML phase	WHO definition 2016
Chronic stable phase	Blasts < 10% in peripheral blood and bone marrow
Accelerated phase	• Blasts 10-19% of white blood cells (WBCs) in peripheral and/or nucleated bone marrow cells • Peripheral blood myeloblasts and promyelocytes combined ≥30% • Peripheral blood basophils ≥20% • Persistent thrombocytopenia (< 100 × 10^9/L) unrelated to therapy or persistent thrombocytosis (> 1000 × 10^9/L) unresponsive to therapy • Increasing WBC counts and spleen size unresponsive to therapy • Additional clonal cytogenetic abnormalities in Philadelphia chromosome–positive cells
Blast crisis	• Blasts ≥ 20% of peripheral blood WBCs or nucleated bone marrow cells • Extramedullary blast proliferation • Large foci or clusters of blasts on bone marrow biopsy

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<u>TREATMENT:</u>

➢ Cytogenetic response: absence of Ph + metaphases

➢ Molecular response: <0.1 % of BCR-ABL transcript containing cells are present in blood

>3 log reduction from baseline

➢ Major molecular response: > 4.5 log reduction from baseline

<0.0032%

PrepLadder

Drugs: Imatinib

- 2nd gen
  - Dasatinib
  - Nilotinib
  - Bosutinib: (imatinib resistant CML)
- 3rd gen
  - Ponatinib:
    - T315 L mutation
    - when there is failure of ≥ 2 TKIs)
  - Omacetaxine

Allogenic stem cell transplantation is the treatment modality only when the patients has progressed to blast cell crisis stage. Other stages can be managed with TKI.

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PrepLadder

ACUTE MYELOBLASTIC LEUKEMIA

- 5 year of survival rate of AML with all advancement is **25 %**
- But 10 year of survival rate of CML with advent of tyrosine kinase inhibitor is **85%**
- These survival rate indicates complications associated with management of disease and presentation, also its relatively stormy / aggressive management.

Median age of AML: 67 years

In children with Down syndrome: M7 is M/C type (otherwise ALL is M/c in children with less than 3 years of age)

→ CAUSES:

1. **Idiopathic (M/C)**
2. **Bone marrow failure**
   - Fanconi anemia → Congenital aplastic anemia which leads to AML in future.
   - (Fanconi syndrome due to RTA because of damage to PCT)
   - Schwachman diamond syndrome
   - Diamond black fan syndrome
3. **Down syndrome (M7 AML)**
4. **Defective DNA repair**
   - Bloom syndrome
   - Ataxia telangiectasia
5. **Exposure to alkylating agent** $\xrightarrow[\text{Monosomy 5}]{\text{Monosomy 7}}$ **4-6 yrs → AML**

   Exposure to topoisomerase II inhibitors $\xrightarrow{\text{chromosome 11}}$ **1-3 years → AML**
6. **Radiation / benzene / phenylbutazone /chloramphenicol**

- Chloramphenicol can cause aplastic anemia which can later evolve into AML.

7. **Chromosomal swap:**

- t (15:17): forms fusion product **PmL – RARA** → leading to APL(Acute promyelocytic leukemia). It can cause **DIC** (d/t releasing of Auer rods by chemo)
- t (8:21): RUNx1 – RUNx1t1
- Inv 16 t (16:16)

8. Activating mutation of FLT3 gene is incremental to cause 30% of AML cases.

FLT 3 gene	t (8:21)	good prognosis
CEBPA	Inv 16	
NPM1	t (16:16)	

→ C/F: **(Stormy onset):** -

Case scenario: 60 years old male 3 months ago going for a walk or running nearly 4 km without any problem but now develops bone pain, body pain and not even get out from the bed, felt breathlessness while going to bathroom.

1. Fatigue / pallor - present with dyspnea grade 3 / grade 4

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PrepLadder

2. TLC ↓ – fever or

   TLC ↑↑ – >1 LAC / cu.mm

   ↓

   Hyperleukocytosis → Leukostasis

   ↓

   AML > CML in Blast crisis

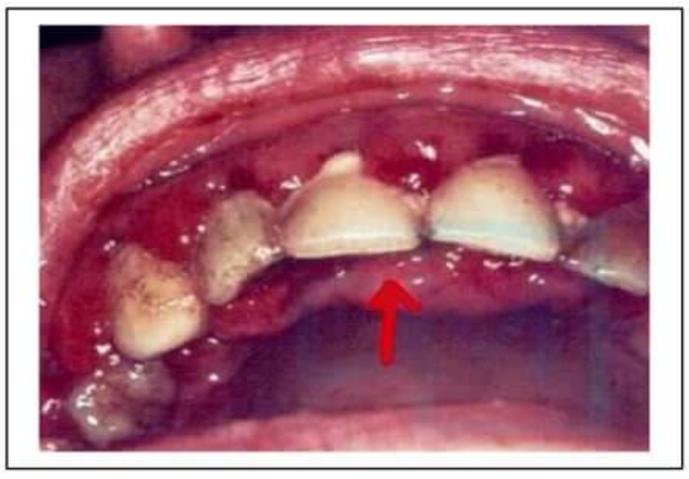
   Viscosity ↑: Blindness, brain – encephalopathy, lung – respiratory distress, priapism.

   So, AML patient soon become bed ridden and oxygen dependent.

3. Petechiae, purpura, Epistaxis
4. **DIC: M/C seen with M3 AML**
5. **Gingival hypertrophy** with bleeding: **M5 (M/C)**

– Also seen in Phenytoin, cyclosporin but bleeding is absent.

6. Hepatosplenomegaly
7. Lymphadenopathy (results in dry cough by compression on air way)
8. Headache



GUM HYPERTROPHY

EXTRA MILES:

CNS leukemia most commonly predisposed by ALL > AML as blasts and can cross the BBB

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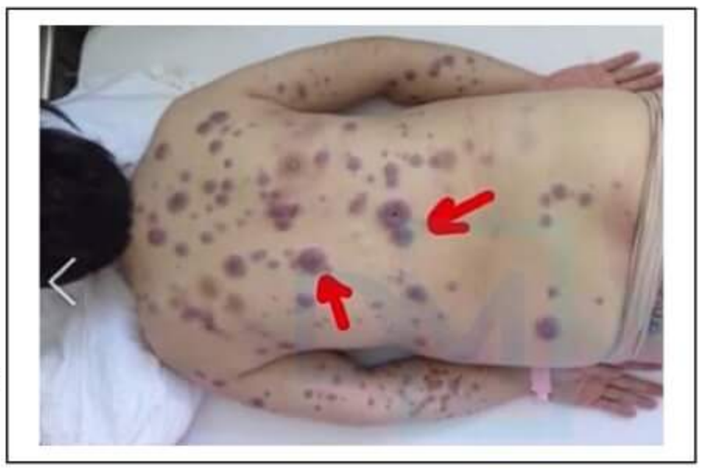
9. **Myeloid sarcoma** (cancer cell infiltrates the skin) →



10. Spinal granulocytic sarcoma

-This can grow fast and compress the spinal cord tissue that leads to paraplegia/ quadriplegia.

→ WORKUP:

1. Bone marrow Aspiration: IOC

   – Site: Posterior Superior iliac spine.

Needles: –

Reusable

- Salah needle
- Klima needle

SALAH NEEDLE

KLIMA NEEDLE

- T- handle needle: bone marrow biopsy needle

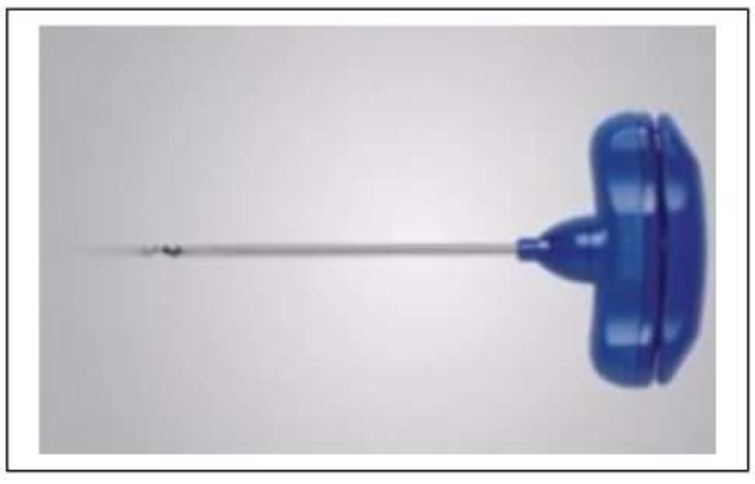
Cut off for diagnosis AML: >20% of myeloblast on biopsy except: –

t (15:17)

t (8:21)

Inv 16

t (16:16)



T- handle needle

- Can diagnose AML if any of above is present with even 10-15 % myeloblast on biopsy.

- Morphology: -

  Auer rods + → eosinophilic granules present in cytoplasm of Auer rods.

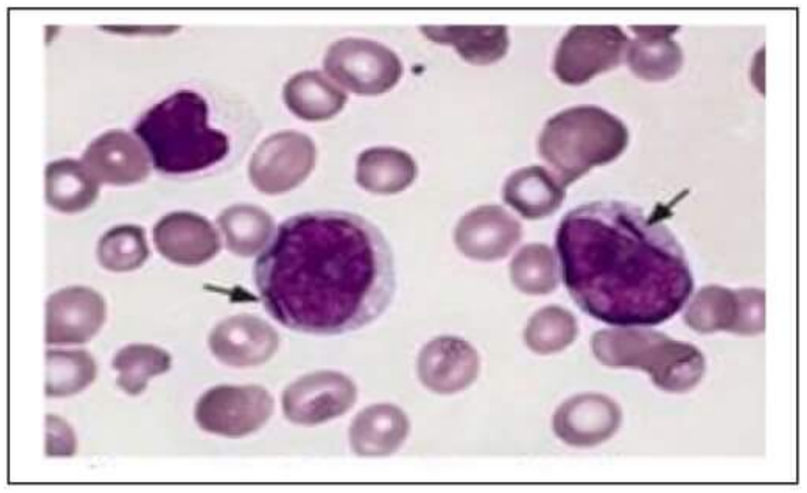
- Flow cytometry for myeloid series: -

  CD 13/14

  CD 41/61 – M7

- Cytogenetics and molecular diagnostic
  - FLT 3
  - CEBPA
  - NPMI

  } Favourable prognosis in the patient



AUER RODS

2. HLA matching
3. CXR
4. Echo
5. KFT – it has been done because sudden rise of creatinine due to tumor lysis syndrome after chemotherapy.
6. On CBC: ↓Hb, TLC↓, Platelet ↓

Classification based on morphology: -

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M0: Undifferentiated

M1: AML with minimal maturation

M2: AML with some maturation – m/c subtype

M3: Acute promyelocytic leukemia - Highest concentration of Auer rods

- Associated with DIC
- Excellent prognosis with ATRA.

M4: Acute myelomonocytic leukemia

M5: Acute monocytic leukemia – Gum hypertrophy

M6: Acute erythroleukemia

M7: Acute megakaryocytic leukemia – a/w Down syndrome (flow cytometry CD41/61)

→ Rx of AML:

- Primary chemotherapeutic agents: **Cytarabine + Anthracycline**

Note: Baseline ECG done before initiating anthracycline drugs because of cardiotoxicity

- Anthracycline which are commonly prescribed in AML: **Daunorubicin, Idarubicin**

On clinical remission: Allogenic stem cell transplantation

PrepLadder

APL: chemotherapy cause death of cancer cells

↓

Release Auer rods

↓

↑ risk of DIC

→ Rx: **ATRA (all trans retinoic acid) + Arsenic trioxide**

- S/E: Differentiation of immature cells to mature called as Differentiation syndrome.

Differentiation Syndrome

↓

these cells adheres to pulmonary endothelium and cause v/p imbalance

↓

Respiratory distress

↓

Rx: Steroids

Mortality rate of differentiation syndrome: 10%

Extra mile:

- **Schwachman diamond syndrome**
  - Pancreatic exocrine defect which manifest as malabsorption syndrome from childhood.
  - Myelodysplastic syndrome cause cytopenia of 2 or >2 cell lines.
- **Diamond black fan syndrome**: manifest only a myelodysplastic syndrome, with physical abnormalities

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ACUTE LYMPHOBLASTIC LEUKEMIA

- M/C tumor in children: ALL > Medulloblastoma> Neuroblastoma
- M/C tumor occurs in Down Syndrome children: ALL
- ALL contributes to CNS leukemia by crossing the blood brain barrier
- Lymphoblast of the tumor cause **Meningismus**

↓

Mx.

CNS Radiation

+

Intrathecal methotrexate

S/E: alopecia

PORTACATH

- **Deliver chemotherapy directly into central vein**, (subclavian vein)
- **Reduce the risk of thrombophlebitis**, (usually central vein catheterization cause – Thrombophlebitis and extravasation of anticancer drug will cause ulceration in the surrounding local tissue but here the risks are minimized.

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Most of the ALL are B cell line around 76%

- **Subtype**: common ALL: expressing CD10
- Associated with t (9:22)

IF T cell line: 24%

- **Subtype**: Cy CD3 (cytoplasmic CD3) / SCD 3 (surface CD3)
- Present in young age
- More Mediastinal involvement and lymphadenopathy → High risk patient.
- Testicular involvement

PORTA CATH

Extra miles: T cell line ALL can cross Blood brain barrier and Blood testicular barrier leading to Meningiomas and testicular lump respectively.

CRITERIA

20% of lymphoblast in a bone marrow will be diagnosed as ALL.

PrepLadder

Causes of ALL: (Mnemonic: ABCDIFKN)

A – Ataxia Telangiectasia

B – Bloom Syndrome, Benzene exposure

C – Chemotherapy (epipodophyllotoxin – Topoisomerase II inhibitor) → both AML & ALL involved,

D- Down Syndrome (M7 AML > ALL > other subtype of AML)

I – Ionizing radiation (CLL is not a/w ionizing radiation); infection with HTLV-1

F – Fanconi Anemia → associated with both AML & ALL

K – Klinefelter syndrome

N – Neuro fibromatosis

P – Philadelphia Chromosome – t (9:22) → Tyrosine kinase inhibitors are used here.

Chromosomal Translocations Other than Ph chromosome

- t (4:11)
- t (1:19)
- t (8:14)

Extra miles:

Ataxia Telangiectasia

- Damage to spino-cerebellar pathway
- Dilated blood vessels on the white of the eye
- ALL

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Fanconi Syndrome:

- RTA Type: 2
- PCT damage
- Wilson Disease

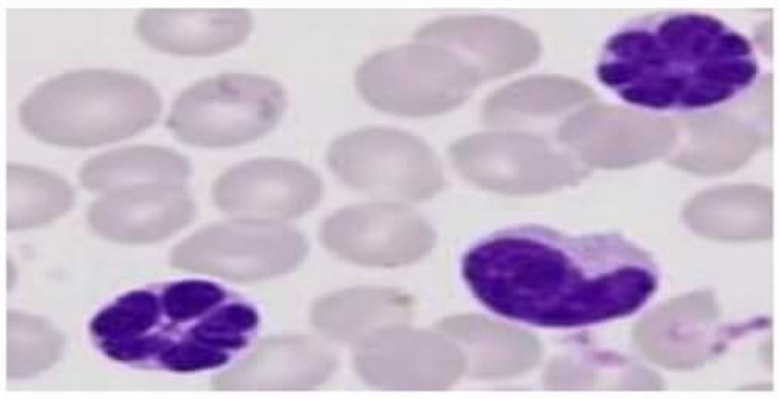
Viral Infection associated with ALL:

- HTLV-1 – Adult T cell Leukemia

↓

Flower cells in the peripheral circulation

On peripheral smear or bone marrow study.

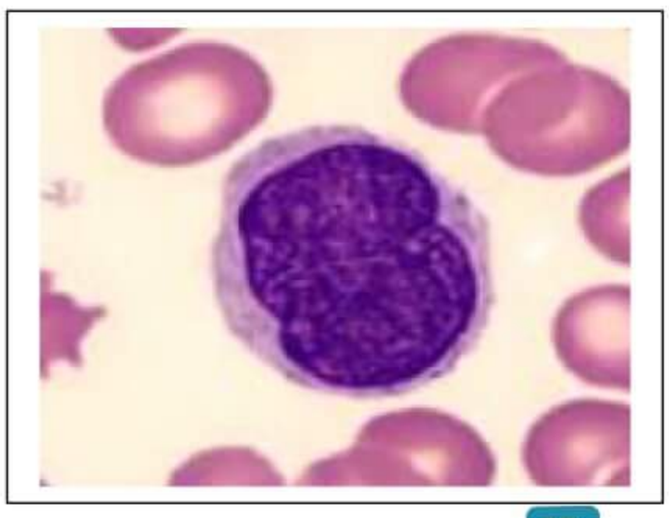


FLOWER CELLS

don't confuse with –

Sezary cell:- present in mycosis fungoides

(Cutaneous T cell lymphoma)



SEZARY CELL

HTLV – 1

Tropical	Adult T cell
Spastic	Leukemia
Paraparesis	Flower Cell

PrepLadder

Extra miles:

- **EBV** associated with HL/NHL/ Nasopharyngeal cancer / Burkitt lymphoma

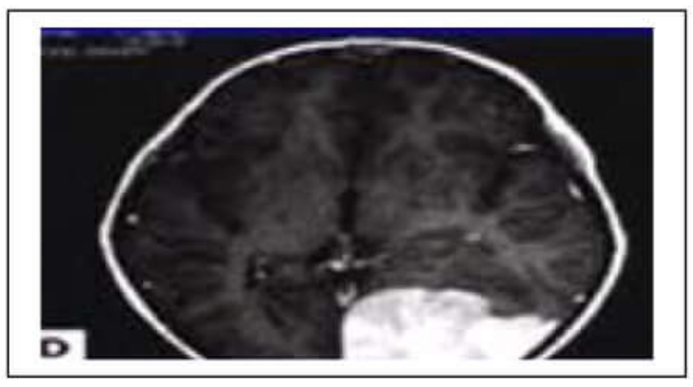
CNS leukemia diagnosed by at least one of the following criteria:

1. **CSF:** ↑ Leukocytic Cell count, n/↓ Glucose, ↑ protein
2. **CT:** Evidence of Leptomeningeal infiltration
3. **Clinical Findings**: Headache, vomiting, visual disturbances findings cranial nerve palsies especially VII, seizures.

C/F of ALL:

2-8 years or >50 years: Stormy onset

1. Hb↓, Pallor ++
2. Platelet ↓: Bleeding
3. Infections: recurrent pneumonia, necrotizing fasciitis
4. **Sternal tenderness (key point)**
5. Bone pain
6. Hepatosplenomegaly
7. Lymphadenopathy
8. CNS leukemia: raised ICP
9. Testicular mass



CT: Leptomeningeal infiltration

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Extra miles:

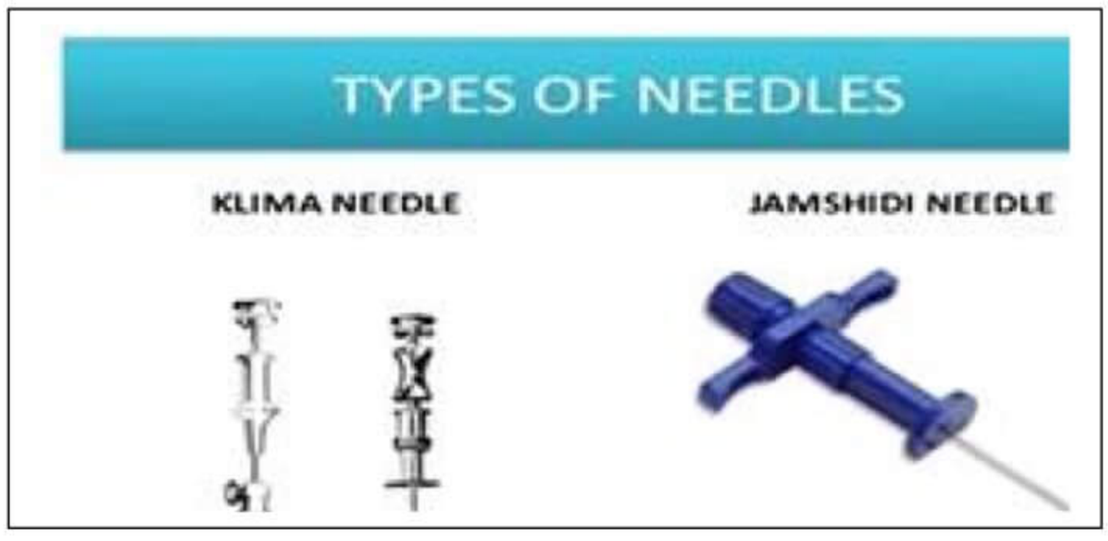
Splenohepatomegaly (spleen > Liver): Features of Extramedullary Hematopoisis.

1. Thalassemia (present in both α and β varieties)
2. Myelofibrosis

→ Work up:-

1. CBC: Hb↓
   - A) TLC: normal / ↑
     - Leukostasis more common in AML > ALL → results in breathing difficulties (D/t ↓ pulmo- circulation) (↑Viscosity)
   - B) Platelet ↓
     - Petechiae → mostly present in ankle
     - Purpura
2. Bone marrow aspiration: - **IOC**

- KLIMA NEEDLE
- JAMSHIDI NEEDLE



Site: **Post. superior iliac spine** > iliac crest , procedure done under cover of Propofol

PrepLadder

Findings:

- a) Blast >20% (WHO criteria)
- b) Morphology

L1 (M/C)

L2

L3 (Burkitt leukemia)

- Mature B cell ALL
- CD 10 +, s Ig + (surface Ig)
- t(8:14), t (8:22), t (2:8)

c) Immunophenotyping: -

- CD 19 → Used for targeted therapy

d) Cytogenetics by using FISH

e) Cytochemistry: TDT (terminal deoxy nucleotide transferase) positivity

↓

+ve for **DNA polymerase** which triggers uncontrolled mitosis in nucleus of the cell.

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3. Lumbar puncture: -

→ During the procedure **intrathecal methotrexate** is given to prevent CNS leukemia

4. Baseline - serum Uric Acid, PO4, K, Ca.

→ To detect Tumor lysis syndrome early.

→ Chemotherapy kills huge number of cancer cells that will result in:

- ↑ Uric acid
- ↑ Po4
- ↑ K+
- ↓ Ca

5. HLA matching for patient / siblings / parents

High risk ALL	Low risk ALL
• Age <1 year (or) >10 year	1-9 year,
• Boys, Dissemination to LN/Liver/Spleen/CNS	Female
• WBC count: ↑	white WBC count: <50 K
• Mature B-cell ALL	Pre-B-Cell
• Absence of C10	
• Hypoploidy	Hyperdiploidy (Imp)
• MLL gene t (9:22), t (8:14), t (1:19), t (4:11)	t (12:21) (Imp)

PrepLadder

- **Low risk** : 1-9 years, WBC <50 K, Pre- B-Cell, hyperdiploidy
- **Standard risk** : 1-9 year, WBC <50 K, Pre-B-Cell, normal Cytogenetics → No chromosomal swap
- **High Risk** : Hypodiploidy
- **Very high risk** : Induction failure, t(9:22)

- Low risk
- Standard risk } **chemotherapy**
- High risk : **stem cell transplantation**
- Very high risk : **Tyrosine kinase inhibitors, Targeted therapy**

→ Rx:

Complete molecular remission: can as early as 6-16 weeks → **minimal residual disease (MRD)**

↓ ↓

High risk patient: 80% **<0.01% of cancer cell left behind**

Standard risk patient: 90% **(or) < 1 leukemia blast for 10,000 cancer cells**

Methods for determination of minimal residual disease:

1. Real time Quantitative PCR (Done Before Rx and After Rx) → best way to identify MRD
2. Flow Cytometry → CD19
3. FISH → Cytogenetic +ve cells

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Adult B cell ALL: 25% of cases presents with Ph+

- Tyrosine kinase inhibitors are used: DASATINIB/NILOTINIB
- Immunological targeting: -
  - BLINATUMOMAB
  - CART-19 – chimeric antigen receptor T cells **(imp)**

} New approach

Chemotherapy for ALL:

Remission induction 1:

V – Vincristine

A – L-asparaginase

P – Prednisolone

D – Daunorubicin

I - Intrathecal Methotrexate

Remission induction 2: Methotrexate, Cranial irradiation, Cyclophosphamide, 6 MP.

- **S/E**: Cranial irradiation in childhood can develop **meningioma** in future

Consolidation (14-28 wks): Vincristine, Daunorubicin, cyclophosphamide, Cytosine Arabinoside

Maintenance (2-2.5 years) : V,D,A,P, 6 MP

Relapse: - **>5% of ALL** cells in blood / bone marrow.

PrepLadder

MULTIPLE MYELOMA

Plasma cell Dyscrasias

Antibodies1 – Heavy chain → G, A, M, D, E

– Light chain → Kappa and λ (lambda)

Over production of light chains of Ab → defective Ab produced → infection (Pneumonia or pyelonephritis) causing Mortality.

* **Most common cause of death in multiple myeloma → infection.**

Note:

→ Normal protein in urine is < 150 mg/day (<30mg is albumin).

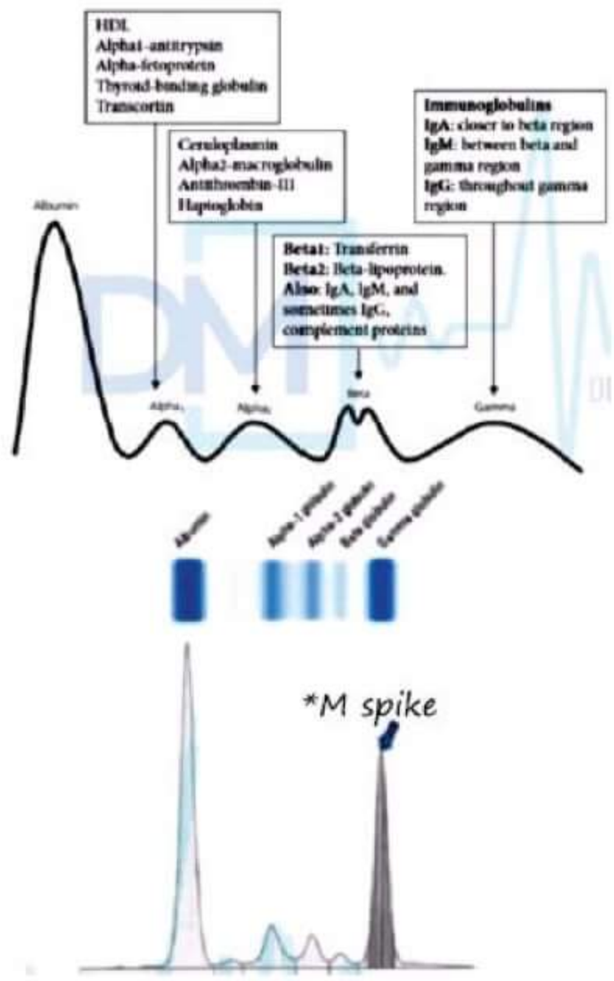
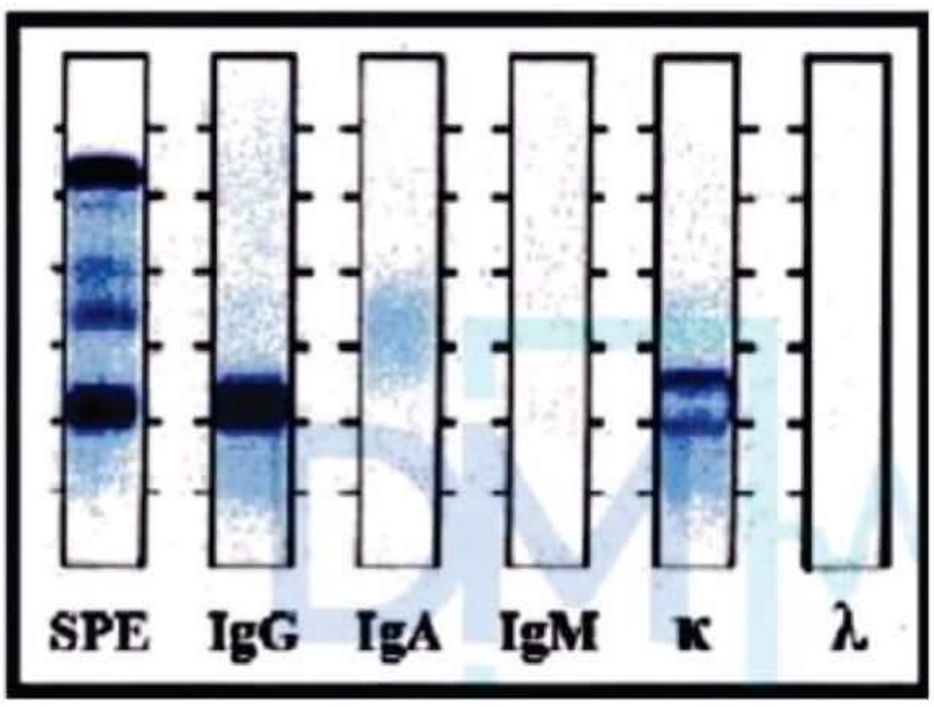
→ Normal light chains in urine < 10 mg/day. These are increased in MM.

→ ∴ serum & urine light chain assays are used for diagnosis of MM.

→ Hyperviscosity develop in patients → symptoms of the headache, visual impairment and ataxia.

→ M – Component (Light chains) → To appear in blood, the tumor load > 10^9 → Causing excessive amount of paraproteins.

To Detect the Paraproteins

Immunoelectrophoresis	Immunofixation
Monoclonal cells are present in spike (CD138 positive) → This appearance in also called "CHURCH SPIRE" 	→ The most common defective Ab produced is IgG → By immunofixation we can find which Ab is over produced **Alpha 2 11.4 7.5 - 13.4 0.9 0.5 - 0.9** **Beta 7.5 8.5 - 13.7 0.5 0.6 - 1.0** **Gamma 40.2 8.8 - 19.2 3.6 H 0.6 - 1.4** 

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PrepLadder

Criteria to make the diagnosis of MM.

→ Bone Marrow plasmacytosis > 10% → Diagnosis criteria for MM

→ Presence of serum/ Urine "M component"

→ Myeloma defining events (Bone pain, infections).

→ Etiology:

1. **Radiation**
2. Wood worker, Farm workers – due to exposure to **petroleum products**.
3. Hyperdiploidy, 13q/4 (Also for Retinoblastoma), t (11:14), t(4:14), t(14:16), deletion 17p, Chromosome 1 q – Amplification or deletion.

Note → No. "14" is repeating in MM, but in case of Burkitt lymphoma No. "8" repeats – t(2:8), t(8:14), t (8:22)

→ Pathology of Multiple myeloma:

1. **Myeloma cell** → Excess of **IL-6** → Causing activation of the osteoclasts resulting in lytic bone lesions
2. **S. calcium ↑↑**,

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3. Serum alkaline phosphate (SAP) is normal.
4. **Renal failure** that causes uremia.
   - The **leading cause of renal failure is ↑↑ Ca**, but there is also presence of amyloidosis (AL) in kidneys.
   - **Pyelonephritis** due to infection also damage renal parenchyma.
   - Due to bone pains, the **NSAID's use on regular basis** sums up the renal damage, because NSAIDS affect prostaglandins which in turn affect filtration of kidney.
5. **Hyperviscosity** causes: headache, visual problems, ataxia.
   - Normally, plasma has 1.8 times the viscosity of water.
   - In MM, the viscosity = 4 x water → causing sluggish circulation in patient and ischemia to tubules (kidney damage)
6. **Hypogammaglobulinemia** (though excessive antibodies are produced but these are **ineffective**) → Resulting in infections – Pneumonia (M/C) & Pyelonephritis.
7. **Normocytic normochromic anemia** developing in a patient → due to infiltration of bone marrow cells by myeloma cell → Replacement of normoblast
8. **Bleeding** → Ab coated platelets → Causing malfunction of platelets and prolonged BT.
9. **Amyloidosis** → Causes manifestations like the carpel tunnel syndrome.

PrepLadder

→ Clinical Features:

→Bone pain is the M/C symptom → starts in vertebra and causes compression myelopathy. There can be sudden onset paraplegia & bladder/bowel incontinence because of lumbosacral nerve roots involvement

→Pelvis is also involved, but the skull is involved last.

→Hypercalcemia causes lethargy, fatigue, CHF,

→Uremia (creatinine can go upto 2 mg% or higher)

→Headache, dizziness, vertigo due to hyperviscosity.

→Pallor and bleeding manifestations.

→Pain in hand d/t Carpal tunnel syndrome (also seen with hypothyroidism, pregnancy and acromegaly)

Components of end organ damage in multiple myeloma:

C – Hypercalcemia > 11 mg%

R – Renal failure: Uremia (Creatinine > 2 mg%)

A – Anemia

B – Bleeding, Bony lytic lesions.

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→ These features are must for diagnosis of multiple myeloma, but we don't need all of them.

→ If any one of these is present along with **Plasmacytosis > 10%**, is sufficient for the diagnosis of MM.

→ WORK UP:

1. **Complete blood count**
   - **ESR ↑↑**
   - **Plasma cell leukemia** → Plasma cell count in blood > **2000/µL**
2. **Albumin: globulin ratio**
   - Disturbed ratio due to ↑↑ globulin
3. KFT: s. Creatinine > 2 mg%
4. PET-CT/ MRI
   - For evaluation of damage to Axial skeleton of patient.
5. Bleeding time ↑↑: Due to platelet coated by Ab.
6. Anion Gap ↓↓: M-Component (paraprotein) is increased (which are positively charged) → so to maintain electroneutrality; kidney start reabsorbing ↑↑ amount of chloride Cl^- and thus Cl^- levels rise.

Anion Gap:

→ [+] – [-]

→ [Na] – [Cl + HCO3]

→ [Na] – [Cl↑↑ in MM + HCO3]

→ Reduced anion gap in MM

PrepLadder

7. **Screening test for MM**

   - **Serum/ Urine electrophoresis** and then the **immunofixation** → to check the type of Ab.

8. Flow Cytometry = CD138 +

9. IOC for MM = Bone marrow biopsy → It reveals **> 10% plasma cells.**

10. **Urine β_2 microglobulin level** → Best test for prognosis of MM.

11. **Abdominal fat pad biopsy** → to check for the amyloidosis.

12. **FISH:** t(4:14), t (11:14) etc.

13. **Serum light chain assay**

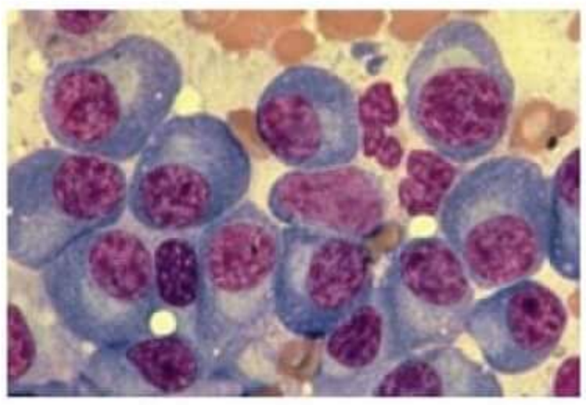
On Histology:

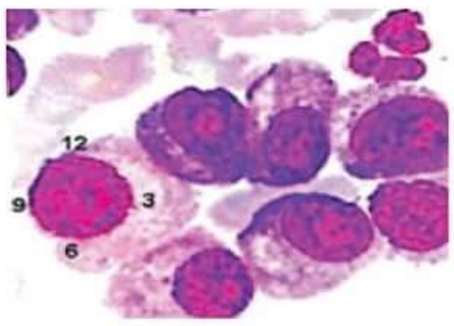
→ Perinuclear halo (clearing)

→ Russel body inclusions are present in cytoplasm.

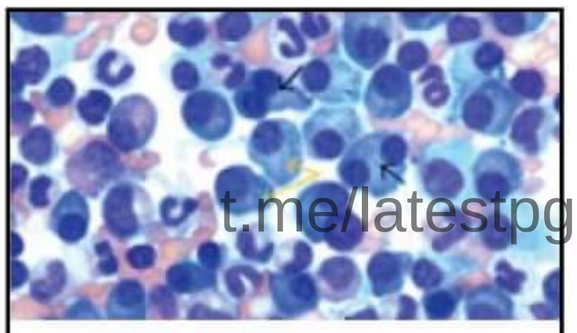
→ Clockface chromatin present in the peripherally of the nucleus.

→ Dutcher bodies accumulation in nucleus.





("clock face" pattern of nuclear chromatin in plasma cells)



(Russel bodies accumulation)

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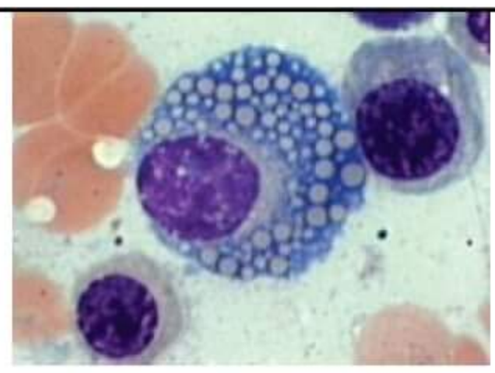
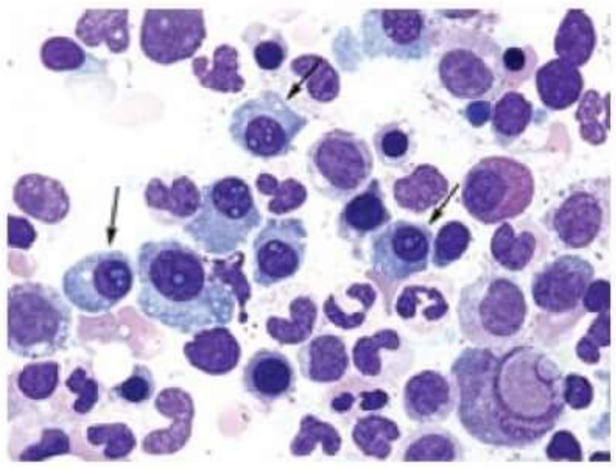


Light chain accumulation inside cell – Mott cell

→ Rain drop pigmentation



Dutcher bodies – Accumulation of Ab (Light chains)

PrepLadder

Best way to identify the disease progress in the patients – PET – CT / MRI

→ Myeloma Kidney → Bence jones protein inside the tubule.

→ Latest Criteria for MM:

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In the NCCN guidelines, active multiple myeloma is no longer diagnosed using the CRAB criteria (hypercalcemia, Renal failure, Anemia, Bone lesions) for End organ damage.

The current diagnostic criteria are as follows:

1. **Bone marrow clonal plasma cells ≥ 10%** or bony or extramedullary plasmacytoma (confirmed by biopsy)
2. **One or more myeloma defining events.**

Myeloma defining events include the following:

- Serum calcium level >11mg/dL
- Renal insufficiency (creatinine > 2 mg/dl)
- Anemia (hemoglobin < 10 g/dL)
- One or more osteolytic bone lesion on skeletal radiography, CT, or PET-CT
- Clonal bone marrow plasma cells ≥60%
- Abnormal serum free light chain (FLC) ratio ≥ 100 (involved kappa) or < 0.01 (involved lambda)
- One or more focal lesion > 5 mm lesion on MRI scans

Note →This means if CRAB is not present still diagnosis of MM can be made if:

→ Clonal bone marrow plasma cells ≥ 60%

→ Abnormal serum free light chain ratio ≥ 100 (involved kappa) or < 0.01 (involved lambda)

→ One or more focal > 5 mm lesions on MRI scan.

PrepLadder

Scenario – 1

Plasma cell in BM < 10%, M – component in plasma < 30 g/L and no evidence of myeloma like events.

↓↓

Dx – "MGUS" Mono clonal gammopathy of unknown significance.

Scenario – 2

Plasma cell in BM > 10%, M – component in plasma > 30 g/L and no evidence of myeloma like events

↓↓

Dx – Smoldering myeloma

Scenario – 3 Plasma cell > 2000 cells in circulation

↓↓

Dx = Plasma cell leukemia

For **prognosis** of patients → β_2-Microglobulin and albumin

Stage	Criteria
I	Serum beta 2 microglobulin < 3.5 mg/l and serum albumin ≥ 3.5 g/dL
II	Serum beta 2 microglobulin < 3.5 mg/l but serum albumin < 3.5 g/dL or Serum beta 2 microglobulin 3.5 to < 5.5 mg/l
III	Serum beta 2 microglobulin ≥ 5.5 g/dL

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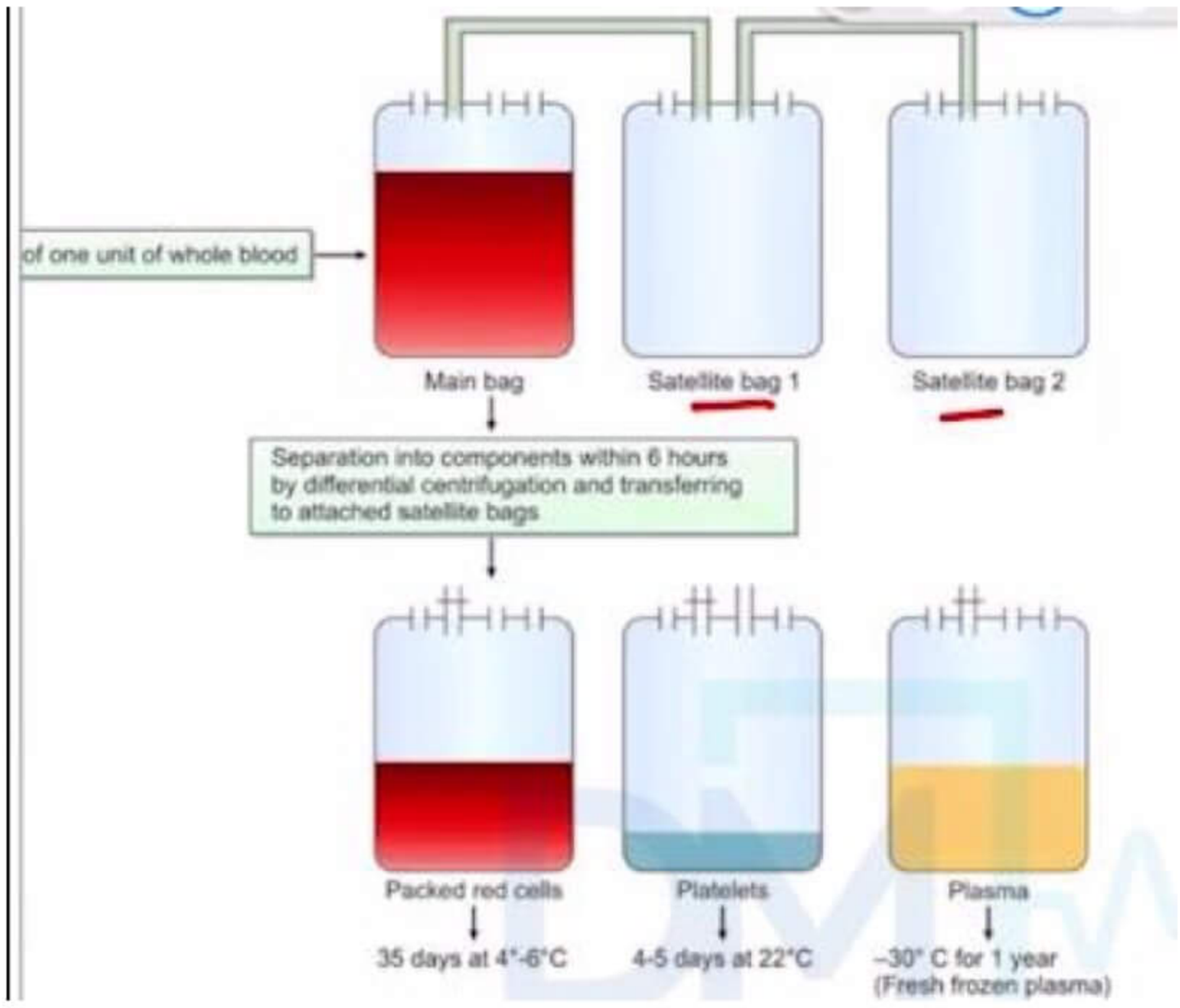
Rx →

- Dexamethasone + Lenalidomide + Bortezomib (Protease inhibitor) – 100% response rate
- Autologous stem cell transplantation

  Normally we do **Allogenic** stem cell transplantation.

PrepLadder

BLOOD COMPONENTS



PRODUCING BLOOD COMPONENTS:

Method 1 → Whole blood

↓ **High speed centrifugation**

- Packed RBC &
- Plasma (stored at -30°C as **FFP**) &
- Buffy Coat (WBC) + Platelets → **low speed centrifugation** → Platelets (Pooled)

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Method 2 → Whole blood

↓ **Low speed centrifugation**

Packed RBC + platelet rich plasma

↓ **High speed centrifugation**

Random donor platelet & FFP

In both of above methods FFP $\xrightarrow{\text{Thaw}}$ Cryoprecipitate

- **PRBC: -**

  -Storage temperature = 4°C

  -Shelf life = 35-42 days (depending upon additive solutions)

  -If CPDA is used = 35 days

  -If SAGM is used = 42 days

PrepLadder

- **Whole blood: -**

  - **1 unit of blood = 450 ml (350ml in India)**
  - Storage temp. = 4°C
  - Shelf life = 35-42 days

CPDA SAGM

  - In government hospital we use = CPDA (Citrate phosphate dextrose adenine)
  - **Uses** = Volume replacement in acute hemorrhagic shock (>25% circulating fluid volume decrease)
  - With **storage** of Whole blood:
    - Platelet count decreases
    - 2,3 BPG falls : ↑ O_2 affinity to RBC (Haldane effect)
    - factor V and VIII decrease (so FFP need to transfuse along with Whole blood)

PRBC : **1 unit PRBC = ↑ Hemoglobin 1 gm %**

↑ Hematocrit by 3%

→ Optimal target Hb. Achieved = 7-8 gm%

Note: Main aim of providing PRBC is to prevent volume overload in severe anemic patients who are already having compensated heart failure.

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- **Platelets: -**

Method

Apheresis (single donor) Pooled platelets (multiple donor)

Volume = 200-400 ml Volume = 50 – 70 ml

  - Rise in mean platelet level = 5000-10,000 cu. Mm (same for both)

To prevent intracranial bleed:

    - If No fever present / No infection then threshold is 5000/cu.mm
    - If dengue Hemorrhagic fever then threshold is 10,000/cu.mm
    - Threshold of platelet transfusion in any primary bleed (in General) = 10,000/cu.mm

  - **Shelf life** = 5 days
  - **Storage temp.** = 20-24°C
  - Chance of injection are higher with platelets.
  - Cannot transmit CMV.

PrepLadder

- **FFP: -**
  - **Volume of Bag** = 200 – 250 ml
  - **Storage temp.** = -30°C
  - Richest source of coagulative factor
  - ↑ coagulation factors in body by 2%
  - **It will provide**: -
    - Fibrinogen
    - Protein C,S
    - Antithrombin III
    - Albumin

Uses: -

1. Reversal of coagulopathy with **warfarin toxicity**
   - Prothrombin complex concentrate can be given when warfarin toxicity INR level→ 20
   - PCC >> FFP in warfarin toxicity (if PCC is not given in the option)
2. **DIC**
3. Thrombotic thrombocytopenic purpura, GBS, Myasthenia gravis during plasmapheresis.

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- **Cryoprecipitate: -**

- Components: - Factor VIII
  - Fibrinogen
  - vW Factor
    - ❖ **Not used for Christmas disease (Hemophilia B)**
- Provide fibrinogen (↑ by 0.3 – 1g %)

Uses: -

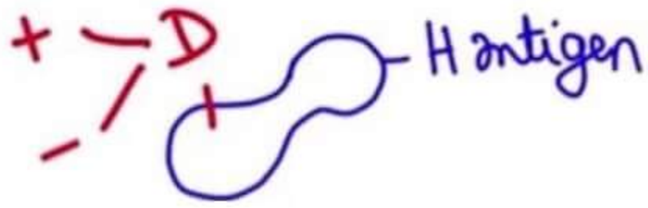
1. Type II Von Willebrand disease: Dysfunctional vWD
2. Type III vWD: Absent vWD
3. Used as topical glue

Indications for Transfusion of Cryoprecipitate	
Adults	**Neonates (continued)**
Hemorrhage after cardiac surgery Massive hemorrhage or transfusion Surgical bleeding	Anticoagulant factor XIII deficiency Congenital dysfibrinogenemia Congenital fibrinogen deficiency
Neonates Anticoagulant factor VIII deficiency	Von Willebrand disease

BLOOD TRANSFUSION & COMPLICATIONS

Blood grouping & cross matching:

- ABO system → Chromosome 9q
  - Pattern of inheritance → Co – dominance
  - Note: H antigen decides the blood groups



- Blood group A = H antigen (Fucose + Glycolipid) + N – acetyl galactosamine
- Blood group B = H antigen + Galactose
- Blood group AB = H antigen + Both (NAG + Galactose)
- Blood group O = H antigen – Both (NAG + Galactose)
- M/C Blood Group: O +ve
- Least common → OH –ve (Bombay Blood G/p) if not given, AB –ve

D antigen on Chromosome 1 will decide Rh +ve / –ve.

- 15% world population = Rh –ve (D antigen Absent)

  Iso-immunization can occur (in pregnancy or transfusion) if Rh +ve blood is exposed to Rh –ve individual

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Lewis antigen: Chromosome 19

- Carbohydrate based Antigen

Q. Most common cause of incompatibility w.r.t. Pre-transfusion screening ?

Ans. Lewis Antigen

MNS antigen: Chromosome 4

Duffy Antigen – Receptor for Plasmodium vivax.

- If person is +ve for Duffy Ag
  - ↑ed susceptibility to P. vivax.
- If person is –ve for Duffy Ag
  - One is resistant to P. vivax

In India, 350 mL blood is donated in bag while it is 450 mL in America

Pre-donation Bag

- Pre-donation Bag → Initial 10-30 mL of blood is diverted, after which blood flows into main bag.

- **Advantage** – Contagious factors from the skin are carried by initial blood which is diverted into Pre-donation bag that minimize the contamination of staph aures, staph epidermis etc, in the residual blood.
- After being released from blood bank, blood should be transfused within 4 hrs as bacterial growth can occur at room temp. and can cause sepsis in patient.

LEUCODEPLETED BLOOD:

- The Filter is used to **stop the transfusion of WBC's** to prevent complications like febrile non hemolytic transfusion reaction, Graft Vs host ds.
- Leucodepleted Blood→ RBC, plasma & platelets are transferred and WBC's are not allowed by using filters.

Filter for leucodepleted blood

CASE SCENARIO: A multigravida female who is already sensitized has a higher chance of transfusion reaction, so this filters is used to prevent this reactions.

- CMV transmission chances decreases as organism is transmitted via WBC

BLOOD BAGS:

Blood bags are always containing preexisting content like anticoagulants, preservatives, eg: CPD, CPDA, to provide standard quality bloods to patients.

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- **Shelf life** **Storage temp → 4°C**

  ACD = 21Days

  CPD = 28Days

  CPD-A = 35Days – used in govt hospitals.

  SAGM = 42Days

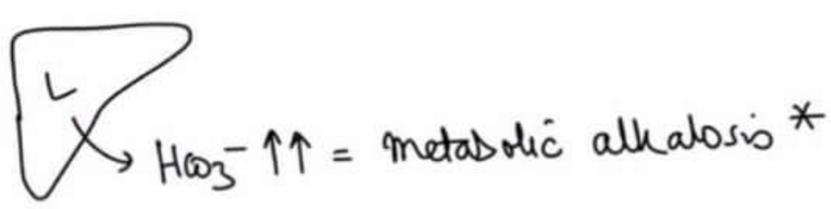
  - Acidified citrate Dextrose (ACD) → not used nowadays because of shorter shelf life. (**Adenine** provides stores of ATP, **Citrate** is Anticlotting agent (binds with calcium), **Dextrose** provides nutrition)
  - Citrate phosphate dextrose (CPD)
  - Citrate phosphate dextrose – Adenine (CPDA)
  - Saline adenine glucose mannitol (SAGM)

Note: 15 ml of **ACD**, 14mL of **CPD or CPDA** is used for preserving 100 mL of blood.

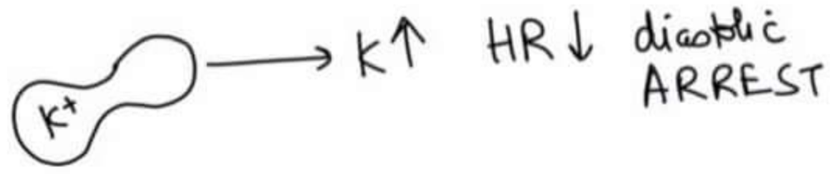
CASE SCENARIO: Pt develops laryngospasm after blood transfusion will presents with difficulty in speech, trousseau sign, Chvostek sign, altered sensorium , all these manifestation are key words for **citrate toxicity**.

- Diagnosis Citrate Toxicity → **Hypocalcemia**

  Tetany → Laryngospasm



- **Metabolic alkalosis** may lead to encephalopathy in patient as it damages the integrity of blood brain barrier
- After prolonged storage of blood, Na^+/ K^+ pump fails and blood levels of K^+ can increase
- RBC's are loaded with K^+ and infusion of near expiry RBC can lead to destruction by spleen which in turn can cause **hyperkalemia** and results in diastolic arrest.



Complications of blood transfusion (B.T): -

1. **Febrile non-hemolytic transfusion reaction (FNHTR)**
   - M/C complication
   - Antibodies to donor leucocytes /HLA Ag are responsible for the FNHTR.

> **Case scenario**: Multiparous woman has higher chance due to increase sensitization in consequent pregnancies or people receiving multiple blood transfusion after massive bleeding will develops preexisting antibody. These antibodies will attack donor leucocytes that results in release of interleukin 1 and cause fever.

   - Temp. increases by 1°C,

     Rx: Antipyretics are given, and this condition is **self-limiting & mild** so **can continue the blood transfusion.**
   - Ideally to prevent this complication, **leucodepleted blood should be transfused.**

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Note: We should differentiate this fever with anaphylactic shock which initially presents with fever so continuous **vital monitoring** has to be done.

2. **Allergic reaction:** - Presents with urticaria and patient feels itching all over body.

   Management: **STOP B.T. temporarily** → inj. Diphenhydramine **(IM)** and continue the transfusion.

3. **Anaphylaxis** → B.P. decreases & H.R. increases due to **release of histamine.**

   Therefore, vital monitoring should be done at every 5 mints for first 15 min then check 15 mins to 30 mins interval.
   - Central cyanosis due to histamine release causing laryngeal edema.
   - Stridor, Rhonchi → d/t Bronchospasm
   - Pruritus.

   Immediately STOP transfusion → 0.5 mg s/c Adrenaline (1:1000) - undiluted form

4. **Acute hemolytic reaction/ Mismatched blood transfusion**
   - Type II hypersensitivity reaction
   - Reason → Clerical error
   - BP falls, H.R. increases, fever, chills, rash → hemodynamic instability profile.

PrepLadder

- **Chest pain** due to ongoing hemolysis affecting coronary circulation and **flank pain** due to hemoglobin blocking the renal tubules that results in ATN.
- These features can differentiate from other complications.
- Hemoglobinuria leading to **black urine** and predisposes to acute tubular necrosis.

Management –

- **STOP blood transfusion**
- **Work up**: Haptoglobin ↓ → consumed in hemolysis.
  LDH ↑ → arises with RBC lysis as present inside the RBC.
  Coagulogram
- Repeat blood grouping & cross Matching
- Diuresis → Furosemide/ mannitol (mannitol not given in established renal failure)

5. **Graft Vs Host Disease** → can occur with post blood transfusion or allogenic stem cell transplantation between first degree relatives.
   - Donor T_8 leucocytes are responsible
   - If person receive blood transfusion from their siblings or any other family donor, there is high chance of developing Graft Vs host disease because they **share common HLA antigens**. So its always better to avoid blood donation between family

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C/F : A younger brother (B +ve) met a RTA and there was severe blood loss at that time, he has been transfused 2 units of blood which was donated by his elder brother (B +ve).

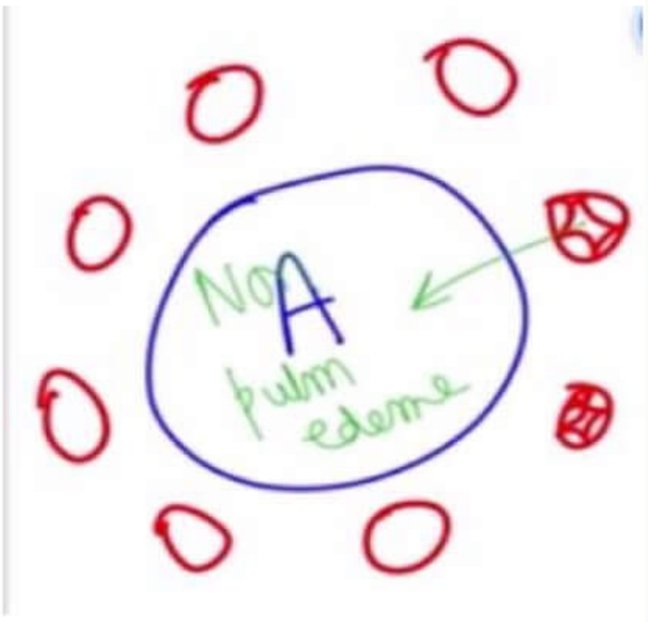
   - Subsequently **8-10 days post blood transfusion** he develops:
     - Fever/ obstructive Jaundice/ diarrhea / pruritus
     - Pancytopenia
     - Death may occur after 3wk. → delayed complication.
   - **Prevention**:
     - Irradiated blood (2500 cGy) → preferred because it kills the lymphocytes
     - Infusion of leucodepleted blood by using filters → but it is more suitable for FNHTR.

Most radiosensitive blood cell – Lymphocyte (which is responsible for GVHD)
Most radioresistant blood cell – Platelet

6. **Transfusion related Acute lung injury (TRALI):**
   - M/C cause of death after blood transfusion
     - Incidence is more common in **first 6 hours** of transfusion and more common with fresh frozen plasma than whole blood transfusion.
     - More common if **donor** is multiparous woman or one who has received multiple transfusion already → has pre-existing anti HLA II antibody, anti HLA I antibody, anti-neutrophils antibody

PrepLadder

- These **antibodies (present in donor blood)** cause leucocyte aggregation in recipient pulmonary capillaries which results in ventilation perfusion imbalance → ARDS like manifestation.
- These antibodies cause release of cytokines leading to increased capillary permeability of pulmonary capillaries → Non-cardiogenic pulmonary edema.



Diagnosis of TRALI: -

- $paO_2 / FiO_2 < 300$ → for confirmation of TRALI
- Evidence of absence of left atrial hypertension
- Insult of lung: within 7 day symptoms develop
- Chest X- Ray: B/L infiltrates present in the lung parenchyma.
- B.P. Normal/ decreased

  Jugular venous pressure – Normal

  BNP → Normal

7. **Transfusion Associated Circulatory Overload (TACO): -**

- Presents with increase BP, increase JVP, increase BNP.

Q → CKD patient scheduled for dialysis but presents with Hb = 7gm% so doctor decides to give 2 units of whole blood transfused over 4 hours. Patient develops resp distress, BP elevated and B/L fine crepitations.

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Diagnosis: **TACO**

Note : B/L fine crepitations are also present in TRALI so, it is not a differentiating feature elevated BP is due to circulatory overload.

Clinical scenario:

→ If blood transfusion patient develops resp. distress: -

a. **TRALI: B/L fine crepitation, BP n / ↓, JVP N; BNP N**
b. **TACO**: B/L fine crepitation, **BP ↑, JVP ↑, BNP ↑**
c. **Tetany (Citrate toxicity):**
   - Laryngospasm, stridor, Cyanosis,
   - Breathlessness
   - Chest: B/L conducted sounds

→ If patent receiving blood transfusion develops fever: -

a) FNHTR
b) Anaphylaxis
c) Mismatched B.T.

} Based on decreasing order of sequence

8. **Electrolyte imbalance**: -

- Metabolic alkalosis → due to **excess of citrate** present in blood.
- Hyperkalemia → due to transfusion of near expiry blood transfusion.
- Calcium ↓ <7 mg % → tetany manifestations are seen.

PrepLadder

9. **Iron toxicity** → develops in patient requiring **recurrent blood transfusions e.g. thalassemia** → secondary hemochromatosis with elevated levels of S. ferritin

- **1 Unit blood: – 200-250 mg iron**
- Usually secondary hemochromatosis features develop after receiving 100 units of blood.
- **> 100 unit blood** = 20 gm iron overload in the body.

Manifestations of secondary hemochromatosis:

- **Hyperpigmentation** → iron deposition in the skin
- Deposition in the liver results in **cirrhosis**
- Deposition in pancreas results in **type I diabetes mellitus** called as Bronze diabetes

Precaution: Iron chelators can be given to these patients.

- Deferoxamine → S/c infusion.
- Deferiprone → Oral (expensive)

10. **Infections**: –

→ Leading cause of Transfusion associated hepatitis = Hepatitis B

–Before blood transfusion atleast these five should be tested: HIV, HBV, HCV, SYPHILIS, MALARIA.

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→ Commonest infection seen in blood transfusion is sepsis then comes hepatitis.

→ But the leading cause of hepatitis in blood transfusion is HBV.

→ Common bacterial infections include like Pseudomonas, Acinetobacter, GN coliforms, Serratia.

→ Fresh frozen plasma doesn't transmit bacteria as it is devoid of cellular components so infection risk ↓.

→ Platelets – Stored at room temp. (20-24°C).

- Coagulase negative staph. (CONS) are usually found as contamination.
- So platelet should be transfused within 30 mins of blood bank release.

→ Other viruses transmitted:

- HTLV – 1 (related to tropical spastic paraplegia, Adult T-cell Leukemia)
- HEV
- HAV (rare)

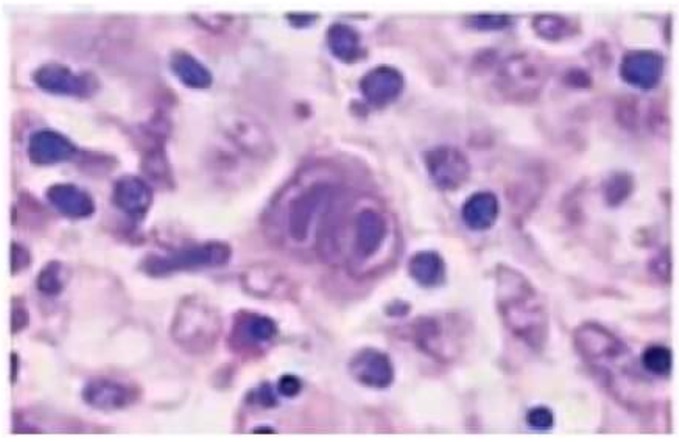
→ Hypotension can occur after blood transfusion in patient on ACE inhibitors because stored blood has bradykinin which is a vasodilator.

→ Immunomodulation can occur after blood transfusion and may result in false positive Mantoux.

→ Also, patients receiving multiple transfusions has **lower chance of rejecting transplants** as they have decreased immunity.

HODGKIN'S & NON-HODGKIN'S LYMPHOMA

HODGKIN'S LYMPHOMA



→ **Etiology:** EBV, HIV

→ **HP Finding:** -OWL EYE Appearance of Reed Sternberg Cell

→ **C/F:**

1. Progressive cervical lymph node enlargement
   - Rubbery consistency of lymph nodes
   - Contiguous spread
2. Hilar LN enlargement
   - SVC Syndrome: Facial Plethora
   - Trachea: STRIDOR
   - Thoracic Duct: Chylous Ascites
3. Porta Hepatis lymph node enlargement
   - CBD Compression: Cholestasis; PRURITUS and ICTERUS
   - Portal vein compression: Portal hypertension
4. Retroperitoneal LN enlargement leading to URETER kinking and development of hydronephrosis
5. Category B Symptoms:
   - Weight loss > 10% wt ↓ over 6 months
   - Drenching night sweats
   - Loss of appetite
6. Pel ebstein fever

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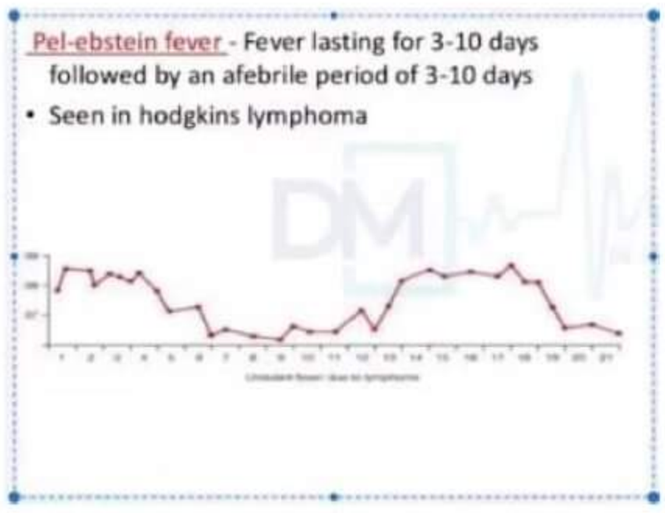
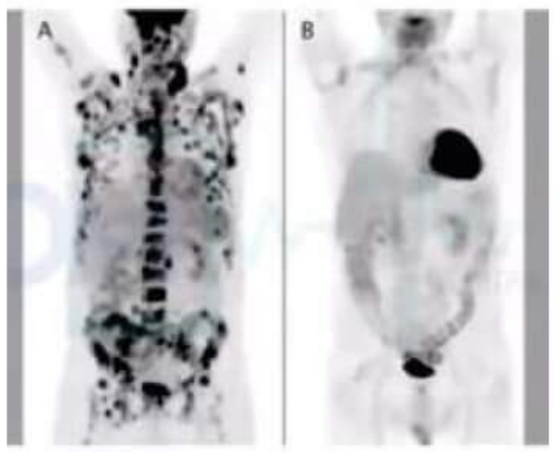


→ **Work Up:**

1. LDH
2. WHOLE BODY PET SCAN for initial staging →
3. CT Chest abdomen
4. IOC – Excision lymph node biopsy
5. **Flow cytometry**: - CD 15/30 +



Extra Miles: -

- Involuntary weight loss in Harrison 20th is given as 5% decrease overs 6 months.
- Category B symptoms as description of Hodgkin's lymphoma given then answer as 10% over 6 months

PrepLadder

→ Staging:

ANN ARBOR Classification: Based on clinical grounds

1. One group LN / lymphatic area
2. 2 group of LN **same side** of diaphragm
3. 2 group of LN **both side** of diaphragm
4. Dissemination

WHO Modified Real Classification: Based on histopathological ground

1. NODULAR SCLEROSIS → (Most common globally) has LACUNAR CELL
2. MIXED CELLULARITY → (Most common in India) has CLASSICAL REED STERNBERG CELL, associated with HIV (as per Harrison, pathology Robbins says Nodular Sclerosis controversial so let it pass)
3. LYMPHOCYTE RICH
4. LYMPHOCYTE DEPLETED (worst prognosis)
5. NODULAR LYMPHOCYTE PREDOMINANT (Atypical variety)
    - Slow growing
    - CD 15 / 30 -ve (negative)
    - POPCORN CELL

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Extra Mile: -

- Popcorn calcification on CXR is a feature of benign lung tumor → Pulmonary hamartoma
- Popcorn lesion seen in mammography is suggestive of Fibroadenoma Breast
- AIDS Positive patient having brain tumor is Primary CNS lymphoma
- NHL (Non-Hodgkin's) → Immunoblastic variety
- HL (Hodgkin's) → Mixed cellularity > lymphocyte deleted

Rx →

- Localized disease → Radiotherapy
- Advanced Disease

  →Chemotherapy: ABVD

A - Adriamycin

B - Bleomycin

V - Vinblastine

D – Dacarbazine

PrepLadder

NON-HODGKIN'S LYMPHOMA

→ **Incidence:** NHL > HL

85% 15%

→ **Etiology:** EBV, HIV, HTLV-1, KSHV, HCV, H. Pylori

- t (14-18): Most common chromosome translocation
- t (11: 14): Mantle cell lymphoma

→ **C/F**: Medium age of presentation 67 years

1. Multigroup of LN ++: Painless adenopathy

2. Burkitt lymphoma:

   → in child (African) presents as jaw swelling

   → in adult involves abdominal group of lymph nodes → intestinal obstruction and hydronephrosis.

3. Category B symptom: wt. loss > 10% over previous 6 months

   : Drenching night sweats

   : Fever > 38^{0} C

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4. Bone marrow involvement: **CYTOPENIA**:

   - Anemia, Infection (recurrent), Petechiae

5. Spinal cord compression (paraplegia, quadriplegia) & Cranial nerve palsy

Extra Mile:

HL is associated with paraneoplastic manifestation like Guillain Barre Syndrome.

→ **Work Up**

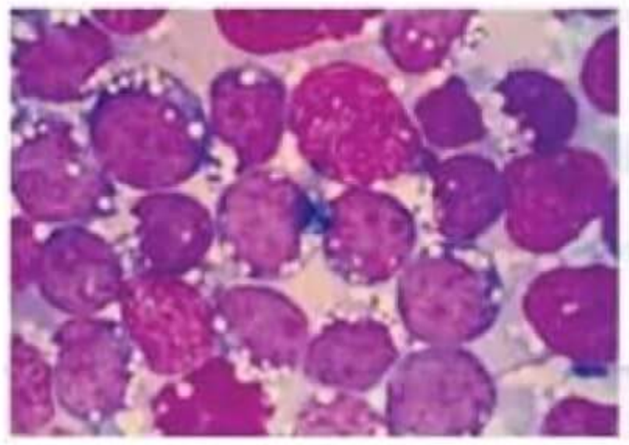
1. Hb ↓; TLC ↓; Platelet ↓
2. LDH ↑
3. β_2 microglobulin urine ↑
4. MRI abdomen / chest
5. PET SCAN (using 18 FDG)
6. MRI Spine / LP
7. **IOC: Excision LN Biopsy**
8. FISH: t (14: 18)

   Burkitt: t (8: 14) (2: 8) (8 :22)

PrepLadder

WHO Modified Real Classification for NHL:

- B Cell (80%) & T Cell (20%)



Starry sky appearance in lymph node biopsy

→ B cell NHL:

1. **Most common: DLBL** (Diffuse Large cell lymphoma)
2. HIV: Immunoblastic lymphoma
3. HCV: lymphoplasmacytic lymphoma
4. H. pylori: M.A.L.Toma
5. KSHV: Kaposi Sarcoma
6. **t (8: 14) (2 :8) (8: 22): Burkitt lymphoma**
   - Histopathological view → **Star sky appearance in lymph node**
   - **# c- myc** → inhibits apoptosis

→ T Cell (20%)

Mycosis Fungoides/ Cutaneous T cell lymphoma

- It presents with erythroderma.
- It spreads hematogenously resulting in hepatosplenomegaly.
- It is referred to as Cutaneous Sezary Syndrome.
- Sezary cell present +
- Bone marrow involvement

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Erythroderma

Sezary Cell

Histopathological view: - Pautrier Microabscess

(MUNRO MICROABSCESS = Psoriasis)

→ Rx of NHL:

ANN ARBOR CLASSIFICATION: -

Stage 1: one lymph node (one extra lymphatic site)

Stage 2: two lymph nodes (same side of diaphragm)

Stage 3: two lymph nodes (both sides of diaphragm)

Stage 4: Dissemination

Using this classification, we determine INTERNATIONAL PROGNOSTIC INDEX.

PrepLadder

INTERNATIONAL PROGNOSTIC INDEX (IPI) takes into consideration following parameters:

1. Age
2. ECOG performance status
3. ↑ LDH
4. > 2 extra nodal sites
5. ANN ARBOR classification: III/IV has bad prognosis

→ **TREATMENT:**

R – CHOP

R – Rituximab
C – Cyclophosphamide
H – Hydroxydaunomycin
O – Oncovin
P – Prednisolone

Clinical Presentation & IOC Summary:

	Clinical Presentation Summary	IOC
CLL	LN + AIHA / Platelets ↓	Flow cytometry
HL	LN + Pel ebstein fever, Rubbery LN	LN Bx Excision
NHL	LN multiple group + cytopenia	LN Bx Excision
CML	Massive spleen	FISH
ALL	Child with Anemia + Petechiae + Sternal tenderness & CNS leukemia	BMA
AML	Anemia + Petechiae + Sternal tenderness plus Gingival hyperplasia / Chloroma / Leukemia cutis	BMA

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Drug of choice:

CLL	Fludarabine
HL	ABVD
NHL	R CHOP
CML	Imatinib
ALL	VALP
AML	ATRA (All Trans Retinoic Acid)

PrepLadder

THALASSEMIA

β-THALASSEMIA

- Autosomal recessive
- Chromosome 11

Hb electrophoresis if done on a newborn:

	Day 0	Adult (6 months of age)
- Hb F = 95% →		2%
- Hb A = 2% →		95% ($\alpha_2\beta_2$)
- Hb A_2 = 3% →		3%

 # First Hb. to develop: GOWER 1 followed by GOWER 2 then Portland

 # Hematopoiesis: 2 weeks: Yolk sac: Gower 1
14 weeks: Liver, spleen: Hb F ++
38 weeks: Bone marrow: Hb A appears

On Day 0 of life, Hematopoiesis is occurring in: -

- skull
- Vertebra
- Sternum
- Ribs
- Clavicle
- Long bones
- Flat bone after 18 yrs.

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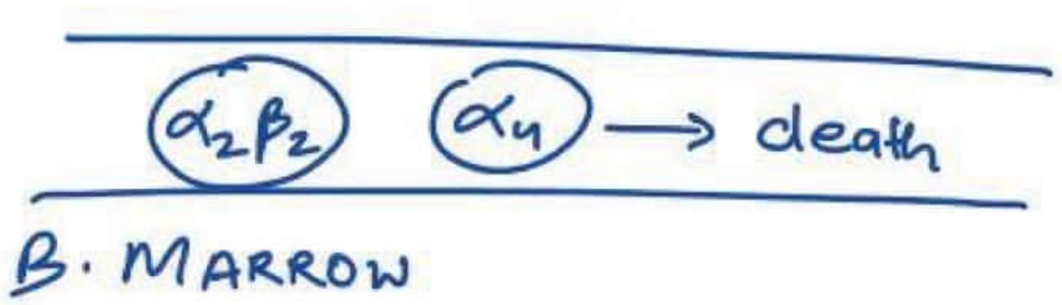
→ **Thalassemia major:**

- β0 β0 → 0 % production of β- chains
- RBC: HbA decreased
- α4 tetramers



- Features of Thalassemia Major:

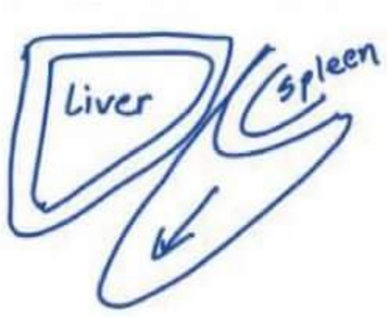
1. Ineffective Erythropoiesis
2. **Reticulocytopenia** d/t in ineffective erythropoiesis (Other hemolytic anemia → Reticulocytosis)
3. RBC containing α4 tetramer are destroyed in spleen → extravascular hemolysis → severe Pallor and splenomegaly.

Clinical features of Thalassemia major

- 6 months child having **severe anemia with CHF**
- Frontal / Maxillary prominence (Bone marrow expansion) -→ **Chipmunk facies**

PrepLadder

- Extra medullary hematopoiesis: Splenohepatomegaly



Prominent cheek bones, upturned nostrils and prominent incision teeth

→ Thalassemia intermedia

- $\beta^0\beta^+$ → 50% production of β-chains
- Hence severity of disease is LESS

C/F: -

- 1yr old child Anemia
- Chipmunk facies
- Splenohepatomegaly

→ Thalassemia minor / Trait

- $\beta^+\beta^+$ → 90% of β- chain

C/F: - Asymptomatic

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Work up of Thalassemia -

1. Screening test: - NESTROFT (Naked eye single tube RBC osmotic fragility test)
   - Osmotic fragility decreased In thalassemia
   - Osmotic fragility increased in hereditary spherocytosis
2. IOC: - H.P.L.C (High Performance Liquid chromatography) > Hemoglobin electrophoresis
3. PRE-NATAL DIAGNOSIS: - Chronic Villi sampling @ 10-12 week of gestation

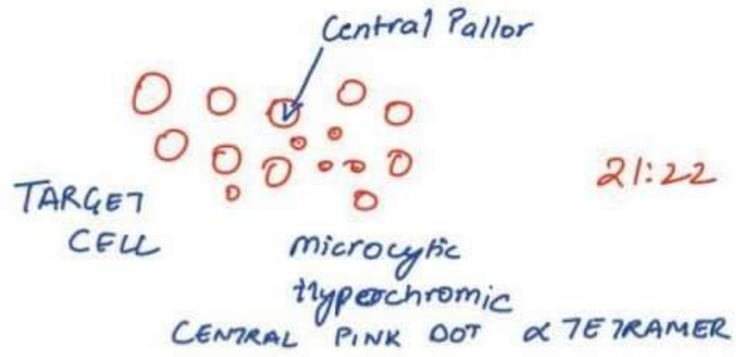
HbA 2 > 3% => Indicative of trait

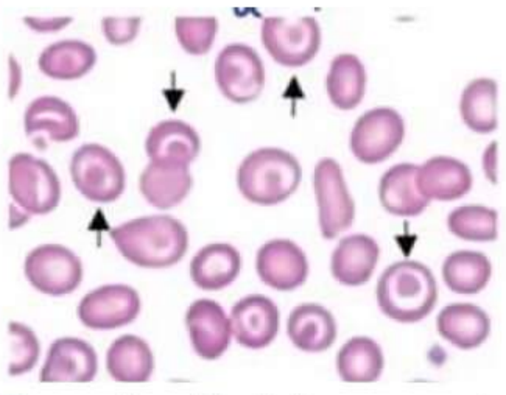
ANEMIA + SPLENOHEPATOMEGALY + Chipmunk facies

↓ ↓ ↓

Hemolytic Extramedullary hematophoresis Bone marrow expansion

4. Hb decreased
5. Peripheral smear:





Target cells (also seen in CLD)

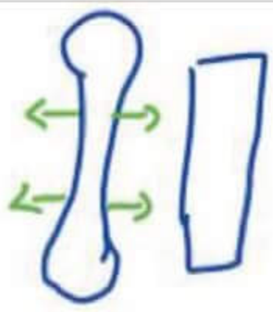
6. Reticulocyte count – decreased (Thalassemia major) / increased

6. X-Ray

HAND – "Squaring of the metacarpals"

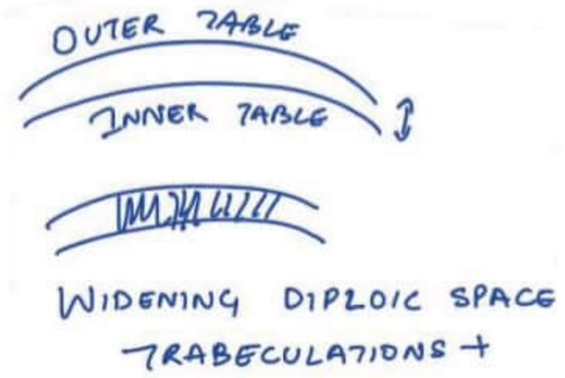
↓

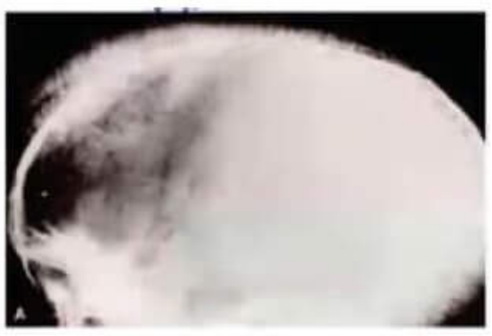
earliest radiological finding



METACARPAL

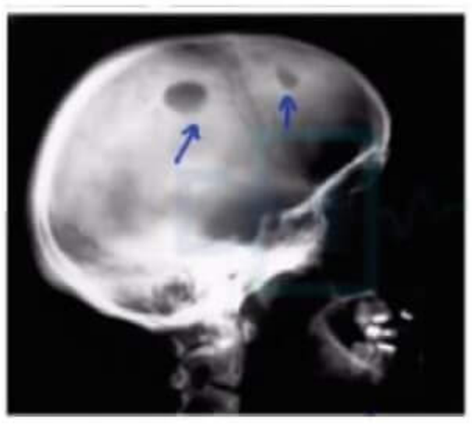
Skull – "Crewcut appearance"



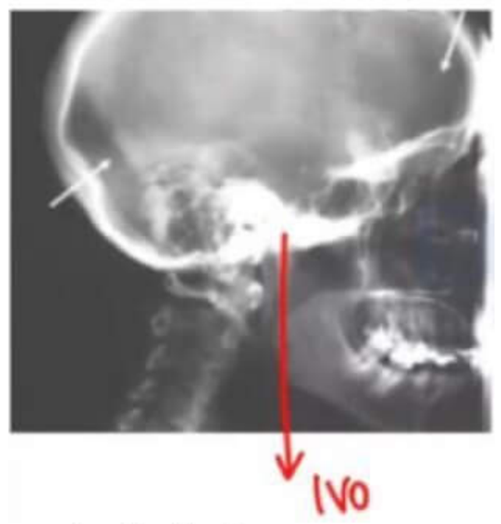


Hair on end / Crewcut appearance

Rain drop lytic lesion (Multiple myeloma)



Child X-ray of Skull, Lytic lesions & floating teeth (Histiocytosis – X / Hand schuller christian disease)



Lytic lesion + Ivory appearance of bone (Paget's disease)

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Rx: -

- Thalassemia major – Transfusion dependent patients
  - Packed RBC need to be transfused on recurrent basis
  - Life span transfused RBC = 60-80 days
  - 6-12 units PRBC / yr

→ Iron toxicity → Bronze diabetes

→ Rx: -ORAL DEFERIPRONE / S.C. DESFEROXAMINE

RxOC → Allogenic Bone Marrow Transplantation

IRON OVERLOAD: - Infection of YERSINIA ENTEROCOLICTA

AUTOSPLENECTOMY:

Capsulated organisms

- Pneumococcus,
- Meningococcus,
- H. influenzae

→ In case of Increased Transfusion dependency by 50% -> plan **Elective splenectomy**

PrepLadder

ALPHA THALASSEMIA

- Autosomal recessive
- Defect in chromosome number 16 (α2 chain = 4 α gene)

-ααα	75% production	Silent Carrier
--αα	50% production	Thalassemia trait
---α	25% production	Hb H disease
----	0% production	Hb BARTS : γ4 high O2 affinity

→ O2 availability to tissue decreased

↓

Anemia

CHF

* HYDROPS fetalis -> non- immune genic

other causes of non immunogenic Hydrops Fetalis
* Congenital Nephrotic Syndrome
* Complete Heart Block: neonatal lupus

- **C / F** – Anemia

  Splenohepatomegaly

  Chipmunk facies

- **Screening:** - NESTROFT
- **IOC:** - H.P.L.C
- **TOC:** - B.M.T. allogenic and initial survival with Packed RBC

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HEREDITARY SPHEROCYTOSIS

RBC flexibility due to: -

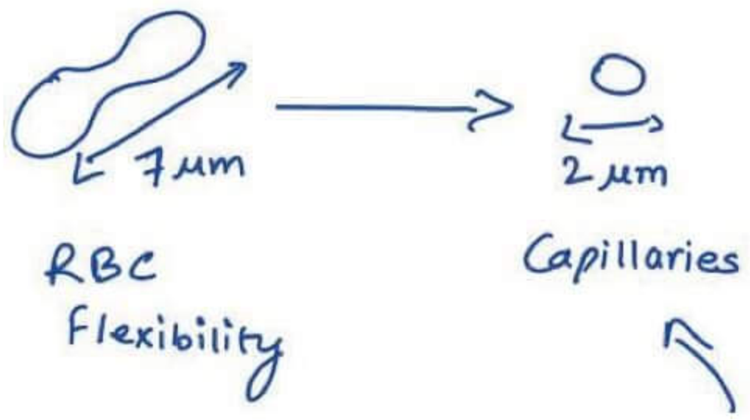
Spectrin

Ankyrin

Pallidin

Protein 4.3

- If ankyrin defect is present, RBC's become rigid
- Rigid RBC's trapped in capillaries of spleen
- Accelerated Hemolysis
- Extravascular hemolysis



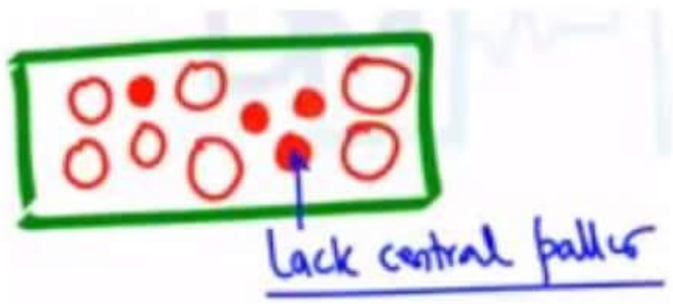
C / F: -

1. Pathological jaundice
2. Anemia
3. Splenomegaly
4. Gall stones: pigment stones: Calcium bilirubinate
5. Non-healing ulcer: medial malleolus
6. Aplastic crisis: - human Parvo virus B19
   (ERYTHEMA infectiosum "slapped check appearance")

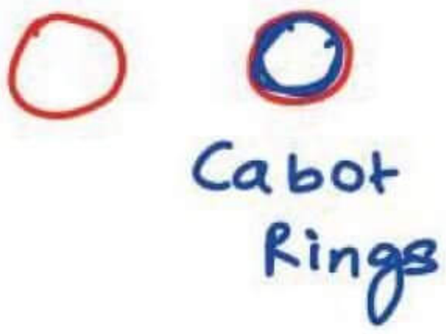
PrepLadder

WORK Up:-

1. Hb decreased
2. Peripheral smear –
   some RBC's without central pallor
   Spherocytes
3. Reticulocyte count increased
4. NESTROFT – O.F. increased (due to reduced surface area)



Rx: – **Elective splenectomy**



- Post splenectomy P. smear → Cabot Rings

* Pneumococcal Vaccine
* Meningococcal Vaccine
* H. influenza Vaccine
* Influenza A Vaccines

] 4 weeks before surgery

Extra Mile:

Cabot Rings are seen in (Remnants of Mitotic Spindle)

1. Megaloblastic Anaemia
2. Myelodysplasia
3. Lead Poisoning
4. Post Splenectomy

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PrepLadder

SICKLE CELL DISEASE, G-6 PD DEFICIENCY AND OTHER HEMOLYTIC ANEMIAS

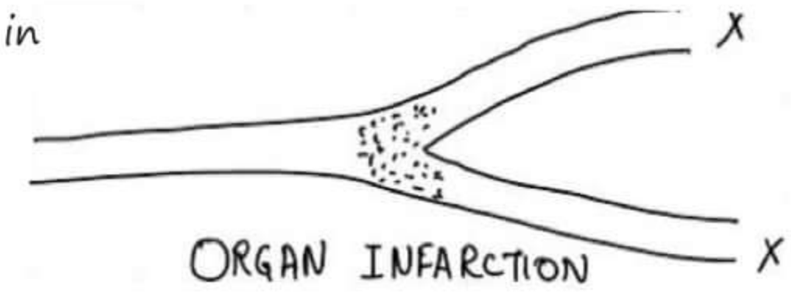
Sickle cell Anemia

→ At β-6 position, glutamate goes out and Valine comes in

→ HbS Polymerization makes RBC sticky

→ leading to micro-occlusions

- < 6 months: HbF protective effect
- > 6 months: HbF decreased



1. **Vaso-occlusive crisis** → fever & pain
2. **Hand foot syndrome** / dactylitis (D/D – Osteomyelitis) < 5yr

Extra Mile

Hand foot syndrome: -

- A/w chemotherapy: Capecitabane / 5-Fu
- k/a **Palmer-Plantar Acrodysthesia**

Hand, foot, Mouth disease: -

- Vesicular eruption
- d/t **Coxsackie A virus**

3. **AVN Bone**: - MRI
4. **Splenic infarction**: - acute abdomen left upper quadrant pain
   AUTOSPLENECTOMY ~ 3yr → capsulated organisms induced sepsis
5. Coronary infarction / ischemic cardiomyopathy [perforators#]

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↓

ACUTE CHEST SYNDROME

Acute coronary syndrome is due to Atherosclerosis

6. Pulmonary vaso-occlusive episodes / (PAH) – Rx: Bosentan.
7. Kidney: **Papillary Necrosis / isosthenuria** - inability to conc. & dilute urine
8. **Hemolytic Gall stones** increased incidence
9. Non-healing ulcer on Medial Malleolus
10. APLASTIC CRISIS: Human Parvo virus B19

Homozygous patients have an early & more severe manifestation.

Heterozygous →Late presentation;

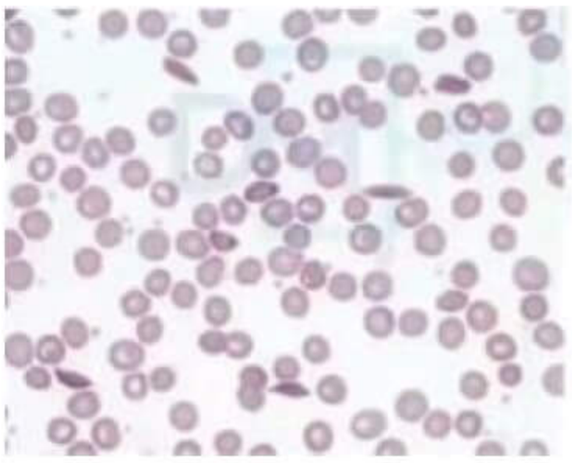
precipitated by:

Dehydration; Hypoxia: → HbS polymerization: sickling episodes

	Heterozygous	Homozygous
HbS	+	+
HbF	+	+
HbA	+	–
HbA_2	+	+

Work up: -

1. Hb decreased: Extra vascular hemolysis
2. Peripheral Smear: Sickle cell
3. Reticulocyte count increased
4. IOC – H.P.L.C > Hb electrophoresis
5. USG abdomen: evaluate spleen size
6. Echo T.T.E.: evaluate ischemic cardiomyopathy
7. X-ray Hand / foot



Rx: -

1. Hydroxyurea: Decreased sickling episodes
2. Fentanyl or Morphine / codeine: Bone pain
3. BOSENTAN: PAH
4. During sickling episodes: Analgesic IVF, Whole blood transfusion

   Packed RBC's Not given as they will increase viscosity of blood leading to increase incidence if sickling crisis.

G6PD (Glucose 6-phosphate dehydrogenase) Deficiency

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- Function of G6PD is to neutralize free radical induced damage inside RBC
- Triggers – fava beans consumption or antimalarials drugs like Primaquine

Unopposed oxidative stress leads to Intravascular hemolysis

↓

Hemoglobinemia

↓

Hemoglobinuria / Black urine → **Acute Tubular Necrosis**

↓

Death

- G6PD deficiency is an example of both extra & intravascular hemolysis

→ **Drugs C/I in G6PD**

-Aspirin, Sulpha Drugs
-Nitrofurantoin
-Primaquine
-Chloroquine
-Mefloquine

→ **Drugs which can be given in G6PD deficiency**

-Artesunate
-Artemisinin

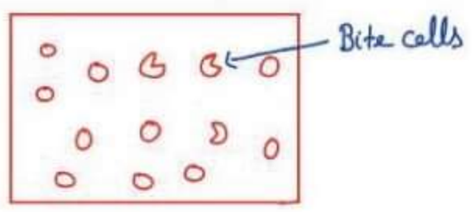
PrepLadder

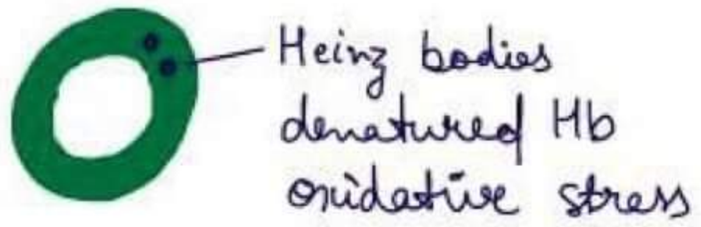
Investigations

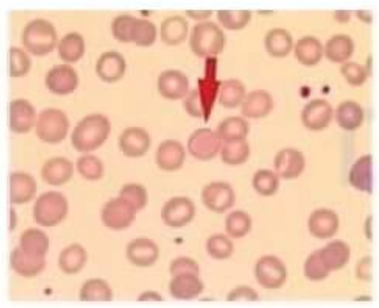
→ **IOC** -> G6PD assay

→ P. smear:

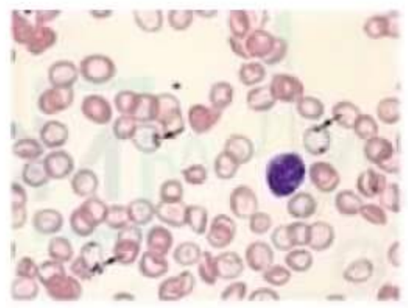
- Hb decreased
- **BITE CELLS**
- Supravital stain (Crystal Violet) → **HEINZ BODIES**







CABOT RINGS



HOWELL JOLLY BODIES

Cabot Ring
Howell Jolly bodies
} Seen in splenectomised pt.

AUTO-IMMUNE HEMOLYTIC ANEMIA

Warm Antibodies (IgG class)	Cold Antibodies
• S.L.E • C.L.L • NHL • α- methyldopa	- **Paroxysmal cold Hemoglobinuria (IgG):** Mycoplasma pneumoniae infection leads to production of **Donath Landsteiner Antibodies** that attack self RBC at low body temperature leading to Hemoglobinuria. - **Cold-agglutinin syndrome (IGM)** * Mottling of acral part * Black Urine

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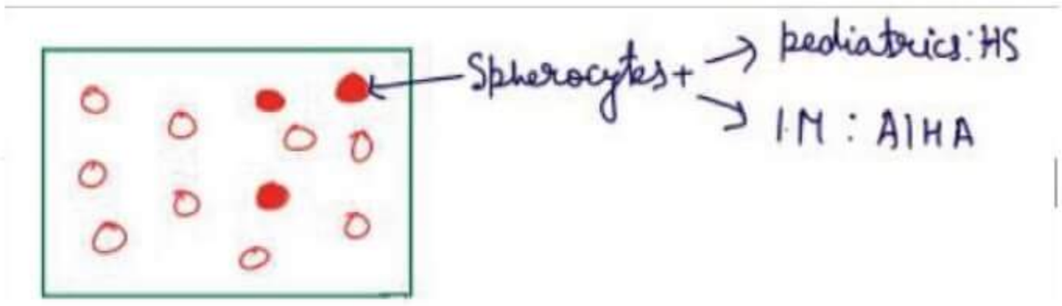
- Pallor +: Malaise / Chest pain
- Palpitations / Pedal edema



Work up: -

1. Hb decreased
2. P. smear: **Spherocytes**
3. **Direct Coombs Test: IOC of AIHA**

Rx: - Steroids

Q. 20 YEAR woman: Anemia, joint pain, feel feverish off and on, RASH and P. SMEAR shows spherocytes

Dx - SLE

Q. 2 YEARS child: Anemia, Spleen INCREASED and P. SMEAR spherocytes, NESTROFT

Dx– Hereditary Spherocytosis

PrepLadder

MICROANGIOPATHIC HEMOLYTIC ANEMIA

- Complement mediated damage to RBC
- Characterized by:

- **Schistocytes / Helmet cells**
- **Echinocytes / BURR cell**

> Extra Mile
>
> Howell Jolly bodies are finding of Basophilic nuclear remnants seen in splenectomized patients

→ Causes:

- Hemolytic Uremic syndrome: E. coli O157: H7, EHEC, Shiga Toxin
- Thrombotic Thrombocytopenic purpura:
  - Fever / Acute Ischemic Stroke
  - Hemolysis = MAHA
  - UREMIA / Renal variety AKI
  - PURPURA (Palpable bleed)
- Metallic Prosthetic Heart valves

→ Work up:

- Direct comb Test = -ve
- Peripheral smear: **Helmet cell & Burr cells**

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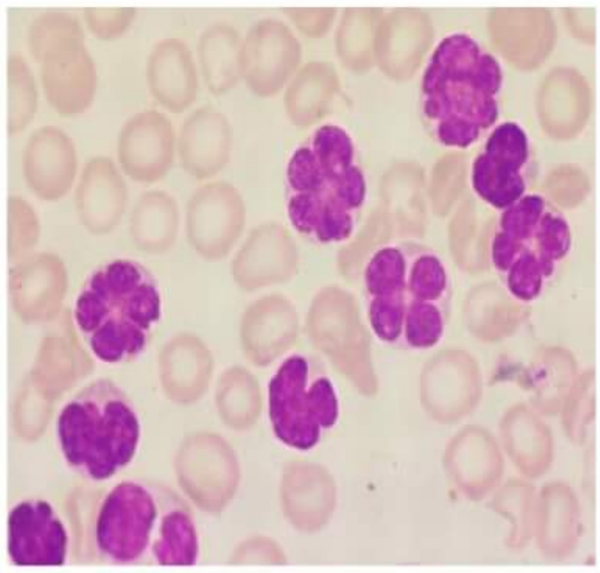
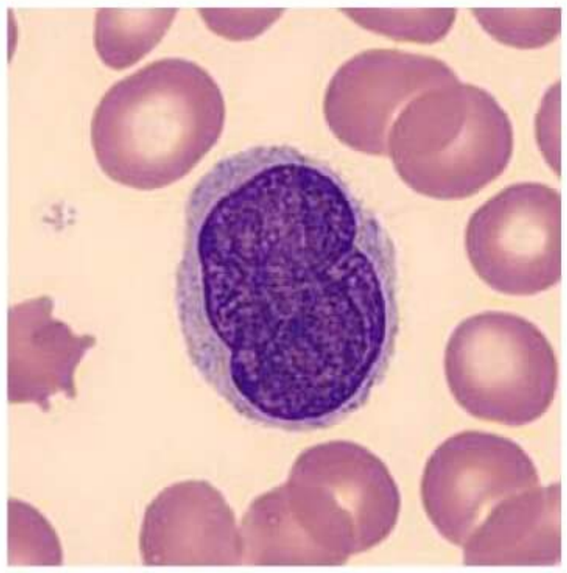
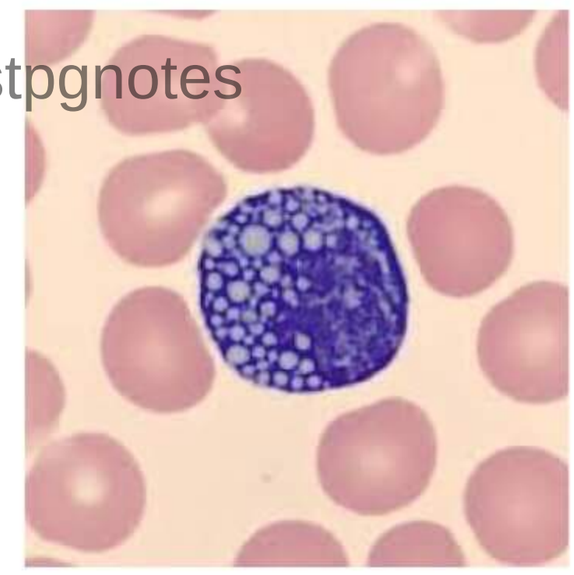
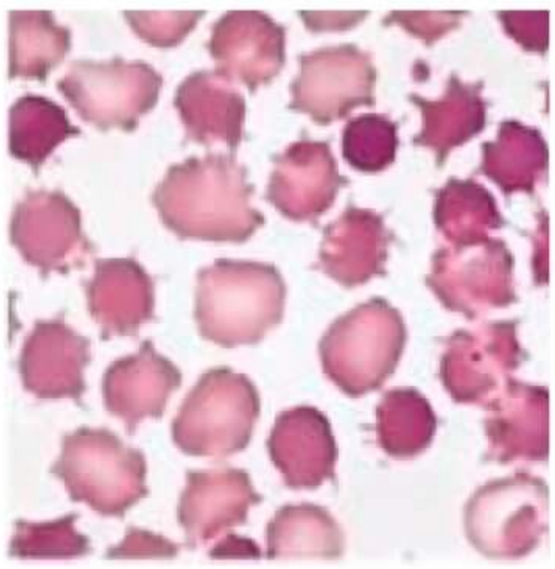
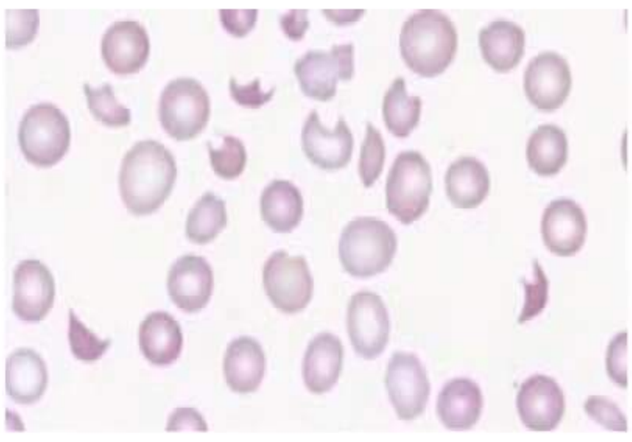
→ Rx: **Cause specific**

Summary of IOC of various anemias

Anemia	Diagnosis
AIHA	Direct Coombs Test
MAHA	Direct Coombs Test – ve, P. Smear
G6PD	G6PD assay, Heinz bodies / bite cell
PCH	Donath Landsteiner
SCA	HPLC > Hb electrophoresis
Thalassemia	
HS	NESTROFT: Fragility Increased

PrepLadder

IMAGE BASED QUESTIONS:

	THEORY	IMAGE
1.	**FLOWER CELLS**: Adult T cell Leukaemia caused by HTLV-1 (also Tropical spastic paraparesis)	
2.	**SEZARY Cell**: Cutaneous T Cell Lymphoma / Mycosis Fungoides → Erythroderma + Hepatosplenomegaly	
3.	**MOTT cell**: Russel bodies, intracytoplasmic inclusions seen in Multiple Myeloma	
4.	**SPUR CELL/ ACANTHOCYTES** which show Irregular spicules seen in Abetalipoproteinemia and vitamin E deficiency.	
5.	**SCHISTOCYTE / HELMET CELL** in HUS/TTP	

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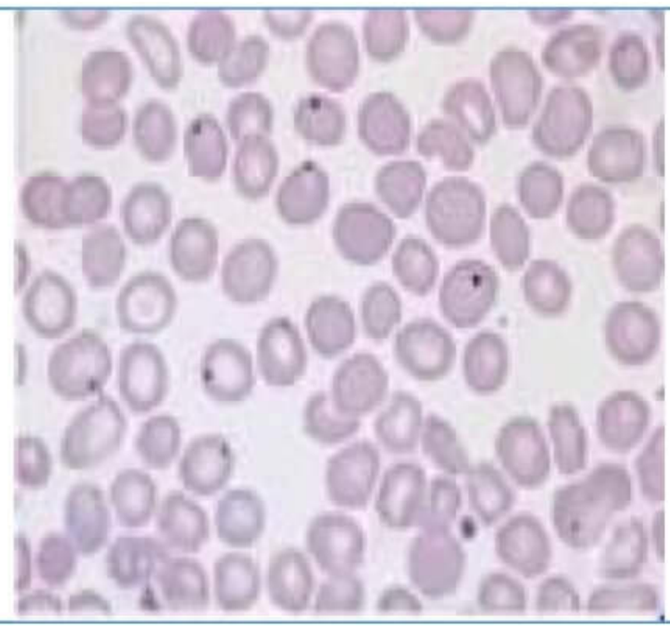
6.	HOWELL JOLLY BODIES seen in Asplenia	

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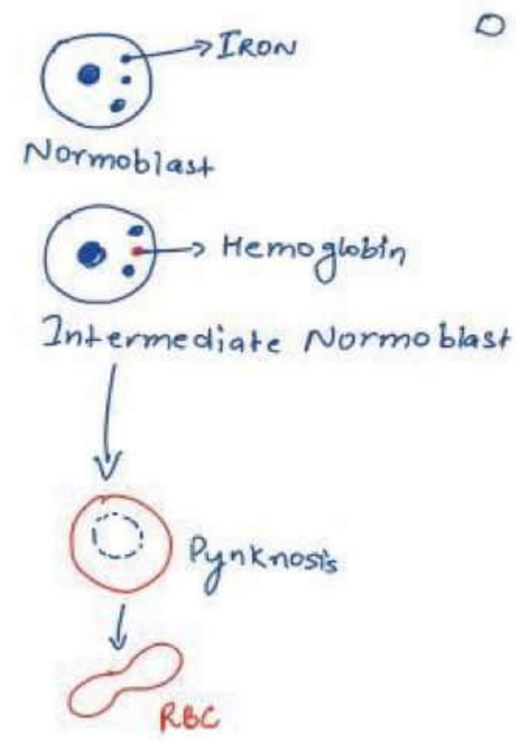
SIDEROBLASTIC ANEMIA

- Antitubercular drug **INH** is toxic to bone marrow.
- INH inhibits Hb synthesis → it leads to the deposition of neutralized iron in intermediate normoblast, less hemoglobin in reticulocyte → results in small size RBC's called as **Pappenheimer Bodies**
- S. iron → ↑
- S. ferritin → ↑

Rx: → **Vit B_6**

Pyridoxine response anemia is sideroblastic anemia



ANEMIA OF CHRONIC DISEASE

- **In Patients Of RA/ UC/ CD**
- In these patients, **liver will produce Hepcidin → inhibit utilization of Iron** in Hb synthesis
- S. Iron → ↓
- S. Ferritin →normal /↑
- NCNC > MCHC anemia

Rx: → **Cause specific**

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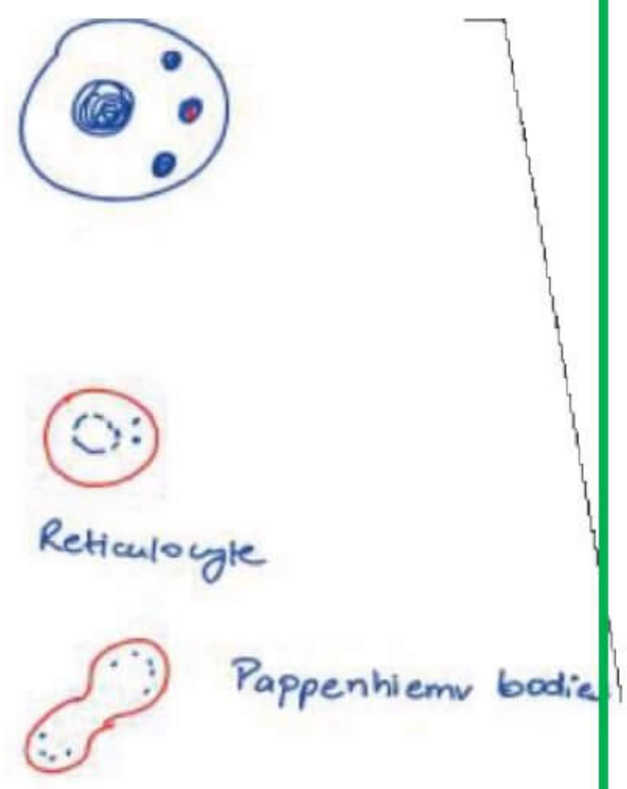

	IDA	SA	ACD
• S. iron	↓	↑	↓
• S. ferritin	↓	↑	↑
• TiBC	↑	↓	↓
(TiBC ∝ 1 / Ferritin)			

→ Causes of MCHC:

- Sideroblastic anemia
- IDA
- Thalassemia
- A. C. D

→ Causes of NCNC anemia:

- Chronic Renal Failure → where Erythropoietin ↓
- A. I. H. A = SLE/ CLL/ Paroxysmal Cell Hemoglobinuria
- NHL/ Leukemias
- Anemia of chronic Disease

PrepLadder

→ Causes of Macrocytic Anemia:

- B12 deficiency: Vegan diet, Diphyllobothrium Latum fish Tapeworm, Type A gastritis
- Folic Acid ↓: Pregnancy, AED, Celiac Sprue
- Chronic liver disease
- Hypothyroidism
- Aplastic anemia/ Fanconi anemia
    - Viral: Hepatitis D virus, EBV can lead to aplastic anemia
    - DDT and other drugs also contribute to sideroblastic anemia

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PrepLadder

PLATELET DISORDERS

Hallmark:

→ **Petechiae:** Non palpable, Non-blanching

→ **Purpura:** Palpable bleed.

- Non- palpable purpura → acute I.TP
- Pinch purpura → Amyloidosis
- Non-thrombocytopenic purpura→ H.S.P ((IgA mediated vasculitis)

→ **Joint space bleeding** seen in:

- Hemophilia A (deficiency of 8)
- Hemophilia B (deficiency of 9)
- Hemophilia C (deficiency of 11)

ACUTE I.T.P

→ **Causes: -**

- **Adults**: SLE/ Acute leukemia/ MDS
- **Children**: Immune mediated, EBV/ CMV/ Rubella

→ **C/F: -**

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1. Epistaxis (Recurrent Episodes)
2. Menorrhagia
3. I.C.H → headache/ altered sensorium
4. Petechiae: Sites: Ankles/ Subconjunctiva/ BP cuff/ Sction cup ECG
5. Purpura
6. Spleen: Not palpable

→ **Work up: -**

- P. Smear: Platelets ↓
- BMA: Megakaryocyte hyperplasia and count ↑

→ **Rx: - IV steroids**

- If disease is progressing:
  - Rh +ive = Rh Immunoglobulin
  - Rh -ive = **IV Ig** (overall best)
- **Elective splenectomy** done in **chronic I.T.P** (and in **Hereditary spherocytosis**)
- **No role of platelet transfusion.**
- Drugs:
  - Romiplostim = Acute / Chronic ITP
  - Eltrombopag = Chronic ITP

PrepLadder

HEMOPHILIA A

- **Factor 8 ↓**
- **X Linked recessive** disorder affecting Boy
- Presentation:
  - Earliest: Excessive circumcision bleed
  - Usual at 1 year: **B/L Hemarthrosis**
  - Easy Bruisability / Purpura
  - Intracranial hemorrhage

Normal Coagulogram:

- **BT**: 2-9 minutes
- **PT**: 11-16 seconds
- **aPTT**: 30-45 seconds

→ **Workup:**

- **Screening**: **Coagulogram**
  - BT: Normal (BT based on Platelet count)
  - PT: Normal (PT based on Extrinsic pathway)
  - **aPTT**: ↑ (aPTT based on Intrinsic pathway)
- IOC: factor 8 levels: ↓

→ **Rx:** factor 8 (DNA R. Technology) I.V concentrates

- If mucosal bleeding in Hemophilia A → **D.D.V.A.P (Desmopressin)**
- If life threatening bleed in Hemophilia A → **F.F.P** (Richest source of clotting factors)

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RULE OUT → **Battered baby syndrome: -**

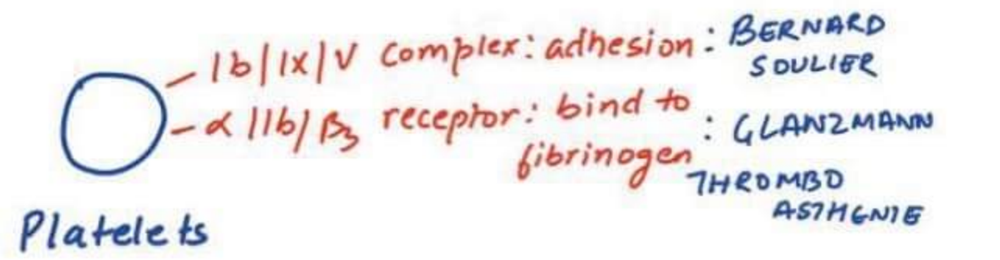
- Asymmetrical injuries
- Bruises: Variation in color
- X-Ray: fracture, healing fracture
- Fundus: Retinal bleeds

BERNARD SOULIER SYNDROME:

- **"1b receptor" defect**
- **AR**
- **GIANT PLATELETS**

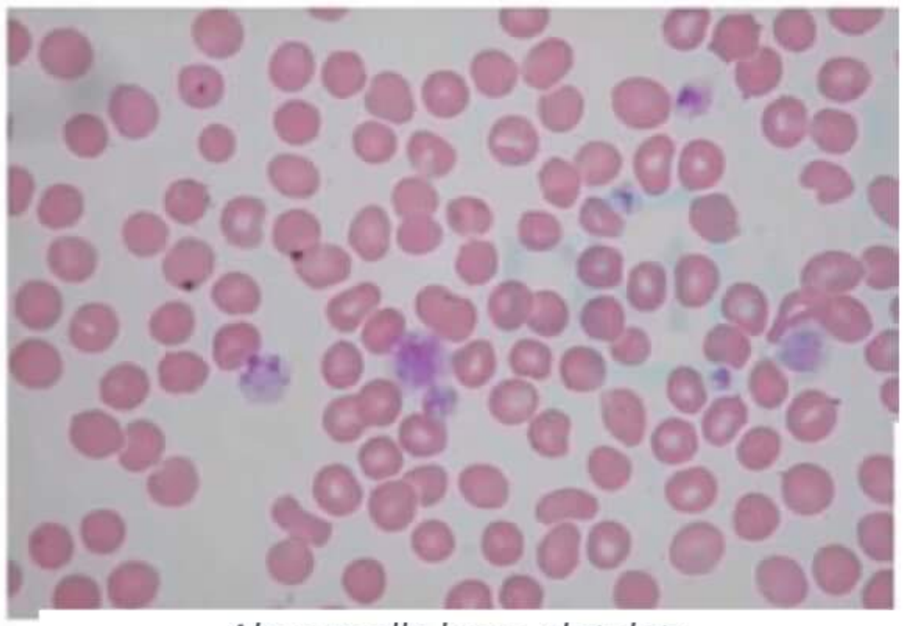
→ **Clinical feature:**

1. Recurrent epistaxis
2. Menorrhagia
3. Easy Bruisability
4. Post-operative bleeding



→ **Work up:**

- Blood count: TLC ↑ (falsely ↑)
- P. Smear → Giant Platelets
- Platelet count → Normal
- Coagulogram → BT ↑
  PT (normal), a PTT (normal)
- Platelet Function Analyzer 100



Abnormally large platelets

PrepLadder

- **Ristocein aggregation test →** ⊖
- Platelet aggregates with ADP, Adenosine, Collagen
- But does not aggregates with Ristocein

→ **Rx:** No definitive treatment.
Post-operative bleeding can be managed by **Platelet Transfusion.**

WISKOTT-ALDRICH SYNDROME

- XLR → Boy
- IgM ↓ → recurrent infections
- IgA ↑, Ig E ↑
- P. Smear: **SMALL PLATELETS**

GLANZMANN THROMBASTHENIA

- "α 2b/ β3 receptor" defect
- **Ristocetin aggregation Test→⊕**

- Platelet aggregates with Ristocein
- But does not aggregates with ADP, Adenosine, Collagen.

To remember the characteristics of Wiskott-Aldrich syndrome, use **WAITER**

Wiskott-
Aldrich
Immunodeficiency
Thrombocytopenia
Eczema
Recurrent pyogenic infections

Wiskott Aldrich is a WAITER!
Also, its X-linked recessive disorder. Typically, IgM levels are low, IgA levels are elevated, and IgE levels may be elevated. IgG can be normal, low, or elevated.

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PrepLadder

STROKE / CVA

In a Rt handed person - Dominant parietal lobe is of Left side = supplied by Left middle cerebral Artery

Function

1. Maths : Acalculia
2. Understand written test : Agraphia
3. Lft - Rt orientation : L → R disorientation, Finger agnosia
4. Speech : Global Aphasia

Non Dominant Parietal Lobe ® = RMCA

Function -

1. Visuospatial skills

   If there is occlusion of right MCA IT LEADS to visuospatial skill loss causing - APRAXIA (Constructional)

2. Hemi – Neglect

Temporal Lobe #

Hippocampus + - seat for Short term memory

Neo-cortex →seat for Long term memory

1. Loss of short term memory - Antegrade amnesia
2. **Prosopagnosia** - impaired memory of faces (Memory of faces)
3. Complex Hallucinations

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   → Smell - of Rotten fish / dead rat

   → Taste – of Metallic taste

   → Hearing - Music

4. Deja Vu - Undue familiarity
5. Jamai Vu - Unfamiliarity

Frontal Lobe #

→ Aggressive, anti-social behaviour

→ Personality damages

→ Urge incontinence – is present due to damage to Para central lobule.

↓ control urinary bladder

Never put foley catheter in this patient .

→ Apathy (Lack of interest in self care)

→ Abulia (Lack of desire to speak)

→ Primitive reflexes are present

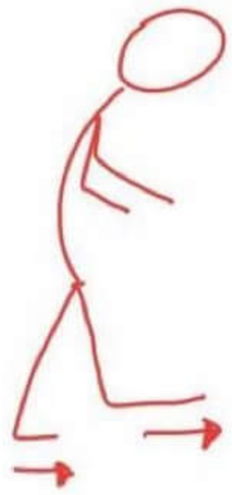
* Grasp reflex - persist up to 4 months in a newborn

PrepLadder

* Rooting reflex - Persist upto 1 month age
  + In adult
* MORO reflex - Persist upto 6 months age
  NEVER REAPPEARS

All primitive reflexes can reappear except MORO reflex

2. Magnetic gait / GAITAPRAXIA
   → Programming of gait is affected.(not able to react to a situation)

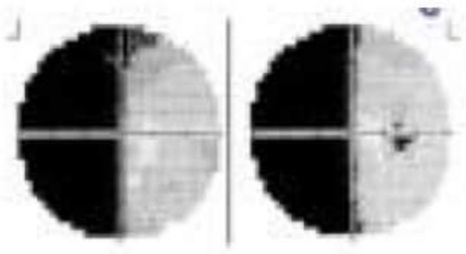


FESTINATING GAIT

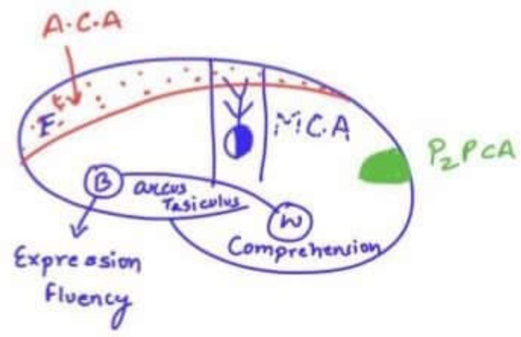
→ Festinating of gait – is seen in Parkinsonism(absent arm swing, stooped posture ,short Schuffling steps).

Occipital Lobe

P_2 PCA (P_2 branch of Post Cerebral Artery)

1. Visual Hallucinations
2. Palinopsia - persistence of an image even when object removed from field of vision
3. 

Homonymous Hemianopia



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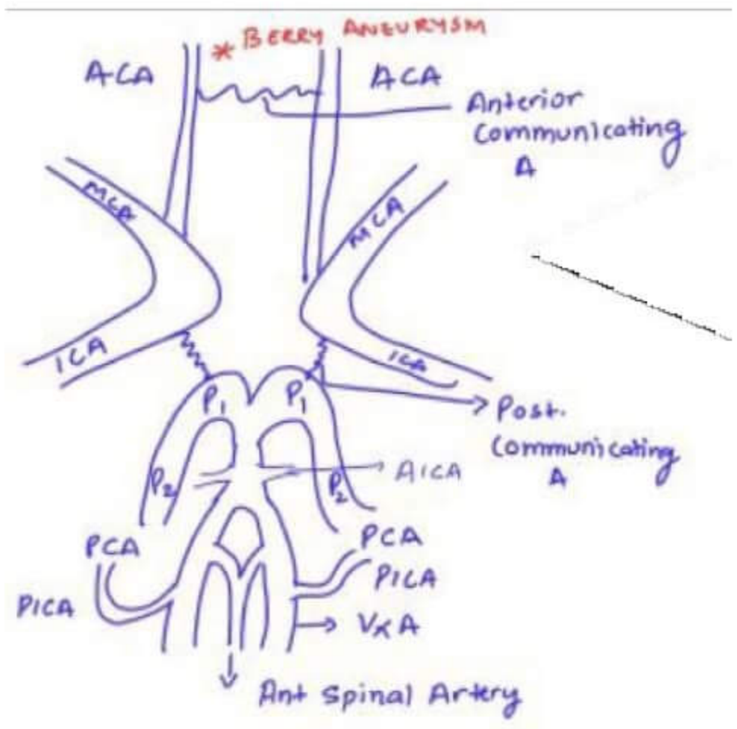
Area 4 - Precentral Gyrus
ACA involvement - Spastic monoplegia / paraplegia / gait apraxia / personality change / urge incontinence
MCA involvement - C/L Spastic Face / Arm paralysis
Left MCA involvement - Aphasia
RMCA # - Apraxia
PCA involvement - Visual Hallucination
P2 PCA Hemi Blindness
→ P1 PCA – supplies midbrain
If involved lead to **Midbrain stroke**
→ Basilar Artery -supplies pons
If involved lead **to Pontine stroke**
→ Vertebral Artery – supplies Medulla
→ Ant Spinal Artery -supplies medial medulla
If involved lead to **Medial medullary syndrome**
→ ACA - Frontal lobe involved
→ MCA - Parietal / temporal lobe involved



Weber Syndrome

→ I/L 3rd N palsy - ptosis, strabismus
→ C/L Hemiplegia

Non Thangel Syndrome

→ I/L 3rd N palsy + C/L ataxia gait

PrepLadder

→ C/L intentional tremors

Benedikt Syndrome

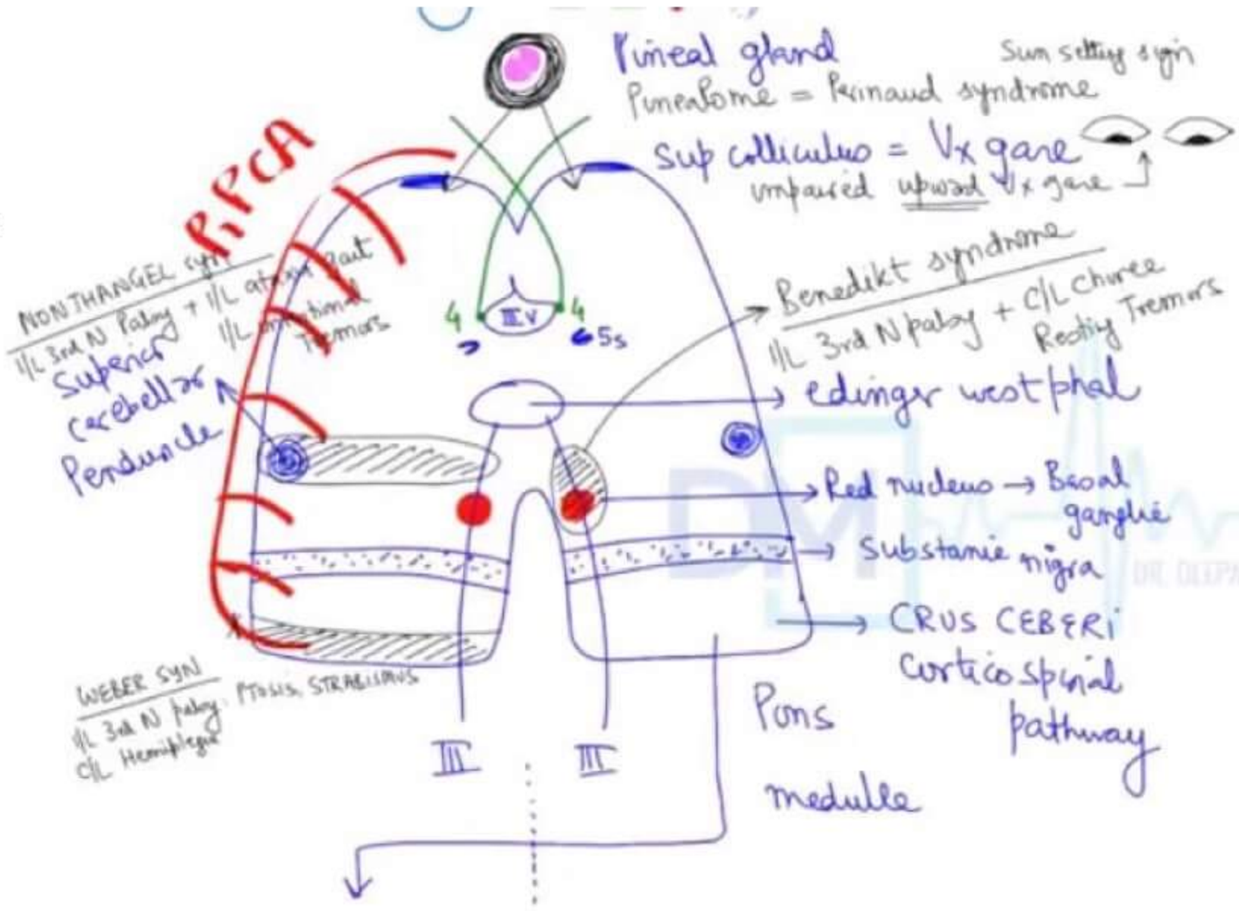
→ I/L 3rd N palsy + C/L Chorea resting tremors

Pinealoma

→Causes Parinaud syndrome

→ Impaired vertical gaze (Upward gaze)

→ Sun setting sign



$V_M V_S$ Integration of Nucleus in pons

M - Jaw Jerk (V_S, V_M)

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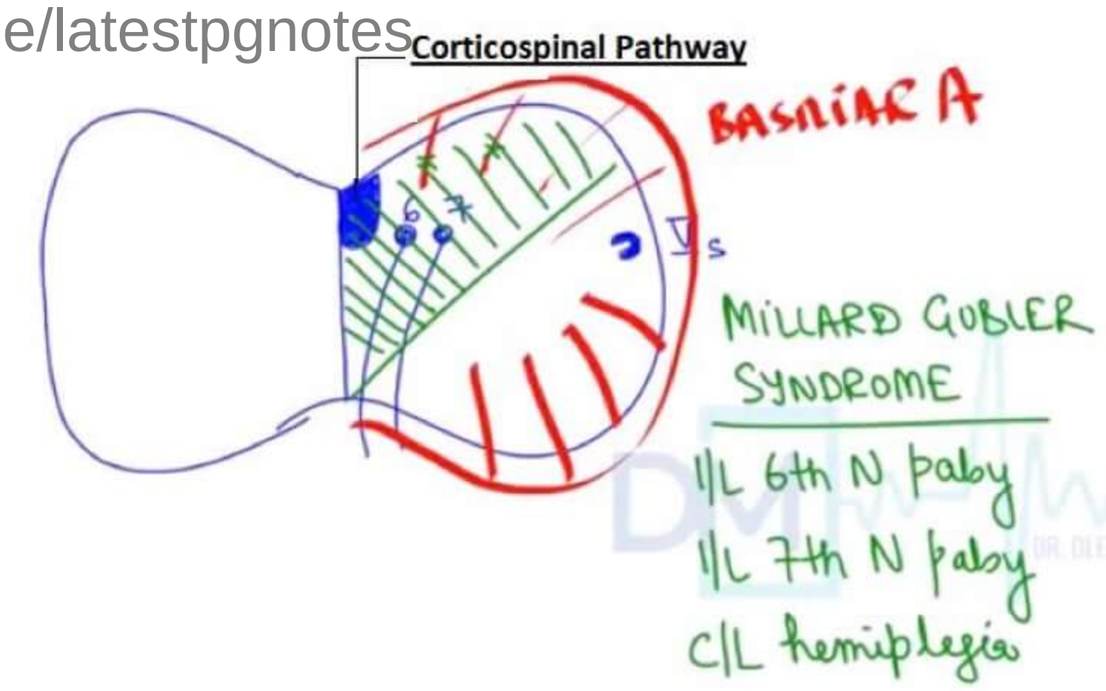
Millard Gubler Syndrome

→ I/L 6th N palsy

→ I/L 7th N palsy

→ C/L Hemiplegia



Lateral Medullary Syndrome

→ N involved - 5 / 7 (Sensory)/ 8 / 9 / 10 / 11

Medial Medullary Syndrome

→ I/L 12th N palsy + C/L Hemiplegia

Hemiplegia

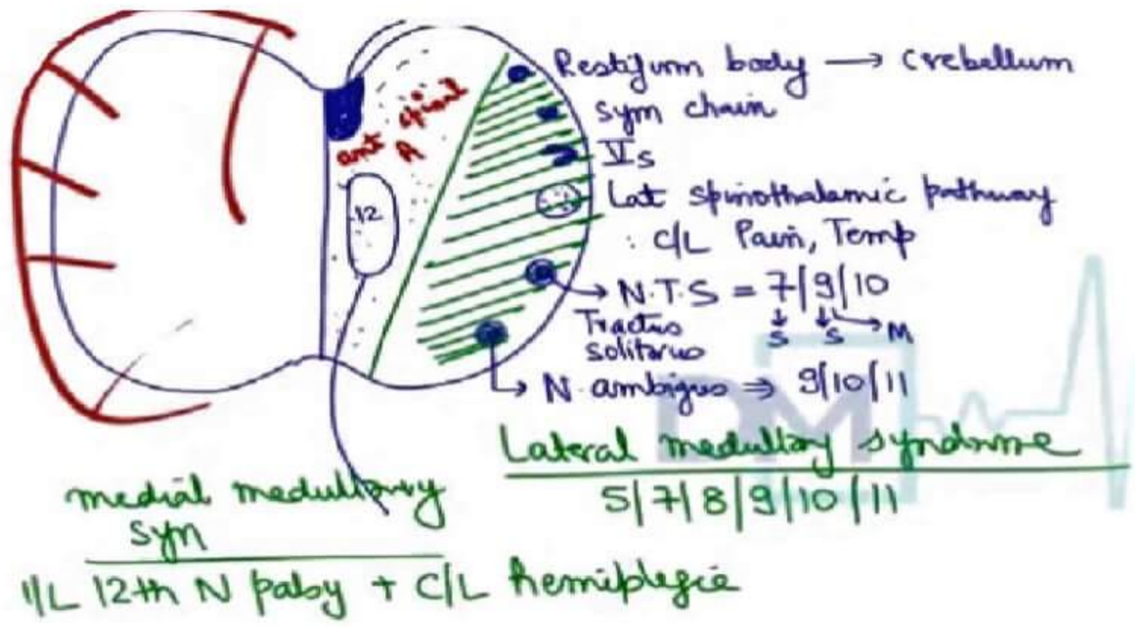
→ MCA involvement

→ P1 PCA : Weber Syndrome - 3 N

→ Basilar A : Millard Gubler Syndrome - 6 / 7 N

→ Ant. Spinal A - Medial medullary syndrome - 12 N

→ In PICA involvement no hemiplegia seen .



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Lateral Medullary Syndrome / Wallenberg Syndrome

→ Vessel involved - Vertebral Artery > PICA

Structures Involved

→ Restiform body → I/L Ataxia, I/L Hypotonia of Arms

→ Sympathetic chain involvement - HORNER SYN. (In Pan coast tumor also)

Features of HORNER SYN

Perfect Meal

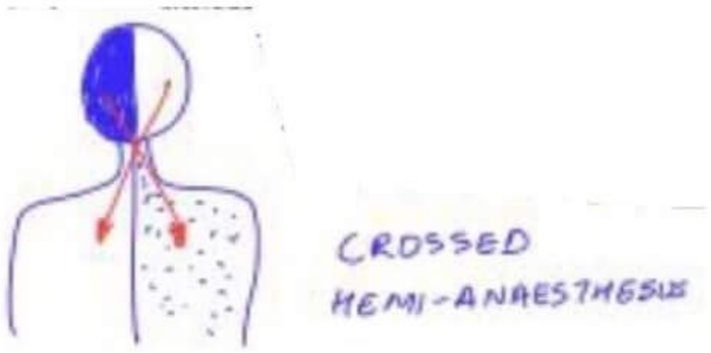
P - Ptosis - Muller Muscle involved

M - Miosis

E - Enophthalmos (Pseudo)

A - Anhidrosis

L - Loss of ciliospinal reflex



→ V_S sensory nucleus of trigeminal N involvement

→ Lateral Spinothalamic pathway involved - C/L pain, temperature sensation affected (CROSSED HEMIANESTHESIA)

→ 7_s / 9_s - Taste - AGEUSIA

→ 9^{th} N palsy - Nasal Regurgitation

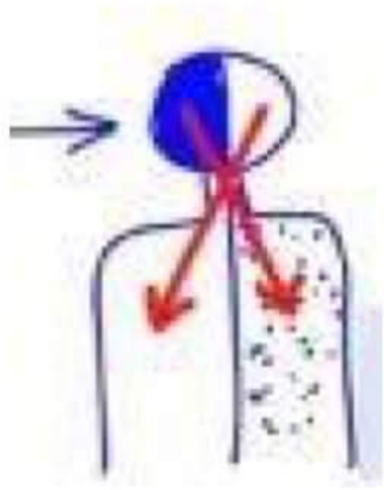
- Nasal twang to voice

→ 10^{th} N palsy → Control HR - Palpitations

- Stomach motility - Gastroparesis
- GIT motility - Constipation
- Gag reflex - Choking / aspiration
- Vocal cords - Dysarthria

→ 11^{th} N palsy - Spinal accessory N

- Shoulder drooping present



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Weber Syndrome - Midbrain = 3N involved - P_1 PCA

Millard Gubler Syndrome - Pons - 6 / 7 involved - Basilar A

Lateral Medullary Syndrome - Medulla - 5 / 7 / 8 / 9 / 10 / 11 - Vertebral A involvement > P.I.C.A

Medial Medullary Syndrome - Medulla 12 - Ant Spinal A involvement

PrepLadder

TRANSIENT ISCHEMIC ATTACK

Symptoms appear and disappear in < 24 hr,

Imaging = Normal

FEATURES-

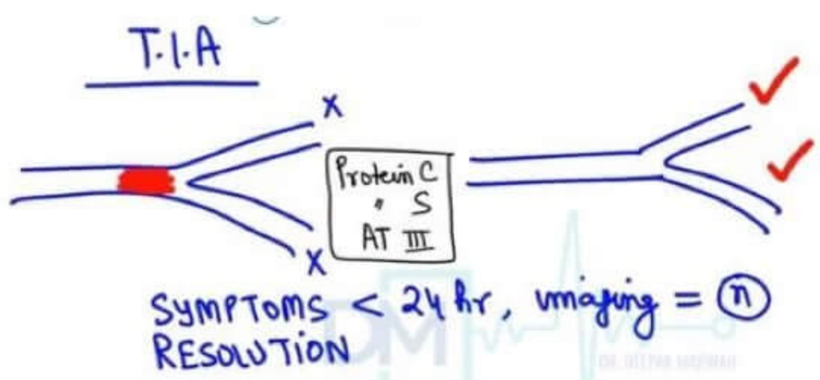
→ **Ophthalmic Artery involvement**
(Transient blindness)
Amaurosis Fugax

→ **MCA involvement**: Arm weakness
Facial Weakness
APHASIA

→ **ACA involvement**: Paraplegia

→ **Vertebral A involvement**: Nasal Regurgitation of fluids (9th Nerve involvement)

→ **Pins and needle sensation**



$ABCD_2$ SCORE

→ used to predict chances of development of stroke → **Maximum score = 7**

- Age > 60 yr =1
- BP > 140 / 90 = 2
- C/F : Arm weakness =2
- Aphasia minus weakness = 1

→ Duration

- < 10 min = 0
- 10-59 min = 1
- > 60 min = 2

→ Diabetes mellitus = Yes / no

↓ ↓

1 so

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Work Up

→ ECG : R/O ATRIAL Fibrillation

→ TTE / TEE : R/O mural thrombus

→ Carotid A doppler to rule out atherosclerotic narrowing of carotid Artery.

→ Lipid profile ↑

→ Homocysteine ↑

Rx

Tab. Aspirin 300 mg + Tab. Clopidogrel 300 mg

[Dual Antiplatelet Therapy]	↓		↓
	75 mg	Lifelong	75 mg

PrepLadder

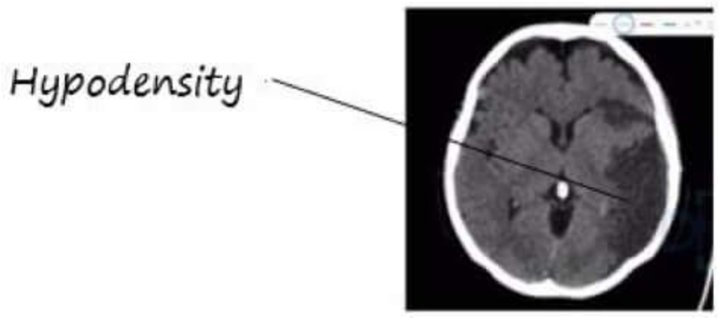
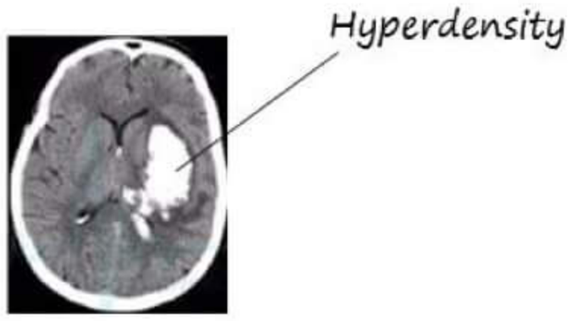
→ Atorvastatin + $B_{6/9/12}$ ± Rivoroxban or Dabigatran

Novel oral anticoagulants (NOAC)

Clinical scenario

A 60 yr old HTN / Smoker goes for morning walk at 6 am and at 6:30 am there occur Sudden onset: Aphasia, along with right arm weakness. At 7:30 am he is brought to Hospital → on examination DTR shows Brisk movement and the plantars are upwards, Fundus examination = Normal

- Door to CT SCAN time < 20 min
- Door to CT SCAN interpretation < 45 min

CT SCAN (Two possibilities)	
	
Acute Ischemic Stroke	**Hemorrhagic Stroke**
→ DOC - Reteplase → Window period < 4.5 hr Of symptom onset → Brain angiography 4.5-6hr Mechanical Thrombectomy/Intra arterial reteplase	↑ ICP Osmotherapy Ventriculostomy ↓ (If fails) Hemicraniectomy Decompressive

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Note: For HTN crisis → Nicardipine/ Labetalol is used

Thrombolysis	
Indication	**Contraindications**
→ STEMI : < 12 hr → AIS : < 4.5 hr → Massive P.E (pulmonary embolism):	→ NSTEMI → Hemorrhagic stroke → Pulmonary embolism → SBP > 185, DBP > 110

PrepLadder

Note: Ischemic Stroke more common than hemorrhagic stroke

Hemorrhagic Stroke (1/3 cases) causes:-

→ HTN

→ Trauma

→ Warfarin Toxicity

→ Cerebral amyloid angiopathy

Ischemic stroke (2/3 cases)

→ Embolic stroke (Non Rheumatic Atrial Fibrillation) >> Cerebral Thrombosis (Atherosclerosis)

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PrepLadder

SUBARACHNOID HEMORRHAGE (SAH)

Causes

→ Most Common Cause: **Trauma** → secondary cause

→ Rupture of Berry aneurysm – primary / intrinsic cause

→ Arterio venous malformation: CHARCOT BOUCHARD ANEURYSM -seen in Hypertension

→ Extension of intracerebral hemorrhage

→ Mycotic aneurysm (complication seen with SABE – subacute aneurysm bacterial endocarditis)

→ **MC site:** Berry aneurysm- 85% Anterior communicating Artery ⟷ Anterior cerebral artery.

→ **Mycotic aneurysm** – site – distal to first bifurcation of the major component or major blood vessel ⟷ **circle** of Willis

→ **Giant aneurysm: > 2.5 cm**

Site: Terminal Internal carotid artery, Middle Cerebral artery, top of Basilar artery

Incidence of rupture:

→ Increases with size and location, If size is >7 mm and is + at top of basilar artery → highest chances of rupture.

→ Rupture causing brain stem ischemia → Mortality around 45% is there.

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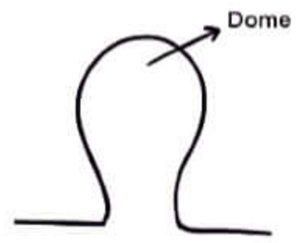
Dome: Prone to tear/ micro leaks

Sentinel Headache: Severe excruciating headache from duration of few seconds to minutes & disappears ,after few days of this headache the actual aneurysm break → blood leaking into the meninges leading to classical thunderclap headache]



Layer defective: Internal Elastic lamina

Clinical manifestation in Berry aneurysm

→ **"Worst headache of my life"** – Thunderclap headache - once headache starts, it reaches peak intensity

within 1 min and last upto (5 min) few min

→ Vomiting (Projectile)

→ Loss Of conscious / Stupor

→ Nuchal rigidity ⊕

Remember – fever +headache+ nuchal rigidity represents meningeal infection.

PrepLadder

Extra Mile

Other condition with thunder clap Headache

→ Post coital headache
→ Exertional headache
→ Benign cough headache
→ Intracranial cysts & tumors
→ **Hypophyseal apoplexy → bleeding in pituitary**
→ **Dissection**
→ **Migraine**
→ **Intracerebral hemorrhage** → should be ruled out before Dx SAH
→ **Sinus thrombosis**
→ Segmental reversible vasospasm

C/F based on site of rupture:

→ **Anterior Communicating Artery**
- Abulia (lack of desire to speak)
- Brocas Aphasia
- Hemiparesis
- Focal neurological deficit ⊕

→ **Posterior Communicating Artery**
- 3rd nerve palsy Q. **m/c nerve involvement with unruptured/ rupture berry**]
- Loss of light reflex
- Retro orbital pain
- Pupillary dilation

→ **Internal Carotid Artery** (goes via cavernous sinus) → 6th nerve palsy, diplopia on looking lateral

→ **PICA / AICA:** Occipital headache / cervical area pain

→ Release of ⟶ B type natriuretic peptide from Brain

↓

Leads to Natriuresis and cause Na^+ loss from body

↓

Dangerous hyponatremia electrolyte imbalance

↓

Seizures

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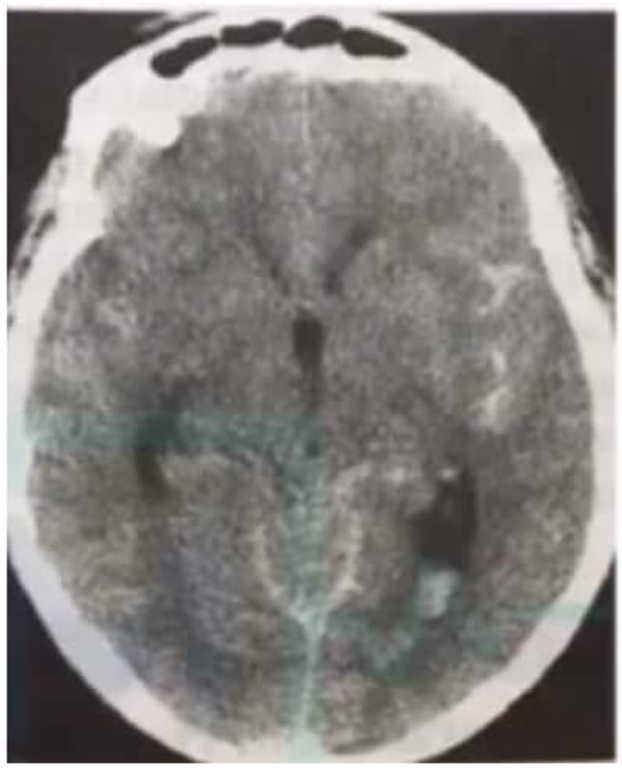
Work up:

→ NCCT head (Non-contrast CT head)

Dx – left sided SAH

Blood in Sylvian fissure



Blood in temporal horns of ventricle

→ Lumbar puncture:

Bloody CSF: → Trauma
→ HSV encephalopathy
→ SAH t.me/latestpgnotes

- RBC lysis (inside the CSF) → Bilirubin → give yellowish tinge to CSF →**Xanthochromic CSF**.
- Starts as early as 6-12 hours after the bleed and peak: 48 hours

→ **CT angiography/ four vessel conventional X-ray angiography**- to identify any other aneurysm.

→ **ECG**: Catecholamine excess can contribute (ECG finding to myocardial Ischemia of stroke) ST ↓ depression, T wave inversion / Peaked T wave, QT prolongation(also seen in hypocalcemia, hypomagnesemia) and Broad QRS.

→ **Electrolytes**: Hyponatremia due to Natriuresis

→ **ECHO**: Presence of regional wall abnormality/ LVH.

HUNT HESS SCALE		World federation of Neurological society	
		Evaluate GCS	
		Grade	prognosis
Mild Headaches	I	I	GCS – 15, No motor deficit, Best prognosis
Severe headaches	II	II	13-14 No motor deficit
Somnolent, confused	III	III	13-14 with motor deficit

PrepLadder

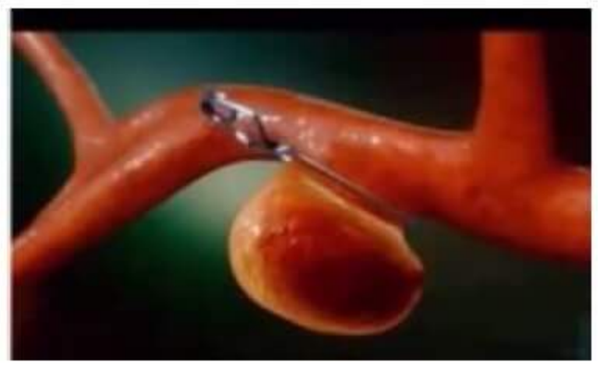
Stupor	IV	IV	7-12 **with/without** motor deficit
Comatose	V	V	3-6 **with/without** motor deficit

Delayed Neurological deficit

→ Rebleeding
→ Hydrocephalus
→ Cerebral ischemia due to vasospasm is Leading cause of death
→ Hyponatremia: B.N.P induced natriuresis AKA cerebral salt wasting syndrome

→ **CVS**: Myocardial infarction/ Ischemia

Rx: For unruptured aneurysm - Aneurysmal clip deployment



Access from femoral Artery Introducing

→ Platinum coil
↓
Thrombi/ fibrosis formation
↓
Prevent berry from rupturing

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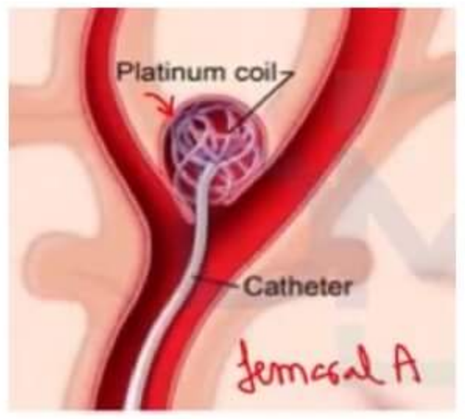
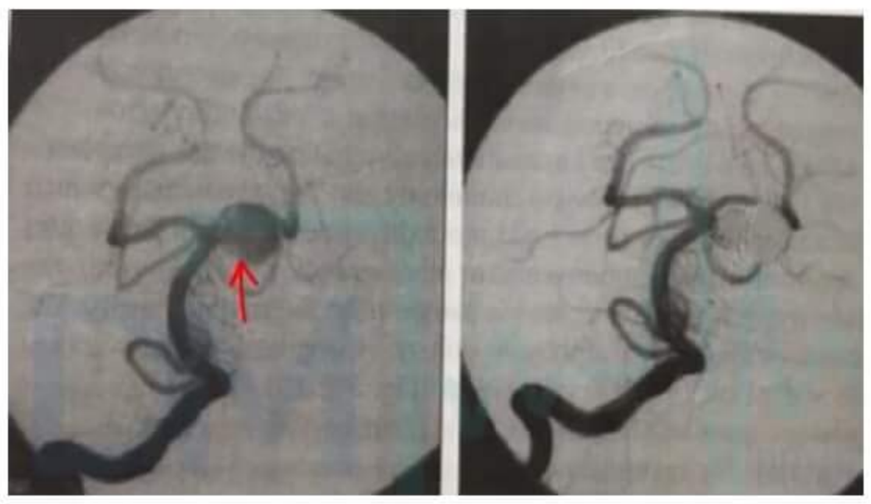


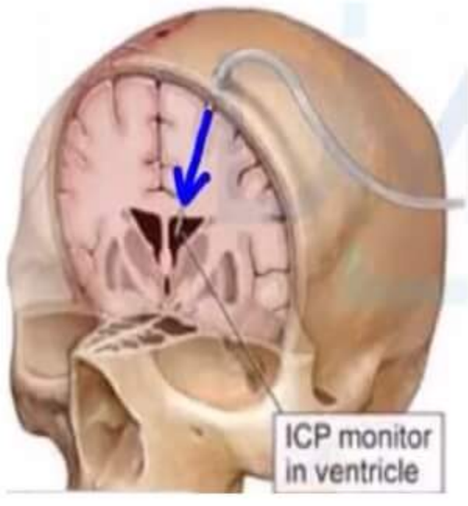
Note → Endovascular coiling is better due to shorter hospital stay and good results.

TOC: For Unruptured berry/ aneurysm → **Endovascular coiling**



Treatment of Ruptured aneurysm malformation

1. **Ventriculostomy** intracranial pressure monitoring catheter in lateral ventricle
↓
Drain out CSF from brain (to reduce the pressure in brain)
↓
Reduced chances of patient dying due to brain herniation



2. Drug of choice for SAH-**Nimodipine** - 1° of cerebral vasospasm that occurs due to Vasospasm

PrepLadder

after rupture of aneurysm.

3. **HTN crisis:** IV Nicardipine > Labetalol

→ Target Blood pressure: =160 mmHg

→ CPP (cerebral perfusion pressure) = MAP (mean arterial pressure) – ICP (intracranial pressure)

CPP target to maintain= 60-70 mmHg.

4. **Vasospasm Rx:** Volume expansion/ Nor-epinephrine/ Phenylephrine

→ Unfractionated Heparin

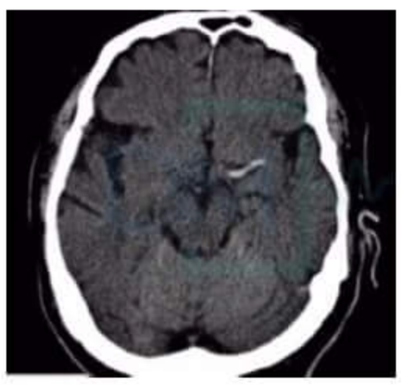
→ Compression stockings (To Prevent DVT)

- Dense/ Hyper dense MCA sign

↓ Thrombus in blood vessel

Early feature seen in acute Ischemic stroke

[Wedge hypodensity – **Dx-AIS** – Later stage]



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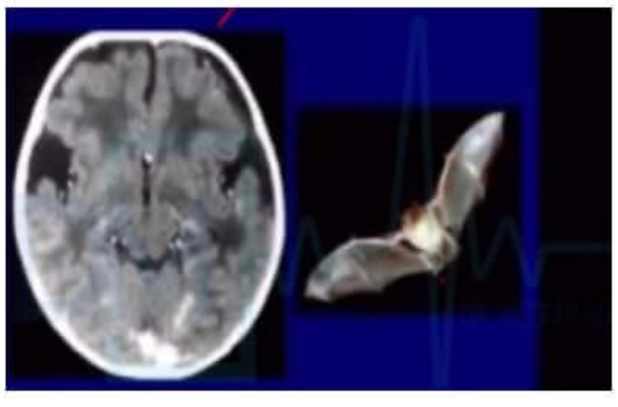
- **BAT WING sylvian fissure**-Develops in inborn error of metabolism of glutaric acidemia



Extra Mile

Blood **in sylvian Fissure/ Interhemispheric fissures → SAH**

→ **Bat Wing Sylvian Fissure** - Glutaric Acidemia

→ **Bat wing pulmonary edema** - CHF/ Bronchopneumonia

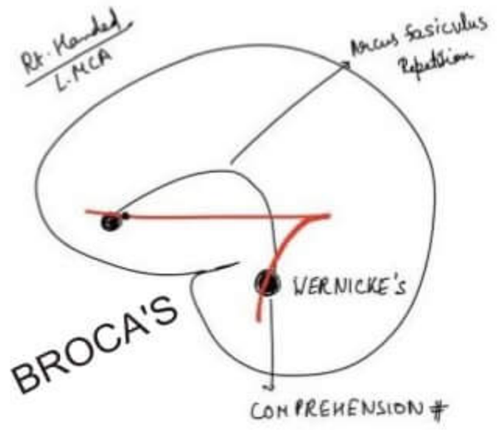
→ **Reverse wing pulmonary edema** - Chronic eosinophilic pneumonia

PrepLadder

INTRAPARENCHYMAL HAEMORRHAGE, EXTRADURAL HAEMORRHAGE & SUBDURAL HAEMORRHAGE

Intraparenchymal Bleeding

BROCA'S area damage	Wernicke's Damage
→ ↓ Fluency Syntax (Grammar) Expression → Motor aphasia	→ Comprehension lost → Receptive Dysphasia → Word Salad → Fluency is Preserved → Jargon Speech

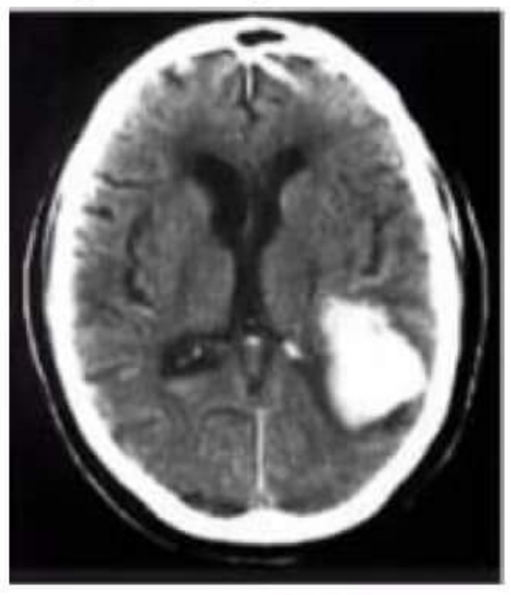


Case Scenario

A 50 yr old, HTN (Non-compliant with medications) comes with the chief C/O → Facial asymmetry and

Sudden onset → Aphasia and weakness in right arm/shoulder

Provisional diagnosis - LMCA Territory stroke O/E → DTR are Brisk and Babinski sign (+), non-cooperative with Fundus examination



→ Door to CT scan time < 20 min

Hyper density / Obstructive

I.P.H / Hydrocephalus

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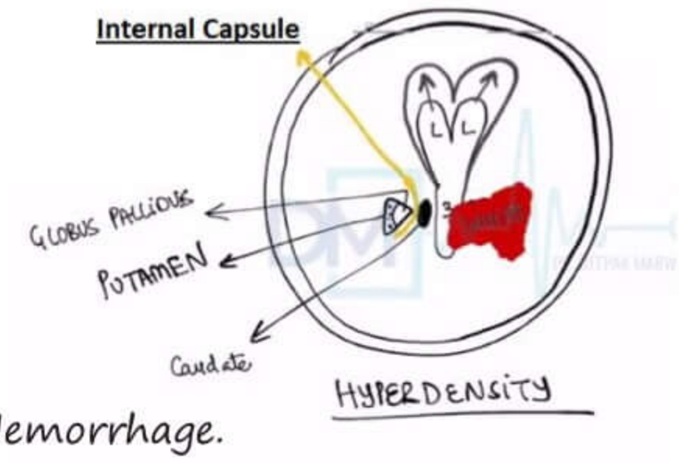
Rx

1. **Control of HTN Crisis**: > 220 / 130 - IV Nicardipine
2. **Control of Raised ICP** → Ventriculostomy

   ↓ Fails

   Decompressive Hemicraniectomy
3. Warfarin ++ → I.P.H.



R_x:- Prothrombin complex concentrate is superior to FFP in warfarin induced Hemorrhage.

Extra Dural Hemorrhage

→ Middle meningeal Artery is the source of bleeding

→ NCCT heads shows Lenticular hyperdensity

→ Mass effect of CNS bleed leads to obstructive **Hydrocephalus**

→ Lucid interval [consciousness between 2 periods of unconsciousness] may be present.

Rx of EDH with Posturing

→ Burr hole

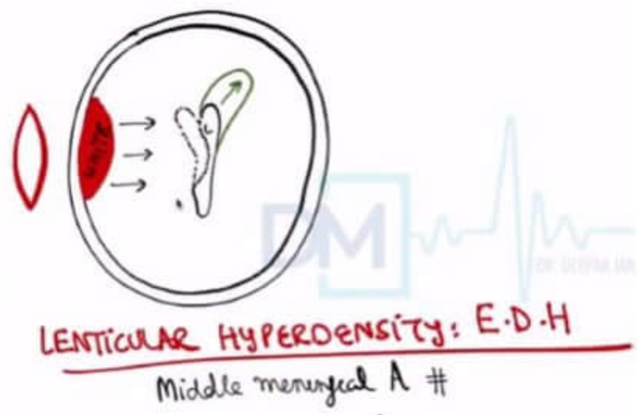
→ Decompressive Hemicraniectomy.

Decision for which side to Perform Burr hole is based on.

→ CT Scan Report

→ I/L mid dilated pupil, sluggish ® to reaction

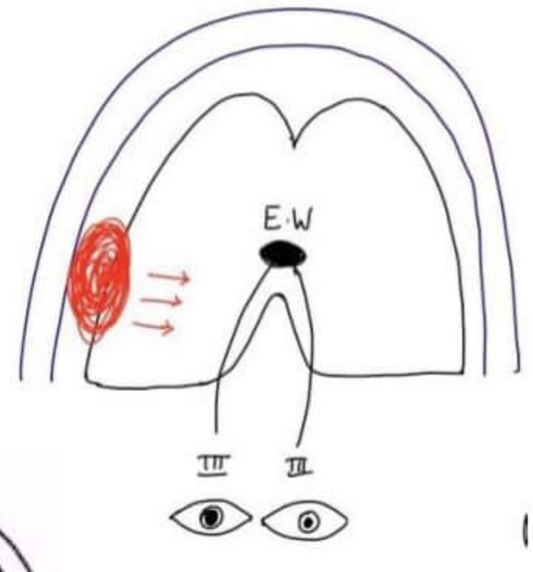
→ **On left side if pupils are equivocal in response to light.**



PrepLadder

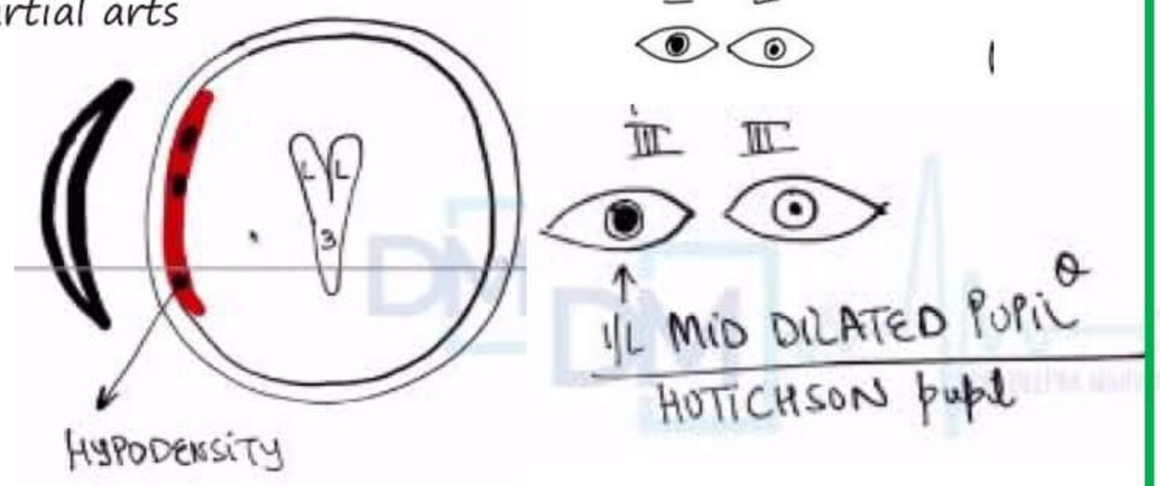
SDH- Subdural Hemorrhage

→ Source of bleeding: Cortical bridging veins



Clinical scenerio → 70 yr male→ Obese, T2 DM, Slipped in Bathroom 7 days back → Bump on head (Subperiosteal Bleeding) + C / O Focal deficit and Arm weakness.

→ People prone to SDH → Stunt actor/ Boxer/ Mixed martial arts
* Parkinsonian patient
* Diabetic neuropathy patients



→ **Acute SDH shows** → Concavo–convex hyperdensity

→ **Chronic SDH shows** → After 2-3 weeks hypodensity is there - Black pockets in white blood collection is there due to reabsorption of the blood.,

Note → Festinating gait + Sensory ataxia later on gradual onset of neurological symptoms. O/E: Fundus shows Papilledema + DTR are Brisk and Babinski sign is elicited. This is the typical history given in exams regarding the chronic SDH.

Rx- The Sx intervention in these cases is not required in all cases and is dependable on ICH score:-

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ICH Score components

→ Age
→ GCS
→ Volume of bleed
→ Location of bleed

Note:- if patient is > 75 yr old and GCS is < 8, volume of bleed > 30 cc and is Infratentorial bleed then in these worst scenario the requirement of Sx intervention is must fort management of the patient.

- **Decompressive Hemicraniectomy**

In other cases where the patient does not have the components mentioned above and got mild neurological deficit then the patient is managed conservatively by:-

- **ORAL Glycerol**
- **Acetazolamide**

PrepLadder

HEADACHE AND MIGRAINE

→ Most common cause of headache = **Tension headache**
→ MC cause of 2° headache = **Infection**
→ MC cause of headache (Female) = **Tension headache > Migraine**
→ MC cause of headache (Male) = **Tension headache > Migraine > Cluster headache**
→ MC cause of frontal headache= **Tension headache**

- HTN
- Refraction error
- ↑ ICP (10-20 mm Hg - Normal) and >25 mm Hg for >5 min needs treatment

→ MC cause of occipital headache = **Tension headache** but rule out HTN but if it is not given in the options then answer is going to be → **Basilar migraine**
→ MC cause of temporal headache = **Giant Cell Vasculitis** (MC vasculitis in geriatric age group)

Migraine

Clinical scenario:- Female standing in sunlight for long duration and having AURA: Blurring of vision and following that the manifestations that occurs are:-

→ Pulsatile headache – U/L – Throbbing in nature
→ Photophobia / phonophobia
→ Nausea (Sight/ smell of food)
→ ↑ intensity of headache on physical neck movements

Most of the times patients have recurrent episodes

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P. O. U. N. D

→ Pulsatile headache
→ One day illness
→ Unilateral – most of the cases
→ Nausea
→ Disabling in character

Note: If 4 out of 5 features should be +ve and ≥ 5 attacks per year should be there to make the diagnosis

Pathogenesis theories related to migraine:-

→ Release of **CGRP-Calcitonin gene related** Peptide (Latest theory) → to be answered as 1st choice
→ Release of **excitatory neurons- Glutamate/Aspartate releases** → irritates the nociceptive receptors of Trigeminal nerve. (More acceptable theory than Vascular theory)
→ **Vascular theory:- Vasoconstriction of intracranial Blood Vessels** and later on **reflex vasodilation of extracranial BV** (they came piercing via Dura matter- pain sensitive structure) that causes pulsatile headache. The Dura matter is innervated by the the nociceptive receptors of trigeminal nerve. Whenever the BV via dura matter dilates they cause pain due to stretching of dura matter.

Note:- Duration of attack: - 4 hrs to 72 hrs and Average duration:- 24 hrs but
If pain persists > 72 hr → **Status Migrainosus**

PrepLadder

Rx:- Mild to moderate attack

→ Indomethacin : Cox-1 inhibitor (s\e Gastritis)

→ Etorocoxib: Cox-2 inhibitor

→ PCM 1 gram: Cox-3 inhibitor

Severe attack

→ Triptan = Sumatriptan (They act on 5HT $1_B/1_D$ receptors present in extra cranial blood vessels)

It is available as:-

- Mouth dissolving tablet
- Nasal spray
- I.M
- Transdermal patch

Triptans are contraindicated

- Pregnancy
- Prinzmetal angina
- Peripheral artery disease
- Basilar migraine

→ **Fastest acting triptan = Rizatriptan**

→ **Longest acting triptan = Frovatriptan**

→ **Status migrainosus = I/M Prochlorperazine**

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Clinical scenerio:- A 25 year female woke up at 5 am with excruciating headache having 2 episodes of vomiting since morning and complains of weakness, O/E there is presence of Nuchal rigidity. Probable diagnosis?

Ans.:- Subarachnoid Hemorrhage: Blood in meanings

Differential diagnosis:-

→ **Meningitis: Triad of Fever,Headache, Nuchal Rigidity** (Seen in 40% patients), photophobia,and seizures.

→ **ICSOL (Imaging of intracranial space occupying lesion):** Ruled out due to short history.

→ **Tension/headache:** Considered only when all other causes have been ruled out.

Terms which give hint of subarachnoid hemorrhage:

- Thunderclap headache
- Worst headache of my life
- Short duration severe excruciating Headache + Nuchal rigidity

SAH
- Rupture of berry aneurysm (Primary cause)
- Trauma (Secondary Cause)

PrepLadder

Migraine variant

Ophthalmoplegic migraine

→ **P.O.U.N.D** features are present and after Rx – Triptans, there is resolution of symptoms → during resolution period there is Ipsilateral 3rd Nerve palsy → Spontaneous improvement.

Investigation- NCCT head to rule out stroke / Cerebrovascular Accident

Symptoms

→ Ptosis
→ Strabismus- Divergent

Familial hemiplegic migraine

→ Ca^+ channel defect
→ P.O.U.N.D + C/L arm weakness/ face → shows Spontaneous resolution
→ NCCT head is mandatory to rule out stroke

Other Ca^+ channel defect:-

→ Lambert- Eaton syndrome
→ Hypokalemic periodic paralysis
→ Familial hemiplegic migraine

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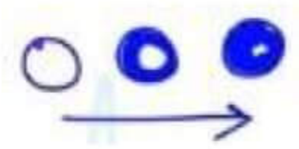
K^+ Channel defect → Episodic ataxia

Q:- 75 year old male, retired military person feels feverish off and on and temporal headache since 4 weeks. Probable diagnosis?

Ans: Giant cell Vasculitis, it can present as:-

→ F.U.O (Fever of unknown origin)
→ Superficial Temporal /Auriculotemporal Artery Vasculitis
→ Ischemia of skin of scalp, TM joint → ischemia Jaw claudication
→ Ophthalmic A Vasculitis causing blindness (Monocular/ binocular)
→ ESR = 100 mm fall/ 1st hour
→ Palpate the cord like structure at TM joint under blood vessel



IOC: - Vessel wall Biopsy
Rx: - Steroids - Prednisolone

Q:- 35 year old female complains of headache: and on enquiring she told that she got 2 children→ they are having poor performance at school and she feels like→ there is compression around her head (Fronto-occipital)

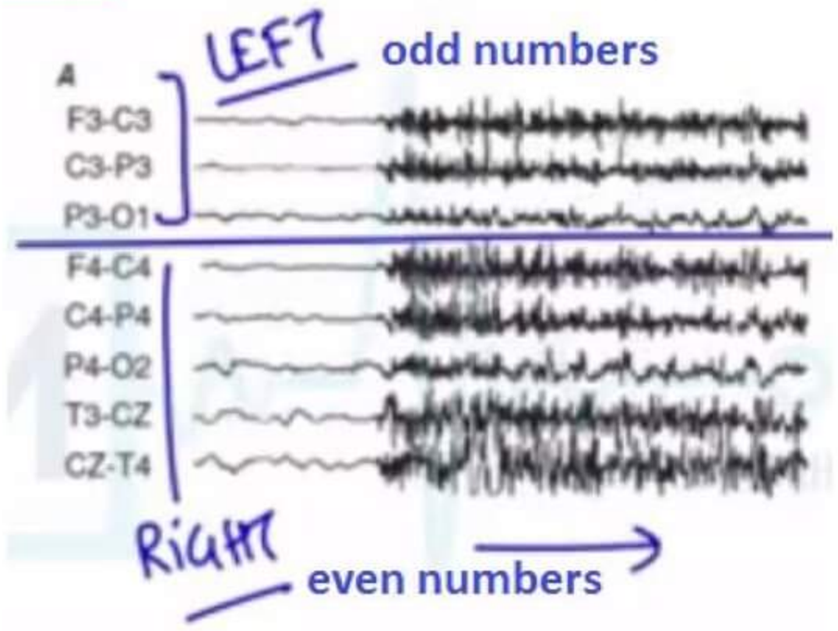
→ O/E: BP = (n)
→ Refraction testing = (n)
→ X-ray PNS = (n)
→ Fundus = (n)
→ Probable diagnosis?

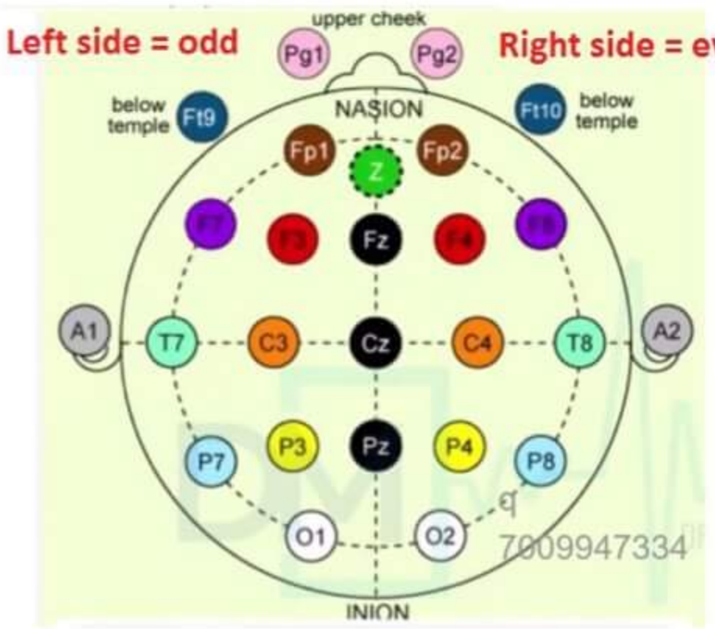
Ans.: Tension headache

PrepLadder

EPILEPSY AND EEG

EEG- EEG invented by **Hans Berger** and it has 10 – 20 lead placement system





→ Alpha rhythm: eyes closed, drowsy, relaxed → **8 – 13 Hz**

→ Beta rhythm: Awake, eyes opened → **13 - 30 Hz**

NREM Phase-

→ **NREM 1** → Myoclonic jerk may occur.
→ Theta rhythm: 4- 7 Hz

→ **NREM 2** → longest phase of NREM
→ μ waves/ sleep spindles
→ 12 - 14 Hz

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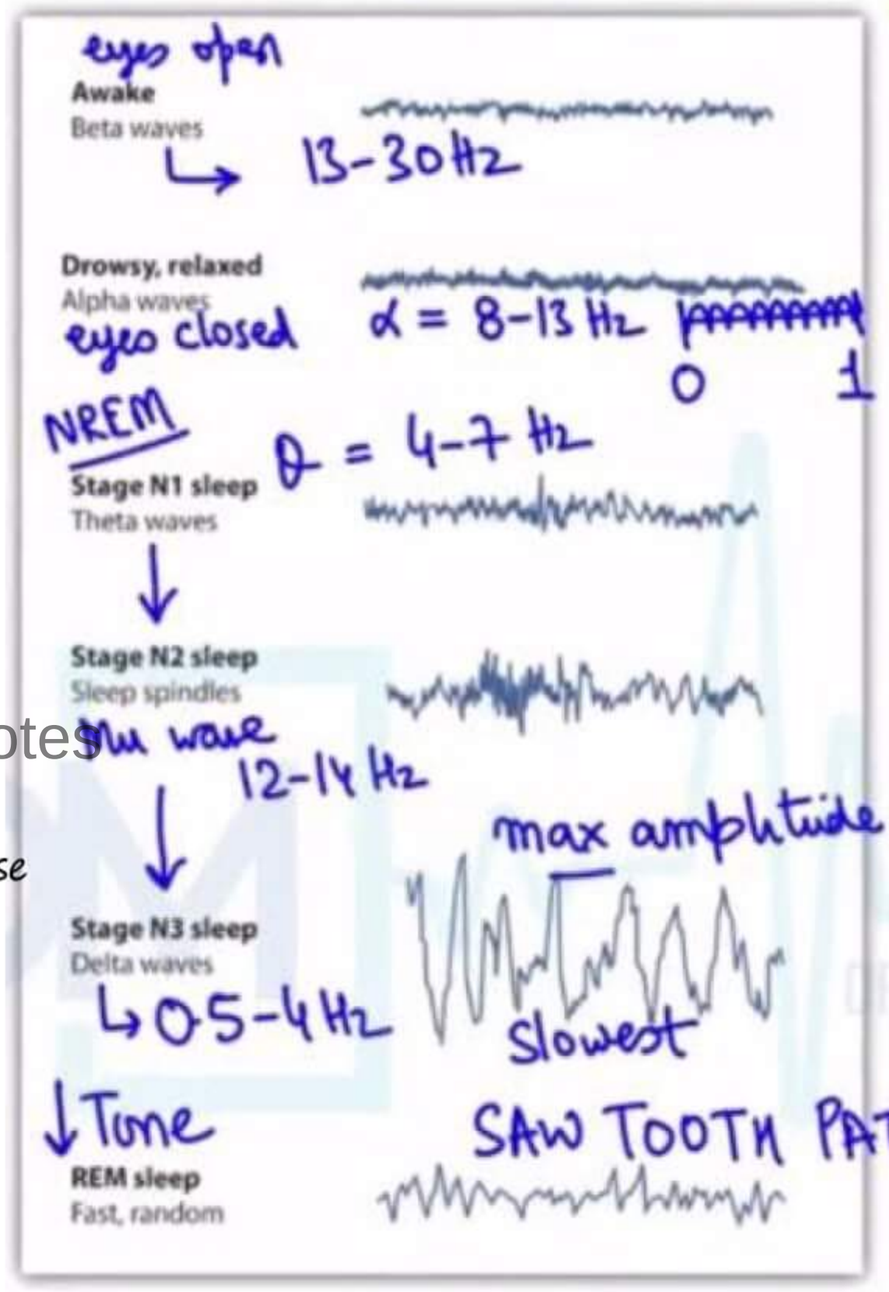
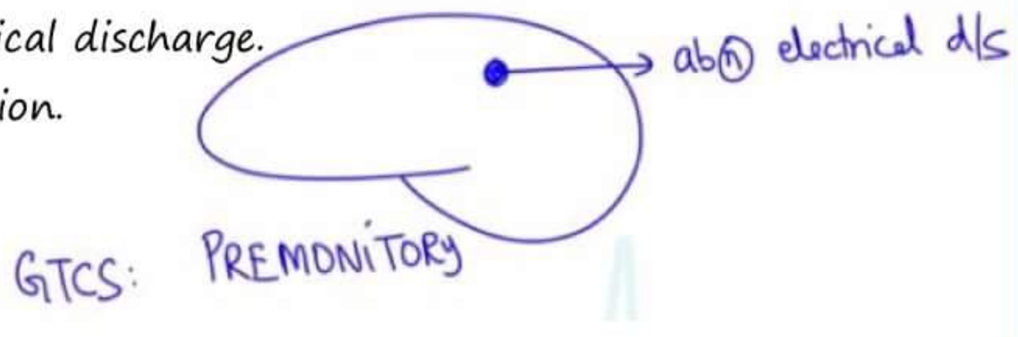
→ **NREM 3** → deepest phase of sleep/ most difficult to arouse
→ Delta waves: 0.5 – 4 Hz
→ Slowest wave pattern
→ Maximum amplitude, least frequency



REM Phase-

→ REM sleep→ decrease tone of muscle
→ EEG- Saw tooth pattern

SEIZURES- Abnormal focus in brain leading to abnormal electrical discharge.
CONVULSION- Motor manifestation of same is called as convulsion.



GTCS = Generalized tonic clonic seizures

Clinical scenario

Premonitory symptoms (general unwellness of the patient) are presenr– and later on loss of consciousness, uprolling of the eye balls and during tonus there is ↑ in Tone of muscles and there occurs sudden contraction of muscles of expiration of vocal cord lead to "ICTAL CRY".

Tonus (10-20 Seconds)
→ Up rolling of eyes
→ Pooling of secretions
→ Tongue bite ±
→ Perioral cyanosis
→ ↑ HR ↑ BP
→ Mydriasis

PrepLadder

GCSE – Convulsions > 5 min

CLONUS: Violent jerking of all limbs followed by post ictal deficit

Note:-

→ < 60 seconds - Usual duration of both tonus and clonus

→ Postictal deficit - confusion, orientation

- Babinski sign present and Corneal reflex absent in unconscious patient and vice versa at the time of regaining consciousness.

Epilepsy: ≥ 2 unprovoked seizures episode

→ To terminate Convulsion = Lorazepam is given intravenously. In case of failure to obtain intravenous access, rectal diazepam is used.

Classification: -

Focal	Generalized	Unknown onset
With intact awareness	**Motor** → Tonic –clonus → Atonic → Myoclonic	Motor
Without intact awareness	**Non – motor** → Absence → Atypical absence	Non – motor
Motor		
Non motor		
Evolution into GTCS		
AURA		

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Aura implies perception of stimulus like bright lights, unpleasant smell of burning rubber

1. **Focal Onset**
   (Can be further described as having intact or impaired awareness, motor or nonmotor onset, or evolve from focal to bilateral tonic clonic)
2. **Generalized Onset**
   a. Motor
      Tonic-clonic
      Other motor (e.g., atonic, myoclonic)
   b. Nonmotor (absence)
3. **Unknown Onset**
   (Can be further described as motor or nonmotor, or unclassified)

Focal seizure:

causes - 1. Neurocysticercosis

2. Hippocampal Sclerosis – causes temporal lobe epilepsy

With intact awareness-

Abnormal electrical activity in left motor cortex-

→ Right hand/face involuntary movements

PrepLadder

Extra edge:-

→ **Jacksonian march**- abnormal movement start from distal part and progress to proximal part.

→ **Todd's palsy**: Weakness persisting for hours to days after manifestation of focal seizurs

→ **Epilepsia partialis continua**- Counterpart of GCSE and manifestation can persist for days & weeks.

→ **Non motor manifestation**:- Paraesthesia / vertigo

- → Sensation of burning rubber
- → Micropsia or macropsia
- → Subjective events that cannot be observed by someone = **AURA** like bright lights, smell of burning rubber.

NOTE-

→ AURA is not a feature of GTCS (generalized tonic clonic seizures)

→ **Automatism** is a feature of focal seizure with impaired awareness:-

- Lip-smacking
- Chewing
- Swallowing
- Picking
- Uncontrollable laughter/ crying

→ Progression of focal seizure:- **AURA → Motionless stare → Automatism.**

There is presence of

- Post ictal confusion
- Antegrade amnesia
- Transient neurological deficit in form of Aphasia

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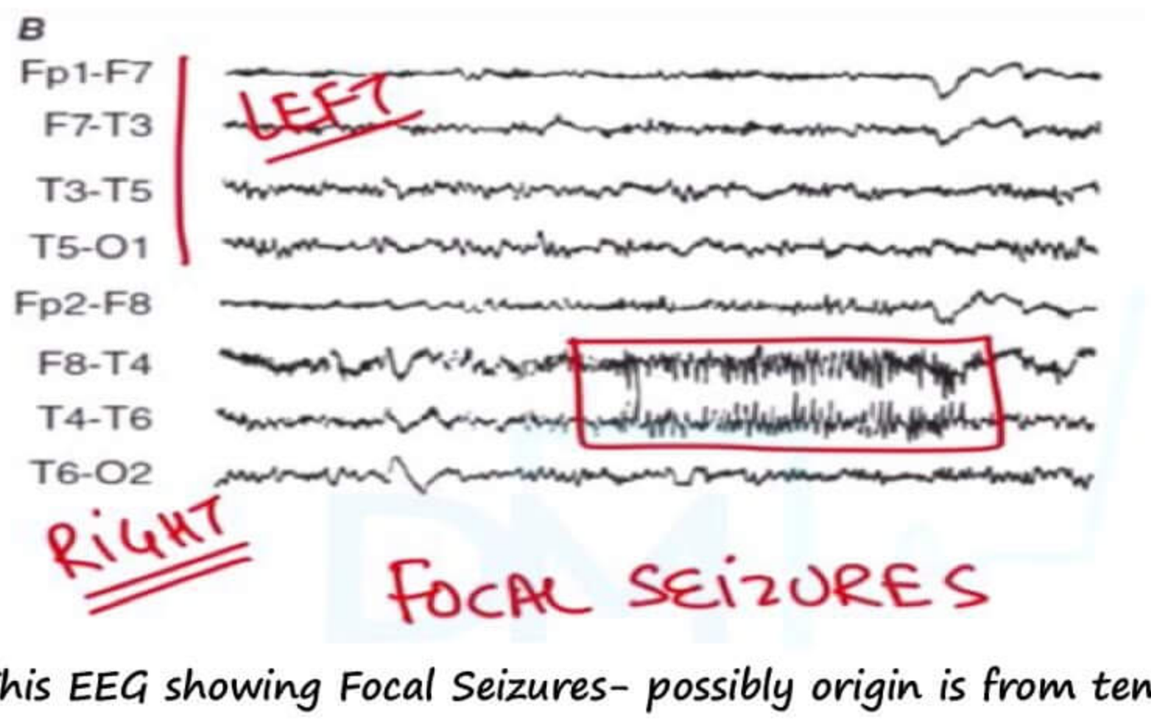
→ EEG can be normal during interictal period

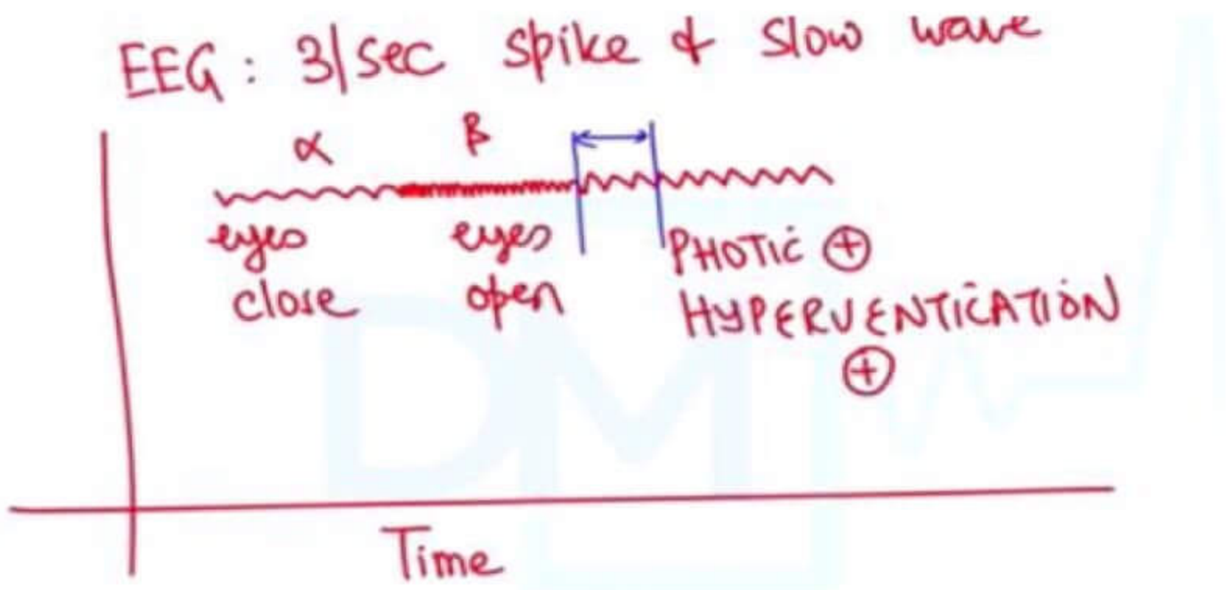


This EEG showing Focal Seizures- possibly origin is from temporal lobe

Generalized onset seizures

1. Typical absence seizures:
   - → Transient loss of consciousness for 1-2 seconds
   - → 4-10 yr child
   - → Postural tone is maintained
   - → Become unresponsive/quiet
   - → Repeated blinking of eye
   - → Post ictal deficit absent
   - → Day dreamers

PrepLadder



EEG = 3 per second spike & slow wave.

Ask patient to first open the eye – alpha wave present, then close the eye – beta wave present. Ask the patient to hyperventilate or give photic trigger resulting in **3 per second spike & slow wave**.

T/t = Valproate/ ethosuximide (in younger child)

2. Atypical absence seizures:

→ EEG ≤ 2.5 Hz spike by slow wave pattern.
→ Lapse of consciousness
→ Mental retardation
→ Lennox gestaut syndrome

3. Atonic seizures:

→ Loss of postural control for 1-2 sec
→ Loss of consciousness for 1-2 sec
→ Sudden onset of head nodding/dropping
→ **Post ictal deficit absent in-**
- Febrile seizure
- Absence seizure
- Atonic seizure

4. Myoclonic seizures:- Sudden/brief myoclonic jerky movements

Causes:-

- Neurodegenerative disorder-variant **Creutzfeldt-Jakob disease**
- Metabolic encephalopathy
- Anoxic cerebral injury - High altitude cerebral edema

5. Epileptic spasm:

→ Infant with "SALAAM SEIZURES" involving trunk muscle
→ On EEG – **Hypsarrhythmia** - grossly chaotic pattern
→ Background rhythm is suppressed (REM, NREM waves suppressed) -Decremental response

6. GTCS:

Premonitory symptoms
→ Ictal cry: Tonus ~ 10 seconds
→ Cyanosis, tongue bite +, up rolling eyes

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PrepLadder

→ Clonus: involuntary jerking

↓

Post ictal deficit, Noisy breathing due to pooling of secretions

→ Urine passed

→ Stool passed

↓

Reorientation

Vasovagal syncope	GTCS
Trigger	Present	None
Tonus & clonus	<15 seconds	30 – 60 seconds
Tongue bite	Rarely seen	±
Headache	Rarely seen	+
Urinary incontinence	+	+
Loss of consciousness	Gradual	Sudden
Recovery	Within seconds, ↑leg raise	Minutes to hours
S. prolactin	Normal	↑↑

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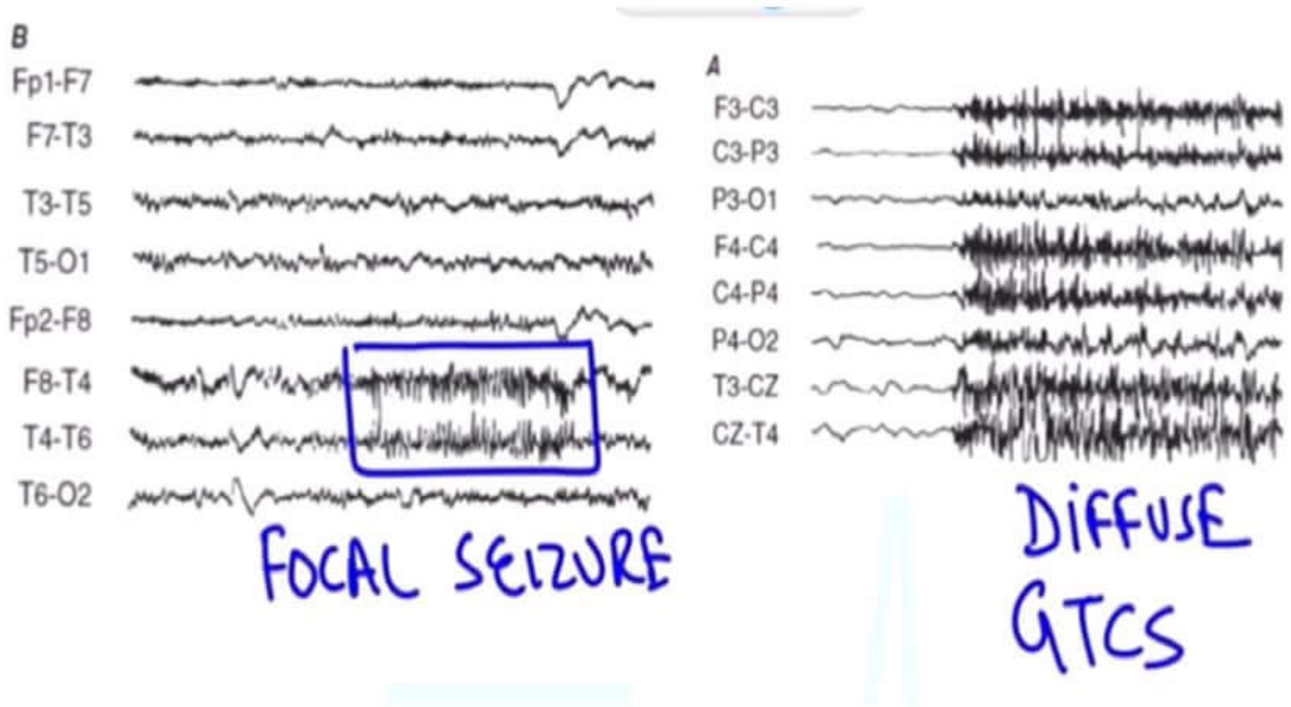


EEG of Focal seizure and Diffuse GTCS

Epilepsy syndrome

1. Lennox Gastaut Syndrome

→ GTCS

→ Atypical absence

→ Atonic seizure

Etiology = multifactorial

EEG = <2.5 Hz spike & slow wave

D.O.C =Na valproate

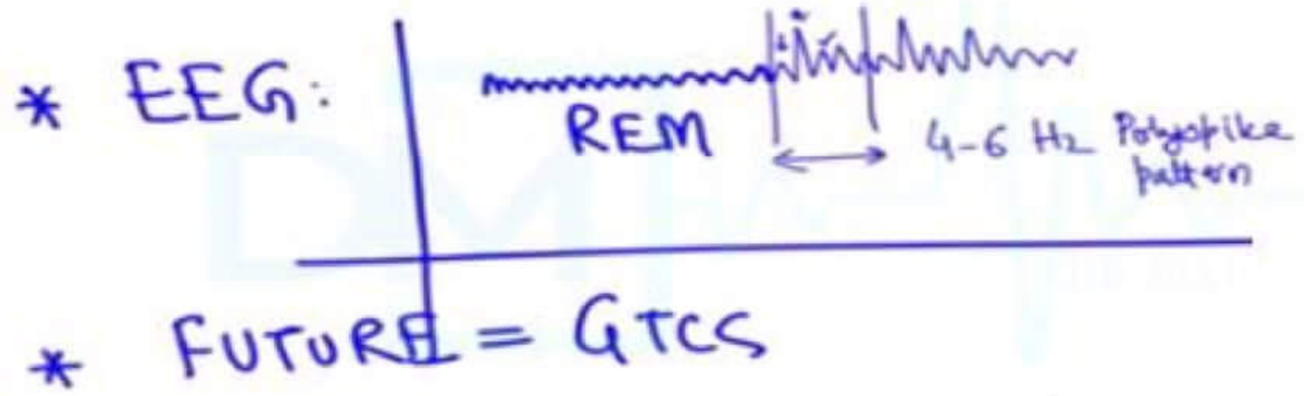
2. JANZ syndrome = Juvenile myoclonic epilepsy

PrepLadder

→ Polygenetic inheritance

→ 10 -19 yrs.

→ Myoclonic Jerk (early morning)



→ EEG: 4-6 Hz Polyspike pattern seen.

→ May develop GTCS in future and in 30% will also develop absence seizure in future

Rx – Valproate (lifelong)

Myoclonus

→ <1 yr = Infantile spasm - salaam seizure, WEST syndrome

→ 8 yr = Unvaccinated child; measles vaccine - Subacute sclerosing panencephalitis

→ 10-19 yr = Juvenile myoclonic epilepsy

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→ 30 yr = consumed Beef = myoclonic JERKS + Dementia = Variant Creutzfeldt Jakob disease

- Infantile spasm = hypsarrhythmia
- Juvenile myoclonic epilepsy = 4-6 HzPolyspike pattern

3. Mesial temporal lobe epilepsy

↓

MRI - **Hippocampal sclerosis**

- Febrile convulsion
- Focal seizures with impaired awareness

  "Automatism"
- EEG - temporal (U/L or B/L) spikes

→ D.O.C = Sodium valproate

→ T.O.C = Surgery- Surgical resection of hippocampal sclerosis lesion

Treatment: -

Focal seizure = Carbamazepine

Pneumonic -L_2COP -

- Levetiracetam → elderly pt. (less interaction with other drugs)
- Lamotrigine → Steven Johnson syndrome risk
- Carbamazepine → Risk factor- anemia, leucopenia and hepatotoxicity
- Oxcarbazepine
- Phenytoin

Generalized seizure = Sodium valproate

PrepLadder

→ Safest Antiepileptic drug in pregnancy = **Levetiracetam (Least teratogenic) > Lamotrigine**

GTCS	Focal seizure	Typical absence	Atypical absence Atonic/ myoclonic
Lamotrigine Valproate Levetiracetam	Lamotrigine Levetiracetam Carbamazepine Oxcarbazepine Phenytoin	Valproate Lamotrigine Ethosuximide	Valproate Lamotrigine Topiramate

- INFANTILE SPASM= D.O.C - **ACTH**

→ D.O.C of infantile spasm with Tuberous sclerosis (Neurocutaneous disorder) = Vigabatrin

- FEBRILE SEIZURES
  - Prophylaxis = Oral clobazam
  - T/t = intranasal midazolam

    Rectal Diazepam (conventional method)

- Most common **epilepsy** in children
  - Benign Rolandic epilepsy
  - Focal seizures
  - Peak age of onset:2-13 yr
  - Treatment = Carbamazepine

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Mc seizures in child = Febrile seizures

Mc seizures in neonate = **Subtle seizures**

↓

'Jitteriness'

↓

Causes → Hypoxic ischemic encephalopathy

→ Hypoglycemia

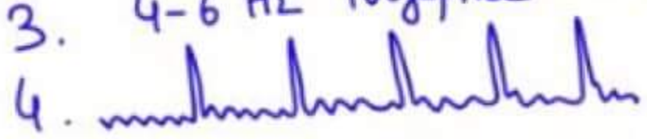
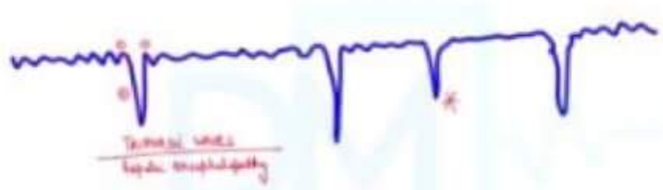
EEG

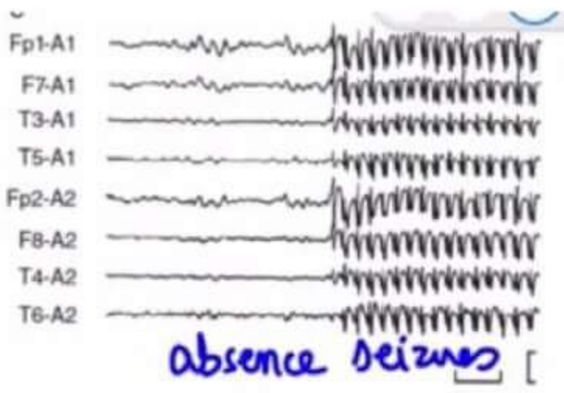
Summary Table

1. <3 Hz spike / slow → Absence
2. <2.5 Hz spike/ slow → Atypical Absence
3. 4-6 Hz**Polyspike** → Juvenile myoclonic epilepsy
4. Periodic sharp wave complexes : VCJD
5. Triphasic waves – Hepatic encephalopathy

PrepLadder

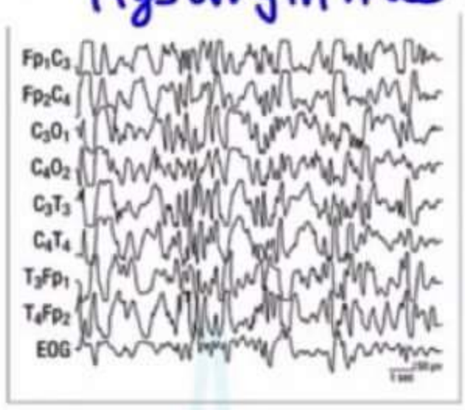
EEG

1. < 3 Hz spike/slow → absence
2. < 2.5 Hz " " → atypical absence, LGS
3. 4-6 Hz Polyspike → J.M.E/JAN2 syn
4.  Periodic sharp wave complexes ↓
5.  VCJD / PRION (BEEF) + myoclonic + dementia

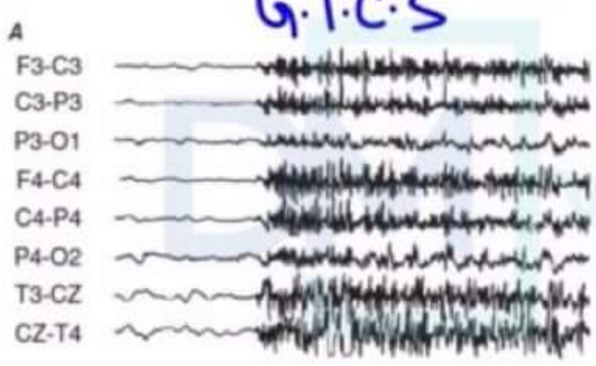


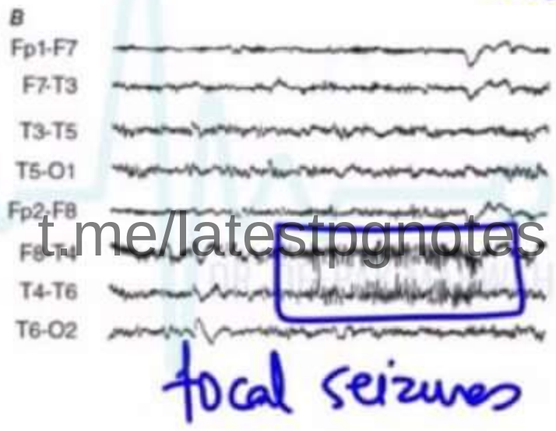
absence seizures

Hysarrythmie ⇒ Infantile Spasm / Salaam Seizures / West syn



G.T.C.S





focal seizures

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Subacute sclerosing panencephalitis – also called as Slow virus disease

→ Late complication of measles

→ On EEG – Periodic sharp wave complex

→ 2 yr = Measles ⊕

→ 8 yr = C/F are:-

- Myoclonic jerk
- Neurodegeneration features – Apathy
- Urinary incontinence
- Stool incontinence

Diagnosis –

1. Clinical		Progressive, subacute metal deterioration with typical signs like myoclonus
2. EEG		Periodic, stereotyped, high voltage discharges
3. Cerebrospinal fluid	*	Raised gammaglobulin or oligoclonal pattern
4. Measles antibodies	*	Raised titre in serum (≥ 1:256) and/or cerebrospinal fluid (≥ 1:4)
5. Brain biopsy		Suggestive of panencephalitis

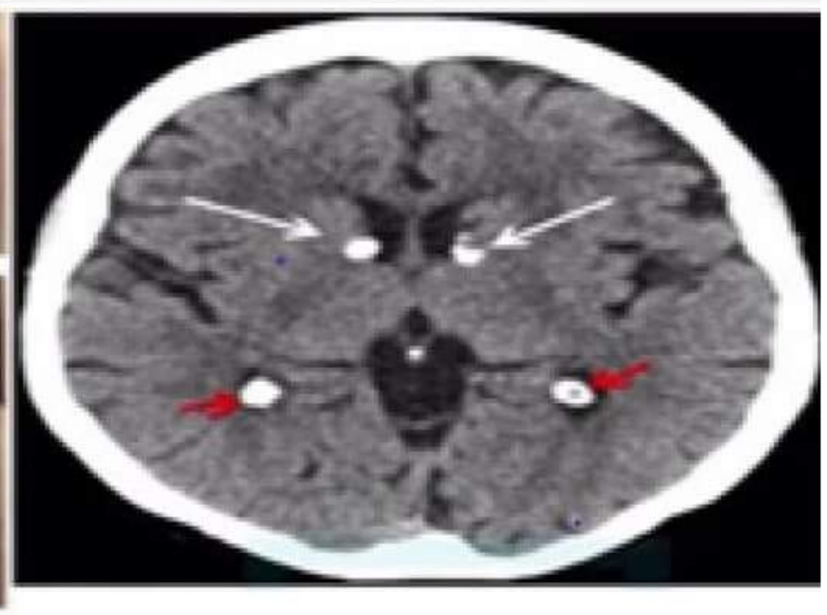
Definitive: criteria 5 with three more criteria; probable: three of the five criteria.

PrepLadder

PHAKOMATOSIS/ NEUROCUTANEOUS DISORDER

Tuberous sclerosis: AD.

→ Family history is present and **TSC1 (Chromosome 9) & TSC2 gene (Chromosome 16) involvement**



- **Adenoma sebaceum** – Acne like lesion in butterfly distribution
- **Shagreen patch** – Irregular appearance of skin
- **Subungual fibroma** – fleshy growth from below the Nail

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Earliest cutaneous manifestation

- Ash – leaf macules = Hypopigmented macules on Trunk

CNS manifestations:–

→ < 1yr: Infantile spasm = **Vigabatrin**

→ > 1 yr : Focal/ seizures = **Carbamazepine**

On CT = **Subependymal astrocytoma**

Lesion in Kidney = Angiomyolipoma (having fat, muscle and blood vessel together)

Bleeding in angiomyolipoma = **Wunderlich syndrome**

Sturge weber syndrome

→ Port wine stain

→ Cavernous angioma

→ Seizures (focal)

S – Seizure

T – Trigeminal Nerve distribution

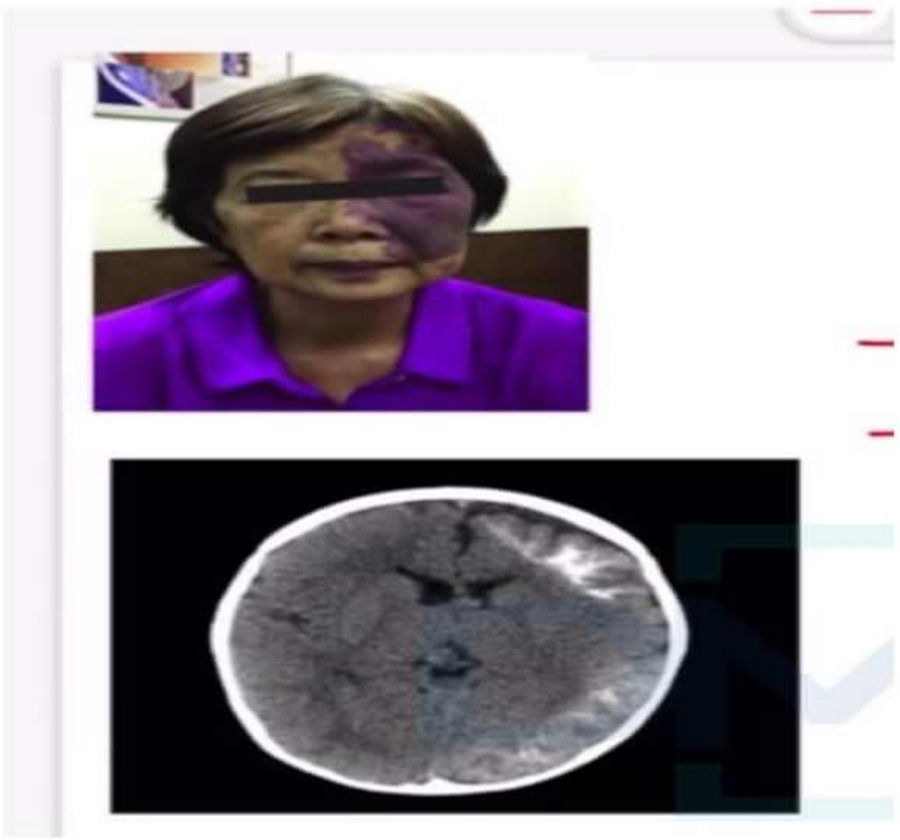
U – U/L weakness

R – Mental Retardation

G – Glaucoma

E – eye = Buphthalmos

CT scan head : TRAM TRACK APPEARANCE



RAISED ICP AND BRAIN DEATH

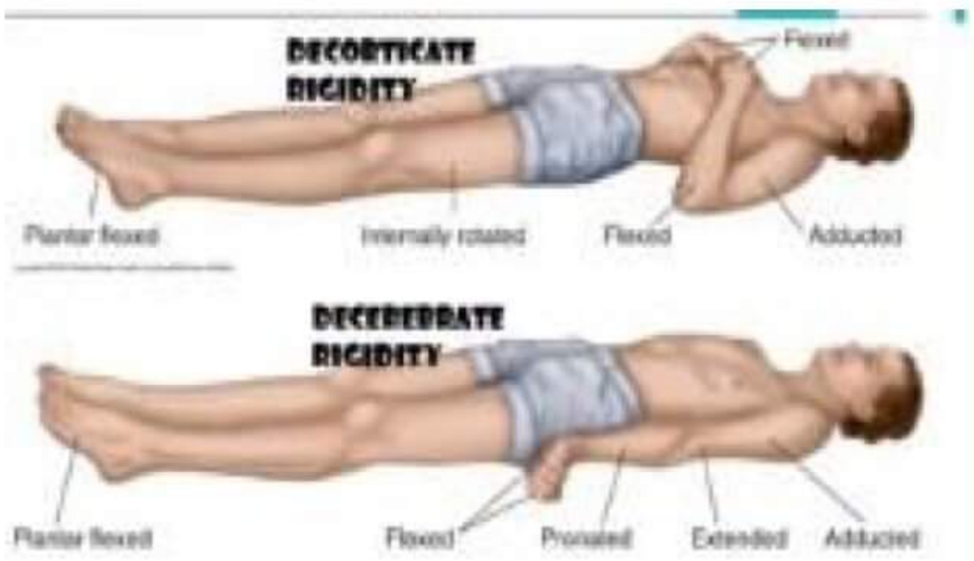
Normal Pressure in brain → 10-20 mm Hg Raised ICP = >25mm Hg for > 5 minutes → indication of osmotherapy

1. Osmotherapy :

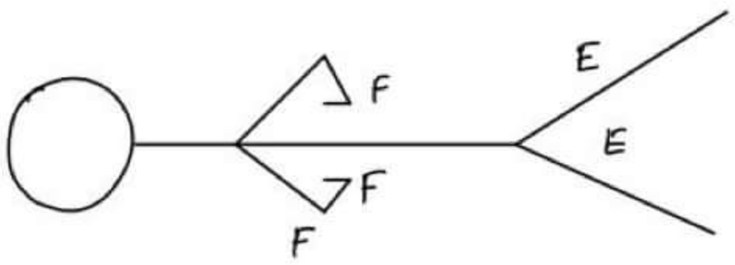
- IV Mannitol,
- IV 3% saline

Note : 5% Dextrose = hypotonic fluid → Contraindicated in stroke patient because it will worsen the neurological status.

- IV acetazolamide
- **Pediatric raised ICT** → IV frusemide
- NG tube Glycerol



CASE SCENARIO : Head injury patient presents with flexion of elbow and wrist joint, extended lower limbs



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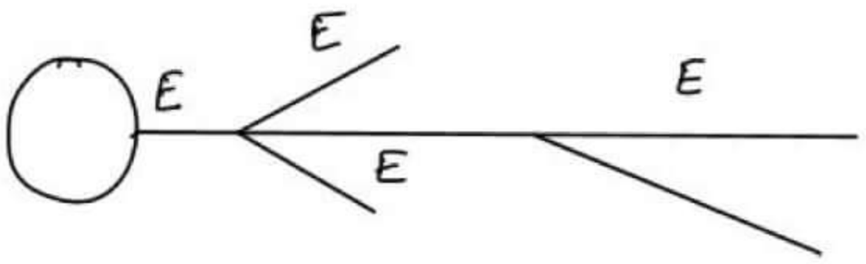
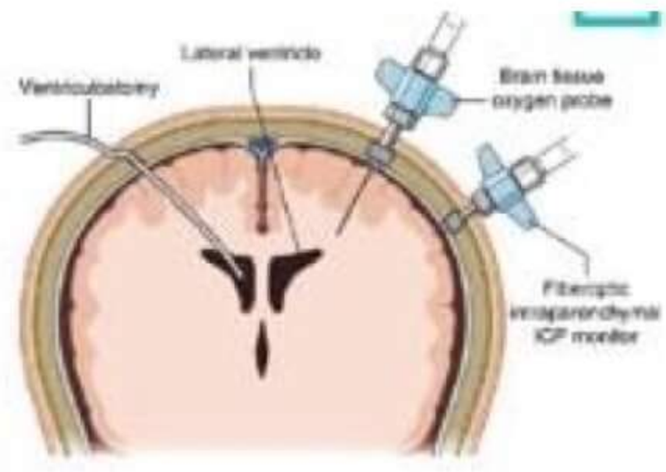
- This is called **Decorticate posturing** also referred as **Uncal herniation**
- Decorticate position later develops into decerebrate posturing and brain death



- **Decerebrate posturing – patient present with extended neck, arms, legs** – this posturing is referred as **central herniation**

2. Vertriculostomy – Most Effective

- ICP monitor catheter in to frontal horn of lateral ventricle, it will sense the pressure continuously when it arise >25mm Hg, valve will opens which is located at the tip of catheter.
- CSF : Flows out sterile container
- It is Fully Automated process.



Vertriculostomy

3. Vasopressors : NE, Dopamine → to increase Mean arterial pressure (MAP) because increasing MAP can compensate for raised ICP therefore Cerebral perfusion pressure can be maintained.

PrepLadder

- Cerebral perfusion pressure = MAP – ICP

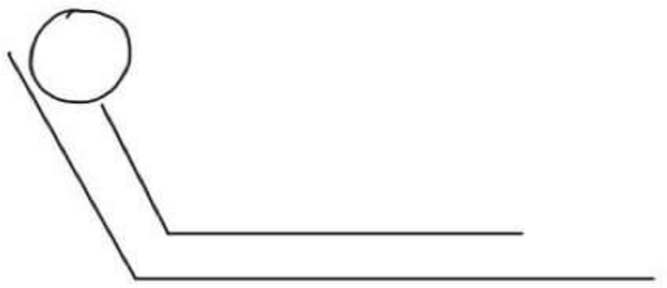
= 93mm Hg – 20mm Hg = 73mmHg (60-80 mm Hg)

4. **Vasogenic edema /Cerebral edema** in brain tumor patient → IV dexamethasone

5. **Positioning** → Reverse Trendelenburg → Head end elevation

- Perfusion of any organ depends on arterial – Venous blood flow so in Reverse Trendelenburg position Venous outflow from heart is better Therefore perfusion of brain increases

Note : Reverse Trendelenburg – also used in **Acute congestive heart failure** to reduce orthopnea.



Reverse Trendelenburg position

6. **NM Paralysis to reduce ICT** : Succinylcholine

7. **E. Tube + Respiratory Rate increase** results in CO_2 washout can exhibit vasoconstriction on Choroid Plexus Capillaries results decreased CSF production therefore it can lower the raised ICP.

- Normal CSF production → 20ml / Hr
- Total amount of CSF = 150 ml

- This method is called as Elective Hyperventilation (Least effective as it has temporary effect)

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Tier II Therapy :

8. **Pentobarbital Coma / Medically induced coma :**

Barbiturates → Decrease Neuronal metabolism can Increase longevity of cell

9. **Therapeutic hypothermia :**

- **Reduce brain temperature from 37°C to 33°C can** decrease Neuronal metabolism tends to Increase longevity of neurons.
- this is FDA approved therapy.

Brain Death

- Raised ICT subsequently develop Brain death , to identifying brain death is clinically very important for organ donation.
- Brain dead is a death of brain stem where pacemaker of respiratory centre 'pre-Botizinger complex ' located in medulla. So patient cant initiate breathing due to damage of respiratory centre which itself criteria for brain dead.

Brain stem Death
- Cortex alive
- Spinal Cord alive: DTR elicited
- Spontaneous Twitching Finger/ Toes may be seen.
- Grasp reflex present

- Brain death patient present with irreversible coma and it can demonstrated by MRI head where brain stem damage is manifested.

Note : if GCS <8 can consider coma.

PrepLadder

Before made a diagnosis of brain dead causes of reversible coma should be ruled out.

- **D.K.A →**
- **Non ketotic Hyperosmolar Coma**
- **Opium overdose → Rx : Naloxone**
- **Uremic Encephalopathy → Rx : Dialysis**

} Causes of reversible coma

Once ruled out reversible cause of coma and patient present with low blood supply to brain stem so following evaluation can be done :

Irreversible Coma :

↓
GCS<8
structural
damage
medulla/ Brainstem

1) Light reflex (route value of light reflex is 2nd and 3rd nerve)

- Pupils fixed, Non reactive to light
- This feature implies damage of Pre - Tectum of Midbrain .

2) Corneal Reflex (route value of 5th and 7th nerve): if B/L blinking is absent while touching the periphery of cornea with cotton swab indicates Pons damage.

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3) GAG Reflex (route value of 9th,10th nerve): absence of Cough indicates while stimulate the posterior pharyngeal wall indicates irreversible damage of Medulla.

4) Caloric stimulation test : cold water (30°C) irrigation cause opposite side nystagmus and warm water (44°C) irrigation on the ear canal can cause same side nystagmus in normal individual. (COWS = nystagmus) → negative caloric stimulation test indicates brain stem damage.

5) Oculocephalic Reflex / Doll's Eye Reflex :

- the eye will going to left side When turns the head to right. Same vise versa occur on when head turns to left. In brain stem damage this oculocephalic reflex is absent.

6) Disconnection of Ventilator :

- Absence of spontaneous breathing efforts after disconnection of ventilator indicates Respiratory center failure. So reconnect the ventilator in this situation.

7) EEG :

- Flat isoelectric line with Intermittent Bursts in between indicates brain death

8) MR Angiography : demonstrate Structural/ Vascular damage to Brain Stem, mostly this could be a irreversible brain damage.

PrepLadder

Organ Transplantation Team :

- To declare brain dead 2 doctors needs to certify the declaration in the gap of 12 hrs.
- Even patient is consider brain dead, their cortical function is still exist.
- If patient's family accepts can proceed for organ transplantation
- 1 Brain dead = 8 lives saved

Leading causes of organ Transplantation

- Heart → D.C.M, RCM
- Lungs → I.L.D and COPD
  - U/L lung transplantation : emphysema
  - B/L lung transplantation : Cystic fibrosis
- Kidney →Nephropathy
- Liver → Hepatitis C induced cirrhosis
- Pancreas → Type 1 DM: β cells from donor given to recipient

  ↓

  go Via portal vein

  ↓

  Liver → becomes the source of insulin production
- Small intestine → CROHN's

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University of Wisconsin Solution used to transport harvested organs. Composition is same as body fluids.

PrepLadder

INTRACRANIAL SPACE OCCUPYING LESION

Neurocysticercosis :

- seen in both Non vegetarian and vegetarian by vegetables from fecal contaminated soil which can cause neurocysticercosis.
- larval form of Tenia Solium enter into the body :

- **Cysticercosis cellulosae** → Parenchymal involvement
  - ➢ Can cause seizures in patients
- **Cysticercosis Racemose** → Ventricular system
  - ➢ Can cause hydrocephalus, raised ICT.

Note : Neurocysticercosis → one of the leading cause of intracranial calcification in india.

Vegetable grown on - Fecally contaminated soil
Eg. Cabbage / lettuce

C/F → 30 yr old male Rickshaw puller presents **multiple** focal seizures episodes and weakness of hand.
O/E →

- Higher mental function, cranial function, Deep tendon reflex all are normal
  But there was multiple lumps/ Bumps in patient Skin which caused by calcification around dead larvae.
- These lumps/ Bumps are Firm in Consistency Limited mobility
- Accidental Host is man

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PrepLadder

Work up:-

1. Lumbar puncture → CSF immunoblot for NCC antigen positive.
   Microscopic examination shows Eosinophils.

Note : CSF immunoblot is highly sensitive test than CSF ELISA so CSF immunoblot is the first test to done.

2. Imaging modality of choice => **Gadolinium enhanced MRI** demonstrating damage to BBB leading to vasogenic cerebral edema,

   Note :

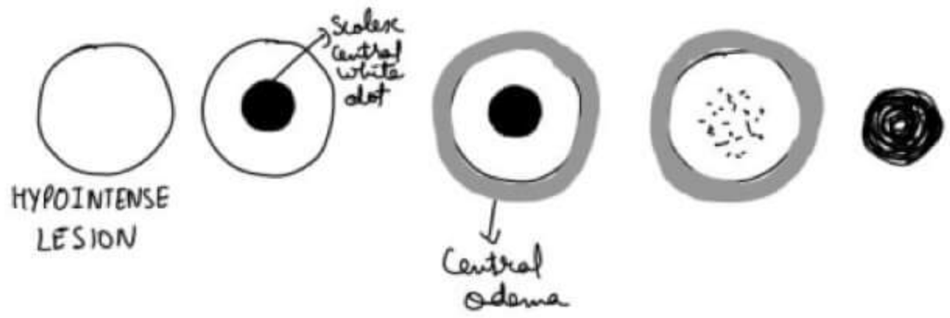
   - CT scan is best to find calcification but in NCC calcification can be seen in later stage.
   - In NCC parenchymal involvement is more common than ventricular involvement.

Hypointense Lesion Vesicular Stage multiple black spots / in some cases scolex present as central white dot on MRI

↓

Colloidal Vesicular → central white dot with cerebral edema d/t attack of immune system, it appears ring enhancing lesion on MRI

↓



Granular nodular → here larvae become disintegrated by immune system and patients presents with symptom like seizures

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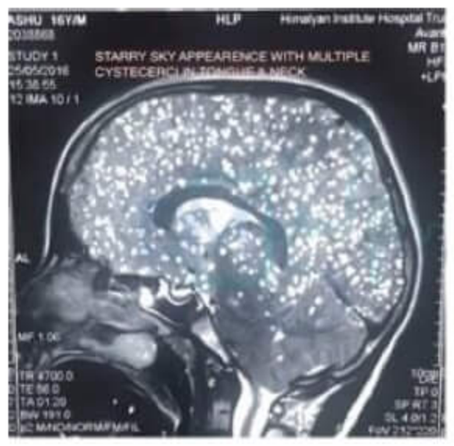
↓

Calcified Nodular stage → edema disappears only calcification presents.

Ring Enhancing Lesions → also seen in tuberculoma where it is single and large lesion

- Starry Sky Appearance on MRI

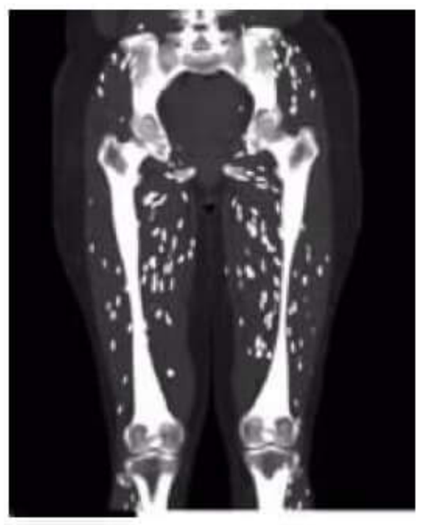


Starry Sky Appearance

3. X- Ray = B / L extremities shows Rice grain Calcification

Rx :

1. IV Dexamethasone to be start at least 48 hrs before initiate albendazole to decrease Cerebral edema and Anaphylaxis risk
2. Albendazole 400 mg BD X 8 day - Q
3. Focal seizures : Carbamazepine – preferred drug for young patient.
   Lamotrigine



Rice grain Calcification

Brain Tumor :

- Brain tumor also can cause concomitant cerebral edema and seizures
- MC Brain Tumor is metastasis, from –
  (1) Oat cell Ca lung
  (2) Ca Breast
  (3) M. Melanoma

PrepLadder

* Primary Malignant → Glioma (Subtype of astrocytoma)
* M/C Benign Tumor of adult → Meningioma

Features of Meningioma

1. Intra cranial Calcification so visible on X ray skull
2. **On CT** : Dural Tail sign
3. Develop in Patient who received CNS Radiation
4. Tumor causes Erosion of calvarium
5. Meningioma > astrocytoma (incidence wise most common is meningioma)
6. **IOC** = gadolinium enhanced MRI

Note : Clinical features of brain tumor mostly due to ↑ ICT, seizures and cerebellar lesion features in cerebellar astrocytoma.

Worst prognosis → Grade IV glioma : Glioblastoma multiforme

In Child :

- MC malignant Brain Tumor : **Cerebellar astrocytoma / Medulloblastoma**
- MC Benign Brain Tumor in children : **Craniopharyngioma**
- Craniopharyngioma presents with intracranial calcification.

Extra mile :

Intracranial calcification are seen in Neurocysticercosis, meningioma, TORCH infections/ Craniopharyngioma.

1. Suprasellar Tumor
2. Rathke Touch
3. Bitemporal hemianopia
4. (Short stature)
5. Central DI polyuria / polydipsia

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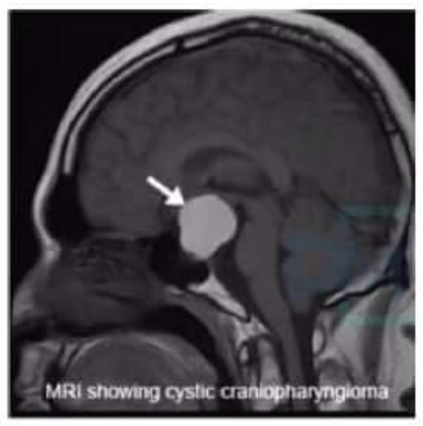
Worst prognosis

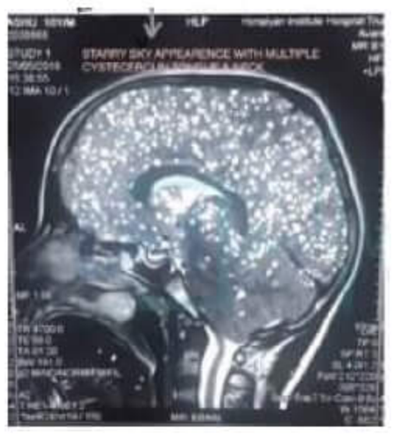
Brain Tumor with worst prognosis in children: Brian stem Glioma.

Note: Medulloblastoma has bad prognosis but not worst.

This is as it shows craniospinal Axis spread.



Craniopharyngioma



Starry sky appearance of NCC

PrepLadder

MENINGITIS PART-1

- **Neonates** - Group B streptococcus (Strep. Agalactiae)
- **India** - Klebsiella > E. Coli **(Cause)**
- **Rare organism** - Listeria Monocytogenes (Sensitive:→ Ampicillin)

Etiology:-

Children:

- Pneumococcus > H. Influenza
- Post meningitis deafness ↑ - -

Gliosis along course of VIII nerve

Adult : Pneumococcus > N. Meningitidis (Sporadic meningitis)
(Epidemics of Meningitis)
Hostel/ Urban Slum

→ N. Meningitidis (Droplets)

- Meningitis
- Sepsis
  - DIC
  - ↓
  - **Adrenal Hemorrhage**

(Addisonian Crisis also called Water house freid schen syndrome)

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- Routine Surgical Mask does not protect doctor/ Health care worker from occupational exposure.
- Person to Person transmission is best managed with use of **N – 99/95 mask**

* Chemoprophylaxis is best way to protect

* Drugs
  - CEFTRIAXONE → Most effective drug in N. Meningitidis (I.M) = health care worker
  - CIPROFLOXACIN → Given in family contact)
  - CEFTRIAXONE → In pregnancy

Viral Meningitis :

Cause - Enterovirus

Viral Encephalitis

- INDIA
  - Japanese B
- GLOBAL
  - (Herpes simplex I)
  - Associated with Temporal lobe
  - Amnesia: Sequalae

- **Lumbar Puncture** : Bloody CSF → SAH
  - → Traumatic LP
  - → HSV 1 Encephalitis

PrepLadder

- **IOC** - PCR HSV 1 on CSF Sample

Rx → Empirical acyclovir.

- EEG: Periodic Lateralized Epileptic form discharge (PLED)

[- Periodic Sharp waves complexes: EEG Variant Creutzfeldt Jacob disease]

Fungal Meningitis :

- Caused by: Cryptococcus neoformans
- Portal of entry → Lungs

Rx → Amphotericin - B. IV

Clinical Features of meningitis

1. Fever, headache, nuchal rigidity (Triad)
2. ↓ consciousness, Nausea, Vomiting, photophobia
3. ↑ ICP : Papilledema, dilated poorly reacting pupil sixth nerve palsy, Decorticate posturing
4. Petechiae (N. Meningitidis)

↓

Headache, Fever + Nuchal rigidity

↓ Check for

Altered Mental Status?

Yes

1. ADEM
2. Meningoencephalitis
3. Encephalopathy
4. MASS lesion

↓

- If such, then

↓

Obtain blood culture, start empirical antibiotics

↓

Imaging

↓

Lumbar Puncture - CSF

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No

1. Meningitis

↓

- Papilledema

(Focal neurological deficit)

- CMI ↓
- Head trauma
- Cancer
- Sinusitis

↓

If answered to anyone is YES

↓

Obtain blood culture

↓

Imaging

↓

Lumbar Puncture

It indicates Bacterial

CSF: ↑ Opening pressure
Pressure: > 180 mm H_2O
↑ PMN ++ > 1000 cells/cu mm

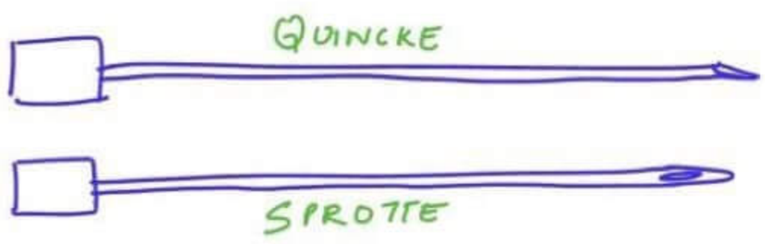
PrepLadder

MENINGITIS PART-2

Work up of patients of meningitis

1. Blood culture
2. Imaging - NCCT head
3. Lumbar puncture - Position : Lateral decubitus

Site - L_3 - L_4



Contraindication of LP:

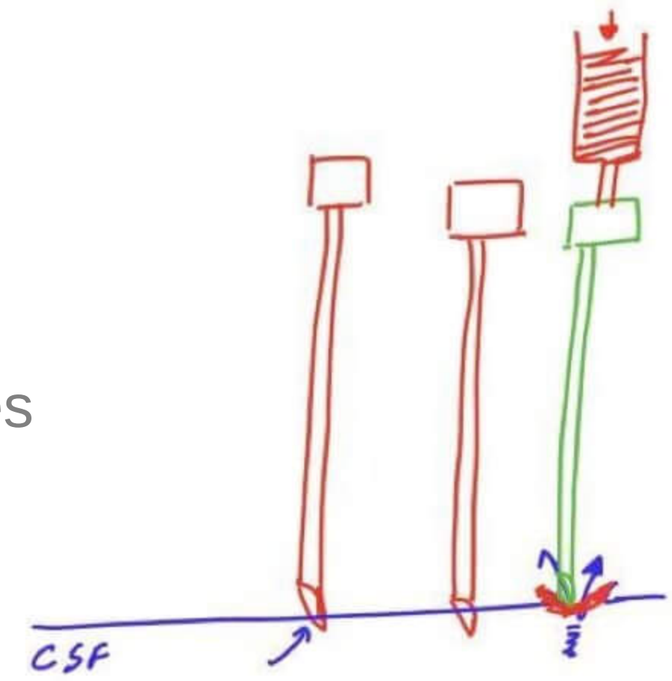
1. Raised ICP (Risk of Transtentorial herniation)
2. Bleeding diathesis
3. Local site infection
4. Kyphoscoliosis
5. Polio

layers pierced during Lumbar Puncture:-

1. Skin SC → Bevel up, Cephalad progression Aim for umbilicus
2. Supra spinous ligament
3. Intra spinous ligament
4. Ligamentum flavum
5. Dura mater

↓

CSF



Max CSF removal → 20 ml (1 sitting)

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If lumbar puncture needle goes deep inside

↓

Eversion of edges of dura

↓

Continuous leakage of CSF

↓

Post lumbar puncture headache

(Rx bed rest

↓

Immobilization

- Headache on straining

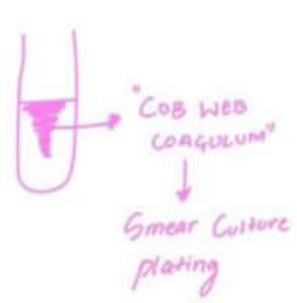
DOC = **IV Caffeine Codeine**

↓

- Low volume blood patch → seal the tear in dura

(10 – 20 ml blood)

PrepLadder

Opening pressure →		Cells	Sugar	Protein	Gross
Normal	50-180 cm	0-4 lympho -cytes cu mm	2/3 blood sugar	15-45 mg%	Clear
Acute Bacterial Meningitis	↑	> 1000 PMN (cu mm)	↓ hypogly - corachia	↑	Turbid
Tubercular Meningitis	↑	> 100 lymphocytes	↓	↑↑ 	Straw
Sub arachnoid Hemorrhage - After 24 hr	↑	RBC ++ Bilirubin +	Normal	Normal	Bloody Xantha chromic
Viral Meningitis	↑	> 50-500 cells	Normal	↑	Clear
Guillain-Barre Syndrome	Normal	lymphocytes Normal	Normal	↑	Normal

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GBS: Autoimmune albumin O - cytological dissociation

Tubercular meningitis

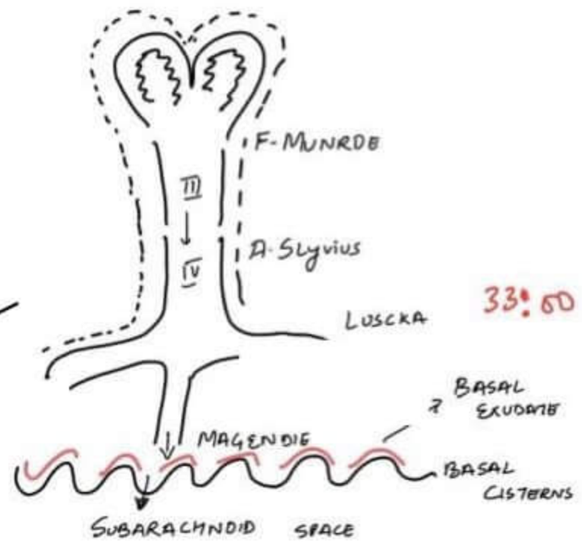
H/O few weeks → Irritable, drowsy, fever
Altered Sensorium, seizures +
Focal deficit +
Nuchal rigidity

↓

TB endarteritis

→ BCG Scar - Absent, PEM grade IV

→ Rich focus



(Hydrocephalus, Crack pot sign, **Macewan sign**, sutural diastasis, Sup. veins scalp visible)

IOC TBM = PCR CSF

PrepLadder

Rx TBM = Anti TT + steroid (6 weeks)

Steroids → ↓ Cerebral edema

↑ Penetration of ATT drugs into CSF

Rx - Acute bacterial Meningitis

Empirical A/b started < 60 min

(Children > 3 months, adults < 55 yrs)

Dexamethasone - Third gen / Fourth gen cephalosporin + Vancomycin

↓	↓
Ceftriaxone	Cefepime
± Acyclovir	± Doxycycline (Tick Season)

Listeria → Ampicillin

Pseudomonas → Cefepime / Meropenem

Encephalitis → Hallucinations, agitation, Personality change Psychotic state

Focal Findings: Aphasias, Apraxia

Nuchal Rigidity: Absent

TBM = ATT + Steroids

ABM / TBM → SIADH: 2/3 rd (Calculated maintenance fluids 4-2-1)

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PrepLadder

CNS INFECTIONS IN AIDS + PATIENTS

Organism Cryptococcal to Neoformans

Portal of entry Via lungs

CD4 < 100 cells / HL

Case→ S. Elisa HIV ⊕ Truck driver presents with
Headache, photophobia X2 day,
feverish O/E→ Nuchal Rigidity

Work – Up

1. β1, 3 glucan Test → P. Jiroveci
   (Invasive fungal infection) → C. Neoformans
   → X Mucormycosis

2 L.P: CSF biochemistry: Lymphocyte count = 20 cells/ cu.mm
Sugar = n Protein = ↑

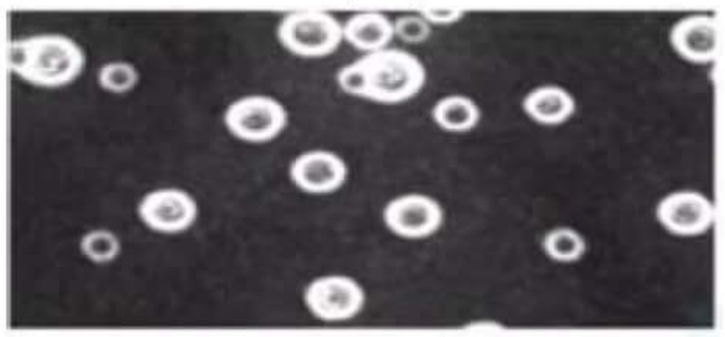
M/e: India ink: Negative stain, Highlights capsule

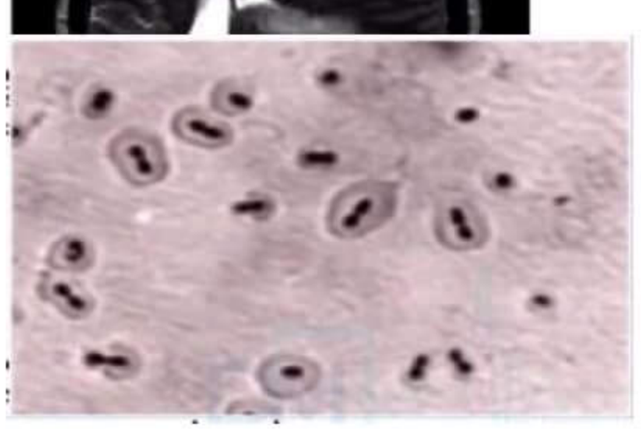
Capsule: Gomori – Methamine stain
Mucicarmine stain

IOC: CSF ELISA for Cryptococcal antigen

3 NCCT Head: Soap bubble → "Soap bubble appearance'
Appearance → X-Ray radius = Osteoclastoma

India ink preparation





Treatment

Liposomal Amphotericin B + 5 – flucytosine

- Pneumococcus can be stained by India ink. It will appear as capsulated diplococci. DOC will change to ceftriaxone and should be started empirically with 60 minutes of probable diagnosis. Even if Person has taken Antibiotics before, Later agglutination can be used for diagnosis.
- MC because Seizures in AIDS HIV associated encephalopathy MC ICSOL, leading to seizures in AIDS = Cerbral Toxoplasmosis

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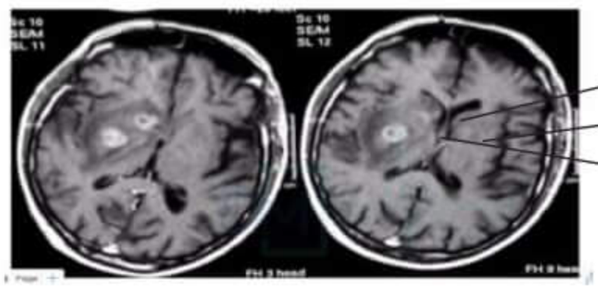
Treatment

Sulfadiazine + Pyrimethamine

Progressive multifocal leukoencephalopathy

Etiology: JC Virus

Settings: Natalizumab, AIDS



Notice the lesions of Cerebral toxoplasmosis localised to Basal ganglia.

Extra Mile

AIDS + Lesions in CNS

1. HIV associated dementia = Subcortical dementia
2. HIV associated encephalopathy = Seizures
3. Meningitis = Cryptococcus Neoformans
4. ICSOL : Seizures : Cerebral toxoplasmosis
5. Primary CNS lymphoma Stereotactic Biopsy

PrepLadder

PARKINSONISM AND PARKINSON'S DISEASE

* Dopamine decrease
* Substantia Nigra is the area involved
* **Lewy bodies**

↑

α -Synuclein protein

Differential Diagnosis: -

Aleihiemer → Ach decrease

Nucleus of Meynert basalis

is the area involved.

Hirona bodies

↑

Tau protein

Causes

1. Parkinson disease :-

* Age related degeneration of basal ganglia
* Chromosome 1 defect # PARK gene, PARKIN gene is ascribed to chromosome 6.

2° parkinsonism

2. Drug induced: Anti psychotics

Dopamine ↓ :Mechanism of action

Ach ↑

Rx: → **Benzhexol**

Trihexyphenidyl

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3. Hyperparathyroidism: Increase PTH: Increase Calcium in basal ganglia.
4. Hypoparathyroidism: Decrease PTH: Increase Po4

Calcium x PO4 > 55 leads to calcium deposition.

5. CO poisoning:

Use of Gas geysers: Small apartment

Carboxy Hb increases ,oxy- Hb ↓ (Basal ganglia malfunction)

Symptoms

A. Headache

B. Bradykinesia

C. Agitated behavior

Rx:- Hyperbaric O_2 therapy

6. Manganese toxicity

Atypical parkinsonism

7. Huntington chorea

Chromosome 4#, AD, Anticipation (↑ Severity of disease with successive generations)

Huntington gene: **Trinucleotide** deposition in neuronal metabolism **repeats** Of CAG segments

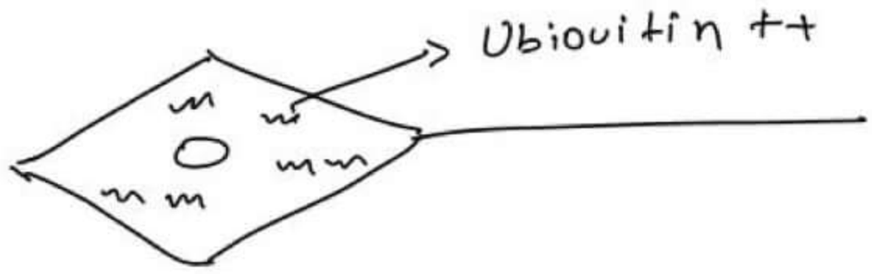
CAG > 40 repeats: Leads to formation of Huntington protein

PrepLadder

Histopathological hallmark of HD is presence of intraneuronal inclusion bodies whose prominent feature is presence of ubiquitin.

Ab (n) protein: (+) neuronal firing

Neuronal death: leads to Dementia



Clinical Features:-

*Develops in 40-50 years age

1. Chorea: Caudate nucleus damage
   Semi purposive fast involuntary movement: Distal
   Athetosis: Globus pallidus # causes slow writhing movements:
   Distal
2. Short term memory loss leading to hampering of daily activities.
   Long term memory loss
   Later stage dementia
3. Bradykinesia (Slowness in doing activities)
4. Cog wheel rigidity: Upper limb
   Lead pipe rigidity: Lower limb

Investigation :- MRI Head : Box car ventricle

Rx:- IN HD: dopamine (Excess)
So Levodopa is contra indicated
Dopamine depleter = Tetrabenazine is DOC of HD.

8. Progressive supranuclear gaze palsy:-

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Damage to superior colliculus = vertical gaze affected

60 year old male : Recurrent falls
: Recurrent spilling of food on clothes
: Rigidity :cog wheel
: Bradykinesia

Work up
1. Electrooculography: - Square wave jerks
2. MRI Head: - Humming bird appearance

Rx: - Poor response to levodopa

9. Multiple System atrophy (Shy dragger Syndrome)

60 year: Bradykinesia, Rigidity
+ Autonomic insufficiency features
*
* Postural Hypotension (Recurrent falls)
* Constipation/ Diarrhea
+ Cerebellar Features : Gait Ataxia
* Intentional tremors

MRI Head : Hot cross bun sign
Rx- : Poor response to Levodopa

PrepLadder

HD	Caudate damage	Box Car Ventricle
PSP	Sup. Colliculus damage	Humming bird appearance
MSA	Brain Stem damage	Hot cross Bun

Square root wave sign: Echo

1. RCM(Restrictive cardiomyopathy)
2. C. P(Constrictive pericarditis)

Square wave Jerks: EOG

Progressive Supranuclear gaze Palsy

Typical Parkinsonism

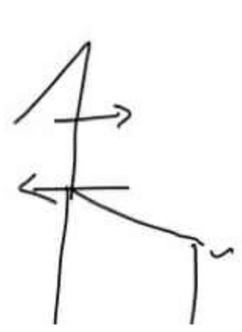
Non- motor Symptoms : Anosmia, Constipation

Motor Symptoms:

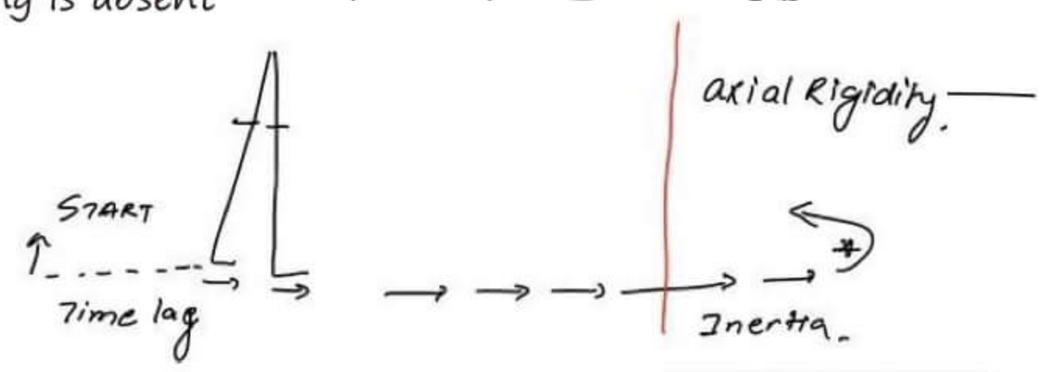
1. Resting tremors:
   4-6 Hz, Asymmetrical, Pill rolling tremor (Disappear on sleep)
2. Bradykinesia : may progress to Akinesia (Akinetic mutism)
3. Rigidity — Cog wheel- Upper limb; Lead pipe- Lower limb

* Out of 3 if 2 symptoms are present diagnosis will be Parkinson disease/ Typical Parkinsonism.

4. Response to levodopa
   Good → In Typical
   Poor → In Atypical
5. Festinating Gait
   * Short shuffling steps
   * Stooped posture
   * Automatic Arm swing is absent

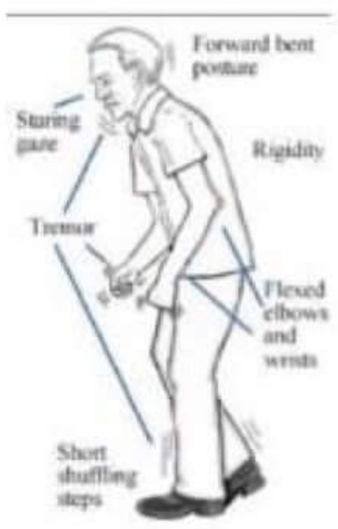


6. Important words to remember
   - Hesitancy
   - Postural instability
   - Freezing
7. On & off Phenomenon



8. **Blink rate ↓ : Exposure keratitis**
9. Myerson sign: Glabellar tap absent.
10. Mask like facies
11. Depression ± : Pseudodementia ±
12. Bradyphrenia, hypomimia(slow/inaudible tone of voice)

* No investigation of choice, it's a clinical diagnosis



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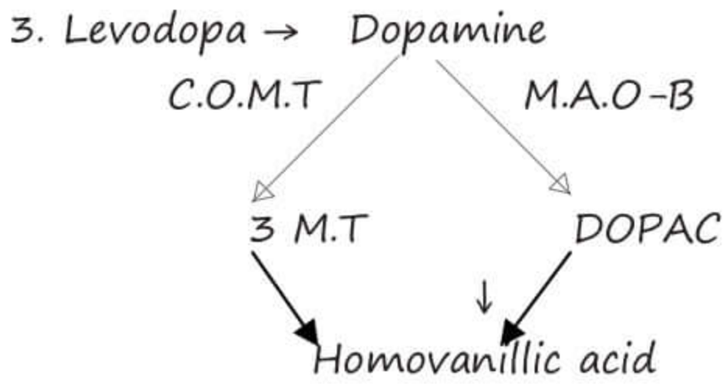
Rx: -

1. Rasagiline : **Neuroprotective drugs**
2. Pramipexole / Ropinirole: D_2 receptor agonists : Transdermal Patch. Rotigotine is a long acting form of dopamine agonist.
3. Levodopa + carbidopa (Peripheral decarboxylase Θ)

PrepLadder



C.O.M.T (Catechol – O – Methyl transferase) :

M.A.O –B (Monoamine oxidase – B)

C.O.M.T inhibitor = Entacapone,

Tolcapone -(Hepatotoxic: Status withdrawn)

5. Other Miscellaneous drugs -Endogenous dopamine releasers

Bromocriptine(causes Raynaud's phenomenon)

Selegeline

Amantadine is used for → Influenza A

6.→ 90 years age, resistant to all above drugs :

Deep Brain Stimulation

Electrode: Subthalamic Nucleus

Impulse generator, Battery: are deployed in Neck

Patients is awake during surgery

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PrepLadder

MYASTHENIA GRAVIS

- Type II Hypersensitivity reaction > Type V Hypersensitivity Reaction.

- Receptor of Acetyl choline are affected. It is a post junctional defect.
- Ach have 5 subunits .
- Alpha subunit activation will lead to sodium influx , subsequently leading to depolarization , thus muscle will contract.

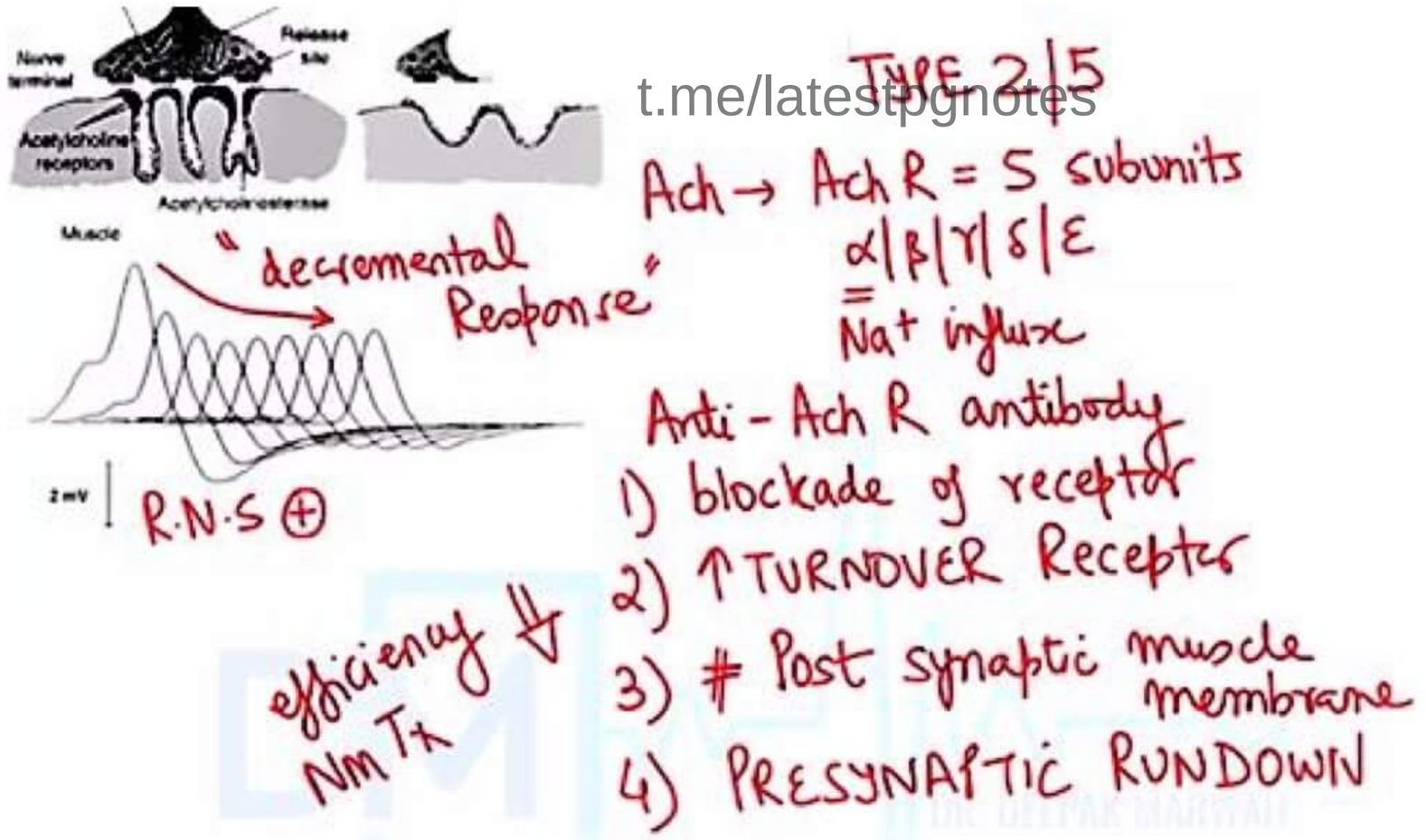
Presence of Anti Acetylcholine Receptor Antibody

1. Blockade of Receptor (mainly effect alpha subunit)
2. Increase turnover of receptor (time for which Ach activate the receptor will substantially reduced)
3. Post synaptic muscle membrane damage
4. Presynaptic rundown

Above four reasons cause decrease in efficiency of neuromuscular transmission

↓

decremental response



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Etiology: -

1. Thymus abnormality 75%
   a. Thymic Hyperplasia -65%
   b. Thymoma -10%
   - Myoid cells in thymus
   - Myoid cell contains alloantigen. It has chemical structure resemblance to Ach receptor
   - Antibody Ig4 T cell dependent

Names of anti Ach receptor antibody-

1. Anti A-ch Receptor Antibody (85%)
2. Anti-MUSK Antibody (Muscle Specific Kinase Antibody) (10%)

PrepLadder

3. Anti LRP-4 (Low density lipoprotein related protein 4)
4. Anti-Netrin – 1 receptor
5. Anti CASPR – 2
6. Anti-striated muscle Antibody against TITIN

Prevalence

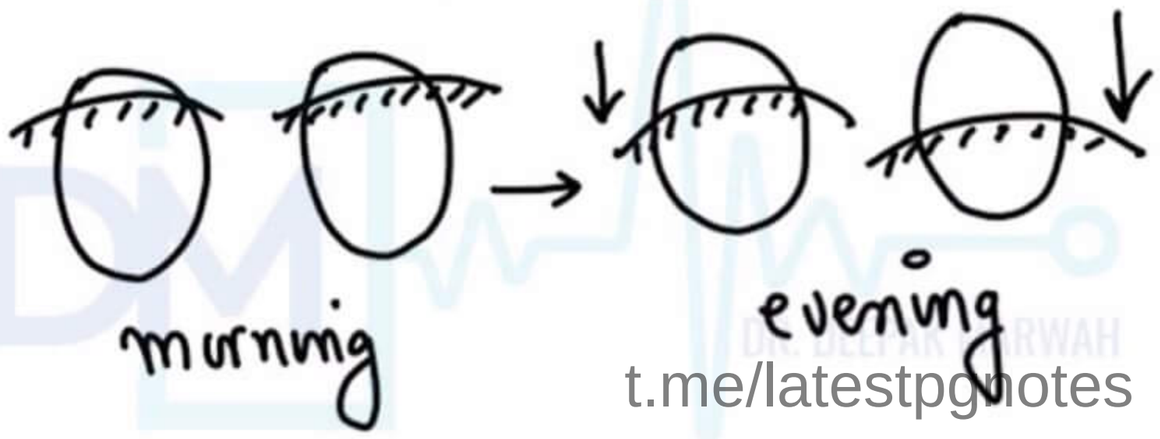
- 200: 100,000

♀ : ♂

- Exacerbation (waxing waning course)

C/F:

1. **Ptosis:** Asymmetrical ptosis
   Weakness
   Easy Fatiguability
   (Evening> morning) – "Diurnal Variation" of symptoms.



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2. **Diplopia**
   Ask patient for Upward gaze > 30 seconds → Ptosis and Diplopia

If only extra ocular mus cles involve for 3 years

↓

Ocular myasthenia gravis

3. Snarling facies – When asked to smile
4. Chewing muscle weakness
5. Nasal Twang. to voice – weakness of soft palate

PrepLadder

6. Nasal Regurgitation of food
7. Aspiration risk is high
8. Dysphagia - Oropharyngeal Dysphagia
9. Dysarthria – muscles of vocal cords affected
10. **Deep tendon reflexes are preserved**
11. Sensory function normal
12. Proximal Muscle weakness

Work up: -

1. Anti Ach Receptor blocking Antibody = 85% +ve

Limitation:-

a. –ve antibody report doesn't rule out the disease
b. Doesn't correlate with severity of disease

2. Anti-MUSK Antibody
3. Anti LRP 4 Antibody
4. Single fiber electromyography (SFEMG)=Jitter and blocking - **Confirmatory test**
5. Repetitive nerve stimulation test.

↓

Decremental Response

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6. Tensilon test, Or Anticholinesterase test

Sustained upward gaze leads to Ptosis

↓

IV line 10 mg edrophonium

Onset 30 sec

Duration: 5 min

- Edrophonium inhibits dehydration of Ach

↓

Ptosis become lesser than absent after 5 min it again reappear

During test Pt. may develop cholinergic crisis during the test – SLUDGE symptoms.

↓

- ↑Secretions = Hyper salivation
  - Hyper Lacrimation
  - Frequent Urination
    - Diarrhea

For treatment of cholinergic crisis – Atropine given

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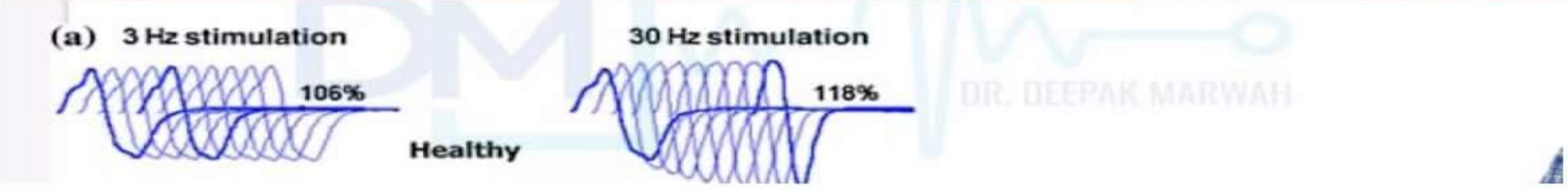
7. **Ice Pack Test**



Sustained Upward gaze

↓

Ptosis

↓

Ice Bag Application (3 – 5 min)

↓

Ptosis is substantially reduced

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↓ Activation of A-Ch esterase (sensitive to temperature) at NMJ

↓ Turnover of receptor

8. **CT/MRI HEAD:**

   - For Ocular Myasthenia gravis

9. **CT chest**

   - Thymoma / Thymic Hyperplasia

10. **Hashimoto/Graves / SLE / RA**

    TSH , ANA, RA Factor

11. **Pulmonary function test – to plan thymectomy and to evaluate lung function**

12. HbA1c and Tuberculin skin Test (Rule out Diabetes mellitus, Tuberculosis, as steroids may be started in ocular M. Gravis.

Management:

1. Pyridostigmine – **DOC**

   Onset – 15 min

   Total – 4 hr

PrepLadder

- If Anti-Musk Antibody +nt then they have poor response may lead to worsening of symptom.

T.O.C – Thymectomy

Resection of Thymoma

Decrease in Requirement of immunosuppression

Ocular Myasthenia gravis (Thymectomy not recommended)

↓

Pyridostigmine (first line drug)

↓

If Poor Response

↓

Start Steroids +++ / azathioprine

Generalized myasthenia gravis

↓

Pyridostigmine

↓

Substantially good response

If Forced vital capacity good

↓

Thymectomy done

↓

Post-op Steroid dose + (minimal)

Myasthenia Crisis (Trigger = Infection or Pregnancy)

↓

Plasmapheresis

Or

IV immunoglobulin

1st line in Myasthenia Crisis = Elective intubation + Assisted controlled Mechanical Ventilation

Neonatal Transient Myasthenia Gravis

Acquired from Mother to child.

IgG = Transplacental Spread

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Neonate = Difficulty in establishing respiration
Difficulty in breast feeding
Neostigmine (DOC) drops 4 hourly X 1 month

Self-limiting as antibody formed are destroyed by immune system of child.

LAMBERT EATON SYNDROME

♂ with - Small cell cancer Lung produce the Ab that acts against Ca^{+} channels on presynaptic membrane

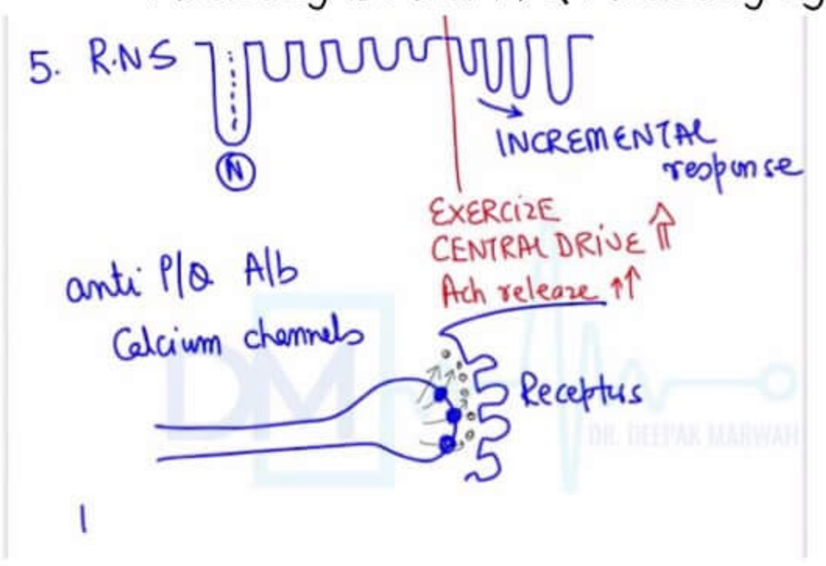
Presynaptic disease → ACh ↓↓ release

- Antibody formed act on pre-junctional site – that decrease the release of Ach.

C/F: -

1. Proximal Muscle weakness
2. Ptosis / diplopia
3. **DTR ↓↓**
4. **Autonomic features**
   - Dry Mouth
   - Impotence
5. Repetitive nerve Stimulation – to differentiate with Myasthenia gravis
   After RNS- ask patient to exercise which lead to increase Ach release at NMJ- leading to substantial increase of amplitude – **Incremental response.**

Antibody is Anti P/Q Antibody against Voltage sensitive Ca^{++} channels



T/t = D.O.C = 3,4 Diamino Pyridine (k+ channel blocker)

NEURAESTHENIA: -

- Myasthenic fatigue
- No organic Basis

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Botulism:

Home delivery- Honey given to baby by grandmother

↓

Given to newborn ♂

↓

Spores of botulinum grows in gut and produce toxin

Leading to paralysis (descending)

- Pre-Junctional ↓↓ Ach release

C/F-

1. Bulbar palsy
2. Diaphragmatic Palsy

T/t – Antitoxin

Myasthenia Gravis	LEMS
→ Thymus Abnormality	→ Small cell lung carcinoma
→Ach Release normal but Receptor defective	→ Ach release decreases but receptor normal
→ Anti ACH R Antibody anti musk Antibody	→ Anti P/Q antibody against calcium channel
→ ♀ Ptosis, Diplopia chewing muscle weakness	
→ DTR Normal	→ DTR decreases
→ Decremental response	→ Incremental response
→ D.O.C Pyridostigmine/ steroids	→ D.O.C - 3,4 diamino pyridine - Pyridostigmine can also be used

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GUILLIAN BARRE SYNDROME

- Type IV hypersensitivity reaction

- H / O – Acute dysentery (Campylobacter jejuni)

  - Fever + Blood, mucus in stool

R_x:- Quinolones

- Recovery

- Antibodies against C.jejuni cross react with myelin component of spinal cord Segmental demyelination – P. Nerves and spinal cord

- 2 week Later

1 Flaccid paraplegia (Tone decreased)

2 Truncal paralysis

3 Quadriplegia

4 Respiratory Muscle paralysis (MC)

Death – Respiratory Acidosis – CO_2 increased

- Type II R. failure

5. Neck floppiness

6. Facial diplegia (LMN Lesion#) ⟶ also in 1. Sarcoidosis

MC-CN- in GBS – 7th (N) palsy 2. Melkerson Rosenthal syndrome

7. Sensory # - PARASTHESIAS 3. Myaesthenia Gravis

4. Lyme disease

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GBS

- Paralysis starts from legs

↓

Trunk

↓

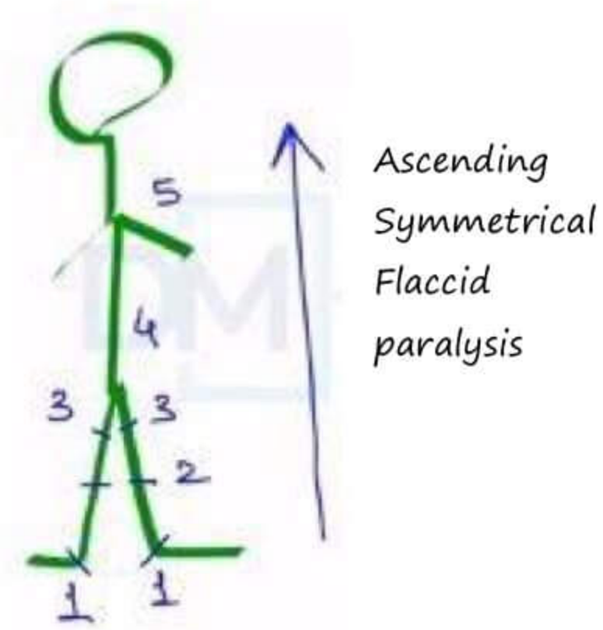
Arms

↓

Neck

↓

Face



Ascending Symmetrical Flaccid paralysis

GBS – Ascending paralysis

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- Symmetrical, flaccid paralysis

Earliest Manifestation - Distal areflexia

8. Autonomic – T_1-T_4 # - cardiac accelerator

fibres # HR ↓, BP ↓

Neurogenic shock

9. Bladder / Bowel – Spared

GBS Subtypes

· Acute Motor axonal neuropathy – AMAN

· Acute-Motor- Sensory axonal neuropathy – AMSAN

· Acute inflammatory demyelinating polyneuropathy : AIDP → MC

· Miller fisher Syndrome ..... : MFS → Rare

↓

CN palsy – 3rd (N) palsy

O –

Ophthalmoplegia

A – Areflexia

A – Ataxia – Sensory

Work up

1 L.P – CSF opening pressure – (n)

Cells – (n)

Sugar – (n)

Color

– (n)

Protein

– ↑

- **Albumino – cytological dissociation**

- Also Seen in Froin Syndrome

Spinal Cord block: -

Tumor

- TB

2 Nerve conduction velocity - F – Reflex

- Latency period↑

3. **MRI spine** – Demyelination

4. **Antibody of G.B.S :** anti GM1 A/b

Antibody of M.F.S : anti GQ1A/b

Rx- I.V Immunoglobulin's – DOC

Plasmapheresis – Efficacy of IV Ig & plasmapheresis is equal.

Transverse Myelitis

H/O URTI / AGE – Recovery from Symptoms

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Extra Mile

Brighton Criteria of GBS diagnosis
1. Bilateral Flaccid limb weakness 2. Decreased / Absent Tendon Reflexes 3. Monophasic illness with interval between onset and nadir of weakness between 12 hrs – 28 days 4. Electrophysiological findings consistent with GBS 5. Albuminocytological dissociation

Ab: Inflammation of spinal cord C/F develops after 2 weeks

1 Flaccid paraplegia

2 Truncal paraplegia

3 Quadriplegia

4 Diaphragm paralysis

5 Sensory : - Sensory level

- Radicular pain / Lancinating pain

6 Autonomic # - T_1-T_4 #

HR ↓ BP ↓

7 Bladder / Bowel involvement

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50 ml urine in Bladder – pt aware – S_2 / S_3 / S_4 – Sensory

150 ml urine in Bladder – urge to urinate – S_2 / 3 / 4 – Motor

- Flaccid Bladder – No urge

↓

Overflow incontinence (Post voidal Residual urine)

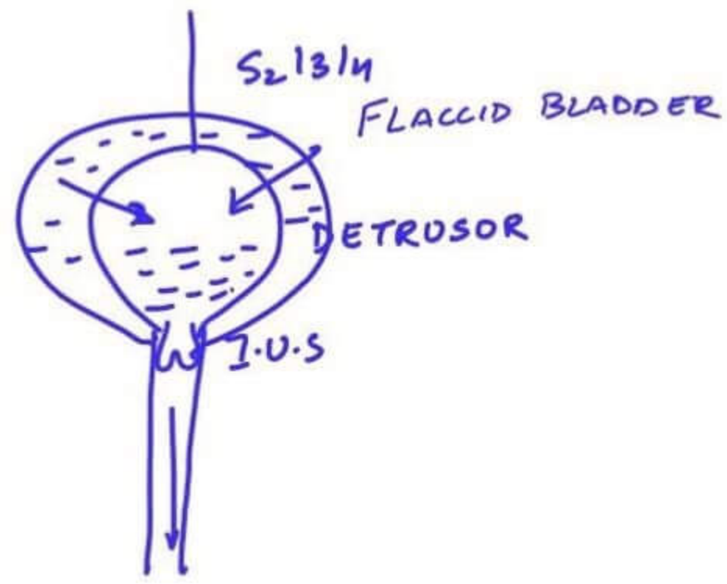
Stroke Pt – Spastic Bladder

↓

Urge

Incontinence **IOC** – MRI spine

(Inflammation) **DOC** - Methyl Prednisolone



Flaccid paraplegia / quadriplegia > 9 weeks

Chronic inflammatory demyelinating Poly neuropathy

R_x – Steroids

Steroids recommended for

1 Ocular Myasthenia Gravis

2 CIDP (Chronic inflammatory Demyelinating

PrepLadder

Polyneuropathy)

3. Transverse myelitis

4. Multiple Sclerosis – Sudden onset blindness

IV Ig recommended for

1. Kawasaki disease
2. Acute ITP
3. Myasthenic Crisis
4. GBS

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ALZHEIMER DISEASE

→ Characterized by Ach deficiency

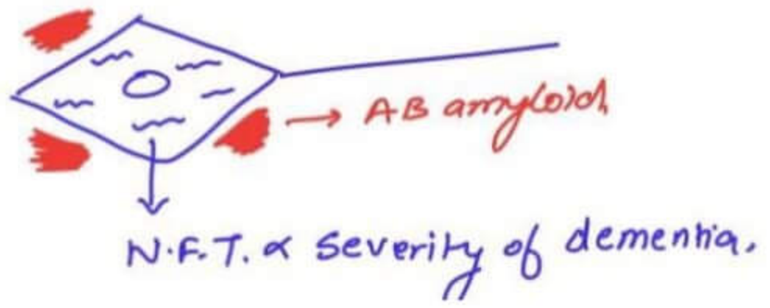
→ occurs in Nucleus of Meynert Basalis

Etiology:

Defects in Ch 1 / 14 / 19 / 21

(If pt.'s with Down Syndrome survive uptil 35 yr. can develop Pre senile dementia)

chr.19 Apo E_4 over expression leads to Alzheimer dz



→ severity of dementia is decided by intraneuronal amount of neurofibrillary tangles

(extraneuronal finding of Aβ amyloid is usually related to ageing and not associated with severity of dz.)

$Aβ_2$ amyloid related to dialysis dementia

C/features :-

1. Amnesia (Temporal lobe is affected) → Short term memory loss (social interaction initially is preservred) but later turns into Long term memory loss(unable to recall his name etc.)
2. Aphasia (Dominant parietal lobe affected)
3. Apraxia (Non dominant parietal lobe affected)
4. Anosognosia

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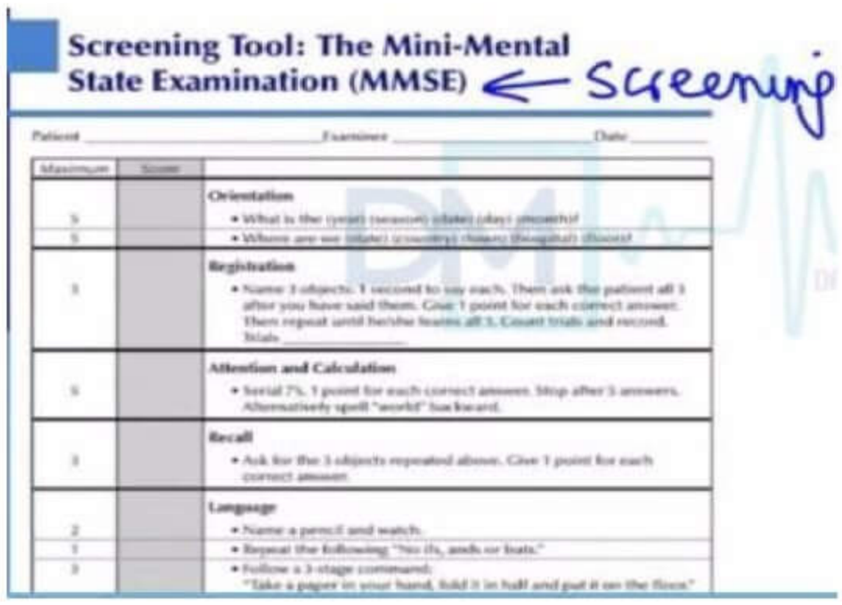
(Acalculia is not a manifestation of this dz.)

Screening tool (is MMSE) if its < 24 /30 = dementia



→ can be Falsely low → in depression

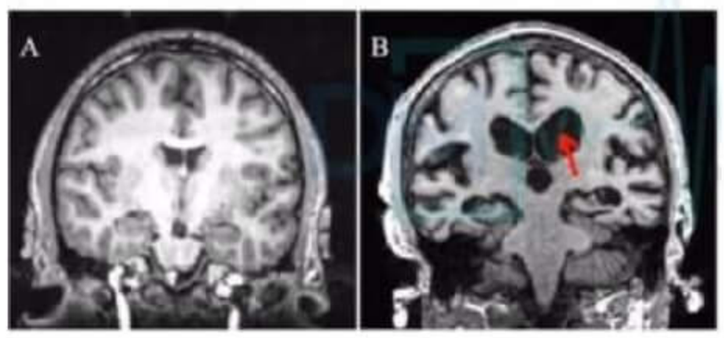
21 - 24 = Mild

10 - 20 = Moderate

< 10 = Severe

IOC = f MRI (Functional MRI)

MRI Brain: Normal vs. AD



MRI findings (plain) → Cortical Atrophy

(ventricular size appears relatively bigger k/a Pseudo Enlargement of ventricles ,is a late finding)

Treatment

DOC: Donepezil

Rivastigmine Galantamine Memantine

Tacrine (withdrawn as it Causes Hepatotoxicity)

Extra Mile

Subcortical Dementia : PD
Cortical Dementia → AD
Dementia + Myoclonus → VCJD
Dementia + Chorea → Huntingtons Ds
Pseudodementia → Depression

PrepLadder

MULTIPLE SCLEROSIS

(Autoimmune demyelinating disorder)

- Myelin is produced by oligodendrocytes. Main target of this disease is autoimmunity that mainly attacks Myelin basic protein (MBP).
- Myelin advantage is to provide insulation over axon.
- Saltatory conduction
  - Allows very fast conduction across nerve Fiber in brain
  - Normal speed of conduction across axon is 1m/ sec
  - but saltatory conduction is very fast Up to 70m/ second

Features

1. Autoimmunity
2. More common in females than male
3. Environmental risk factor- Vitamin- D deficiency
4. More common in North America (sunlight exposure is lesser – disease is more common, probably vitamin – D play role in immunomodulation)

Pathophysiology –

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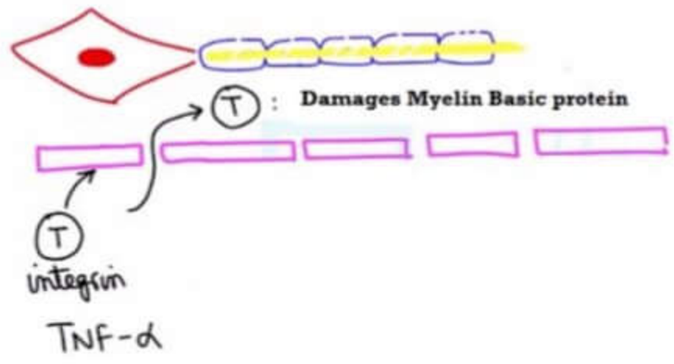

- ↑se in blood brain barrier permeability (Damage by immune system)

1. T cell attack blood vessel Endothelium. On surface of T cell, we have CAM (cellular adhesion molecule) called as Integrin.

NOTE- Natalizumab–interferes with T cell binding to endothelial cell. Thus, prevents further damage.

T cell cause direct damage to myelin by producing various cytokines like –TNF-α,

↓

Main pathological determinant of disease apart from demyelination is axonal damage.

↓

Self-reactive T cell damages myelin basic protein
= Axonal degeneration**
= Myelin degeneration*

↓

2. B cell of brain produces antibody against MOG (myelin oligodendrocyte glycoprotein).

↓

Repair process started

↓

3. **GLIOSIS – FORMATION OF PERIVENTRICULAR PLAQUES** (MAINLY PRESENT IN WHITE MATTER AREA)

PrepLadder

4. Periventricular plaques = Dawson finger on MRI

5. Neurological symptoms triggered on heat exposure (Hot shower) , as core temperature increases and is called **Uhthoff phenomenon**

Clinical Features:

Prevalence - sensory symptom> optic neuritis

1. Sensory symptoms (37%)
   - → Paraesthesia
   - → Pin and needle sensation
   - → Sensory level present + Torso
   - → Pain multifocal

2. Optic neuritis (36%)
   - → ↓se in visual acuity U/l > B/L
   - → Decrease in colors perception (desaturation)

     If uveitis present with above ophthalmological features →**SARCOIDOSIS**
   - → Fundus normal or papillitis

→ Visual loss U/L > B/L
   - → Periorbital pain ↑se on movement
   - → Internuclear ophthalmoplegia

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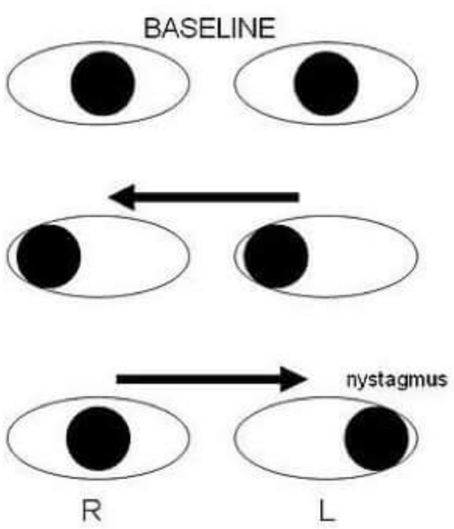
INTERNUCLEAR OPHTHALMOPLEGIA - Lesion of medial longitudinal fasciculus that result in impaired adduction of one particular eye and contralateral eye will move normally in patient.



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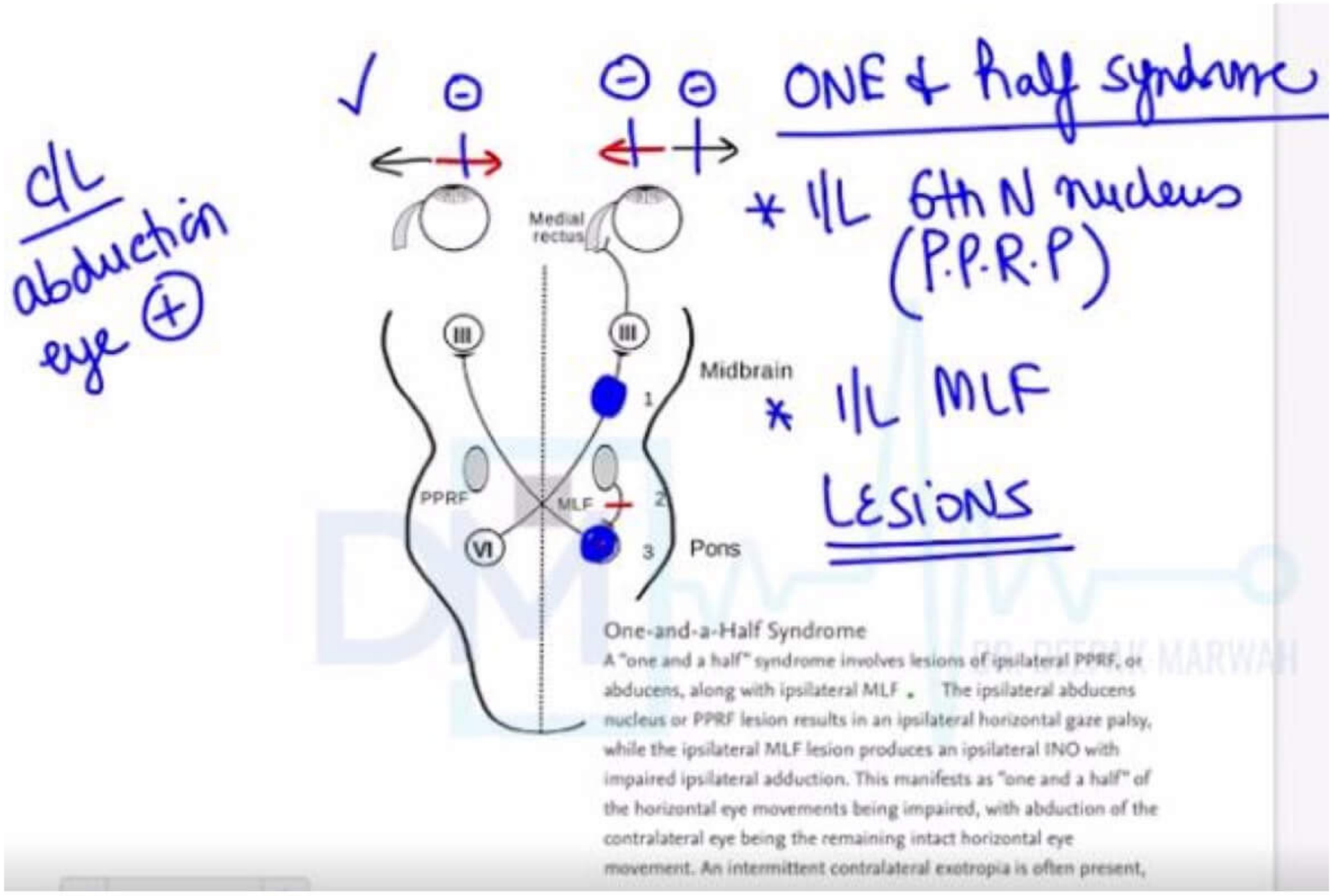

One and half syndrome:

Plaque in 6th nerve nucleus responsible for abduction movement (Lateral rectus) – inability to move eye laterally 6th nerve also connected to contralateral 3rd nerve nucleus which helps in adduction of opposite eye.

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↓

opposite eye adduction is affected

↓

Second plaque in medial longitudinal fasciculus affecting 3rd nerve nucleus. Hence one eye is not moving at all.

Other eye only one movement (Abduction component). As contralateral 6th nerve not involved

↓

Manifestation of → One and half syndrome

→ I/L 6th nerve palsy lesion

→ I/L medial longitudinal fasciculus lesion

→ **C/L abduction of eye present**

3. Weakness:

↑ses on activity

Spasticity: Increase in tone

Upper motor neuron lesion

→ Brisk deep tendon reflex, Babinski ⊕

Lower motor neuron lesion

→ Areflexia

PrepLadder

4. Facial nerve palsy

   = Due to lesion of nucleus of 7th **nerve in pons.**

   = Taste sensation **preserved**

5. Ataxia

   Gait ataxia : Paleocerebellum (GP)

   Truncal ataxia : Archicerebellum

   Scanning speech

6. Vertigo / deafness – 8th nerve
7. Trigeminal neuralgia – 5th nerve
8. Glossopharyngeal neuralgia – pain on swallowing
9. Ancillary symptoms

- LHERMITTE SIGN: Neck flexion

  ↓

  Radicular Pain (shooting pain) in legs

  Also seen in

  = Tabes dorsalis

  = Cervical spondylosis

- Facial myokymia: Flickering movements of muscles

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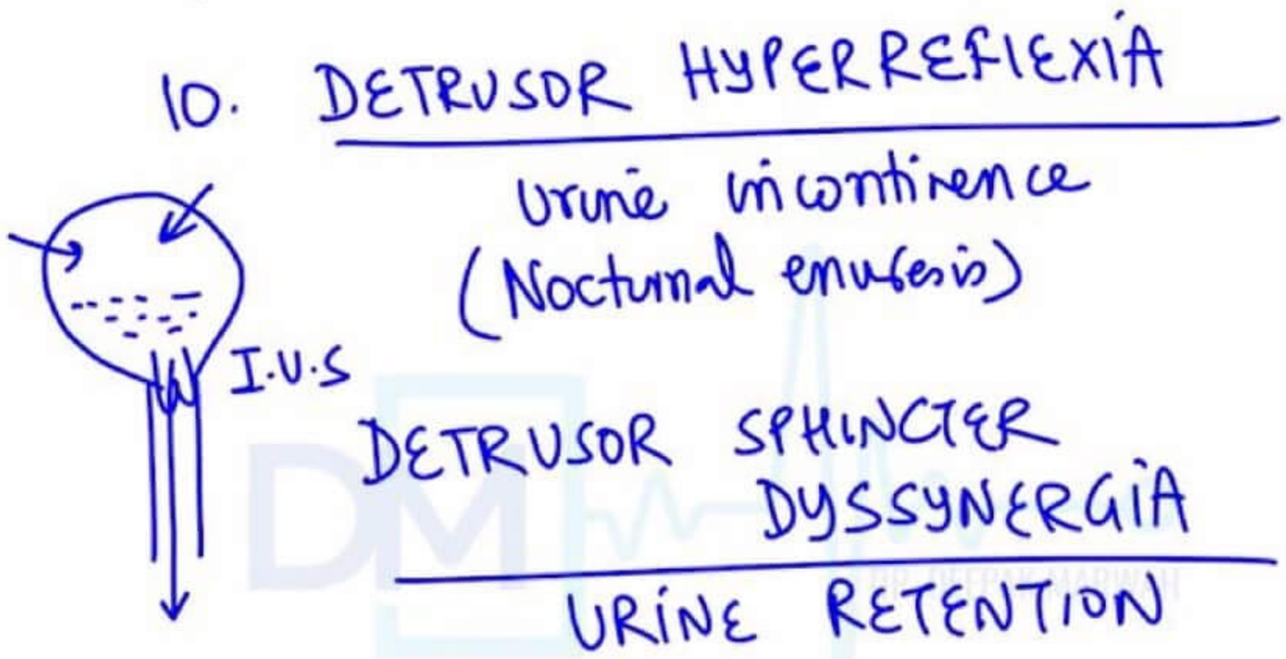
10. Detrusor hyperreflexia



→ Detrusor hyperreflexia -In CNS lesion there is loss of inhibitory control causing Urine incontinence (nocturnal) enuresis)

11. Detrusor sphincters dyssynergia - detrusor muscle contracts but sphincter does not relax causing urine retention and cystitis.

PrepLadder

Expanded disability severity score (EDSS)

3.5	9	9.5	10
↓	↓	↓	↓
Ambulatory	Bedridden Can talk Can drink	Bedridden Can't talk Can't drink	Death

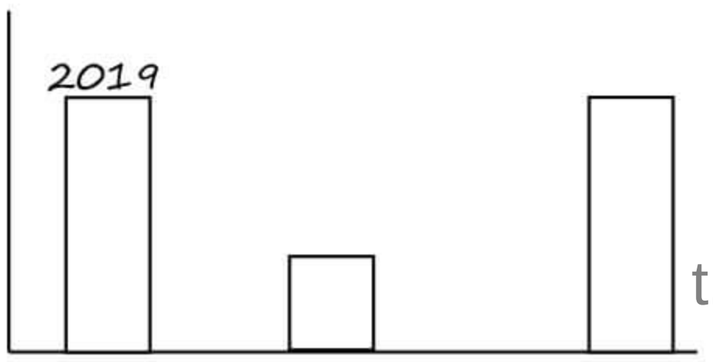
For acute attack of M.S = IV methyl prednisolone

Disease modifying treatment = interferon-β (used initially)

Diagnosis

- Revised McDonald criteria

1. Relapsing multiple sclerosis



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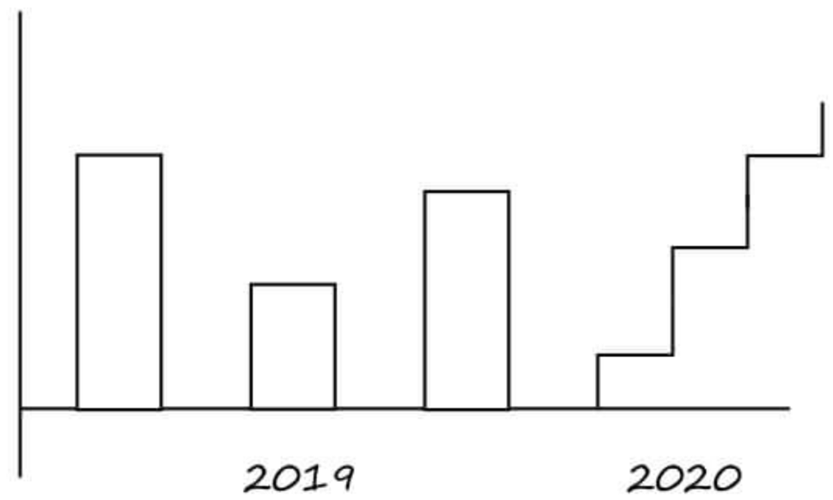
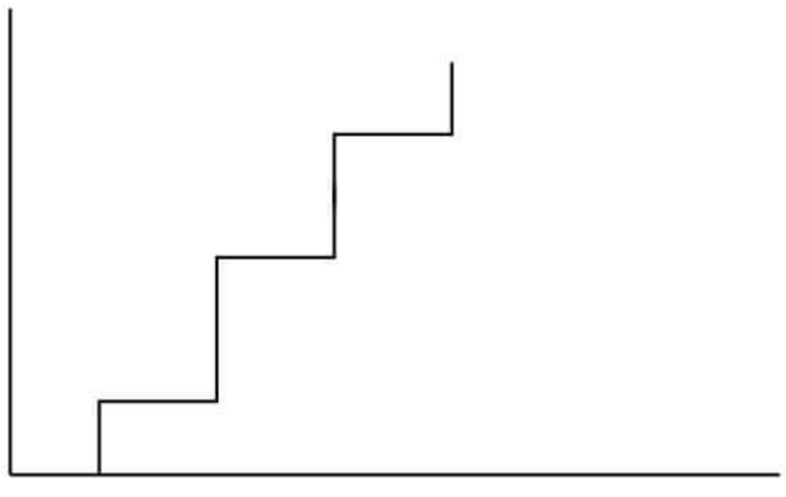
Jan	April	July
↓	↓	↓
Spasticity	Incontinence	Visual acuity decreases

2. Secondary progressive multiple sclerosis (S.P.M.S)



3. Primary progressive multiple sclerosis



PrepLadder

Primary progressive multiple sclerosis:

- 10% case (Least common)
- Base
- Most severe

Revised McDonald criteria

2 symptoms, symptoms > 24 hrs duration

↓

Symptoms separated by 4 weeks or more

WORK UP-

1. In gadolinium enhanced MRI = Plaques / Dawson Fingers

↓

I.O.C ↓

Periventricular (white matter area) / juxtacortical or Infratentorial(cerebellum)

- FLAIR- Fluid Attenuated Inversion Recovery suppress signal of CSF, periventricular lesion will stand up relatively better

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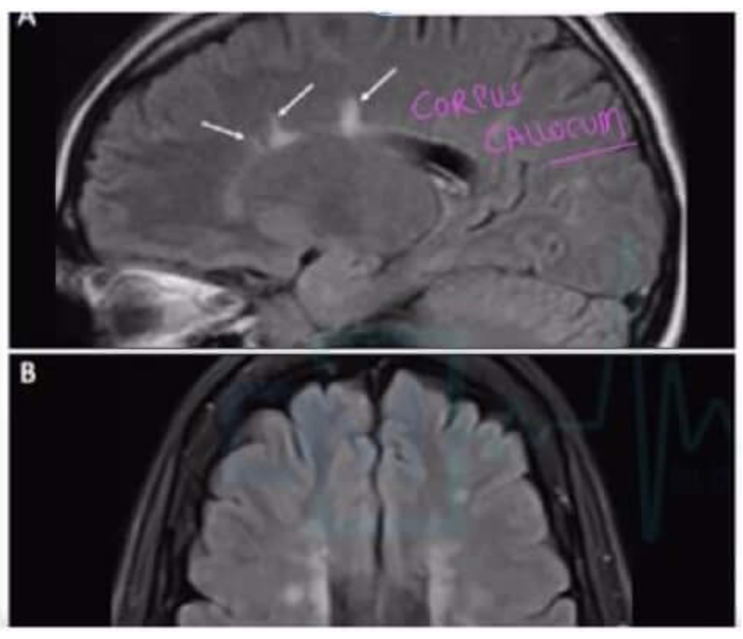

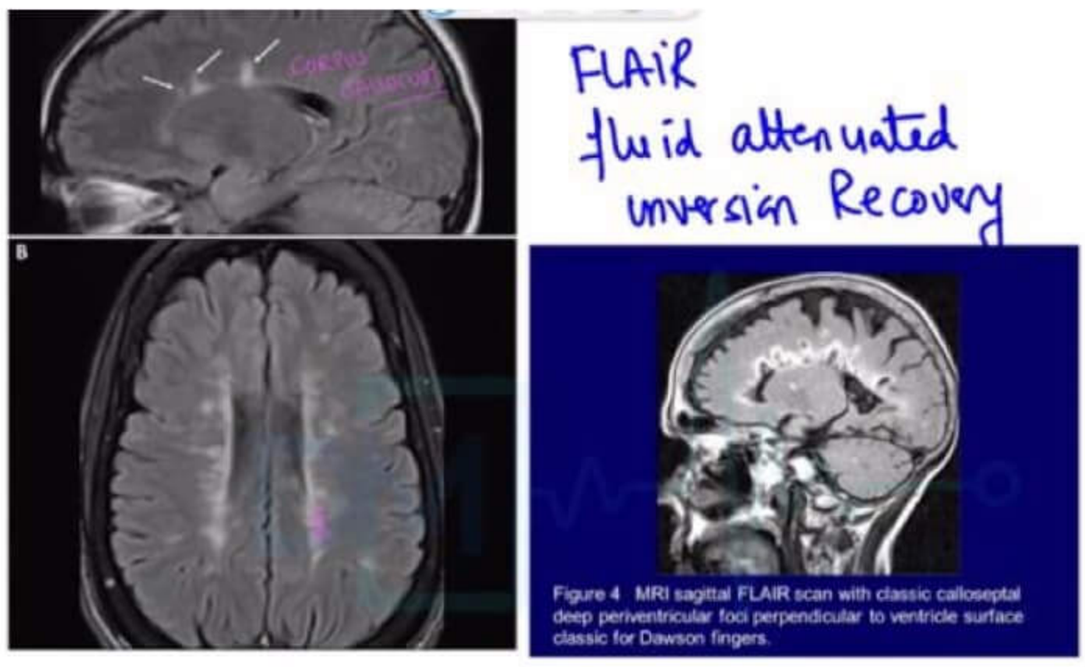

2. Visual evoke potential (VEP)= Plaque formation is smaller in size, voltage generated decreased leading to ↑ Latency period.

3. CSF = mild to moderate Pleocytosis

Proteins slightly increase

4. CSF electrophoresis

↓

Oligoclonal band in CSF

PrepLadder

Treatment – Acute attack of optic neuritis = IV methylprednisolone

Disease modifying drugs (to prevent disease)

1. B interferon
2. Glatiramer (immunomodulatory) = Glutamic acid, lysin, alanine, tyrosine
3. Oral fingolimod
4. Oral dimethyl fumarate (DMF)
5. Natalizumab = Once a month infusion

↓

Inhibit binding of T lymphocyte to capillaries related to blood brain barrier

↓

Damage to BBB is minimised

S/E = JC virus (John Cunningham virus) activation leading to PMF Progressive multifocal leukoencephalopathy - worsening of neurological features.

- It is ideal for patient with JC virus negative are eligible to get Infusion of natalizumab.

6. Ocrelizumab = acts by attacking mature B cell which express CD 20
   Is allowed for management of P.P.M.S

- NOTES-Mitoxantrone is Cardiotoxic. It is highly efficacious but it is NOT currently recommended for management of multiple sclerosis.

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PrepLadder

NEUROMYELITIS OPTICA

Neuromyelitis Optica Spectrum Disorder/ Devic's DS.

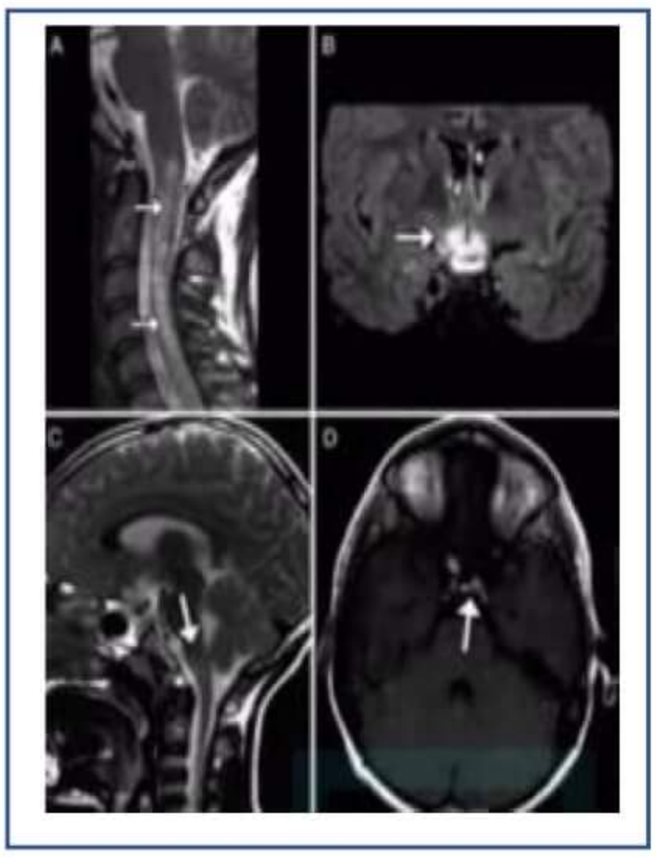
→ **Female: Male = 3:1** autoimmune disorder

→ **Target** → damage to Astrocytes {Astrocytopathy}
Involvement of foot processes of Astrocytes & Aquaporin -4 damage – Compromises BBB.

Case Scenario

♀ with sudden onset blindness and features of Transverse myelitis with presence of Anti Aquaporin – 4 Ab.
Ans. N.O.S.D- Neuromyelitis Optica spectrum disorder

Core clinical features



1. **Optic neuritis** - Sudden onset blindness, fast progressing, B/L {D/D: multiple Sclerosis – It is gradual onset, Asymmetrical presentation U/L}

2. **Transverse myelitis** - (**LETM**=longitudinally extensive transverse myelitis {i.e. Involvement of >3 segment of spinal cord})
   - Initial presentation – Pt C/O **pins & needle sensations** inability to work, **woody leg**

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3. **Area postrema syndrome** : Protracted vomiting (due to direct , damage to the BBB, not due to raised ICT)

4. **Diencephalic syndrome**: Lesions in Hypothalamus
   characterized by progressive anorexia + wt. loss, Narcolepsy {increased day time sleepiness}

5. **Acute brainstem syndrome:** 3rd n/v Palsy + C/L Hemiplegia (due to damage of CRUS CEREBRI)

6. **Cerebral syndrome** (cortical syndrome): Contributes to development of seizures & encephalopathy

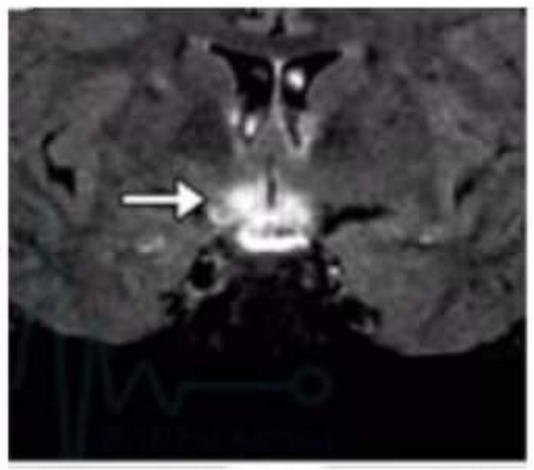
Diagnosis

1. Any **1** Core Clinical Feature
   +
   Anti-aquaporin – 4 Ab {which damages BBB}
   Or
2. If. Anti-aquaporin - 4 Ab not detected
   then **2** core clinical feature
   +
   MRI findings (gadolinium MRI)

"Dissemination Over Space"
I.e. clinical features don't occur simultaneously in a patient but occur over couple of days.

PrepLadder

Hyperintensity found in spinal cord present over multiple area



Cloud like lesion in brain parenchyma of pt.

- >1/2 length optic n/v inflamed
- Longitudinal extensive transverse myelitis {spreading over >3 segment}
- Area postrema damage
- Cloud appearance on MRI
- Peri ependymal brain lesions.

Management

Rx : **Mainstay:**

DOC- Methyl prednisolone

↓ if poor response

Plasmapheresis X 7 consecutive days

{1.5 times of actual plasma of Patient)

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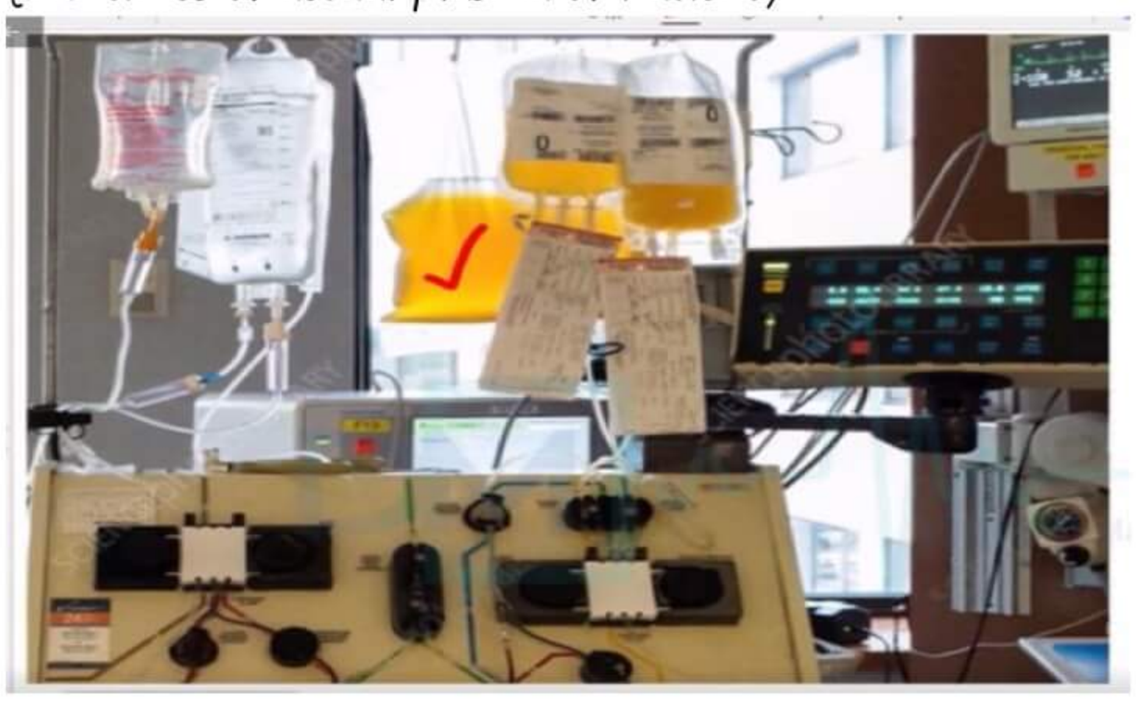


Best way of 1° prevention: **Mycophenolate** / (Anti CD_{20}) Rituximab/ Prednisolone + Azathioprine

Plasmapheresis in other condition:

- Hemolytic uremic syndrome
- Thrombotic thrombocytopenic purpura
- NMO

Note: Glatiramer/ β-**interferon** cause **worsening of symptoms** so its contraindicated.

- Mortality = D/t Respiratory paralysis
- **Anti MOG Ab** → Also detected in pediatric disorder ADEM (acute disseminated Encephalomyelitis)

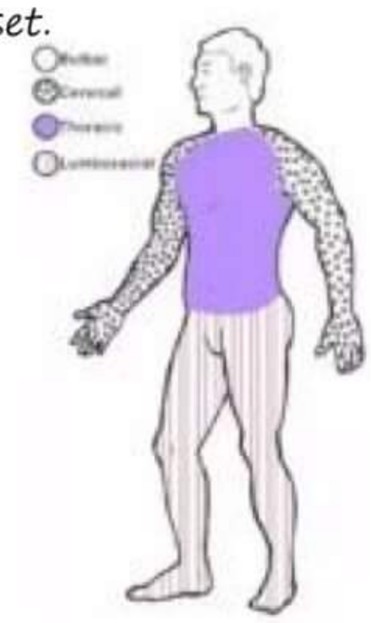
PrepLadder

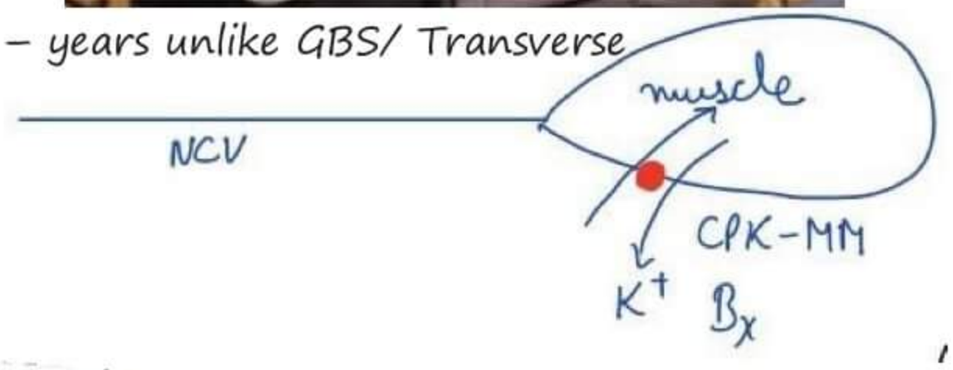
AMYOTROPHIC LATERAL SCLEROSIS

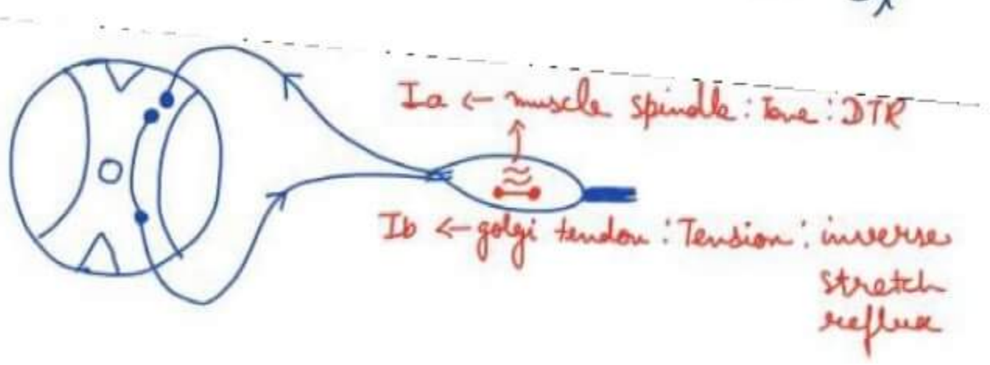
Motor Neuron Disease

- Neurodegenerative disorder : Adult onset
- Most common
- Etiology – **Hexanucleotide repeats**
  - It is a glutamate induced free radical damage
  - Damages mainly # **Pyramidal Neurons**
    # **Anterior Horn Cells of spinal cord**

C/F = Gradual Weakness of extremities developing over months – years unlike GBS/ Transverse myelitis which have rapid onset.







* **Ant. Horn** Cell degeneration	#	LMNL	Spinal muscle atrophy
* **Pyramidal** Neurons	#	UMNL	Primary lateral Sclerosis
* **COMBO**	# #	UMNL LMNL	Amyotrophic Lateral sclerosis

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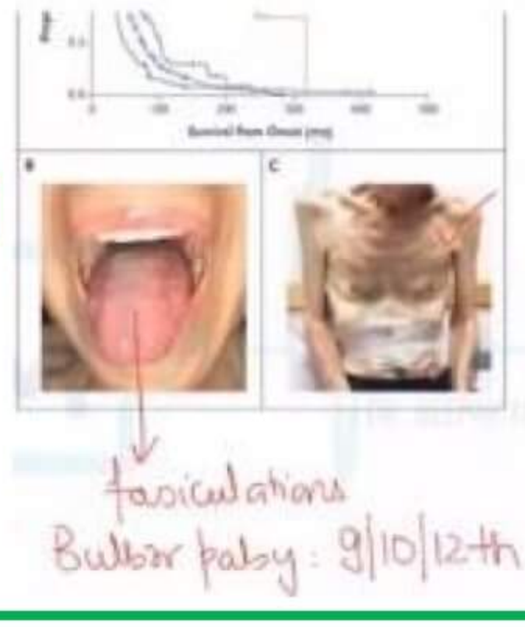
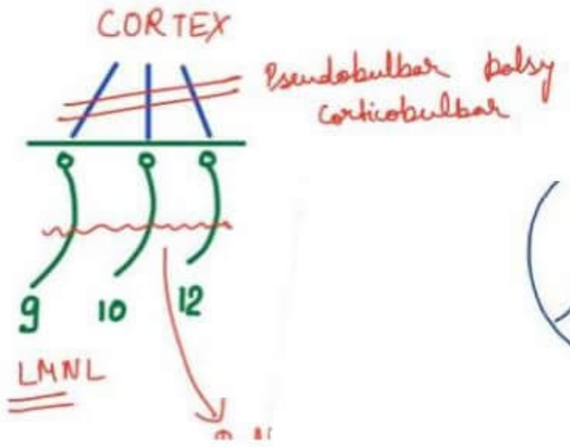
- Upper limb can have features of corticospinal involvement and lower limb may be develop flaccid weakness.
  - Normal higher mental functions
  - No ptosis, No eye involvement
  - No bladder / Bowel involvement

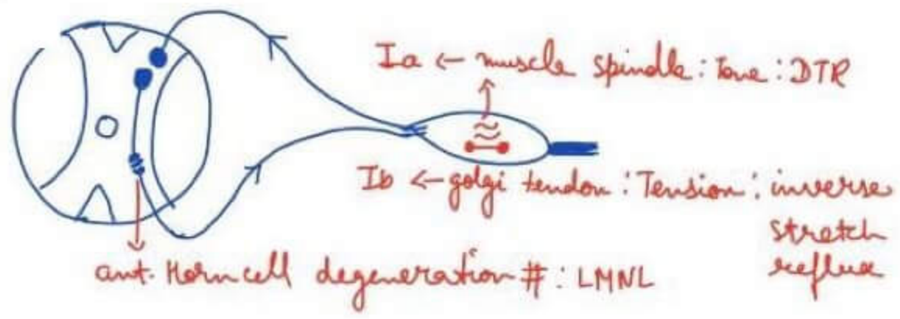
- Most common cause for death in motor neuron disease is # **respiratory failure**



- Fasciculations of tongue
- Bulbar palsy : 9 /10 / 12th nerve palsy

  - **Can't drink**
  - **Can't speak**
  - **Can't eat**





Diagnosis

- EMG - Myopathic Potential
  - Fasciculations ⊕

R_x: 1. Riluzole
2. Edaravone

Bulbar palsy: 9/10

Extra Mile:

Riluzole inhibits glutamic acid release due to inactivation of voltage dependent sodium channels. The objective is to neutralize the excitotoxic hypothesis of neurodegeneration

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PrepLadder

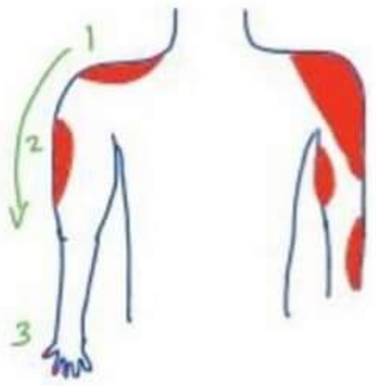
SYRINGOMELIA AND CONUS MEDULLARIS SYNDROME

Syringomelia

Major cause: - Arnold chiari Malformation Type 1

C/F :-

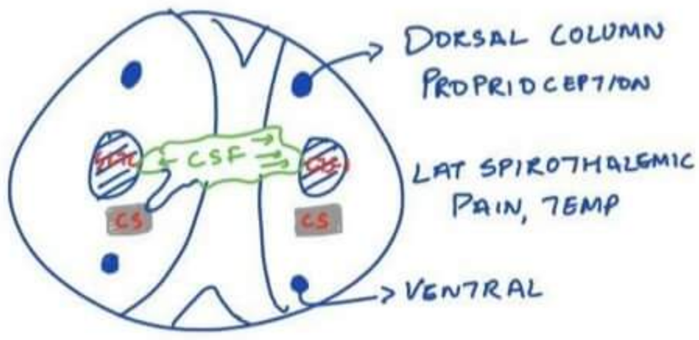
1 Painless burns in hand
2 Non healing ulcer in hand
3 **Charcot Joints** : painless paralysed joints (Hands)
4 Proximal to distal progression of sensory deficit



cape like distribution of sensory deficit

1. Due to involvement of corticospinal pathway on one side ,it will cause motor manifestations in the patient :
   - Ipsilateral spasticity
   - Ipsilateral Brisk Deep Tendon Reflex
   - Ipsilateral Babinski sign

   (If both CS pathways are involved then b/l manifestations will occur)



IOC:- MRI spine

Rx:- Surgical decompression

 # If surgical decompression not done, syringomelin can progress to Syringo bulbia → 9th / 10th /12th nerve palsy

↓

Can't drink
Can't eat
Can't talk
| **Complication of untreated Syringomelia**

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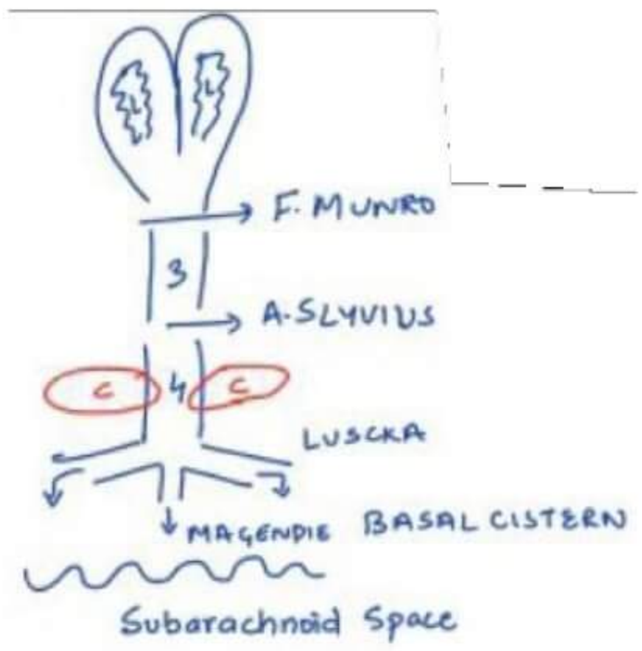


Arnold Chiari Malformation Type II

- Characterized by **herniation of cerebellar tonsills**
- Congenital hydrocephalus
- Associated with myelomeningocele
- Small posterior fossa (Large posterior fossa [in Dandy walker syndrome)]

Rx:- V.P. shunt

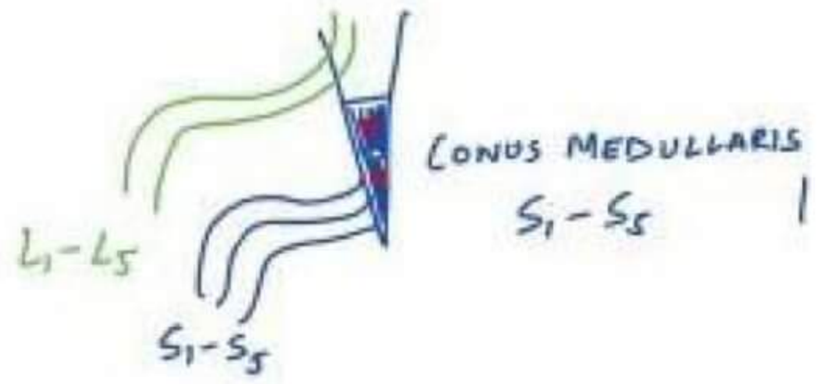
Cause:- Inferior displacement of cerebellar tonsil

Conus Medullaris Syndrome

- Damage to S_1-S_5 fibres
- Usually due to cancer metastasis from cancer prostate

C/F

1 Ankle jerk (S_1, S_2) = Absent
2 Knee jerk (L_2 / 3 / 4) = Preserved
3 Sensation perineum (S_2 / 3 / 4) = Saddle anaesthesia
4 Bladder sensation (S_2 / 3 / 4) → Overflow Incontinence.

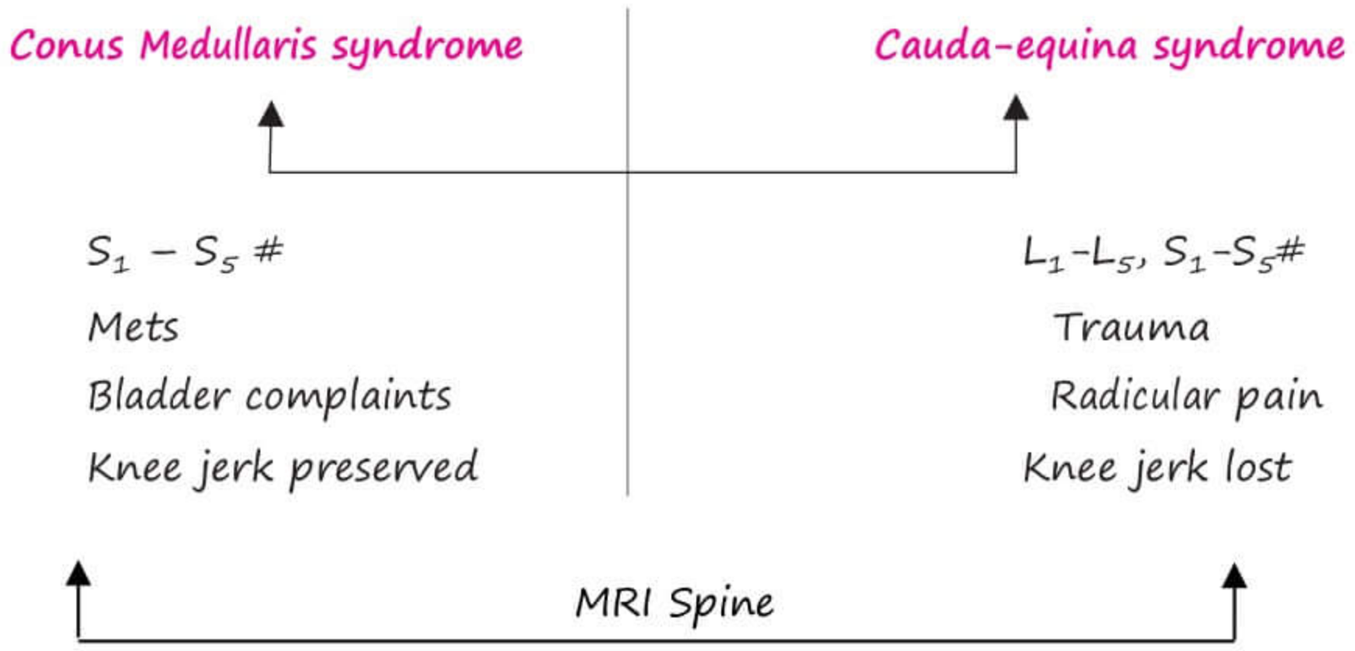


Cauda equina syndrome :

- Damage to L_1-L_5, S_1-S_5
- Usually due to trauma

1 Ankle jerk = Absent
2 Knee jerk = Absent
3 Sensation jerineum = Saddle anaesthesia
5 Bladder Overflow incontinence

PrepLadder



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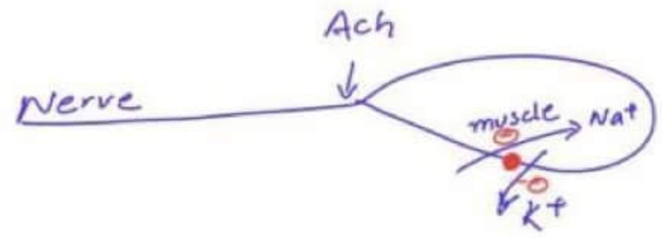
CHANNELOPATHIES



SCN4A:→ Loss of function

Hypokalemic Periodic Paralysis → Slow depolarization

Hypokalemic Periodic Paralysis:- → Slow Repolarization

- AD
- Post high carbohydrate diet:- weakness

Slow depolarization and repolarization is responsible for weakness in the patient.

Work up

- 1. S. Potassium decreased
- 2. NCV (Normal) (N)
- 3. CK MM : (N)

- IOC → Genetic studies are required for diagnosis of the patient
- EMG→ Reveal weak contractions and weak relaxations

  This patient is told to avoid carbohydrates and to take potassium supplements in the diet.

  More common in young males

- CACN1A channel: Ca^{++} present release decreases from sarcoplasmic reticulum→interaction between actin and myosin also decreases →Muscle weakness
- Primary defect – Ca channel defect > Sodium channel defect

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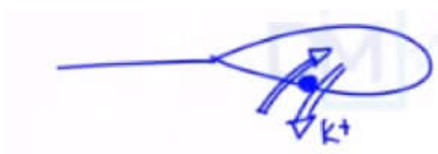
Rx: - POTCHLOR (Symptomatic intake of KCL),Coconut water can also be taken.

Hyperkalemic P. Paralysis:- SCN4A: gain of Function



This will lead to Fast depolarization and fast repolarization→ The total duration for which the muscle contraction will be lesser.

If we compare the twitch duration→ It will be lesser

Hyperkalemic P. Paralysis is diagnosis of exclusion (Rule out other causes of weakness like electrolyte imbalance, Nueropathies, Myopathies)

C/F:- Myotonia

Myoclonus – Twitching Jerking

↓

In. few muscle groups

Management of Hyperkalemic Periodic Paralysis: High Carbohydrate diet

(Because high carbohydrate diet → More sugar will cause→ more insulin to be produced→Potassium goes inside cell→ Muscle relax faster , This is an symptomatic management)

Causes of Myoclonus

1. Salaam Seizure / Spasm-<1 year
2. SSPE : 8 yrs
3. JME : 10-19 yrs
4. VCJD : 30-40 yrs

Channelopathis :- Channelopathies Types →

1. Hypokalemic P. Paralysis – (Loss)
2. Hyperkalemic P. Paralysis – (gain)
3. Paramyotonia congenital :- Variant of Hyperkalemic P. Paralysis (Gain) – Myotonia – Cold Exposure

Calcium Channel defect is seen in

- 1. Hypokalemic P. Paralysis
- 2. Lambert Eaton Syndrome
- 3. Familial hemiplegic migraine

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K^+ channel defect

-1. Episodic ataxia

All these channelopathies are related to the musculoskeletal system.

SCN5A defect → Brugade Syndrome

- **most common cause of death (Nocturnal)**
- In South east Asian Males

There is Defective inward current in myocardium

- Voltage gradient : V. Tachycardia → Sudden cardiac death

Investigation :- E.C.G : V_1 V_2 : ST↑ (Asymptomatic), cove pattern, T wave inversion

Rx :- TOC :- I.C.D

Comparison of Neuropathy versus Myopathy

Neuropathies are mostly acquired, and present with distal weakness whereas Myopathies present with proximal weakness.

PrepLadder

Distal weakness	Proximal Weakness
Difficulty in the turning on ignition Key of car Recurrent slipping	Difficulty in climbing stairs Difficulty in combing the hair
Areflexia	DTR (normal)
Glove & Stocking anaesthesia	Nil
NCV (Nerve Conduction Velocity)	CPK MM increased - Biopsy

Diabetic Neuropathy

- **Sensory involvement** → Distal sensory loss unmyelinated fibres (Earliest finding)
- **Motor involvement** → 3rd nerve palsy (Most common cranial nerve involvement) with pupillary sparing. --> Light reflex preserved ,nut ptosis and squint will be present
- **Autonomic** → Silent MI

Charcot MARIE Tooth Disease– "Hereditary sensorimotor neuropathy"

1. Peroneal muscle atrophy
2. Stork leg appearance
3. Thickened nerves
4. Bx nerves = onion bulb appearance
5. Distal weakness (Flexion Contractures)

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Duchenne Muscular Dystrophy

1. Progressive weakness
2. Calf muscle involvement
3. Pseudo hypertrophy
4. XCR : Boy 4 yr : Difficulty in climbing stairs
5. Gower sign present (+)
6. Wheel chair Bound Patient
7. Death – CHF/ R. Pneumonia
8. : CPK MM: increased Presentation
   (N) 10-12 yrs : wasting (+)
   decreased 15 yrs

IOC:- PCR for dystrophin gene

Rx:- Chest Physiotherapy

PrepLadder

Becker's Muscular Dystrophy

- Presentation = 10-12 yrs
- Wheel chair bound at = 25 yrs bound
- Milder disease
- Death = 40 yrs

↑

CPK mm (n)

Question:- 10 yrs old boy with large leg muscle CPK MM (n) diagnosis ?

Ans:- Duchenne's muscular Dystrophy

Myotonic Dystrophy

- Myopathic Facies
- Myotonia implies muscle relaxation is defective → Weakness (involving jaw muscles→ Partially open mouth and up turned upperlip appearance)
- Rigidity

Leonine leprosy

Overall peripheral nerve involved in leprosy – Ulnar nerve

Most common sensory cranial nerve involved in leprosy = V (Corneal reflex is lost→ Corneal ulcers)

Fig. 1 : Showing masked facies of the patient

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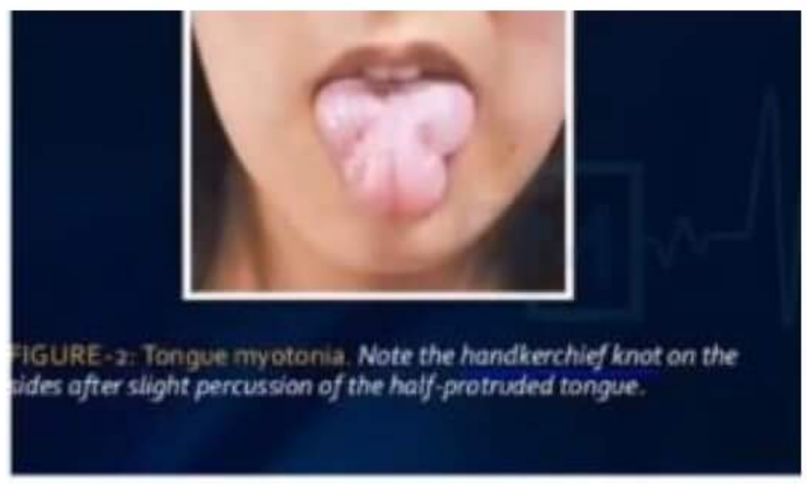

FIGURE-2: Tongue myotonia. Note the handkerchief knot on the sides after slight percussion of the half-protruded tongue.

PrepLadder

SYSTEMIC LUPUS ERYTHEMATOSIS

SLE :

- Type III Hypersensitivity reaction
- Gender ratio : ♀: ♂ 9:1
    - Takayasu
    - SLE
    - Sjogren

  } Diseases can show same gender ratio

- The Severity of the disease ∝ no. of X chromosome

  SLE + ♀ Turner (45XO)

  SLE + ♂ Klinefelter = more severe (47XXY)

Note: Number of X chromosome is directly proportional to severity of SLE so Klinefelter syndrome have more severity than turner syndrome.

For image based Question:

Malar rash, Butterfly rash has **nasolabial fold sparing,**

EXTRA MILE:

- Malar flush is the feature of Mitral stenosis where low cardiac output can cause perioral cyanosis.
- Nasolabial fold is involved in seborrheic dermatitis.

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BUTTERFLY RASH

ANTIBODIES:

Anti nuclease antibody = Best screening → 99% sensitivity.

DS DNA = High titres specific for SLE but problem is there is fluctuation in serum titres.

= Correlate with disease activity

Anti smith antibody = Most specific antibody

Anti RNP antibody = Correlate with Mixed connective tissue disorders so there can be a feature of SLE, RA, Etc.,. so disease are coexist here.

Anti ribosomal – P = Psychosis

= CNS Lupus

CASE SCENARIO : patient presents with low grade fever and joint involvement like MCP, PIP, intermittent polyarthritis manifest with tenderness and joint swelling sometimes presents with seizers.

- So m/c presentation is musculoskeletal system.

Anti neuronal antibody = Lupus cerebritis

Anti Ro (SS-A) = Photosensitivity

= Fetus: SA node =

↓

AV Node = Blocked/ damaged leading to complete heart block.

↓

Bundle of HIS

Note: Anti Ro (SS-A) can cause neonatal lupus where neonates presents with Butterfly rash and Bradycardia.

PrepLadder

SCLE = Subacute cutaneous lupus erythematosis

- Red scaly lesion mimics psoriasis associated with anti Ro (SS-A)

Anti La (SS-B) = Reduces the risk of nephritis,

Note : In Active lupus the main cause of death is lupus nephritis but if a patient is treated aggressively then the cause of death is infections due to reduced cell mediated immunity due to steroid toxicity.

Anti Histone antibody = Drug induced lupus

S – Sulfonamide

H – Hydralazine

I – Isoniazid

P – **Procainamide** (used in emergency management of wolf Parkinson white syndrome)- M/C cause of drug induced lupus

In drug induced SLE = Lupus nephritis
Lupus cerebritis
} Not Seen so its having good prognosis.

Antiphospholipid antibody → main cause of recurrent abortion where fetal loss at the end of first trimester or at 34 weeks there is the unexplained intrauterine death.

To evaluate antiphospholipid antibody:

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- ELISA for cardiolipin antibody
- ELISA for B_2 glycoprotein antibody
- Dilute Russell viper venom time test – specific test/ screening to identify lupus anticoagulant

PATHOLOGY : there is tendency of Clot formation in a uterine artery / vein so that results in compromises of blood supply to the fetus.

↓

Recurrent loss of Fetal

For future prevention of fetal loss and complications : Give lifelong low dose aspirin 75mg

Note: sometimes SLE associated with anti phospholipid antibody which will leads to hypercoagulable state so patients not only present with recurrent fetal loss and also will suffer with stroke, MI, DVP like manifestation in the future.

Anti-erythrocyte antibody = cause Auto immune hemolytic anemia

On P/smear = Spherocytes

CASE SCENARIO : ♀ with anemia, joint pain, skin rash, photosensitivity and positive direct coombs test.

NOTE : Anemia seen in SLE due to Autoimmune hemolytic anemia > anemia in chronic disease.

Anti platelet antibody = Petechiae
= Purpura

C/F -

Mnemonic - MD SOAS BRAIN

SKIN manifestation

1. **Acute SLE Rash** = Malar rash involves bridge of the nose, cheeks and nasolabial folds sparing.

PrepLadder

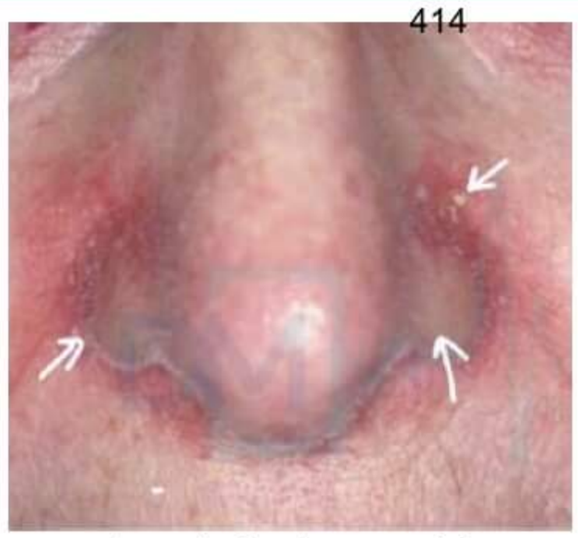
- **Subacute cutaneous LE** = Subacute cutaneous lupus erythematosis

→ irregular Red scaly patch

↓

May mimic psoriasis

But in psoriasis there is no photosensitivity



Seborrheic dermatitis

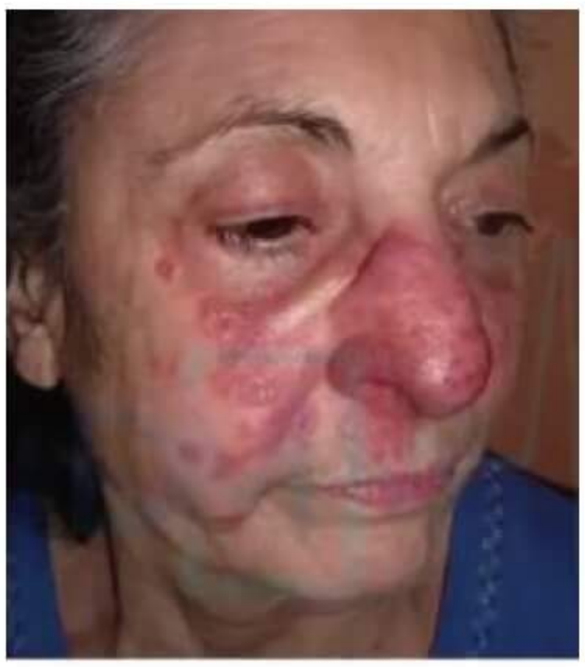
2. **Chronic cutaneous LE** :

- Also called as **discoid lupus erythematous**
- Circular lesion with hyperpigmented periphery and Hypopigmented central part.
- Loss of dermal appendages like sweat and sebaceous glands.
- Non scarring Alopecia seen.

Note :

M/C involvement in SLE is musculoskeletal system.

Rx: = Topical steroids + Hydroxy chloroquine



LUPUS PERNIO - SARCOIDOSIS

Extra Mile

40 years old ♀ present with Dyspnea (Gd. IV) Chest x Ray = B/L Hilar lymphadenopathy Lupus pernio	SARCOIDOSIS

3. S – Serositis :

	Lung	Heart
Most common		
Least common	Pleuritis Shrinking Lung syndrome	Pericarditis Libman-sacks Endocarditis

- Pleuritis and Pericarditis can be differentiated with chest pain, where patient felt chest during inspiration can suggest pleuritis but irrespective of respiration patient felt chest pain suggest pericarditis.
- On ECG : ST elevated with upward concave pattern in all leads suggestiv pericarditis.

Libman sacks endocarditis → also called sterile endocarditis, fibrin deposit under the s of cardiac valve.

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- Long standing of sterile vegetation leads to damage of chordae tendineae and

Results in Mitral valve incompetency so blood leaks from ventricle to atria.

- In most of the cases seen with mitral regurgitation.

Rx:

chronic MR/ Symptomatic = Valvuloplasty

Steroids = no role because it is not prevent mitral regurgitation of the patient

4. O= Oral ulcer present as aphthous ulcer = Painless / painful (rare)

- In SLE patients there is multiple ulcers are present in oral cavity with recurrent basis. It can be controlled by topical steroids.

CASE SCENARIO :

- ➢ ♀ Recurrent aphthous ulcers in oral cavity and vulva
- ➢ If Male patient present with recurrent aphthous ulcer in oral cavity and scrotum

} Behcet's disease

MD SOAS

⇩ ⇩

5. DLE Non scarring alopecia

6. S = Synovitis > 2 joints

SLE arthritis is categories as synovitis with Absent of deformities.

- Proximal interphalangeal joint
- Wrist
- Knee

} Asymmetrical involvement

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- Intermittent polyarthritis – different joints involvement in a various time.
- Erosions < 10% of cases so called as synovitis.
- RHUPUS = RA + SLE features coexistence.
  - Rx of musculoskeletal joint pain : = Steroids
  - S/E of steroids = Avascular necrosis of bone
  - Joint pain increases in spite of steroids and now involved single joint → MRI → AVN of Bone.

7. B = Brain :

→ M/C CNS Involvement = Cognition defect

= Lupus cerebritis due to antineuronal antibody = Cerebral edema
Headache
Seizures

= Psychosis → Psychiatric profile

= Antibody responsible is Anti ribosomal – P antibody.

8. R = Renal :

Important cause of the Death = active lupus

Asymptomatic

Urine microscopic examination = microscopic hematuria and proteinuria

↓

Nephrotic syndrome (protein loss > 3.5 gm in urine)

↓

End stage renal disease

PrepLadder

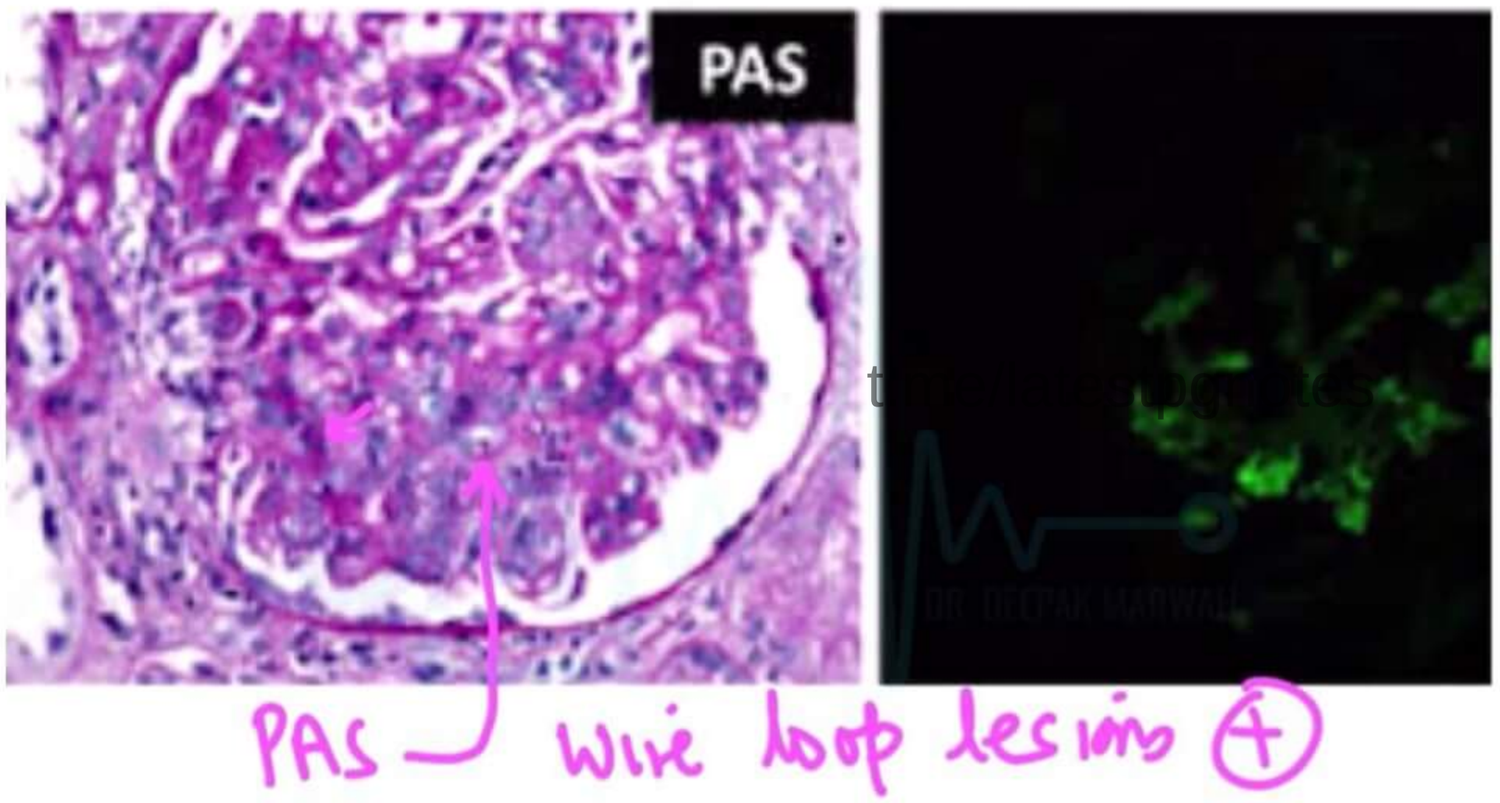
On BIOPSY :

Classification of lupus nephritis :

Pathology So[illegible]cation of lupus nephritis (LN)	
Class	Abbreviated ISN/RPS classification of LN (2003)[22]
Class I	Minimal mesangial LN
Class II	Mesangial proliferative LN
Class III	Focal LN (<50% glomeruli)
Class IV	Diffuse LN (>50% glomeruli)
Class V	Membranous LN
Class VI	Advanced sclerosing LN

Adapted and modified with permission from Ref 22

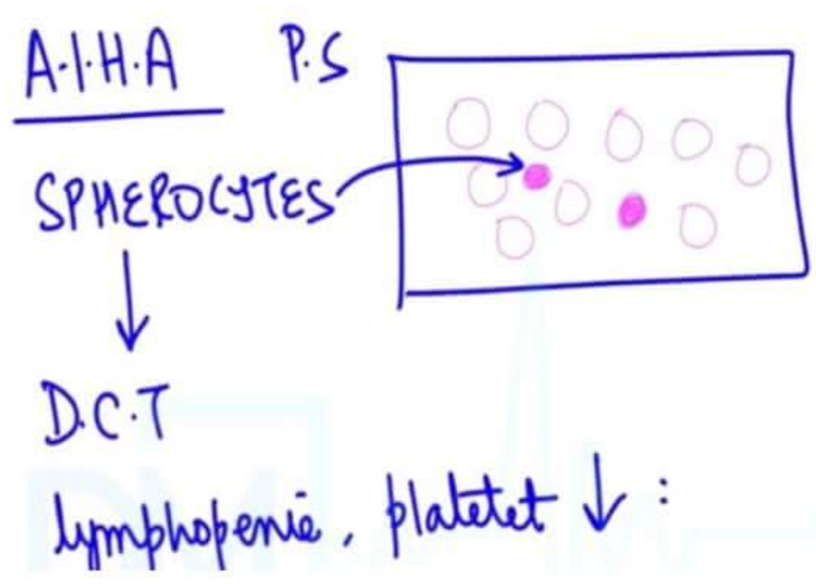
- **M/C type of lupus nephritis** : class 4 : diffuse LN
- **Wire loop lesions** are demonstrated on **PAS** of lupus nephritis.
- Immunofluorescence = **IgG, IgA, IgM, C3, C1,** "FULL HOUSE EFFECT" -Q



9. A = Anemia = Autoimmune hemolytic anemia

On P/smear : some of the RBC's are smaller With lacking of central pallor.

- If spherocyte +nt then we do direct Coombs' test So can be treated with steroids rather than blood transfusion to avoid jaundice caused by preformed antibodies .
- Lymphopenia
- Platelet ↓↓ = Petechiae, purpura.
- Sometimes patient presents with autoimmune peritonitis so the patient of SLE always felt abdominal pain here patient can be treated with opioids.



10. IN = **Immunological features** present due to various antibodies are formed in the body.

If at least four features should be present for diagnostic criteria :

PrepLadder

11. A. **N**. A Positive

↓

Bold

Clinical

M – Malar rash = Acute SLE rash, SCLE.

D – Discoid rash = Chronic cutaneous Lupus erythematosis

S – Serositis

O – Oral ulcer

A – Alopecia – non Scarring rash

S – Synovitis (more than equal to 2 Joints)

B – Brain Manifestation

R – **Renal** = lupus nephritis

A – Anemia = Autoimmune Hemolytic anemia

I – Immunological Features

N

Lab	– A.N.A – ds DNA antibody – Anti Smith antibody – C_3 C_4 ↓ – Antiphospholipid Antibody

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To test antiphospholipid antibody:

- Elisa anticardiolipin antibody
- Elisa B_2 Glycoprotein antibody
- Dilute Russel Viper Venom Test to identify Lupus anticoagulant.
- Direct Coombs test : positive even in absent of hemolytic anemia.

Note : Antiphospholipid antibodies cross react with VDRL kit so it can be manifest as False +ve VDRL.

- **Total 4 features should be positive**
- **At least 1 clinical feature and**
- **At least 1 lab features**

} **To diagnosis for SLE**

- If renal features positive alone is enough to diagnosis SLE.

T/t:-

- D.O.C in S.L.E = steroids
- S.L.E in Pregnancy = Hydroxychloroquine given because deactivation of steroids by placental enzymes can occur so steroids are not given .
- Mortality in SLE show Bimodal Pattern
  - In early years after diagnosis, infections – especially with opportunistic organisms are the leading cause of death followed by active SLE (where patient without Rx), chiefly due to kidney or CNS disease.
  - In later years- > 45 years, Accelerated atherosclerosis linked to chronic inflammation, becomes a major cause of death.

PrepLadder

Note : Autoimmune disorder decreases in severity during pregnancy = Rheumatoid arthritis.
Most of the auto immune disorders are worsen during pregnancy except RA.

	ANA	Native DNA	Rheumatoid Factor	Anti-Sm	Anti-SS-A	Anti-SS-B	Anti-SCL-70	Anti-Centromere	Anti-Jo-1
Rheumatoid arthritis	30–60	0–5	70	0	0–5	0–2	0	0	0
Systemic lupus erythematosus → anti Ro and anti La	95–100	60	20	10–25	15–20	5–20	0	0	0
Sjögren syndrome →	95	0	75	0	65	65	0	0	0
Diffuse scleroderma → anti Topoisomerase	>95	0	[illegible]	[illegible]	[illegible]	[illegible]	33	1	0
Limited scleroderma (CREST syndrome) → anti CENTROMERE	>95	0	[illegible]	[illegible]	[illegible]	[illegible]	[illegible]	50	0
Polymyositis/ dermatomyositis	80	0	33	0	0	0	0	0	20–30
Granulomatosis with polyangiitis	0–15	0	50	0	0	0	0	0	0

- Most sensitive test for Sjogren syndrome
- A Main test is perform in Sjogren syndrome anti Ro and Anti La antibodies.
- For diffuse scleroderma → anti - topoisomerase antibody.
- For limited scleroderma → anti-centromere antibody.

Antiphospholipid syndrome Criteria :

Antiphospholipid Syndrome Criteria
Sydney revision of Sapporo criteria 2006

CLINICAL CRITERIA

1. **Vascular Thrombosis**
2. **Pregnancy Morbidity**:
   a) death of normal fetus at ≥ 10 wks
   b) premature birth at ≤ 34 wks due to preeclampsia
   c) ≥3 consecutive abortions at <10wks
   d) placental insufficiency at < 34 wks

LAB CRITERA

1. anti-Cardiolipin IgG / IgM
2. anti–beta-2 glycoprotein I (GP1)
3. Lupus anticoagulant (LAC)
   - *medium to - high titer*
   - *at least X 2 times*
   - *12 wks apart*

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- Antiphospholipid antibody associated with SLE is called as 2° Antiphospholipid antibody syndrome.
- If not associated with SLE is called as primary antiphospholipid antibody syndrome.
- **1 c/f +2 lab feature at 12 wk apart** to diagnose APAS. -**imp**

PrepLadder

Rheumatoid Arthritis

C/Features –

- Young females mostly affected
- 25-55 yrs
- PIP, MCP, wrist painful, tender joints
- Bilaterally symmetrical involvement
- Morning stiffness > 1 hr
  → Symptoms ↓: Physical activity
  < 4 joints : Monoarticular
  > 5 joints : Polyarticular

Flexor Tenosynovitis	↓ Range of movement
(Hallmark Feature)	↓ Grip strength
	↓ Trigger fingers

Deformities associated –

E	F	→	S- Swan neck
↑	↑		
PIP	DIP		
↓	↓		
F	E	→	B- Boutonniere

1. Z Line deformity
*
*
2. Subluxation of distal ulna
* Piano key movement of ulnar styloid
3. Feet : MTP, ankle, mid tarsal joint, flat feet
4. Cervical spine → Atlantoaxial dislocation
→ Compressive myelopathy

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Extra articular manifestation:

- MC Rheumatoid nodules: Non tender and found in Extensor distribution
- Rheumatoid arthritis can co-exist with any other Rheumatological conditions
  - Secondary SJOGREN syndrome – Rheumatoid arthritis + SJOGREN

Example: Interstitial lung Disease, Pulm nodules

- Keratoconjunctivitis Sicca, Xerostomia, Atlanto Axial Dislocation Quadriplegia
- Pleuritis: Pleural Effusion : Exudative

- **Heart Involvement** – Pericarditis, myocarditis, cardiomyopathy ischemic Heart disease (Death), arrhythmias, Heart block mitral regurgitation

- **Kidney Involvement** : Membranous Glomerulopathy, 2° Amyloidosis

PrepLadder

Genital Involvement

- Hypoandrogenism
- Osteoporotic deformities
- Purpura, ulcers on the tip of toe

Hematological conditions: Anemia of chronic Disease present **as normocytic normochromic anemia.**

EXTRA MILE :

CAPLAN Syndrome: Coal worker pneumoconiosis + Rheumatoid nodules

Felty syndrome

Felty Syndrome =

Pathology

- Synovial inflammation
  - Pannus → Erosion Cartilage
  - Focal Bone Damage

Diagnostic criteria :

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J – Joint Involvement	1 large joint	1 – 3SJ	>10 small joint
	2 – 10 LJ	4 – 10 SJ	
S – serology	RA Factor	Anti CCP	(<3 ULN)
	Low ⊕	Low ⊕	(> 3 ULN)
	High ⊕	High ⊕	
A – Acute phase reactant	(n) ESR	(n) CRP	
	Ab (n) ESR	Ab (n) CRP	
D – Duration of symptoms	< 6 wk	> 6 wk	

Composite score = > 6

Work up:

1. MRI : Synovitis, joint effusion, marrow edema
2. RA factor : IgM : ⊕ Biologically False +ve = 5% population
3. Anti Cyclic citrulline Peptide a/b
   Most specific ↑
4. Synovial fluid: 5000 – 50000 cells /Cu mm

PrepLadder

5. X ray hand → Joint Space loss
→ Subchondral erosion
→ Periarticular erosion

Treatment :

Preferred DMARD (Disease modifying anti rheumatoid drug) Ā Methotrexate : High disease activity ⊕

↓

MTX + Sulfasalazine + Hydroxychloroquine

Triple therapy OR

MTX + Biologicals →
→
→
→

Or

MTX + TOFACITINIB

MOA : JAK3 inhibitor

Steroids Loss ⊕ Benefits +

Θ Signaling of receptors responsible for cytokine release

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PrepLadder

CRYSTAL ARTHROPATHY

ACUTE GOUT:

- Middle aged male
- Post-menopausal female with HTN (on diuretics)

- **Podagra**
  - Warm
  - Tender
  - Red inflammed
  - Tarsal joints, ankle, knee joint

- **Tophi**
- **Nephrolithiasis**

Work –Up: -

1. **IOC:** Joint aspiration:

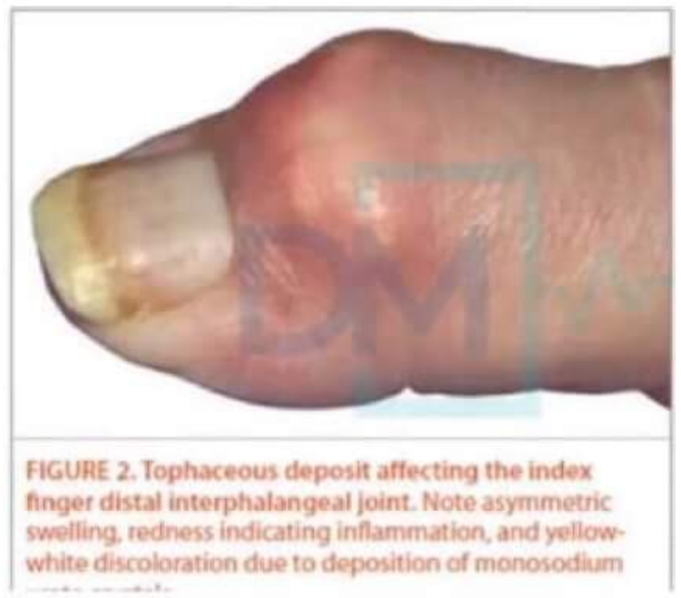

FIGURE 2. Tophaceous deposit affecting the index finger distal interphalangeal joint. Note asymmetric swelling, redness indicating inflammation, and yellow-white discoloration due to deposition of monosodium

- Turbid
- Chalky white
- Cell count: 2K-6K
- Polarized light
- Negatively Birefringent
- Needle shaped

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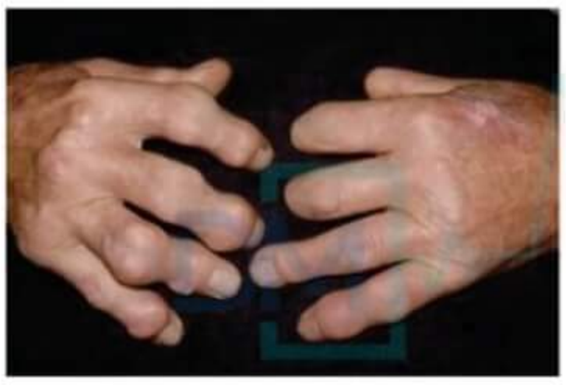
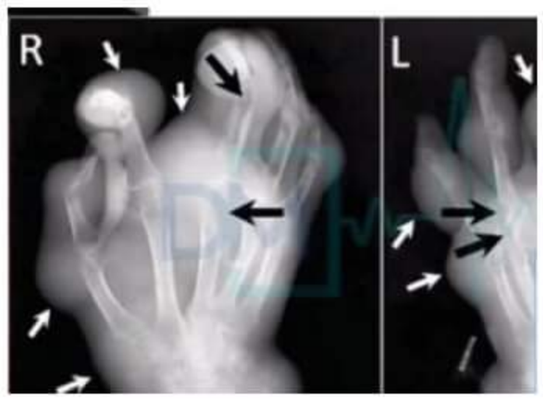
2. 24 hour urinary uric acid evaluation
3. Urine m/e
4. KFT/LFT/ lipid profile
5. **X Ray: "Martel sign"** These are erosions with sclerotic margin)
6. USG: - Joints: double contour sign



Rx:-

- Ice Pack
- Indomethacin/ Naproxen
- Colchicine 0.6mg 8hrly (S/E diarrhea)
- Steroids:
- Aspirin contraindicated in acute/gout.



Hypouricemic therapy:

- Control weight
- Low purine diet
- Intake of H_2O to be increased
- Excess of diuretics

Extra Mile

Needle shaped crystals E/M – calcium apatite

PrepLadder

Over-producer

Allopurinol: granulomatous hepatitis SJS/TEN

Febuxostat pegloticase i.v:
Refractory ch. Gout

Under producer

Probenecid: Increase uric acid excretion
Benz bromarone (Co-existent)
Lesinurad (-) uric acid reabsorption

Extra Mile

Needle shaped crystals: P|M: negative birefringent **Monosodium Urate**
Needle shaped crystals E|M: **calcium apatite**
Rhomboid, rectangular P|M: (Birefringence) **C.P.P.D**
Bipyramidal: LM **calcium oxalate**

Saturnine gout is related with **Lead poisoning.**

Categories of synovial fluid findings

Measure	Normal	Noninflammatory	Inflammatory	Septic	Hemorrhagic
Volume, ml	<3.5	Often >3.5	Often >3.5	Often >3.5	Usually >3.5
Clarity	Transparent	Transparent	Translucent-opaque	Opaque	Bloody
Color	Clear	Yellow	Yellow to clear	Yellow/green	Red
Viscosity	High	High	Low	Variable	Variable
WBC/mm3	<200	0-2,000	2,000-100,000	15,000->100,000	200-2000
% PMN	<25	<25	>50	>75%	50-75
Culture	Negative	Negative	Negative	Often positive	Negative

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PrepLadder

VASCULITIS

Most common cause in children - H.S.P (related to excess of Hb. A)

Most common cause in Adults - Idiopathic cutaneous vasculitis > Giant cell arteritis

GIANT CELL ARTERITIS:

CLINICAL SCENARIO :

70 years old patient, feels feverish, for past 3 weeks and takes PCM off & on. He also has Temporal headache and Jaw claudication

On examination: CORD like Structure at TM joint

- Ischemia skin of scalp explains Temporal headache
- Ischemia of TMJ explains Jaw Claudication

Ophthalmic artery involvement →Blindness monocular/binocular

Work up:

1. ESR=100mm fall (grossly elevated ESR)
2. IOC: Vessel wall biopsy

RxOC: Steroids

Extra Mile

ESR = 100 mm fall/ 1st hour
1. SABE
2. Giant cell Arteritis
3. Multiple Myeloma

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- STEROIDS
  - Most common cause of headache = Tension headache
  - Most common cause of 2° headache = Infection
  - Most common cause of Pulsatile headache = Migraine
  - Most common cause of Temporal headache = Giant cell arteritis
  - Most common cause of occipital headache Tension headache>= HTN> BasilarMigraine

HENOCH SCHONLEIN PURPURA (H.S.P) :

Commonest cause of vasculitis in children

IgA is in excess

↓

Activate complement system

↓

Damage to blood vessels

H.S.P is characterized by complement mediated vasculitis.

PrepLadder

C/F :

1. Extensor PURPURA: - RASH on Buttock, Back of thigh
2. Abdominal pain, hematochezia
3. Arthralgia
4. Normal platelet count/ Non thrombocytopenic purpura

Rx.: Steroids

BEHCET DISEASE/ SILK ROUTE DISEASE

- Seen in female pts. Origin from central Asia i.e Turkey/ China/ Arab

C|F:

(HALLMARK for diagnosis)

↓

1. Recurrent CROPS of APTHOUS ULCERS every month, Painful
2. Seen in ORAL CAVITY and
   - In females → Vulva
   - In male → Scrotum
3. Ocular manifestation– Hypopyon

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(ORO – OCULO – GENITAL – SYNDROME)

WORK UP:-

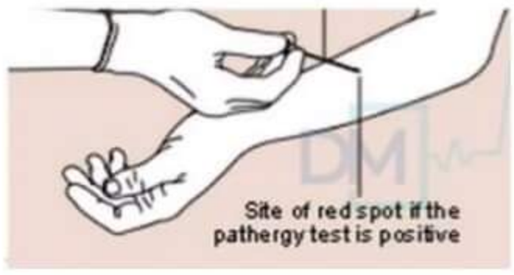
Pathergy Test: Hypodermic needle

[Example of Type IV hyper Sensitivity rxn.]

prick: - Flexor aspect of forearm

↓ after 48-72 hrs.

STERILE PUSTULE



Extra Mile:

PATCH TEST: - Ex. Of type IV hyper sensitivity reaction.

- Done in patients having Contact dermatitis

Complications : -PA Vasculitis

Rx: -

1. Topical steroids for oral ulcers
2. Proper hygiene for genital ulcers

KAWASAKI DISEASE

Clinical scenario : – ECG findings of MI in 4 year old child

4 yrs: Fever > 5 days (oral PCM) Amoxy- Clavulanic acid)

C|F

3. Cervical lymphadenopathy U/L

   D/D – Tonsillitis

4. STRAWBERRY Tongue D/D – scarlet fever
5. RASH- Trunk, Pubic area
6. **Perianal peeling of skin/ desquamation**

   Periungual peeling of skin/desquamation
7. Bulbar Congestion: (B\L: Non Purulent)

(Muco – Cutaneous – Lymph Node Disease)

If not treated earlier then the condition will be: -

4 yr child

Day 14: MI: Syncope

↓

ECG

↓

Rx

a. No. Percutaneous Coronary Intervention

b. Streptokinase Thrombolysis /Thrombolysis is done

c. IVIG injections

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To prevent above condition :

Echocardiography: Coronary Artery Aneurysm > 1cm

Tab Aspirin + IVIG

Case Scenario

A 5 year child with fever X 4 days is found to have Cervical LN : B/L Strawberry tongue Red.

Rash extremities having Sand paper consistency

Flexural area: - PASTIA lines

SCARLET FEVER = caused by Streptococcus Pyogenes.

PrepLadder

Diagnosis:

Rx : Ampicillin| Amoxicillin

White Strawberry Tongue

That desquamates to

⇩

Kawasaki disease

Red Strawberry tongue

⇩

Scarlet fever

Extra Mile

- **Strawberry nose** – Rhinosporidiosis
- **Strawberry gingiva** – Wegener's granulomatosis/ granulomatosis with in angitis.
- **Strawberry cervix** – Trichomoniasis
- **Strawberry gall bladder** – Cholesterolosis

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Strawberry gall bladder

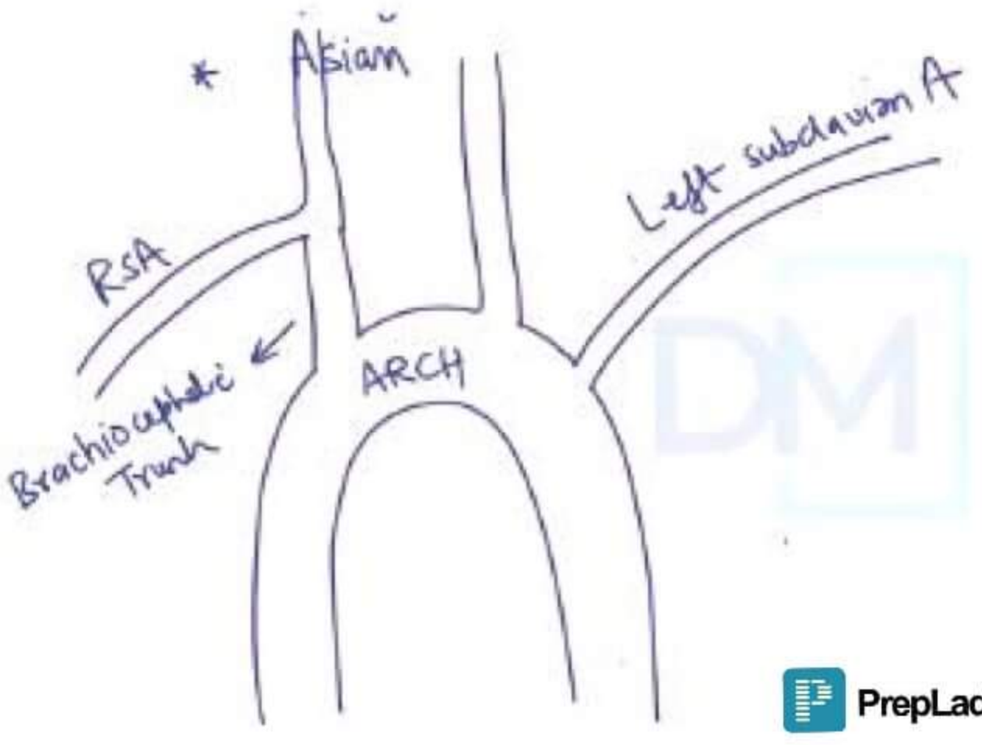
Strawberry cervix

TAKAYASU ARTERITIS /Pulseless disease/ or Non specific arteritis

- Seen in young, Asian population.

C/F :

1. ARM CLAUDICATION (Vascular)
   - MRI spine- normal
2. Unequal B.P in (L) & (R) arm
   - D|D :-
     - **Coarctation of aorta (preductal)**
     - **Obstructive & aorto arteritis**
     - **Supra valvular A.S.**



* In case of COA (post ductal)

- BP of upper limb increased and lower limb is decreased.

3. Renal A. ostial narrowing.

- GFR ↓, RAAS +, RENIN ↑

Cause of Renovascular hypertension :

- Rx :

1. ACE inhibitors / CCB
2. ACE Inhibitors are contra-indicated in B|L RAS
3. Management of B/L RAS : **Percutaneous transluminal renal angioplasty + Stenting**

Note : Most common cause RAS, in 60 years old smoker is Atherosclerosis

Investigation :

IOC : Magnetic resonance angiography.

Rx :- Steroids

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WEGENER GRANULOMATOSIS/GRANULOMATOSIS with ANGITIS

C/F :

Vasculitis of

1. URT= Epistaxis
   (Oral cavity Strawberry gingivitis)
2. LRT= Hemoptysis
   (Cavity formation in lungs)
3. Kidney = Hematuria

IOC: C- ANCA

Rx :

-Cyclophosphamide

Pulmonary A. not involved

Polyarteritis nodosa (PAN):

- necrotizing vasculitis

1) kidney vasculitis leads to hypertension
(Glomerulonephritis)is not a features

2) Skin vasculitis Livedo Reticularis
Hematuria
(fish net app. Of superficial skin BV)

3) Digital circulation - gangrene U|L, B|L
Asymmetrical distribution

4) MI

5) Stroke

Investigations for PAN :-

1) HBs Ag

2) IOC = skin Biopsy

Rx - STEROIDS

PrepLadder

KEY FEATURES OF VASCULITIS:

H.S.P	→ EXTENSOR PURPURA
G.C.A	→ Temporal head ache
Behcet	→ R. aphthous ulcer: Oral cavity + vulva + painful
Takayasu	→ Unequal BP L|R arm, RAS
Granulomatosis with angitis	→ Epistaxis, Hemoptysis, Hematuria
P.A.N	→ Hematuria livedo reticularis + Gangrene +HTN

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PrepLadder

SCLERODERMA

Clinical Features

1. Raynaud's phenomenon

- Fibrosis of skin around digital blood vessels

On Cold exposure → Tip of fingers.

→ Abnormal Vasoconstriction – **White**

→ Deoxy Hb > 4.0 gm % - Blue

→ Abnormal Vasodilation - Red

Raynaud's Disease

↓

Idiopathic Raynaud's Phenomenon

Extra Mile:

On Heat exposure :

- Toes – Red ++ Violet/ purple
- K/A Erythromelalgia and is seen in – Polycythemia Vera

Raynaud's Phenomenon

2. Sclerodactyly
3. Flexion contractures
4. Leather like skin
5. Microstomia
6. Salivary gland fibrosis : Saliva ↓

- Halitosis
- Dysphagia oropharyngeal (chips/ Biscuits)
- Dental caries

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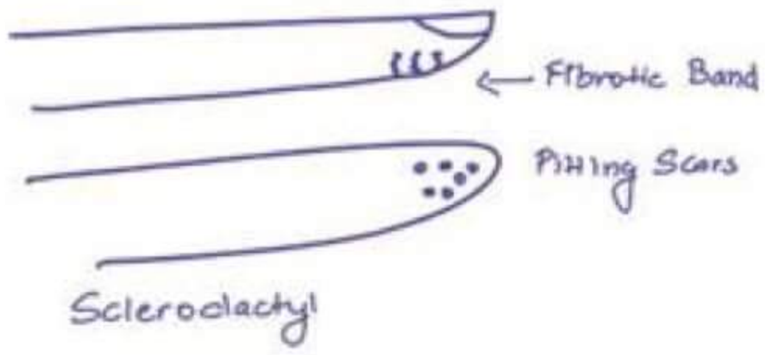

7. Esophageal dysmotility
8. LES fibrosis – Tone↓

- GERD
- Heart burn
- Horse voice
- Nocturnal cough due to chemical tracheitis.

9. Pulmonary Fibrosis –

- Timed vital capacity / Normal/ Increased
- Clubbing
- Pulm. Artery Hypertension: DL co

Extra Mile:

Mc cause of death in Scl– PAH> Pulm. Fibrosis

MC cause of Death SLE- Infection

MC cause of Death in Active SLE: Renal Failure

MC cause of death in RA- Accelerated Atherosclerosis

PrepLadder

10. **Heat- RCM**
    - KUSSMUAL sign ⊕
11. **Kidney – Size ↓ ↓**

Key Points:

♀ ANA+

- Raynaud's phenomenon
- Leather like skin
- HTN
- DLCO ↓

} Systemic Sclerosis

GFR ↓ ↓ ↓
Renin ↑↑↑
Malignant HTN (Scleroderma Crisis)
↓
Rx- Oral ACE inhibitors

HTN crisis in – Stroke → I.V Nicardipine
HTN Crisis in – Sx → I.V. Sodium Nitroprusside
- In Pregnancy/ labor pain – IV labetalol
↑

IOC- Anti-topoisomerase Ab
Rx – Steroids/ Azathioprine

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LIMITED SCLERODERMA

CREST Syndrome

- **C** – Calcinosis
- **R** – Raynaud
- **E** – Esophageal dysmotility
- **S** – Sclerodactyly
- **T** – Telangiectasia
- **IOC** – Anti- centromere Ab

LOCALISED SCLERODERMA

MORPHEA
- Idiopathic Scar formation

Mixed connective tissue disorder

♀ ESR ↑
- Photosensitivity
- Malar Rash
- Raynaud's phenomenon
- Leather like skin
- PIP, MCP, wrist B/L
- These mixed connective Tissue disorder

IOC- U_1 RNP Ab (ribonucleoprotein – Protein antibody)
NOTE : Anti- Ribosomal -P antibody.

PrepLadder

SLE – ANA ⊕

- Anti smith Ab

SLE photosensitivity – Anti Ro Ab

SLE : Neonatal lupus – anti Ro Ab can cause 3rd degree H. Block

SLE Psychosis : anti Ribosomal – P Antibody

SUMMARY :

Generalized scleroderma	Anti Topoisomerase antibody
Limited scleroderma	anti Centromere antibody
MCTD	U1RNP
Sjogren syndrome	Anti Ro and anti La ↓ ↓ SS-A SS-B
Hashimoto thyroiditis	Anti TPO
Graves disease	LATS
PBC	anti mitochondrial Antibody
PSC	p-ANCA
Ulcerative colitis	p-ANCA
Crohn's disease	A.S.C.A

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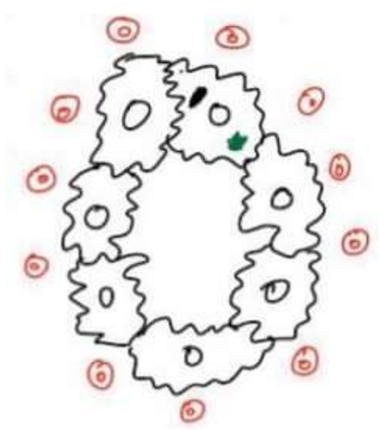
Extra Mile:

- Anti Jo-1/ anti histidyl – tRNA synthetase antibody is commonly seen in anti synthetase syndrome and seen in dermatomyositis
- Gower sign is seen in dermatomyositis due to proximal muscle weakness
- Heliotrope Rash, Gottron Papules, Mechanic Hands are characteristic features of Dermatomyositis

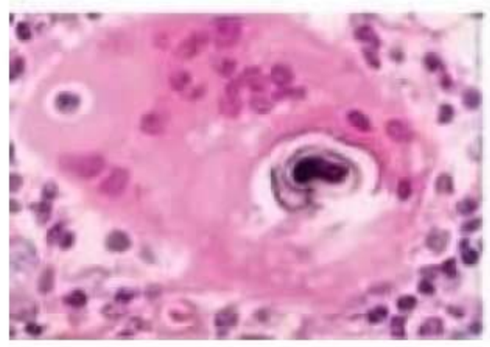
SARCOIDOSIS

- Non caseating granulomas
- MC organ involved – Lung
- LC organ – Heart
- MC cause of Death – Respiratory failure >> Angio-invasive mycetoma
- 50% cases – Spontaneous remission
- Etiology – P. Acnes

- MTB catalase peroxidase mKATG Ag APC
  ↓
  CD_4 cells in LN
  ↙ ↓ ↘
  γ-IFN IL-2
  granuloma (+)



Asteroid Bodies



Schaumann bodies

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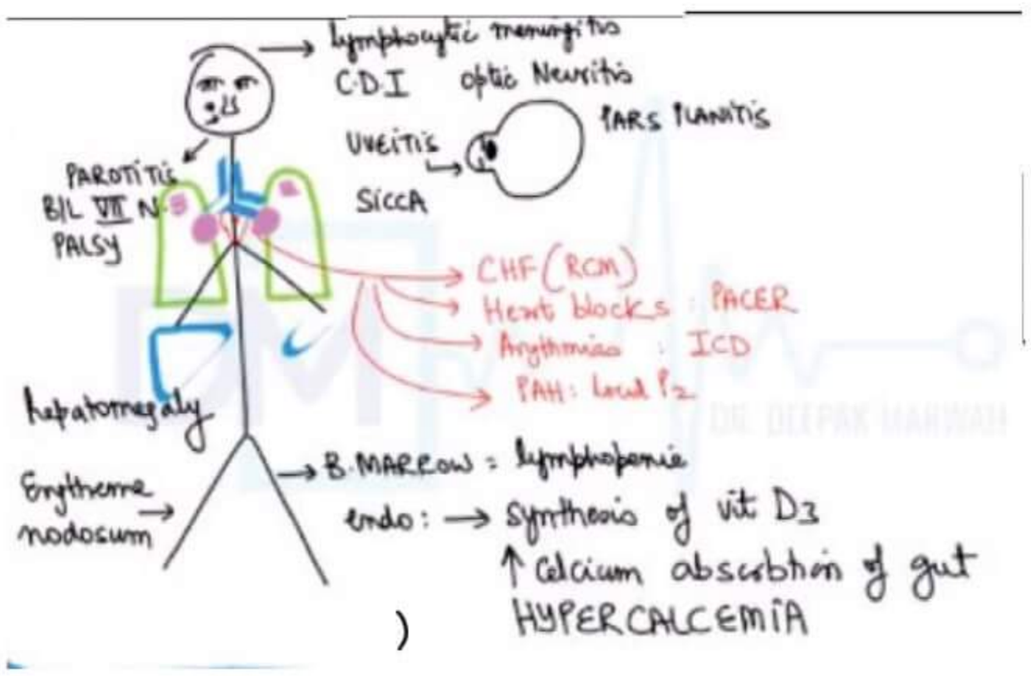
C/F – 1) 35 yrs – cough / dyspnea on exertion / stridor
Dyspnea on Rest

- Night sweats
- Weight loss

2) Lupus pernio – pain less lesion
   - involve – bridge of nose
   - cheeks (no Butterfly appearance)
3) LOFGEN Syndrome
   - Erythema Nodosum
   - Painful
   - EN + B/L hilar LN

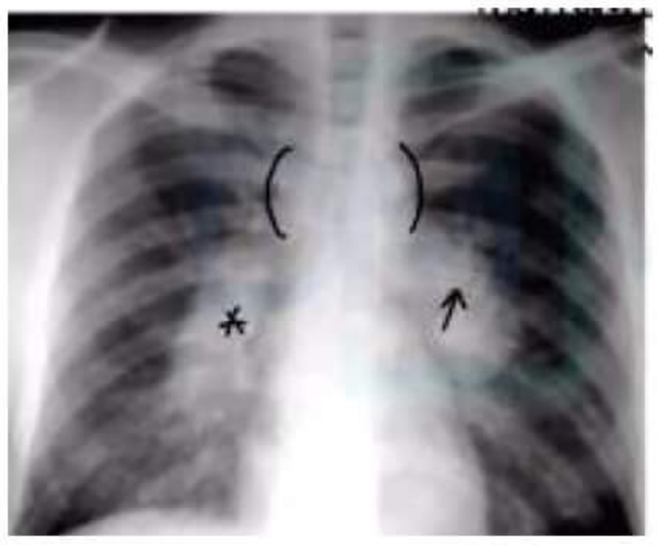
± Arthritis



Work Up->

1. CXR => MC used method to identify lung involvement

   Stage 1 – Hilar LN
   2 – Hilar LN + infiltrates
   3 – Infiltrates
   4 – fibrosis



PrepLadder

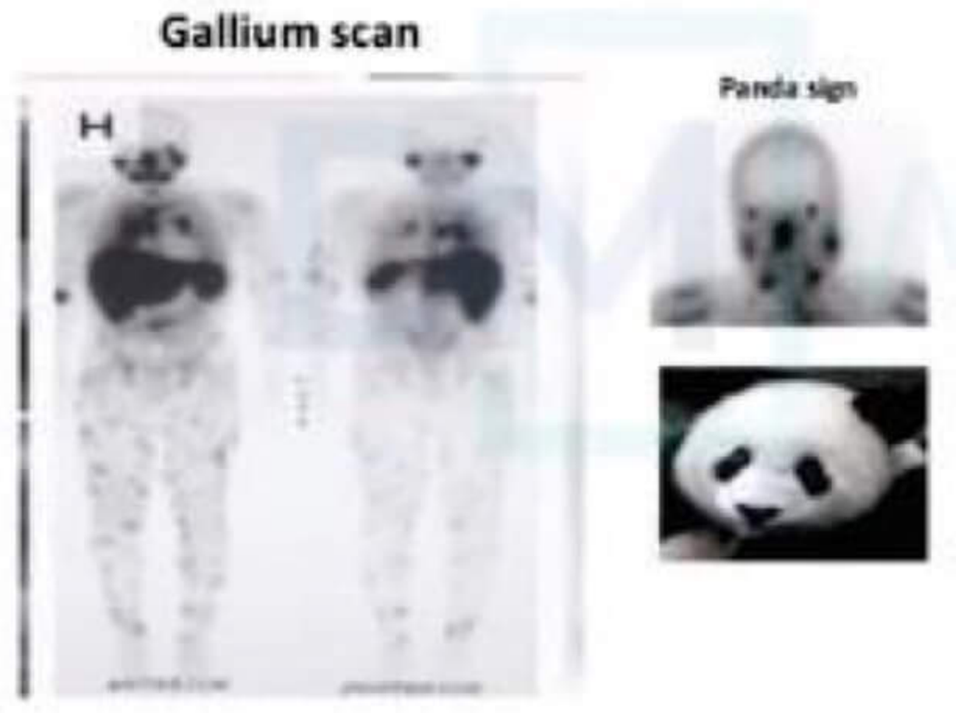
2. **IOC** – Endobronchial USG guider B_x
   - Transbronchial B_x (If Parenchymal involvement)
   - If both then Endobronchial USG guider B_x
3. BAL – (Broncho alveolar lavage lymphocytosis)

   >> CD4 / CD3 > 3.5^{θ}

4. HRCT – galaxy sign
5. DLCO decreased
6. PET scan – extra pulm. Sarcoidosis
7. Cardiac MRI
8. ACE levels increased
   - Mnemonic SGLT
   - Sarcoidosis
   - Gaucher
   - Leprosy
   - TB (Miliary)
9. Gallium Scan 67
10. Kveim test

R_x – **steroids**

- Taper dose < 10mg within 6 months
- Steroids sparing agent → Hydroxy chloroquine
  - MTX
  - Azathioprine
  - Infliximab



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Causes of bilateral facial nerve palsy:

1. Guillain–Barré's syndrome.
2. Bilateral Bulbar/pseudobulbar palsy.
3. Bilateral Bell's palsy.
4. Bilateral parotid infiltration (Mikulicz's syndrome).
5. Bilateral facial muscles weakness (myasthenia gravis; myopathy).
6. Sarcoidosis.
7. Lyme disease.

PrepLadder

ANKYLOSING SPONDYLITIS

- Associated with HLA B27.
- Seen in young males most commonly.

Clinical Features: -

1. Lower back pain despite of taking analgesics for > 3 months, morning stiffness > 30 min.
   Note : morning stiffness also seen RA where small joints are involved.
2. Pain increased with inactivity
3. Alternating buttock pain
4. Neck stiffness
5. Heel pain / enthesopathy → disorder involving insertion of tendons or ligaments in to bone. Usually patient felt pain over calcaneum.

Note : Leading cause of death is **fracture of Rigid osteoporotic spine O/E:**

-

1. Tenderness at Sacroiliac joint and also involve
   - **Sternoclavicular joint**
   - **Spinous process of Vertebra**
   - **Tibial tuberosity**
2. Buttock atrophy
3. Modified Schober test **< 4 cm**

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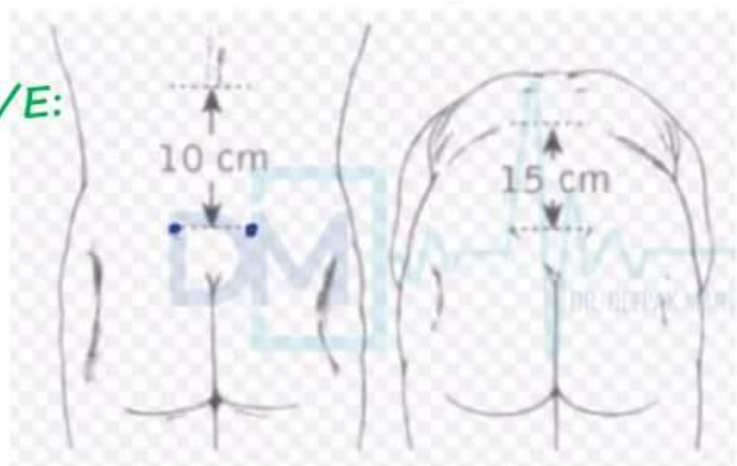
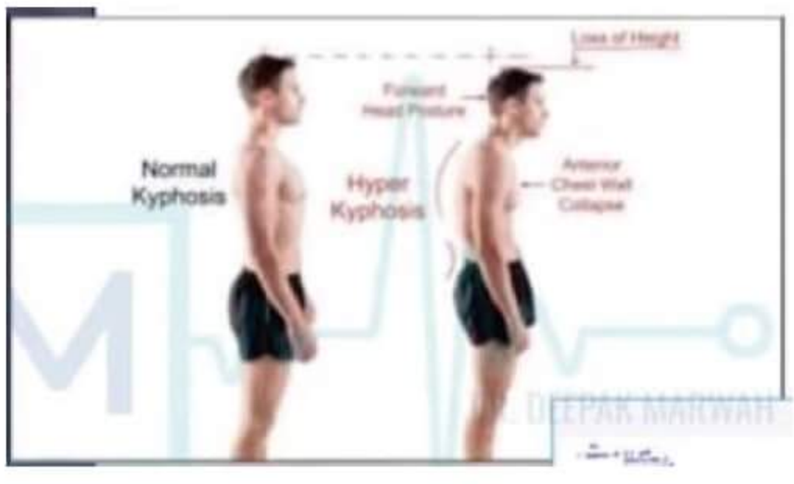


Modified Schober test

- Draw a line between posterior superior iliac spine of both sides then Using measuring tape and marking the line superiorly on spine by approximately 10 cm from intersection of both psis.
  So when asked the patient to bend forward the lines separated more than 15 cm. but in ankylosing spondylitis lines doesn't separate more than 14 cm. (14 -10 = 4)

4. Hyper kyphosis of thoracic spine-decrease height
5. Chest expansion < 5 cm
6. Spondyloarthropathy (SPA): spine ache

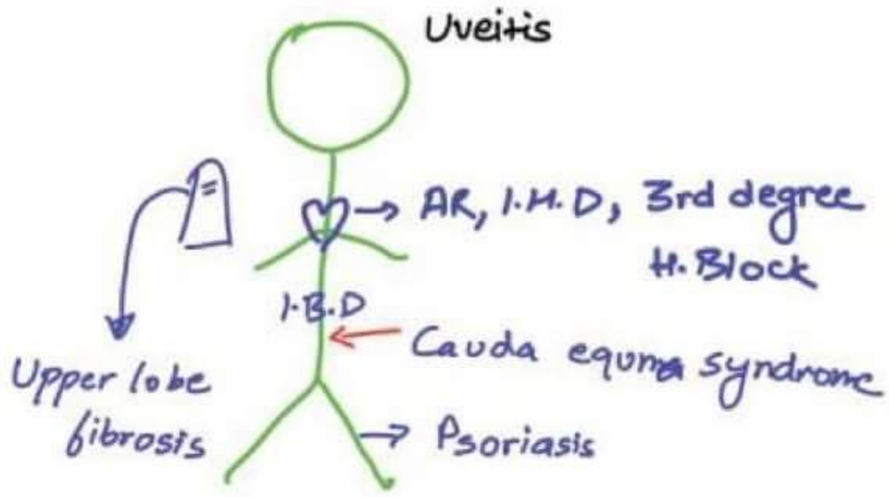


Mneumonic for features of SPA :
SPINE- ACHE

- Sausage digits
- Psoriasis
- Inflammatory back pain
- NSAIDS responsive

PrepLadder

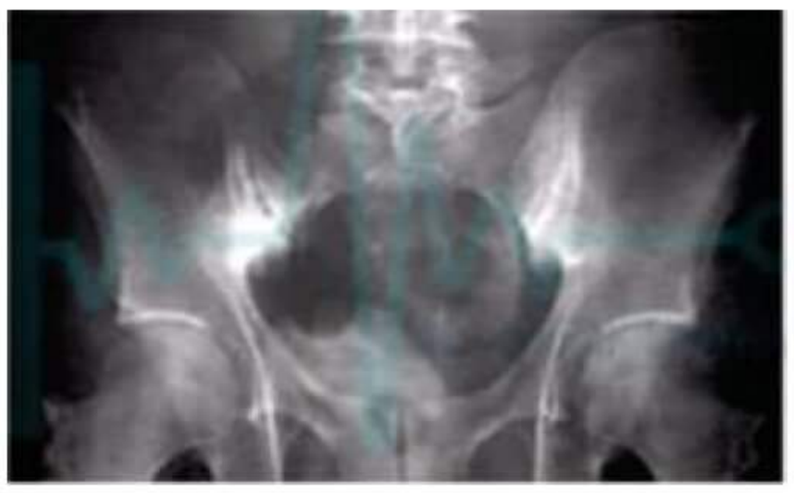
- Enthesopathy
- Arthritis
- Crohn/UC
- HLA B_{27} +
- Eye: uveitis – **MC extra- articular manifestation of ankylosing spondylitis**



- ➢ MC cause of death in AS: fracture of rigid osteoporotic spine > A.R
- ➢ MC valve involvement in spondylitis patient – Aortic valve (aortic regurgitation)
- These patient also have IHD and 3rd degree heart block.
- ➢ Upper lobe fibrosis are seen in this patient.
- ➢ Spinal cord involvement manifest as Cauda equina syndrome.

Work Up:-

1. X –Ray → LS spine
   - Dagger sign will be seen
2. MRI spine: (Most preferred method)
   - Bone marrow edema (early manifestation)
   - Bone marrow inflammation
   - B/L sacroiliitis
3. Serum matrix metalloproteinase 3: disease activity
4. ESR, CRP, SAP, IgA↑.



Sacroiliitis

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Bamboo spine-Dagger sign

Algorithm for diagnosis → 1. sacroiliitis on MRI + 1 SPA feature

1. HLA B_{27} + 2 SPA feature

Rx: –

1.NSAIDS – 1st line management.

2. Sulphasalazine for Peripheral arthritis

If BASDAI >4 in spite of 2 NSAIDS used.

↓

3. Infliximab
   - Contraindicated in malignancy, SLE.
4. MTX, gold salts, steroids: no role

IgG_4 RELATED DISEASE

* Tendency to form tumefactive lesions

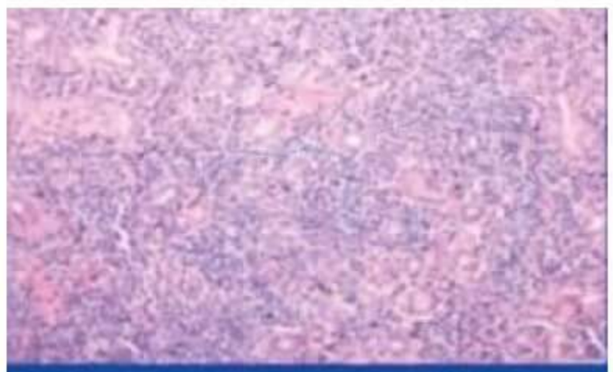
Involves -> * Salivary / lacrimal gland

* Biliary tree

* Lung

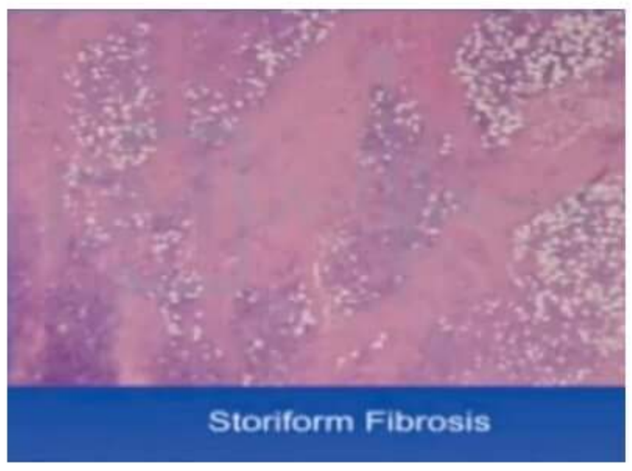
MICULICZ Syndrome = Subtype of Sjogren with parotid enlargement

Ormond Syndrome = Idiopathic Retroperitoneal fibrosis


Dense Lymphoplasmacytic Infiltrate

On Histopathology :-

1. Infiltration of Ig G_4 plasma cell in to salivary gland
2. Storiform fibrosis
3. Obliterative phlebitis


Storiform Fibrosis

Clinical Features :

1. Middle age Male
2. Isolated submandibular enlargement / orbital pseudotumor.
3. Allergic rhinitis, nasal polyps
4. Lungs : Pseudotumor
5. Riedel's thyroiditis
6. Retroperitoneal fibrosis
7. Autoimmune pancreatitis **(Sausage shaped pancreas)**
8. Aortitis

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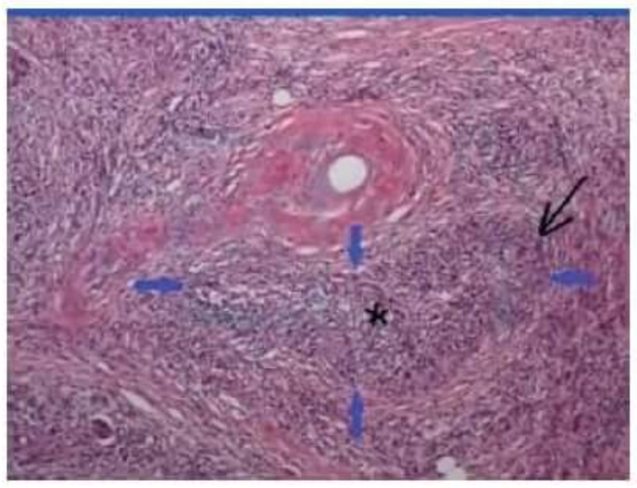
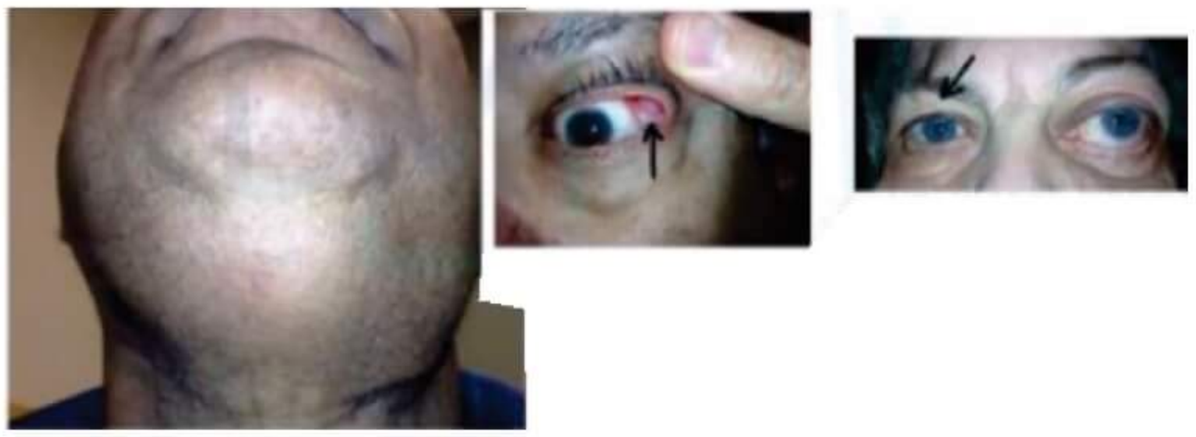

Obliterative phlebitis

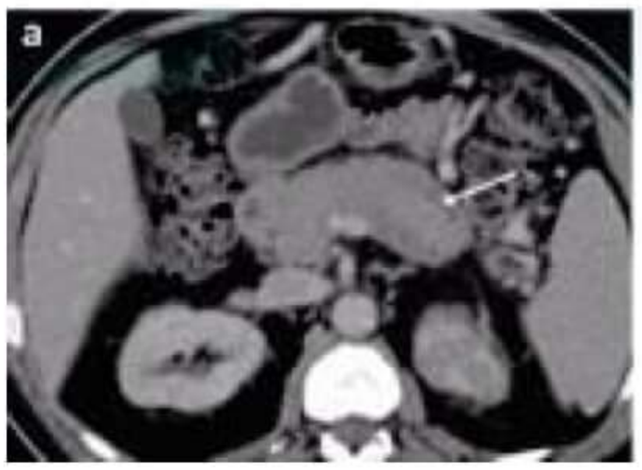


Work-up

1. Whole body PET scan
2. IgG_4 levels increased up to 40 times (normal 2.4 -120 mg/dl)
3. Biopsy
4. ERCP
5. CT abdomen

D_x- Biopsy (**IOC**)

R_x- Steroids / Rituximab.


Sausage shaped pancreas

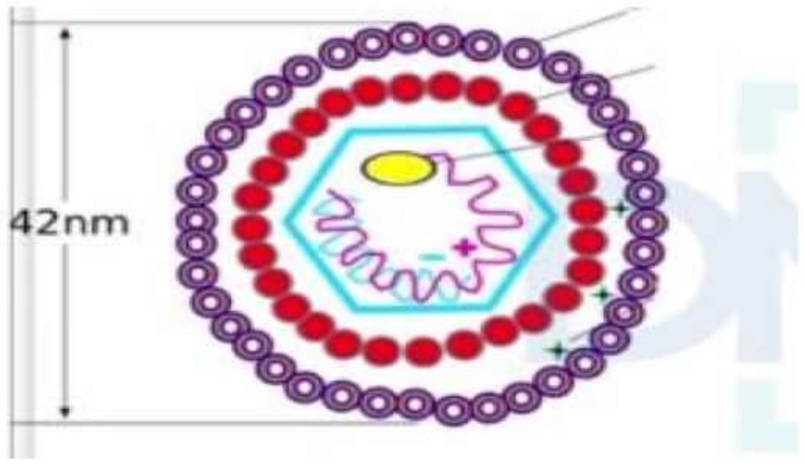
Pseudotumor

PrepLadder

Hepatitis – B

- Leading cause of transfusion associated hepatitis = Hepatitis B

- On electron microscopy view virus is either spherical or tubular in shape



- **HBsAg**: surface antigen
- **HBcAg**: Core antigen → Found in nucleus of hepatocytes but never found in blood howeverantibody to it is seen in blood
- **HBV DNA**
- **HBeAg**: Marker for replication/infectivity of virus
- **Pre- core mutant** = HBeAg absent
  - More severe
  - Replication not detected routinely
  - Seen in Russia and Central Europe (Russian Virus> Indian V)

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Genome = partially Ss and partially Ds circular DNA (3.2 kb) - Double shelled virion and the usual size is 42nm

- Route of transmission: -

1. M/c - Percutaneous route: Sexual transmission
2. Blood transfusion

Note:-Hep B usually recovers (90%) even without any medications → due to seroconversion and medication is only given in chronic phase not given in patients of Acute Hep-B.

- Blood is tested for: -
  - **HBV** (HBsAg = Australian antigen)
  - **HCV** (EIA - anti HCV antibody, PCR HCV RNA)
  - **HIV** (ELISA HIV, **PCR HIV→ for earlier identification of disease esp. in window period**)
  - **Syphilis** (FTA- ABS), **VDRL for Neurosyphilis and Vertical transmission**
  - Malaria (HRP -2 dipstick test)

3. **Vertical transmission**- mother to baby

PrepLadder

Case scenario:-Commercial sex worker in 3rd trimester of pregnancyand her test report as: -

HBsAg⊕HBeAg⊕

Mother

↓ 90% chance

Baby

Rx → HBIg I/M to be given asap within <12 hours (To the child)

+

Hepatitis B vaccine – 3 doses (0, 6, 10/ 14 wks.)

4. **Accidental needle stick injury**
   - Occurs mostly while recapping of needle.
   - Chance of transmission = 30%
   - Conjunctival inoculation → due to splattering of blood on face while handling trauma patient- risk of infection present
   - Rx→ HBIg I/M ASAP (within 6 hrs.)

- **Serum markers: -**

1. **HBsAg**
   - 1st to appear - 1-12 wks. of infection
   - Earliest serological evidence of hepatitis-B infection
   - Precedes SGPT ↑ = 2-6 wk
   - Sequence of appearance:

     HBsAg positive →SGPT ↑ → jaundice → disappear in reverse direction

2. **HBcAg** → Never appears in blood
3. **HBeAg** → Replication/ infectivity of virus
4. **HBxAg** → CD 95 inhibitor → inhibit extrinsic pathway of apoptosis

↓

Trigger development of hepatocellular carcinoma (HBV >HCV)

5. **PCR HBV DNA** → Quantify the viral load

Case scenario: pt. is diagnosed case of Hep. B and HBeAg: reactive and viral load is >2 x 10^4 IU/ml with raised SGPT 2x.

RX → Tenofovir (DOC) / Entecavir

→ Pegylated interferon + Lamivudine

- **Antibodies against Hep B: -**

1. **Anti HBsAg** → Protective antibody
2. **Anti HBcAg**

   IgM = **Acute viral hepatitis** and Ab present in **Gap period**/Window period.

   IgG = Chronic hepatitis
3. **Anti HBeAg** → Replication rate reduce & Infectivity reduces

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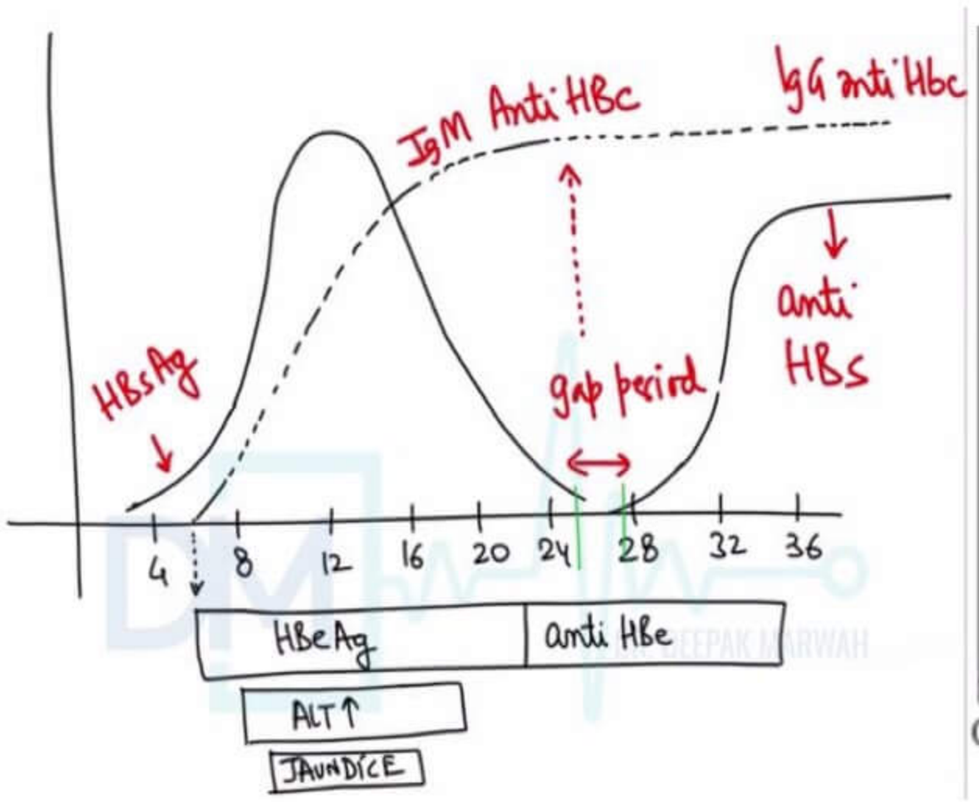
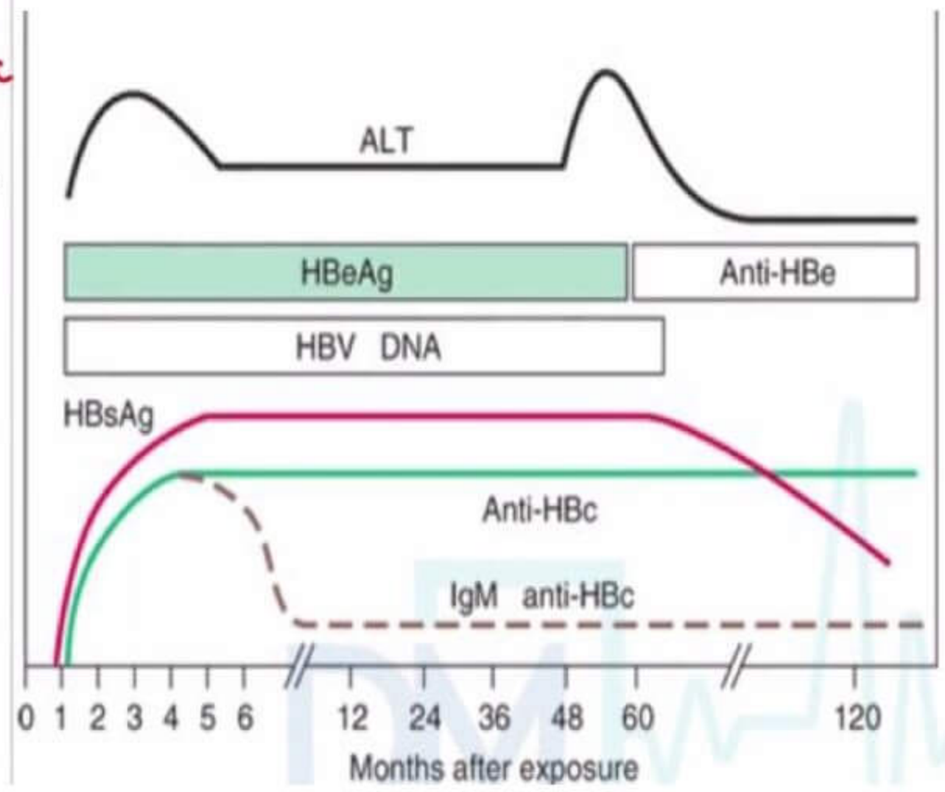
Note:- Jaundice will appear at last and is the first to disappear.

HBeAg → anti HBe → ALT ↑↑ → Jaundice (but first to disappear)





Above diagram shows chronic hepatitis B which leads to cirrhosis and ultimately develop End Stage Liver Disease.

Case Scenario – 22 yr male comes with nausea, vomiting and aversion to smoking (change in olfaction and taste). Low grade fever present with right upper quadrant discomfort for past one week.

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O/E → Icterus+/Jaundice + → S.Bil > 2mg%

Frenulum → Sclera(High conc of Elastin that binds with bilirubin) is yellow

Tender hepatomegaly

No ascites

No caput medusae

No pedal edema

D/d is β Carotenemia → Yellow skin but sclera is normal

Work –up of patient

1. **LFT =** S. bilirubin ↑ (unconjugated)
   SGOT ↑
   SGPT ↑↑
   S. alkaline phosphatase normal

} **Seen in Hepatocellular jaundice.**

In obstructive jaundice: –

S. bilirubin ↑ (conjugated)
SGOT normal
SGPT normal
S. alkaline phosphatase ↑↑↑↑

In hemolytic jaundice: –

S. bilirubin ↑ (unconjugated)
SGOT normal
SGPT normal
S. alkaline phosphatase normal and Splenomegaly can also be seen

PrepLadder

2. **USG** → to check echo texture and span to liver

If on USG report came → **STARRY SKY LIVER** and Liver span ↑↑ → seen in Viral hepatitis

3. **Simplified diagnostic algorithm for finding etiology of acute viral hepatitis**

Condition	HBsAg	IgM anti HAV	IgM HBc	Anti HCV
Acute Hep B	+	–	+	–
Acute Hep A	–	+	–	–
Acute Hep C	–	–	–	+
Non-A Non-B Non-C	–	–	–	–

Note:- Non-A, Non-B, Non-C'' infection means it is either due to Hep-D or E. As in India Hep E is more common due to feco-oral contamination.

Treatment: -

Acute Hep B →

- Bed rest
- Rx – "**Itopride/Mosapride**" for Nausea
- I/v fluids (10% dextrose or NS)
- Monitoring

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HBsAg	Anti HBs	Anti HBc	HBE Ag	
+	–	IgM	+	**Acute Hep B Highly infectious**
+	–	IgG	+	**Chronic Hep B**
–	+	IgG	–	**Recovery**
–	–	IgM	–	**Gap period**
–	+	–	–	**Vaccinated**
–	–	IgG	–	**Low level carrier/ remote infection**

Notes: -

- HBs Ag⊕ + IgM anti HBc = **Acute Hep B**
- HBs Ag⊕ + IgG anti HBc = **Chronic Hep B**
- IgM anti HBc⊕ = **Gap period**
- Anti HbsAg = **Vaccination**
- IgG anti HBcAg =
    1. Low level carrier
    2. Remote infection

Treatment: -

- **Chronic Hep B**
    - HBeAg = Reactivity
    - PCR HBV DNA = >2 x 10^4 IU/ml + SGPT X 2 times

PrepLadder

- **Compensated cirrhosis patients**

  HBeAg = Reactivity

  PCR HCV DNA = 2 x 10^3 IU/ml + SGPT raised

  DOC = Tenofovir (300 mg OD x 48 weeks) or Entecavir

Escape mutant = Virus will not be inactivated by anti HBs.

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PrepLadder

HEPATITIS C, D AND FULMINANT HEPATITIS

Hepatitis C-

- **Most common cause of Transmission is Parenteral**
  IV drug abusers (IVDA) > B.T (Blood transfusion)
- 90% cases of hepatitis C develops Chronic hepatitis

  ↓

  Activation of stellate cells

  ↓

  Cirrhosis- E.S.L.D (end stage liver disease)

  ↓

  Liver Transplant- MC cause for liver transplant in world is HCV induced cirrhosis.

- **IOC** =E.I.A (enzyme immunoassay)anti HCV antibody
- **PCR HCV RNA**: "no cut off" for management of patient
- Treatment based on Genotype
  Genotype 1: **DOC- Ledipasvir**
  Genotype 2: **Sofosbuvir + Ribavirin**

Note:- Pegylated interferon + Ribavirin; in older mcq

Hepatitis D - Delta:

Weak virus→ for Eradication: 100% coverage of population with HBV vaccine should be done
Route of spread:- Parenteral

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Case-IV drug abuser with HBsAg +. also, IgManti HBcAg + in oct 2018. He had to shift his workplace due to police patrolling. While taking IV drugs he got delta virus in his body in nov 2018. IgM anti HDV Ag +

IgM anti HBcAg + IgM anti HDV Ag = **Co-Infection**

Acute Hep B Acute Hep D

Oct 2018 Nov 2018

Case- IV drug abuser with HBsAg +. also, IgG anti HBcAg + in oct 2018. He had to shift his place due to police patrolling. He got hepatitis D in nov 2018. IgM anti HDV Ag +

IgG anti HBcAg + IgM anti HDV Ag = **Superinfection**

Chronic Hep B **Acute Hep D**

↓

Fulminant hepatitis

- DOC -
  Hep D =α Interferon
  Hep B = Entecavir/Tenofovir
  Hep C = Ledipasvir
  Hep D = α Interferon

PrepLadder

Extra Mile

- Mc cause of acute viral hepatitis = Hepatitis – E
- Mc cause of fulminant hepatic failure (FHF) = Hepatitis – D(20%)
- Mc cause of FHF in pregnancy = HEV

Fulminant hepatic failure

CAUSE: **Toxins** > **Viral hepatitis**, Hep. D, Hep. E(pregnancy)

↓

- PCM toxicity
- Amanita (Mushroom) poisoning
- Halothane
- A.T.T =Pyrazinamide

Cut off: < 8 weeks of liver insult, development of

- Encephalopathy
- Coagulopathy

Sub fulminant: cut off: 8 -26 weeks

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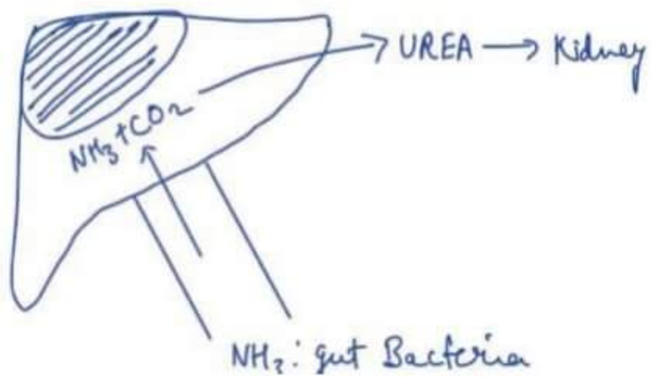
Features of Fulminant hepatic failure-

1. Jaundice = worsen; high affinity in sclera;
   Elastin-Bilirubin

2. Bleeding + = all clotting factors produce in liver
   except - Factor VIII: endothelial cell, Factor IV: calcium- Epistaxis

3. Ammonia intoxication=
   $NH_3 + CO_2$ ⟶ urea ⟶ excreated by kidney
   Ammonia ↑↑ ⟶ Encephalopathy:
   Earlist manifestation of encephalopathy:
   a. Alteration of sleep – awake cycle
   b. Euphoria, slurring of voice
   c. Most Reliable sign:- Asterixis
   d. Number connection test(Constructional apraxia)
   e. Anomic aphasia difficulty in naming an object
   f. Stupor-coma GCS<8



Asterixis/ Flapping Tremors

PrepLadder

Work-up of FHF-

1. **IOC** - Blood ammonia levels
2. **LFT**: SGOT ↑ / SGPT ↑
3. Coagulogram -

	EARLY	LATE
BT	N	N
PT	↑	↑
APTT	N	↑

Factor 7 has shortest t½, PT is the first to get deranged

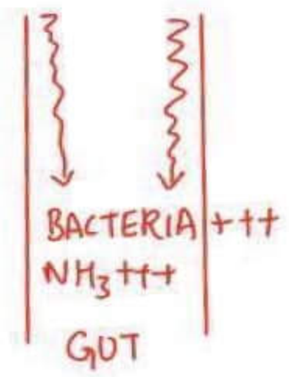
Note:- Internal GI bleeding can worsen hepatic encephalopathy Thus, stabilizing coagulogram is imp.

4. Blood sugar ↓
5. S. Creatinine ↑
6. EEG= Triphasic waves and delta waves (Metabolic encephalopathy)

   In **ECG = WPW**

   EEG = NREM 3

   Discharge frequency of delta waves is 0.5 – 4 Hz



Rx:

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1. **DOC** - Lactulose: Nasogastric tube (Ammonia binder)
2. Rifaximin / Neomycin: NG tube(Bacteriostatic)
3. Enema
4. F.F.P (vit. K is not recommended)
5. IV 10% glucose
6. IV L.O.L.A (L-ornithine -L-aspartate)
7. MARS: Liver dialysis (molecular absorbent re-circulating system)
8. Care of bowel /back/bladder for a comatose patient.

MELD Score: Used to register patient for liver Transplantation

1. Bilirubin
2. I.N.R
3. S. Creatinine

If MELD score > 17: Orthoptic liver Tx

In Orthoptic liver Tx – HLA matching is not mandatory for Cornea, Heart and liver transplantation

Discriminant function score: - Used for alcoholic's hepatitis severity

1. S. bilirubin
2. INR> x seconds above normal

   If discriminant function score >32, it is indication for treatment

Rx: Steroids or Pentoxifylline

PrepLadder

Scores	Decision making Tool for
NAZER index	→ Wilson – for liver Tx
MELD:	→ FHF for Liver Tx
Discriminant function	→ Alcoholic hepatitis for severity of ds
Child – Pugh	→ Cirrhosis for severity of ds and need for Liver Transplantation.

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PrepLadder

HEPATORENAL SYNDROME & HEPATOPULMONARY SYNDROME

Hepatorenal syndrome

- Which happens to be complication of Decompensated cirrhosis.
- Characterized by oliguria/ anuria in a patient with liver failure which is primarily because of toxins and due to imbalance between vasoconstriction and vasodilatation mechanisms in the body
- **Incidence:** 40% of cirrhosis patient with refractory Ascites
- **HPE:** On light Microscopy: Kidney parenchyma (n)
- **On Orthoptic Liver Transplant (OLT):** Restoration of function of kidney

Refractory Ascites

Ascites persisting patient even after optimal Mx of ascites are vulnerable to develop hepatorenal syndrome

Ascites management. :

1. Salt restricted diet/ Salt intake: up to 2 mg/day
2. Diuretics: Spironolactone: 400-600 mg
3. Loop diuretics: Furosemide: 120- 160 mg/day

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Case Scenario

Patient with refractory Ascites, alcoholic/ nonalcoholic, malnourished, everted umbilicus with umbilical hernia, bowel loops floating in massive ascites fluid.

→ **Plan:** Large volume paracentesis with Salt free albumin infusion before the procedure.

→ **Problem:** Ascites patient given less priority, Ascites → massive ascites → infected & spontaneous bacteria peritonitis meanwhile E. coli in bowel loops exhibit Translocation → into mesenteric lymph node → reach ascitic fluid → Pus in ascitic fluid → infection → Systemic inflammatory response in patient.

↓

S.I.R.S, septic shock → compromise renal function (as shock ↓ perfusion of kidney)

→ **Best drug for spontaneous Bacterial Peritonitis:** Cefotaxime

→ **Spontaneous Bacterial peritonitis** has single organism isolated from peritoneal fluid. If the peritonitis is due to 2-3 organism isolated from peritoneal fluid then it is mostly due to perforation of intestine.

PrepLadder

C/F:

1. Fever, tachypnea, tachycardia, Leukocytosis, altered sensorium [in case of septic shock]

2. S. Creatinine ↑ > 1.5 mg% (d/t renal failure)
   or
   ↑ 0.3 mg% Rise in 6 hrs

→ **Indicates Patient has entered Acute kidney injury &**
&Urine output< 0.5 ml/ kg/hr gone into Hepatorenal syndrome

HRS is a complex interplay of:

→ Renal vasoconstriction ↑ and Systemic vascular resistance ↓ - Leads to under perfusion of kidney

(n) PGs Basic function: Responsible for Renal vasodilation (its Best way of ↑ Blood flow to any organ)

↑ Urinary loss of PG occurs in HRS → no vasodilation & ↑ vasoconstriction

Cirrhosis → Causes over production of NO → responsible for ↓ SVR
↓
Blood diverted away from kidney.
↓
Less Blood supply to kidney
↓
Contributing to HRS

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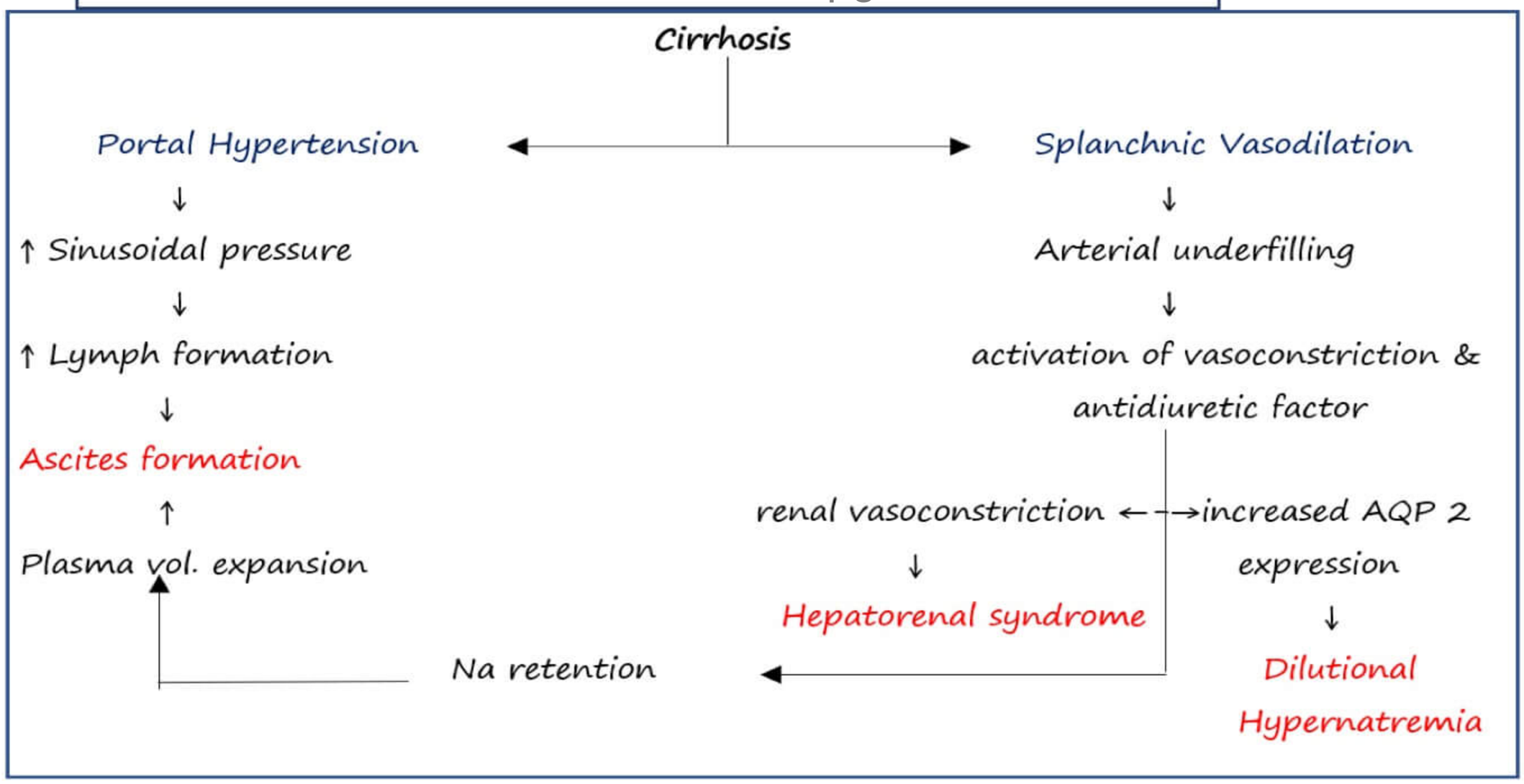

Type I HRS

Ascites
↓
Massive refractory ascites → SBP(Spontaneous bacterial peritonitis) → Septic Shock → Die in 2-10 weeks.

PrepLadder

Type II HRS

- Survival rate: approx. 3-6 months,
- Progresses comparatively slower
- SBP +/-
- In 25% cases no SBP.
- It is d/t imbalance between vasoconstriction & vasodilation resulting in under perfusion of kidney → Uremia

C/F

1. Palmar Erythema
2. Leukonychia
3. Asterixis [Most reliable sign of Metabolic encephalopathy]
4. Clubbing
5. Spider naevi [over d/t overexposure of estrogen found in SVC distribution in Head, Neck, Chest]
6. Xanthelasma [observed in eye skin fold]
7. Fetor hepaticus [Smell of mercaptan & ammonia]
8. Caput medusae [dilation of portosystemic collaterals, flow is away from umbilicus]

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Diagnosis

Major criteria

1. Low GRF, as indicated by serum creatinine greater than 1.5 mg/dl or 24 hr creatinine clearance lower than 40 ml/min.
2. Absence of shock, ongoing bacterial infection, fluid losses & current treatment with nephrotoxic drugs.
3. No sustained improvement in renal function (decrease in serum creatinine to 1.5 mg/dl or less or increase in creatinine clearance to 40 ml/min or more) following diuretic withdrawal, and expansion vol. with 1.5 l of a plasma expander
4. Proteinuria lower than 500 mg/day & no ultrasonographic evidence of obstructive uropathy & parenchymal renal disease

PrepLadder

Additional criteria

1. Urine volume lower than 500 ml/day
2. Urine sodium lower than 10 mmol/l

} Prerenal cause of AKI

3. Urine osmolality greater than plasma osmolality
4. Urine RBC less than 50 per high power field.
5. Serum sodium conc. lower than 130 mmol/L.

Note:- HRS is a diagnosis of exclusion and all the major criteria should be present for diagnosis of HRS. Additional criteria are not necessary for diagnosis but they provide supportive evidence

WORK UP

1. **Low GFR**
   - S creatinine ↑ > 1.5 mg
   - Creatinine clearance < 40 ml/min.

   To demonstrate low GFR

   Central line & also put in Foley catheter
2. Give 1.5 litre NS: Plasma vol. expansion

   No change in urine output
3. No fluid loss, shock
4. Proteinuria < 500 mg/ day
5. USG no parenchymal change & No obstructive Uropathy

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Q **Chronic Liver Ds.** Patient had massive GI bleeding f/b renal failure U.O = 100 ml/12 hr.
Urine sodium = 50 [Elevated]
Dx: Acute Tubular Necrosis

Rx of Choice: Orthoptic Liver Transplantation

Earlier Dopamine → Vasodilation of kidney vessel
&
PGs infusion were used

} Failure of this approach

Drugs: Midodrine + Octreotide

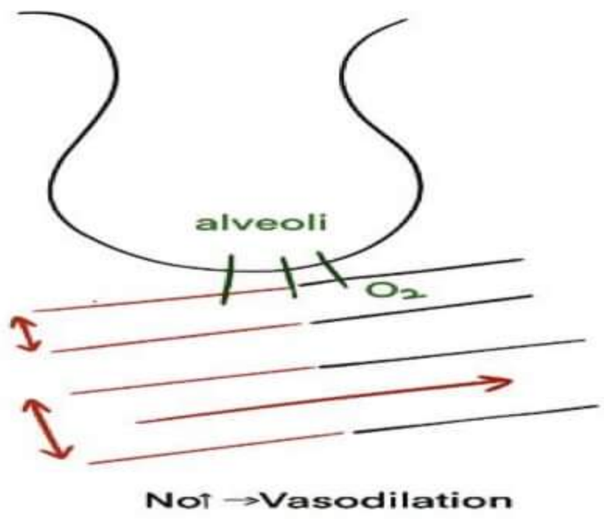
MOA: Vasoconstriction of splanchnic vessel facilitates better renal blood flow

PrepLadder

Hepatopulmonary syndrome

Damaged cirrhotic liver produces a lot of NO. NO causes increase in blood vessel caliber, and the blood travels faster across the vessel without being Oxygenated → RBC inside blood vessel will not be oxygenated and the perfusion of lung starts increasing.

→ Therefore, change in V/Q - ventilation/ perfusion ratio occurs → shunting in lungs of pt. → Responsible for desaturation → Hypoxia → Vicious cycle where d/t Hypoxia liver again starts producing NO → resulting in V/P (Ventilation/perfusion) imbalance



Note:- (N) V/P ratio → 3.5L/4.2 L = 0.8

In HPS, $\frac{V}{P\uparrow}$ = so V/P Ratio decreases.

Manifestation of HPS

1. Platypnea
2. Orthodeoxia

→ **Platypnea:** Dyspnea in sitting position and is relieved on lying down

→ **Orthodeoxia:** Decrease in the arterial oxygen tension (by > 4 mmHg) or arterial oxyhemoglobin desaturation (by > 5%) when the patient moves from a supine to an upright position, which is improved by returning to the recumbentposition

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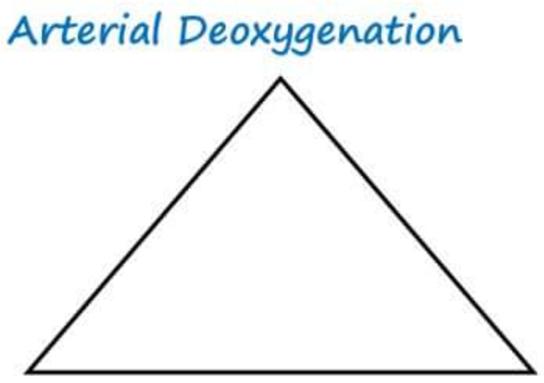
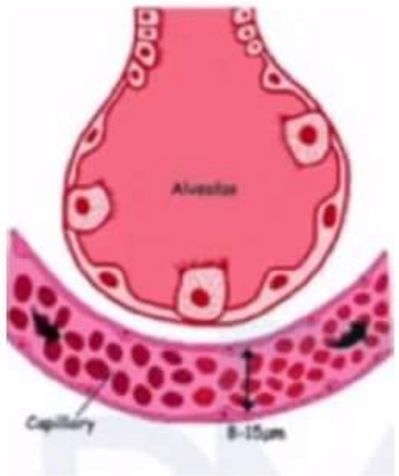
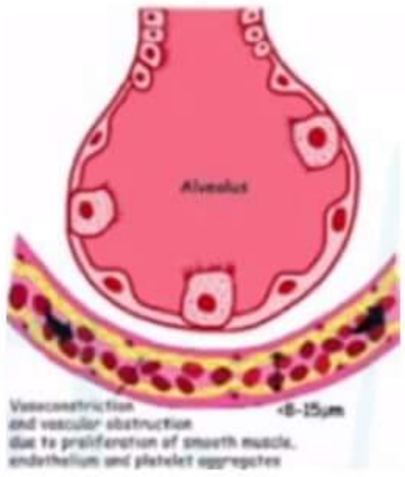
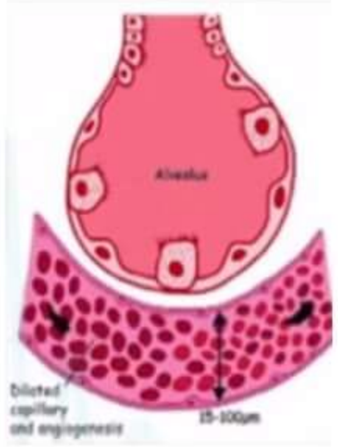
Triad for HPS



Normal	Porto-pulmonary Hypertension (POPH)	Hepatopulmonary syndrome (HPS)
		

→ **Orthopnea:** Dyspnea increase in supine position → In CHF

→ **Trepepnea:** Dyspnea increase in lateral decubitus position

↓

Massive U/L pleural effusion (mc d/t malignancy)

PrepLadder

Causes of platypnea - Orthodeoxia

Cardiac disease - Associated with atrial septal defect (ASD)

→ Interatrial septum aneurism

→ Severe kyphosis

→ Atrial myxoma

→ Aneurysms of the ascending aorta

→ After to pneumonectomy

→ Constrictive pericarditis/pericardial effusion

Pulmonary disease

→ Vascular

Hepatopulmonary syndrome (HPS):

→ Liver cirrhosis

→ Portal hypertension non cirrhosis

→ Fulminant hepatitis

→ Rejection after liver transplantation

Pulmonary arteriovenous malformations

→ Parenchymal lung diseases

→ Pulmonary emphysema

→ Interstitial lung disease (ILD)

Respiratory distress syndrome

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→ Obstructive

→ Larynx cancer

→ Lung cancer

IOC:- Bubble contrast Echocardiography

Technical in puts into this procedure → Push agitated saline → Right chamber of via antecubital vein risk of air embolism absent as amount of air entering heart is miniscule but it will help pick up any shunt in heart, also help known if any shunt in lung that is there is faster traversing across pulmonary vasculature

So we can simultaneously use doppler to measure speed with which blood is moving across lung vasculature and identify arteriovenous shunting occurring in lungs of patient.

Normal Heart

→ Opacification on right side of heart → d/t air going into right side and bubbles of air escaping on left side can also be seen.

Amount of bubbles escaped in left side of Heart have dramatically increased compared to earlier d/t shunting from right → left atria due to patient fossa ovalis.

Rx: Orthoptic liver transplant

For survival:- Positive pressure ventilation.

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PrepLadder

AUTOIMMUNE HEPATITIS

Aka Lupoid Hepatitis /Plasma Cell Hepatitis

- Untreated autoimmune hepatitis → mortality rate of 6 months is 40% (high)

Pathophysiology:

- Cell mediated damage to liver parenchyma
- Cause
  - Idiopathic
  - Loss of immunological tolerance to self-liver Ag's.

  It is T8 cell mediated attack on liver antigens directly.

Triggers/ Conditions A/W:

- HAV, HBV, HCV
- Drugs: minocycline (used in Rx of acne)

- Autoimmune as associated with routine autoimmune disorders like:

  → Hashimoto's thyroiditis

  → Celiac spruce

  → Ulcerative colitis

  → Membranoproliferative Glomerulonephritis

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Type 1 Autoimmune Hepatitis	Type 2 Autoimmune hepatitis
- Young ♀ - Ethnicity: North America - Ab: a/w ANA⊕ (which is also seen in SLE, so it's aka lupoid hepatitis) - Anti SMA (actin) - Anti-soluble liver antigen - Atypical p-ANCA (x-ANCA) HLA a/w - HLA DR3 - HLA DR4	- More common with children - Mediterranean / central Europe - ANA absent - Anti LKM_1 {can contribute to false Δ_x of Hep C} To confirm:- Hep. C Δx:- EIA/ELISA + PCR for HCV RNA - Anti-liver cytosol – 1 Ab - HLA DR B_1 - HLA DQ B_8

PrepLadder

Note:

- **x-ANCA** – Autoimmune Hepatitis
- **c-ANCA** – Wegener`s Granulomatosis
- **p-ANCA** – Microscopic polyangiitis
  - Churg Strauss

Antibodies association with infections:

Anti LKM1 : HCV

Anti LKM2: Drug induced

Anti LKM3: HDV

Clinical feature:

1. Initially – asymptomatic

   On Routine LFT → SGPT↑
2. Symptomatic – Non-specific symptom
   - Fatigue
   - Anorexia
   - Acne
   - Amenorrhea
3. Jaundice (waxing & waning course)
4. SICCA syndrome (Dry eyes & mouth)
5. Erythema nodosum
6. Cirrhosis (decompensated: Ascites, pedal edema)
7. Incidence of HCC isincreased

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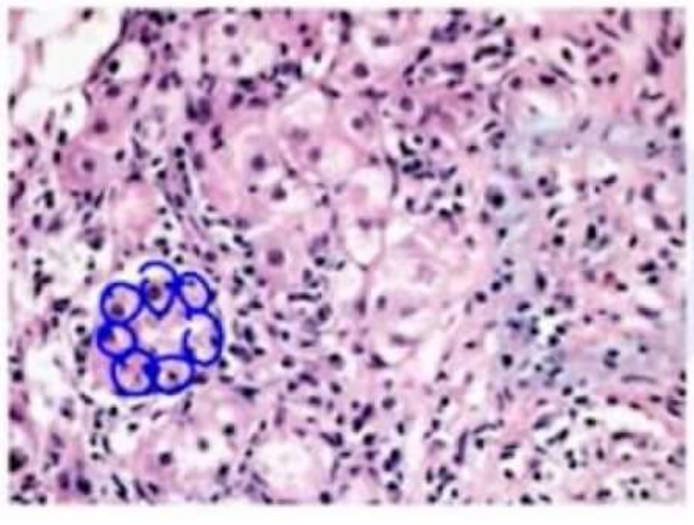
Work Up:

1. LFT: S. bilirubin: ↑

   SGPT: ↑↑

   S. Alkaline Phosphatase normal / ↑
2. Albumin ↓ and γ- globulin ↑↑ and as No catabolism of this protein occurs therefore it keeps on elevating - D/d: Multi myeloma:- Albumin is normal and γ- globulin ↑↑
3. Viral serology
4. PT↑
5. RA factor +
6. **ANA ⊕, SMA (actin), Anti LKM-1 Ab, Liver cytosol 1 Ab.**
7. Liver Biopsy
   - Interface hepatitis
   - **Rosette formation** {this indicates regenerating hepatocytes}



PrepLadder

Diagnostic criteria: Diagnosis of Exclusion

Excluded causes	Include
- Virus	- Ab
- Drugs	- Bx finding
- Alcohol	
- Genetic ds	
{α-1 AT def, Wilson disease, Meineke's disease}	

Rx:

1. Steroids + Azathioprine
2. Late representation – Orthoptic Liver Transplantation

   In case of decompensated cirrhosis

   - On basis of child Pugh score → < 7-8 - listed for liver transplantation
   - Disease can reoccur incidence is rare

Q. Which disease has propensity to reoccur in a transplanted liver?

A. Autoimmune Hepatitis

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PrepLadder

CIRRHOSIS AND ITS COMPLICATIONS

- **Child Pugh Score**:-

Parameters - Bilirubin

INR

Albumin

Ascites

Asterixis

Category

A = 5-6

B = 7-9 (decompensated)

C = >10

→ **Category B** = Enlist for liver transplantation

- MELD Score (Model for end stage liver disease)
  - Parameter
    - S. bilirubin
    - INR
    - S. creatinine

If Liver transplant has to be done it should be planned before the value of 20, because after this steep rise in mortality rate occurs.

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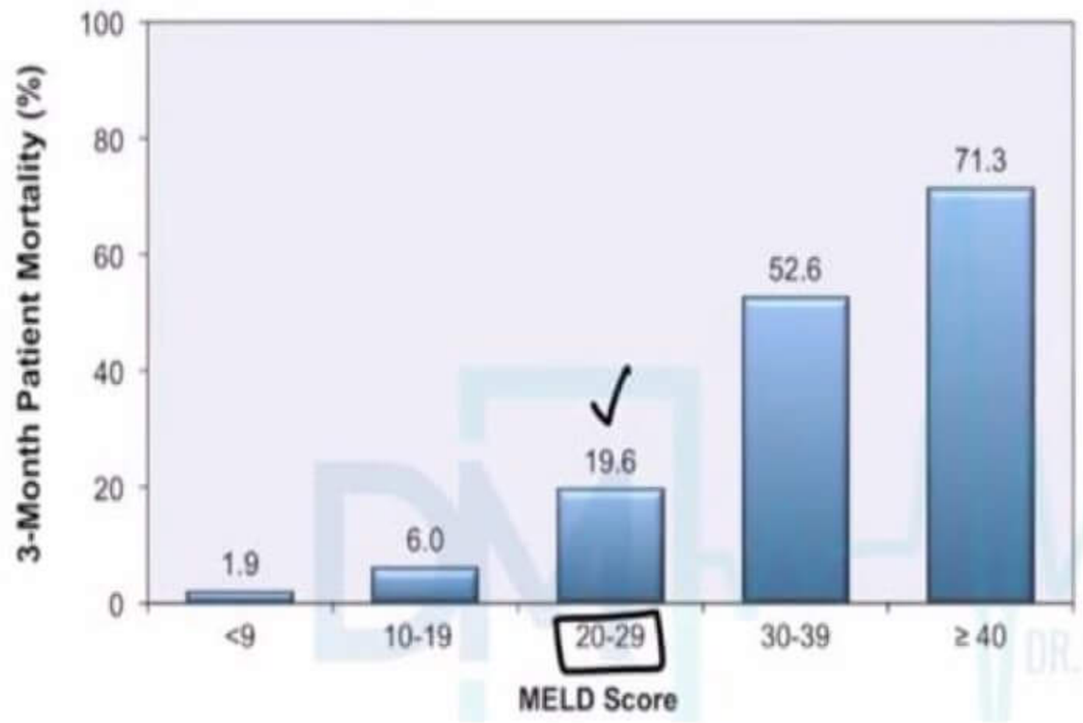

- Biopsy: Invasive test and can`t tell % mortality and whether the case is compensated or decompensated

Metavir score system	Fibrosis stage
F0	No fibrosis can be detected
F1	Fibrosis exists with expansion of portal zones
F2	Fibrosis exists with expansion of most portal zones, and occasional bridging
F3	Fibrosis exists with expansion of most portal zones, marked bridging, and occasional modules.

- Liver biopsy is done at midaxillary line 7th / 8th intercostal space (always USG guided)
- Complications like bleeding and pain at the site or shoulder pain.
- Coagulogram should always be normalized before liver biopsy, as bleeding chances will be high in cirrhotic pts.

  - Liver biopsy
    ↓
    Sent to pathologist

Metavir scale Ishak scale

- Transient elastography (Fibroscan) = Measure velocity of shear wave
- Fibrosure
  - Bilirubin
  - Gamma- GGT
  - Haptoglobin
  - Apolipoprotein A
  - Macroglobulin

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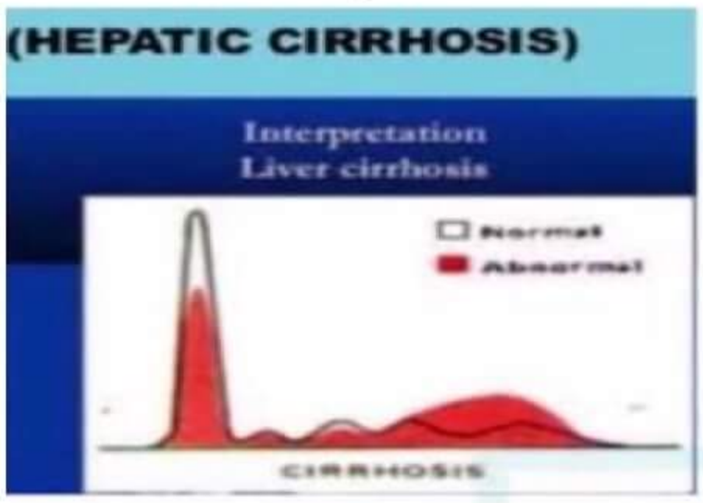

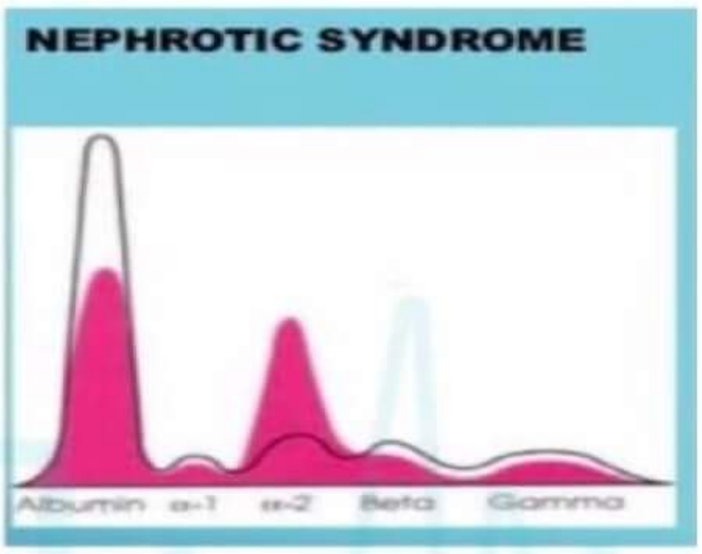

- Whenever liver is damage → albumin decreases and Globulin is elevated (because catabolism of globulin occurs in liver and if liver is damaged it will not occur)
- In Nephrotic syndrome → albumin decreases, Globulin decreases

→ **Church spire** (multiple myeloma)

PrepLadder

- Catabolism of globulin occur in liver

Albumin	Globulin	Condition
↓	↓	Nephrotic syndrome
↓	↑	Cirrhosis
N	↑↑↑	Multiple myeloma/plasmacytoma

	Compensated Cirrhosis		Decompensated cirrhosis	
Stage	**Stage 1**	**Stage 2**	**Stage 3**	**Stage 4**
Clinical	No Varices No Ascites	Varices + No Ascites	Ascites +/- Varices +	Bleeding +/- Ascites +
Death (at 1 year)	1%	3%	20%	57%

- **Causes Of Cirrhosis: -**

1. Alcoholic cirrhosis (MC)
2. Hep. C and B
3. Wilson's disease
4. α_1 antitrypsin deficiency
5. Hemochromatosis
6. Biliary cirrhosis (PBC/ PSC)
7. Autoimmune hepatitis(Anti LKM1 Ab)
8. Non cirrhotic portal fibrosis (NCPF →seen in india)
9. Cardiac cirrhois (constrictive pericarditis/cor pulmonale)

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Extra Mile

Primary biliary cirrhosis:Antimitochondrial antibody

Primary sclerosing cholangitis: p-ANCA antibody

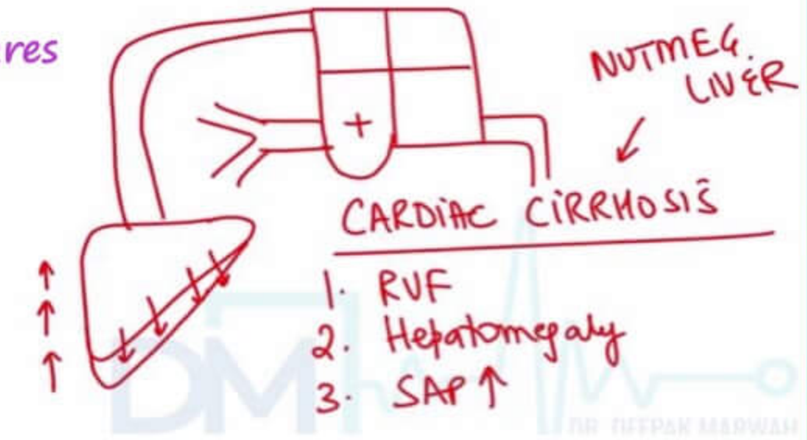
Autoimmune hepatitis: anti LKM 1 antibody

- **Compensated Cirrhosis Features: -**

1. Spider Naevi/ angioma
   - Due to ↑ Estrogen
   - Present in superior vena cava distribution(shoulder and back)
   - Also seen in – Rheumatoid arthritis
     - Pregnancy
2. Palmar erythema
3. Dupuytren`s contracture
4. Clubbing
5. Gynecomastia/ decreased body hair/ testis atrophy
6. Parotid gland enlargement

PrepLadder

- Budd Chiari syndrome does not have right sided heart failure features



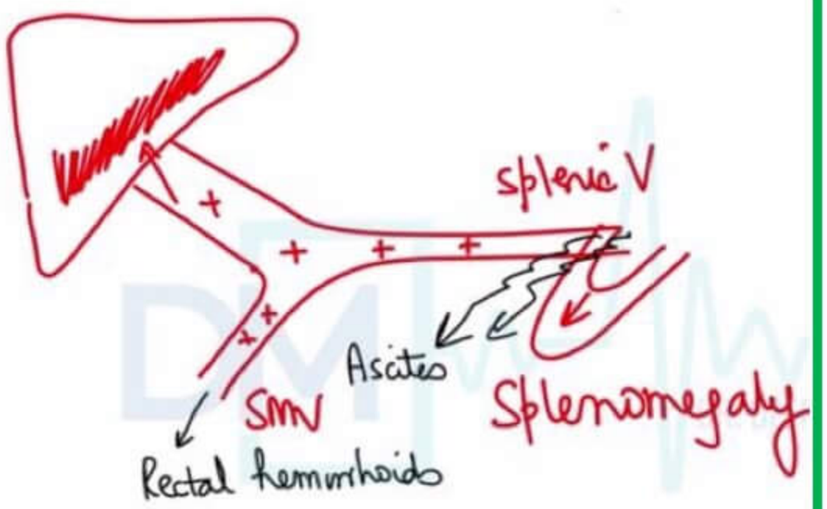
Complications of Cirrhosis

1. Portal hypertension

- Hepatic venous pressure gradient (HVPG) > 5mm Hg
- If HVPG> 12 mm Hg → Variceal bleeding

Sequence of events:

Splenomegaly → ascites (d/t increased pressure leakage of fluid from capillary bed occurs) → portosystemic collaterals (rectal hemorrhoids and esophageal varices)



- IOC = Doppler USG
- M/C/Cause = Alcoholic cirrhosis (seen in western countries)

Q. if the person is non alcoholic, viral markers -ve, no genetic disease, no autoimmune ds. And no cardiac involvement but cirrhosis is present

→ Cryptogenic cirrhosis/Non Cirrhotic Portal Fibrosis (NCPF)

Note:- In non bleeding esophageal varices DOC - Propranolol

- Bleeding esophageal varices DOC - Octreotide
- M/C/C of hematemesis is Peptic ulcer (splenomegaly never occurs in PUD)

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Scenario: Pt. has developed hematemesis + splenomegaly with un-recordable BP

Low BP

↓

- Target BP = 90/60 mm Hg (BP more than this can lead to increased bleeding)

↓

- Put I/V cannula orange (14 G) / Grey (16G)

+

- I/V fluids (Normal Saline)

+

- Massive transfusion protocol (FFP, Packed RBCs and Platelets if reqd.)

↓

I/V Octreotide = DOC (it reduces the pressure in splanchnic circulation so the bleed will ease off)

↓

Upper GI endoscopy + sclerotherapy = TOC of Bleeding O. Varices

PrepLadder

- Causes of Portal Hypertension: -

Pre hepatic	Hepatic	Post hepatic

• Portal vein thrombosis
• Splenic vein thrombosis
• Banti syndrome (massive splenomegaly)
	• **Pre- sinusoidal**
	  ○ Schistosomiasis
	• **Sinusoidal**
	  ○ Cirrhosis
	• **Post sinusoidal**
	  ○ Veno occlusive disease
	Radiation ◄ ► Herbal tea
		• Budd Chiari Syndrome
		• Inferior vena cava webs
		• Restrictive cardio myopathy
		• Constrictive pericarditis

2. Ascites:-

- How much peritoneal fluid is present in normal man = 0 ml
- How much peritoneal fluid is present in normal female = 0 ml

  In mid cycle ovulatory female ≈ 10 ml

→ Pleural space = 5-15 ml

→ Pericardial space = 20-50 ml

- > 100 ml peritoneal fluid = Puddle sign ⊕
- > 500 ml peritoneal fluid = Shifting dullness

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→ Massive ascites:-

- Based on
  - Fluid thrill ⊕
  - Respiratory difficulty
  - Superficial veins of anterior abdominal wall become more prominent and caput medusae will be visible.

Massive Ascites

↓ may progress to

Tense Ascites

↓

Abdominal compartment syndrome (>25 mm Hg in peritoneal cavity and compression of SMV (Superior mesenteric vein) and IMV (Inferior mesenteric vein) occurs lead to gangrene of intestine)

- Abdominal paracentesis prevent the deterioration of patient. But at the same time it leads to dehydration, increase ammonia (asterixis)

  +

  Salt free albumin (to prevent dehydration)

  ↓

  Leads to increase oncotic pressure

  ↓

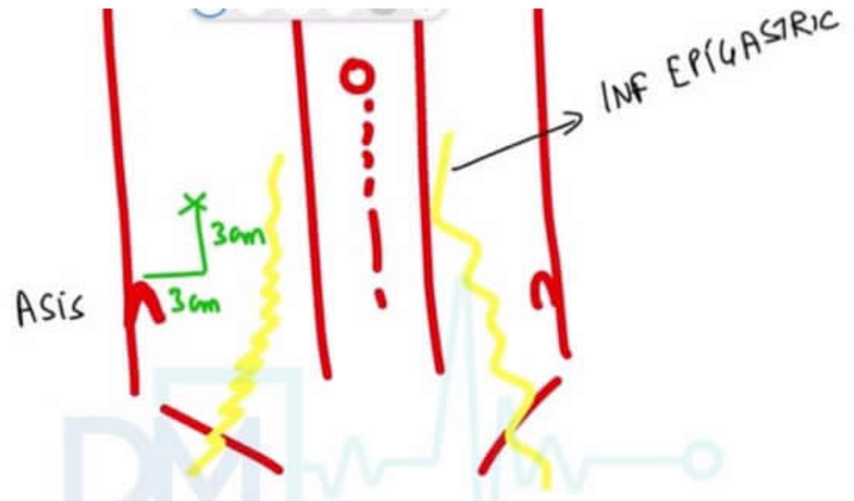
  Cause mobilization of fluid from peritoneal cavity to intravascular compartment (chances of dehydration are less) and then we perform Large volume paracentesis.

- **Treatment of Ascites:-**

1. Salt restricted diet
2. Spironolactone
   - In massive Ascites → Salt free albumin + large volume paracentesis
   - Refractory Ascites →
     - **Spironolactone** 400-600 mg/day
     - **Furosemide** 120-160 mg/day

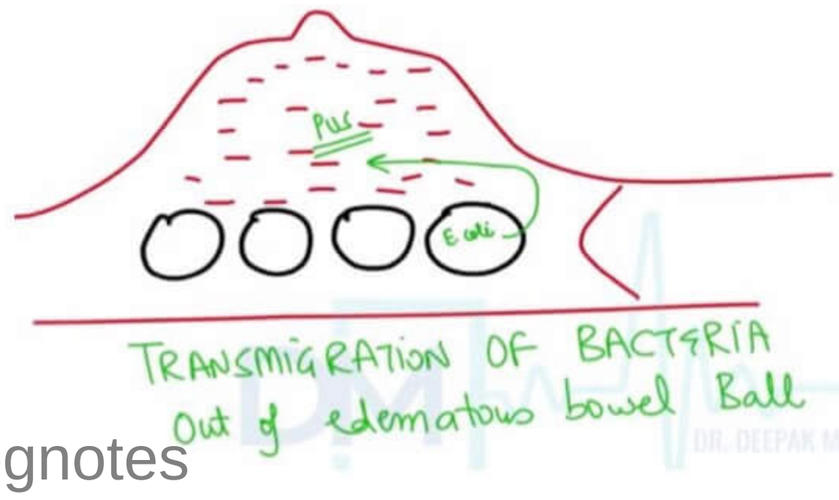
     +

     Ascites ⊕
   - Site for Ascitic tap = **Flanks**



   - Inferior epigastric artery can be traumatized during Ascitic tap.

3. **Spontaneous Bacterial Peritonitis: -**
   - **Patient may go into: -**
     - Sepsis
     - Septic shock
     - Kidney perfusion decreases
     - Hepatorenal syndrome



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4. **Hepatorenal syndrome:-**
   - Kidney biopsy = Normal
   - Pre – renal failure occurs
   - DOC=midodrine
   - TOC= Orthoptic Liver Transplantation (OLT)

5. **Hepatopulmonary syndrome: -**
   - Platypnea
   - Orthodeoxia

PrepLadder

6. Ascites: -

- Serum albumin Ascitic gradient (SAAG)

>1.1g/dl

- Increasepressure in hepatic sinusoids

Ascitic protein	Ascitic protein
<2.5 g	> 2.5g
(Synthesis decreases)	↓
↓	* CHF
Cirrhosis portal hypertension	* Restrictive cardiomyopathy
	* Constrictive pericarditis

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<1.1 g/dl

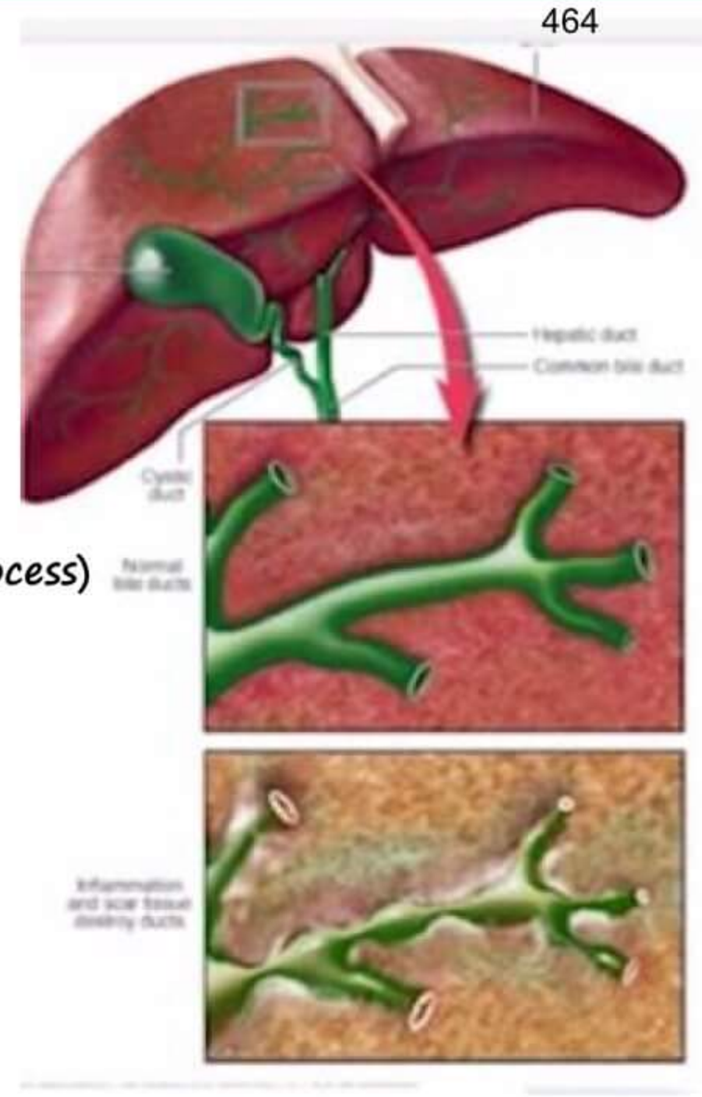
↓

- Bile leak
- Nephrotic syndrome
- Peritoneal carcinomatosis
- Pancreatitis
- Tuberculosis

(mnemonic = BNPT)

PrepLadder

PBC & PSC



Primary Biliary Cholangitis

- Autoimmune disorder:

  d/t A.M.A (Antimitochondrial Ab)

  ↓

  Cause damage to Portal tract and biliary pathway (**intrahepatic process**)

  is affected

- Attack cholangiocytes which are lining biliary radicles
- Cholestasis causes c/f: obstructive jaundice
- With progressive liver damage: Cirrhosis
- (Micronodular **(MC)** / Macronodular)

C/f:

1. Fatigue (Mc Presentation)
2. **Pruritus** (d/t bile salts accumulation)

   ↓ followed by

   Lichenification
3. Jaundice ↑
4. Splenomegaly / pedal edema/ Ascites
5. Xanthoma / xanthelasma – {d/t defective cholesterol transport}
6. Osteopenia/bone pain (2° to steatorrhea- causing def. of fat soluble vitamins-ADEK)

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Work up:

1. LFT:
   - Bilirubin :↑
   - SGOT, SGPT } normal
   - S. Alkaline phosphatase: ↑
2. AMA ⊕
3. ANA absent
4. Prothrombin time ↑

   INR derangement
5. Hb ↓ TLC ↓, Platelet account ↓ - {Hypersplenism – d/t portal HTN}

Rx:

1. UDCA (Ursodeoxycholic acid): Slow the progression of ds.
2. For symptomatic relief
   - Cholestyramine
   - Anti histaminics
   - Naltrexone
   - Plasmapheresis

PrepLadder

3. If it progresses to cirrhosis then depending on child pugh score or MELD score of the pt. can be taken for orthoptic liver transplant.

Primary sclerosing cholangitis (PSC)

- Cause damage to **entire** biliary tree, **both intrahepatic & extrahepatic** component damage.
- ERCP in patient: Strictures (Characteristic) in extrahepatic component (bead appearance)

C/f:

1. Obstructive jaundice
   - Characterized by Pruritus predominantly in palm& soles of pt.
   - Icterus
   - Mustard yellow urine/ {d/t conjugated bilirubin} high colored urine

2. Steatorrhea: def. of fat-soluble vitamins ADEK

   c/o: Bone pain

   Work up: LFT: S. Alk. phosphatase. ↑ 4x

   Albumin ↓

   PT ↑

65% of total cases → a/w **p-ANCA**

50% of total cases → a/w **Ulcerative colitis**

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- IOC: MRCP > ERCP.

On ERCP: -

- **Beaded appearance/ strictures.**

Rx:

1. UDCA: {not so effective}
2. Endoscopic dilatation
3. Orthotopic liver transplant (for patient with decompensated liver failure)

PrepLadder

Wilson Disease

- Total Body Cu → 50-100 mg and Consumption of Cu → 2-5 mg

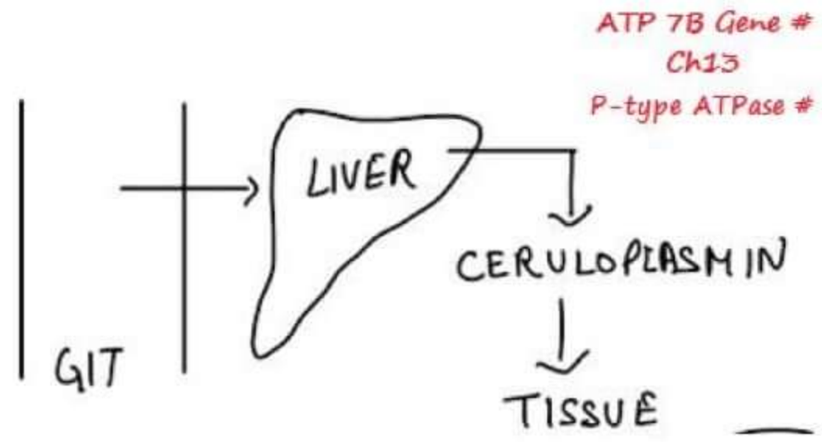
In Wilson absorption of Cu from gut is absolutely normal

Ceruloplasmin levels are reduced in Wilson disease

Ceruloplasmin is ↓ in: → Alcoholic cirrhosis

→ Nephrotic Sx

→ Kwashiorkor



ATP7A → Menkes disease (Cu deficiency)

So the problem is defective biliary excretion of Cu d/t defect in gene **ATP7B Gene** (on chromosome 13)

There is P-type ATPase enzyme activity linked to this gene and this activity is defective.

So earliest manif. Is damage to liver in form of chronic active Hepatitis/ Cirrhosis → (Commonest liver presentation) / fulminant Hepatic failure.

→ **In 1st 10 year of life:** Cirrhosis → (Compensated: Spider nevii, dupuytren's contractures)

Decompensated: Ascites, Portal HTN, Caput medusae

> 10 year → Lenticular Nucleus damaged (Globus pallidus + putamen)

1. Asymmetrical tremors: Earliest neurologic manifestation → Resting, postural, kinetic
2. **Dysarthria**
3. Impulsiveness, disinhibition
4. Dystonia (Late Neurological presentation)
5. Pallor, **Coombs Θ Hemolytic anemia**
6. Hemolysis
7. Premature osteoarthritis

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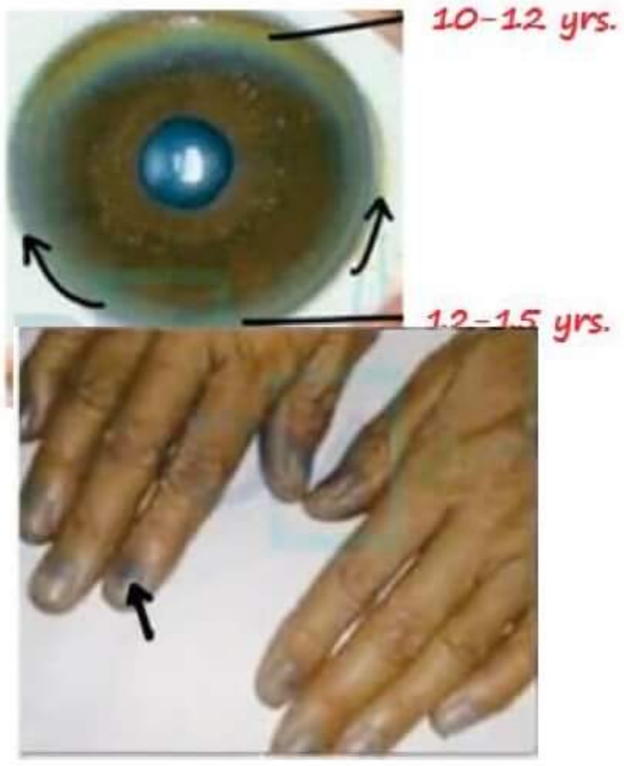


Eyes → KF ring → Develops in upper part of cornea b/w 10-12 years

and then in lower part in b/w 12-15 years

then ↑ circumferentially

- Examined under Slit lamp.
- Descment membrane Is involved.

KF Ring + CNS features has diagnostic accuracy of 98%

Azure lunulae → Blue Nails (but also seen in silver toxicity)

Hemolytic episodes ⊕: Urinary Cu^{++} is significantly Increased leading to damage of PCT which is responsible for absorption of Salt, sugar HCO^{-}_{3}, amine ads, PO_4^{-}

↓

So, all these will not be absorbed

↓

Leads to Salt wasting, Renal glycosuria, aminoaciduria

PrepLadder

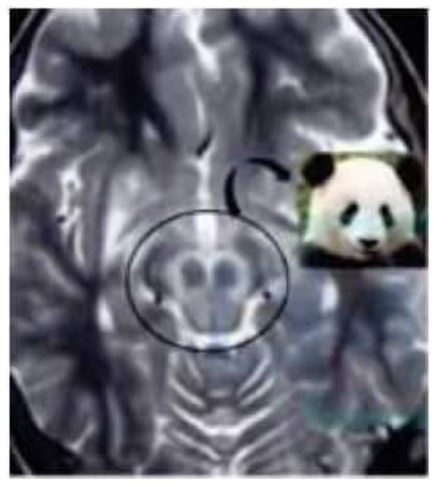
Organs involved in WILSON

Liver	: Cirrhosis (m/c)
RBC	: Hemolytic anemia
B. ganglia	: Tremors
Nails	: Azure lunulae
Kidneys	: Fanconi Sx
Eye	: KF ring

Note:- In hemochromatosis : Bronze diabetes, Pancreas, skin liver involved

Workup:

1) 24 hr urinary copper value → Screening test → (↑) (> 100 mg/d)
2) D-Penicillamine challenge test
3) Liver Biopsy – **IOC** → Estimation of Hepatic Copper
   Content → > 250 mg/g of dry weight of liver
4) S. ceruloplasmin: < 20 mg/dl
5) Imaging: MRI Head – **Face of panda appearance**



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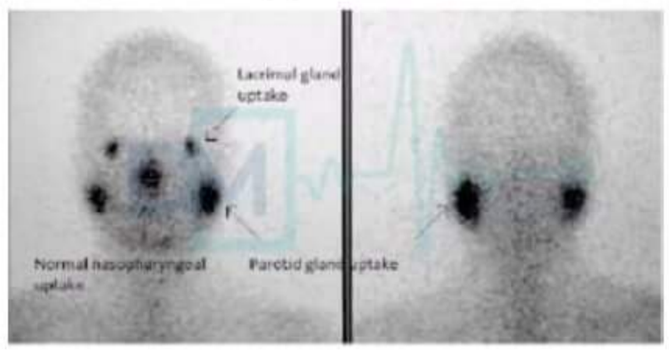
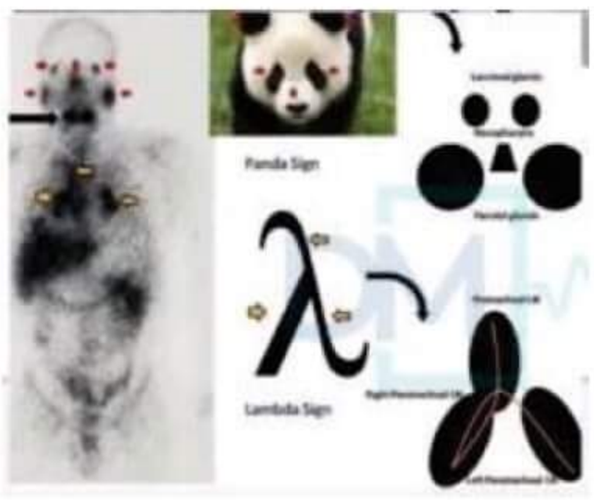
→ ↑ Signal intensity in tegmentum
→ Pars reticularis of substantia Nigra } Involvement of these 3 lead to face of panda appear
→ Superior colliculus also involved



Panda Sign → Seen in gallium scan: In sarcoidosis patients

Lambda sign → d/t Hilar LN involvement in sarcoidosis patients

Panda Sign/ Raccoon eyes→ Seen in ant. Cranial fossa fractures



Rx

1.**DOC**: Zinc acetate (Helps in excretion of Cu as it induces metallothionein, cause negative Cu balance)

2.**DOC for CNS features:** Tetra-thio-molybdate

Tetrabenazine → used in Huntington cholera

3. Need for liver transplantation is evaluated by:

NAZER index:- S. Bilirubin
INR (BIT)
SGOT

PrepLadder

MELD score: BIL

INR

S. creatinine

Child pugh classification

- Bilirubin ↑
- Albumin ↓ (t1/2 → 18-21 days)
- Ascites ↑
- Asterixis ↑
- INR ↑

Score: ≥ 7 Need to list patient for liver transplantations.

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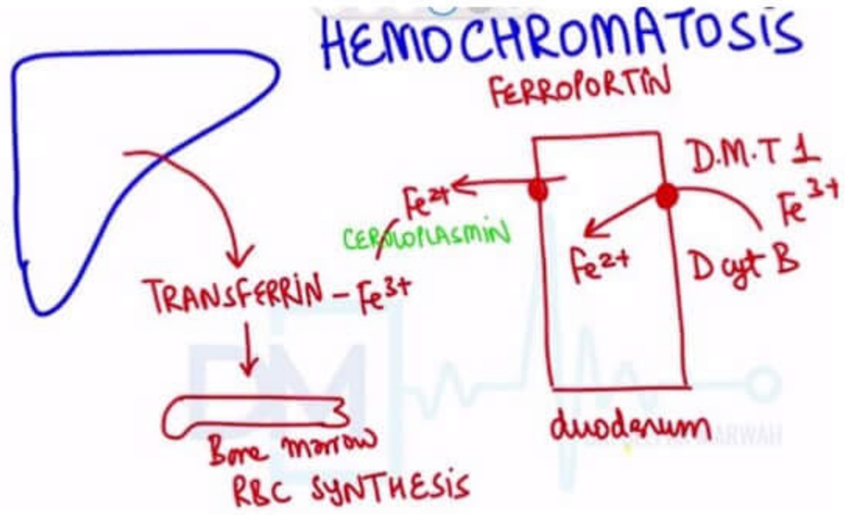
PrepLadder

HEMOCHROMATOSIS



→ Duodenum is main site for absorption of iron

- **DMT 1 (Divalent Metal Transporter 1)**: transports the iron into enterocyte in Fe 2+ form
- **Duodenal Cyt B** helps in reduction of Fe 3+ to Fe 2+
- **Ferroportin**: exporter of iron from enterocyte into circulation.
- **Ceruloplasmin** converts Fe 2+ into Fe 3+ and Fe 3+ binds to Transferrin for transport to bone marrow

→ Etiology

- Deficiency of ceruloplasmin → Iron Toxicity → gets deposited in basal ganglia and cause neuro degeneration

- Any damage to liver → ↓↓ hepcidin → Iron Toxicity occurs.

Hereditary Hemochromatosis

- Gene mutation – **HFE gene**

→ ↓↓ Hepcidin

→ ↑↑ DMT–1 activity

→ Iron Toxicity due to excessive absorption of Iron from gut

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- Chronic Liver disease → ↓↓ Hepcidin
- Aceruloplasminemia → Fe 2+ is not converted into Fe 3+,so excess Fe 2+ is present in circulation.

Normal Iron values → 3–4 gm

RDA:

Child – 10 mg

Adult male – 20 mg

Adult female – 30 mg (values can be different based on menstrual losses)

→ Bioavailability of Iron → 10%

→ Cereal based diet contains phytates and tannic acid (in tea) are the competitive inhibitors for iron absorption

Note:- In hemochromatosis → Iron level → 25 gm and Vit C should not be given hemochromatosis pts as it can increase its bioavailability.

PrepLadder

Hemochromatosis

Hereditary	Acquired
Type I → HFE gene 6p, AR, C282 Y Homozygosity	a) **Chronic liver disease** → Alcohol → **Hepatitis C (MCC)** → N.A.S.H (Non acholic steatohepatitis) → Cirrhosis
Type II → Hepcidin/ Hemojuvelin mutation	b) → Thalassemia (transfusion related iron overload) → Sideroblastic anemia → Chronic hemolytic anemia
Type III → Transferrin Receptor mutation	
Type IV → Ferroprotein mutation	

Note:- The common pathology behind all these types of mutations is that → Hepcidin ↓↓ and it results in the ↑↑ iron absorption in the body and it causes damage at different levels.

→ **Pancreas – Type I DM**

→ **Arthropathy**

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Misc. causes:

→ Aceruloplasminemia → Fe in excess

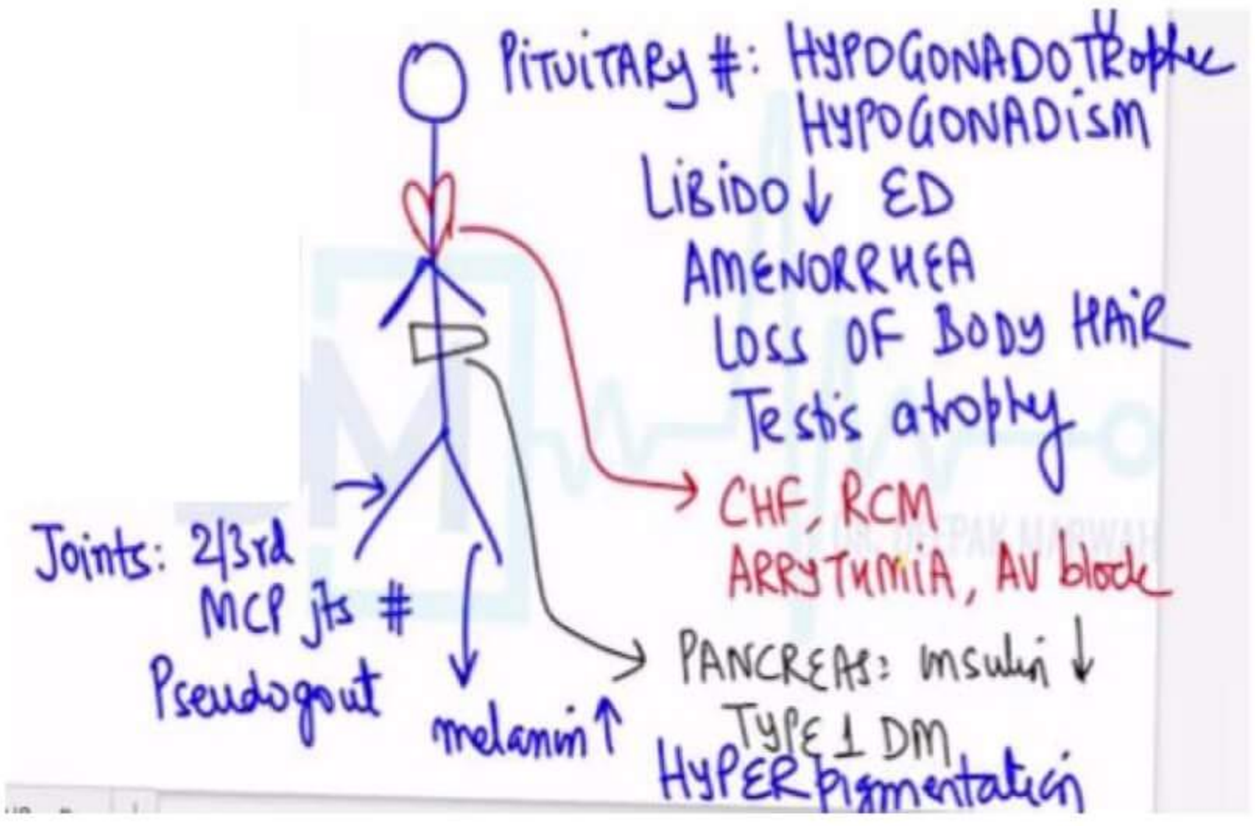
→ Porphyria Cutanea Tarda

Clinical features

Most common symptom → Arthralgia > Pigmentation of skin

Most common organ involved → Liver

Most common presentation → Hepatomegaly



-Excess iron will damage the pituitary.

PrepLadder

a) **Pituitary damage** - hypogonadotropic hypogonadism (LH and FSH decreased)

→ Testosterone and estrogen decreases

→ Libido ↓↓

→ Erectile dysfunction

→ Amenorrhea

→ Loss of body hair

→ Testicular atrophy

b) **Heart**

→ Congestive Heart failure (Right sided)

→ RCM(Restrictive cardiomyopathy)

→ Arrhythmia (tachyarrhythmia or bradyarrhythmia)

→ AV block

c) **Pancreas**

→ Insulin ↓↓ (Type – 1 DM)

→Bronze diabetes (because there is also bronzing of skin along with diabetes)

d) **Joints → 2nd and 3rd MCP joints (MC)** and knee joint can also be involved (Pseudogout)

e) **Melanin ↑↑** (Hyperpigmentation)

→ Most common cause of death in hemochromatosis → Congestive Heart failure (CHF)

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Work up in the patient of hemochromatosis

1)

- Serum Iron ↑↑
- TIBC ↑↑
- Percentage saturation of Transferrin ↑↑ - > 45% (Screening) –Better modality
- Serum Ferritin ↑ = >1000-6000 micro gm /l (Screening)
- **Liver Biopsy with estimation of Iron content → IOC**
- Hepatic Iron index > 2

2) HbA1C

3) Echocardiography

4) X-ray hand

5) USG liver (To pick up Hepatomegaly and Liver cirrhosis)

Case scenario: Adult patient with positive family history of liver disease without neurological involvement or there can be unexplained liver disease with deranged LFT and pt. is non alcoholic

PrepLadder

Ix → [Transferrin saturation + Serum Ferritin] ↑↑

↓

HFE genotype

↓

Liver Biopsy + LFT

Treatment

1. **Weekly Phlebotomy for 1-2 yrs. (TOC)**
2. Don't give Vit C

   1 unit of blood removes only → **200-250 mg iron**

   25 gm Iron ++ in pt.

   S. Ferritin < 100 µg/dl: TARGET

3. Deferoxamine –DOC for transfusion associated HH (hereditary hemochromatosis)

   → Given as Subcutaneous infusions

Note:- For each infusion 10-20 mg iron per day can be removed

4. **Deferasirox (oral)**-S/E +, **Deferiprone (oral)** - better

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Note:- Death is generally due to:- **Heart Failure > Liver failure > HCC**

→ After removal of Iron from body following features continue of Hemochromatosis to progress:

1. ↑↑ Arthropathy
2. Hypogonadotropic hypogonadism

PrepLadder

ALCOHOLIC HEPATITIS

→ Only 10-20% alcoholics develop alcoholic hepatitis

→ Alcohol is the third largest disease burden in world after CAD & DM

→ **Male:** 40-80 gms/day = Fatty Liver and **160 gms/ day = Hepatitis → Cirrhosis**

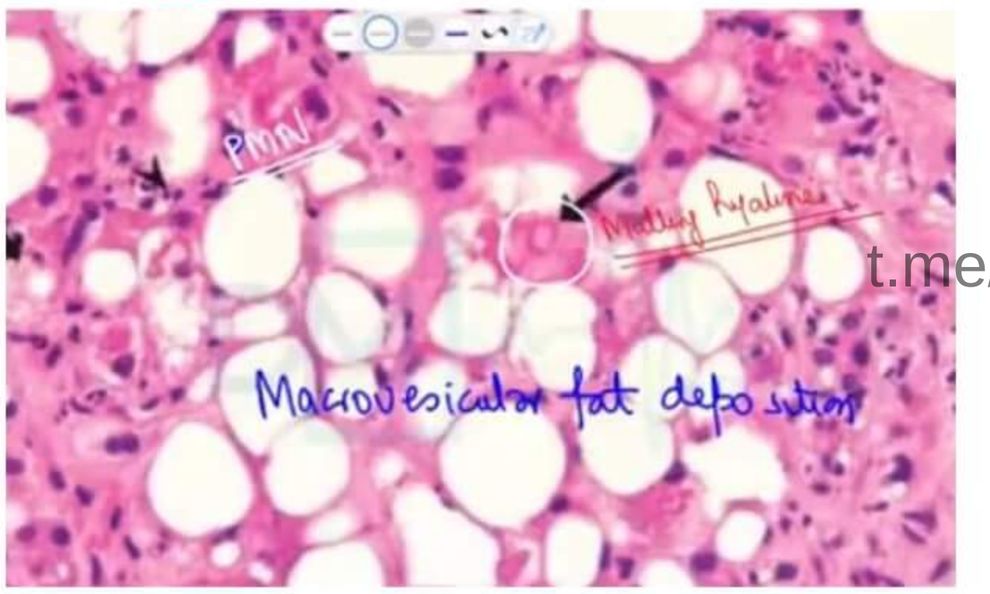
→ **Female:** 20 gms/ day

Note:- Binge drinking is seen mostly in youngsters who have just started earning. Sudden cardiac death occurs in Holiday Heart Syndrome d/t development of atrial fibrillation

Concomitant factors for Alcoholic cirrhosis

- → HCV
- → Genetics
- → NAFLD
- → Obesity

Pathology



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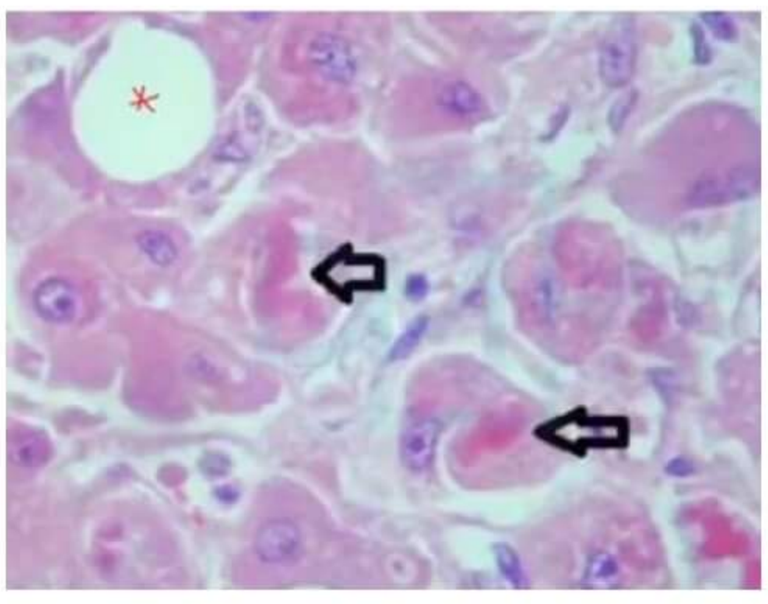
- Macro vesicular fat deposition can be seen
- Neutrophilic infiltrate can be seen
- **Mallory hyaline bodies** → Eosinophilic deposits seen in hepatocytes



- Mallory hyaline bodies in ballooned hepatocytes can be seen (subsequently ballooning degeneration or spotty degeneration occurs)

PrepLadder

Causes of Mallory hyaline bodies (mnemonic- I Will Break Alcoholic Status)

→ Indian childhood cirrhosis - ↑ Cu (due to use of copper utensils)

→ Wilson Disease

→ Primary Biliary cirrhosis (Anti mitochondrial Ab)

→ Alcoholic Hepatitis

→ Non Alcoholic Steatohepatitis (NASH)

Alcoholic hepatitis clinical features:

→ Asymptomatic

→ Right upper quadrant discomfort

- Nausea
- Vomiting
- Jaundice Absent

3. Portal HTN → Splenomegaly

→ Caput medusae

Work up

Liver function test

1. AST or SGOT → 2-7 times elevated (most specific test) for alcoholic hepatitis

→ for Viral hepatitis most specific test is SGPT and for obstructive jaundice is SAP

2. S.A.P → Increased

So LFT will reveal Anicteric hepatitis (as jaundice is absent)

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3. **USG:** Initially echotexture will give away, Later Portal vein flow reversal is seen.

4. **PT:-** Elevated (Normal: 11-15 sec)

5. **Albumin:** Normal and later on ↓↓

6. **Kidney function test:-** S. creatinine Normal and later on ↑↑

MADDREY'S/ DISCRIMINANT FUNCTION/ SCORE:

→ **4.6 x [↑PT above the upper limit of control] + S. Bilirubin**

Note:- If value > 32 → indication of starting t/t

If M.E.L.D score > 21 → indication of starting t/t

GLASGOW ALCOHOLIC HEPATITIS SCORE:

- Age
- WBC count
- BUN
- Bilirubin
- PT

PrepLadder

Laboratory Diagnosis of Alcoholic Fatty Liver and Alcoholic Hepatitis	
Test	**Comment**
AST	Increased two to sevenfold, < 400 IU/L, greater than ALT
ALT	Increased two to sevenfold, < 400 IU/L
AST/ALT	Usually > 1
GGTP	Not specific to alcohol, easily inducible, elevated in all forms of fatty liver
Bilirubin	May be markedly increased in alcoholic hepatitis despite modest elevation in alkaline phosphatase

- Most specific liver function test → **S.G.P.T or A.L.T**

Note:- SGOT is present in cardiac myocytes also. So it is non-specific and it may be produced from damaged liver or heart but SGPT is elevated only in liver disease.

- Most specific liver function test for **Alcoholic hepatitis** → **AST/ALT > 1 (if ratio is not asked then SGOT/AST)**

Management

1. Alcohol Deaddiction → Naltrexone
   → Acamprosate
2. **D.O.C for** Alcoholic Hepatitis → **Prednisolone 32 mg/ day x 4 weeks**
   → **Lille score** → For response to steroid in Alcoholic hepatitis
3. **TNF-α inhibitor**:- Pentoxyphylline

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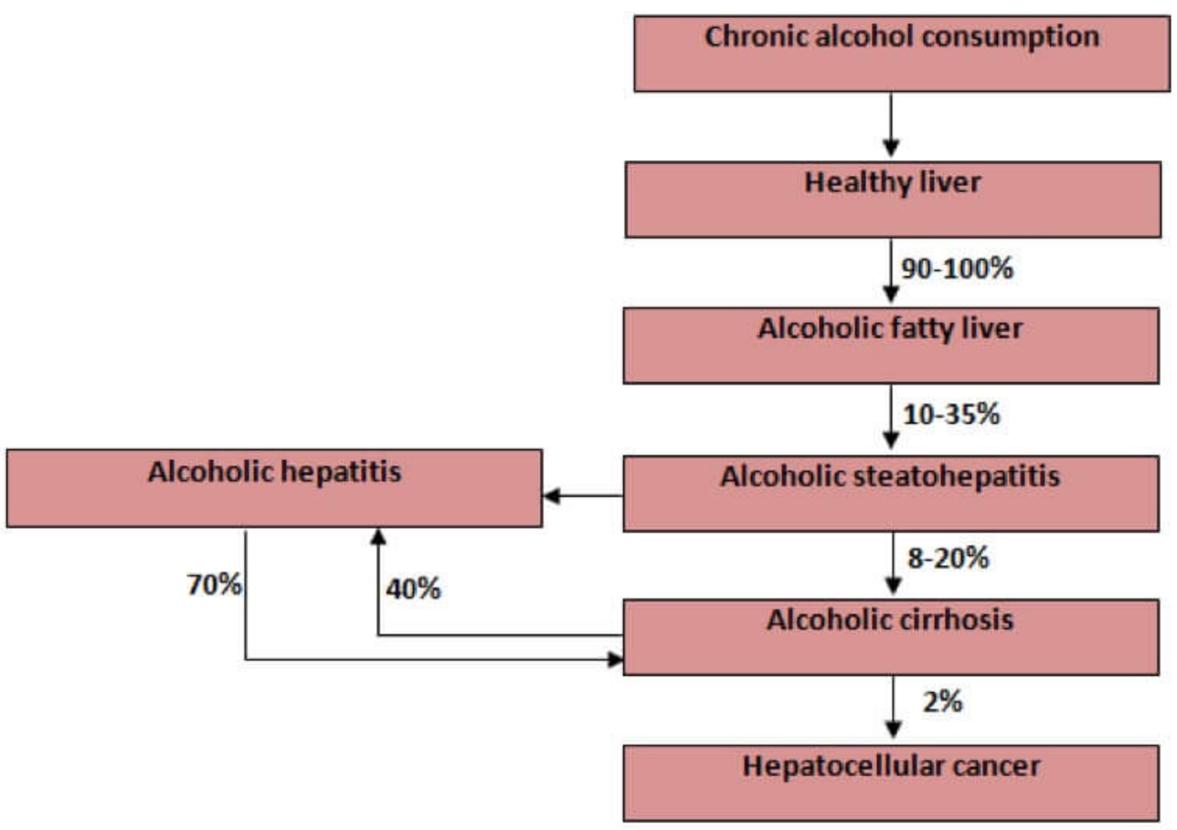

PrepLadder

Selected Noninvasive Methods of Assessing hepatic Fibrosis and Cirrhosis			
METHOD	PARAMETERS	ADVANCED FIBROSIS	CIRRHOSIS
APRI (AST to platelet Ratio Index)	AST, Platelet count	> 1	> 1.5 (1-2)
ELF (Enhanced Liver Fibrosis)	Age, Hyaluronic acid, MMP-3 [Metalloproteinase], TIMP 1 (Tissue Inhibitor of Metalloproteinase)	> 7.7	> 9.3
FIB – 4	Age, AST, ALT, platelet count	> 1.45	> 3.25
Fibro Test	Haptoglobin, α2-macroglobulin, apolipoprotein A1, γ GT, total bilirubin	> 0.45	> 0.63
TE (Transient Elastography/Fibrosure)	Measure speed of a shear wave generated by vibration through liver tissue	> 7.3 kPa	> 15 KPa (9-26.5 kPa)
ARFT [Acoustic Radiation force imaging]	Measure speed of shear wave generated by acoustic radiation force through liver tissue	> 1.3 m/s	> 1.87 m/s

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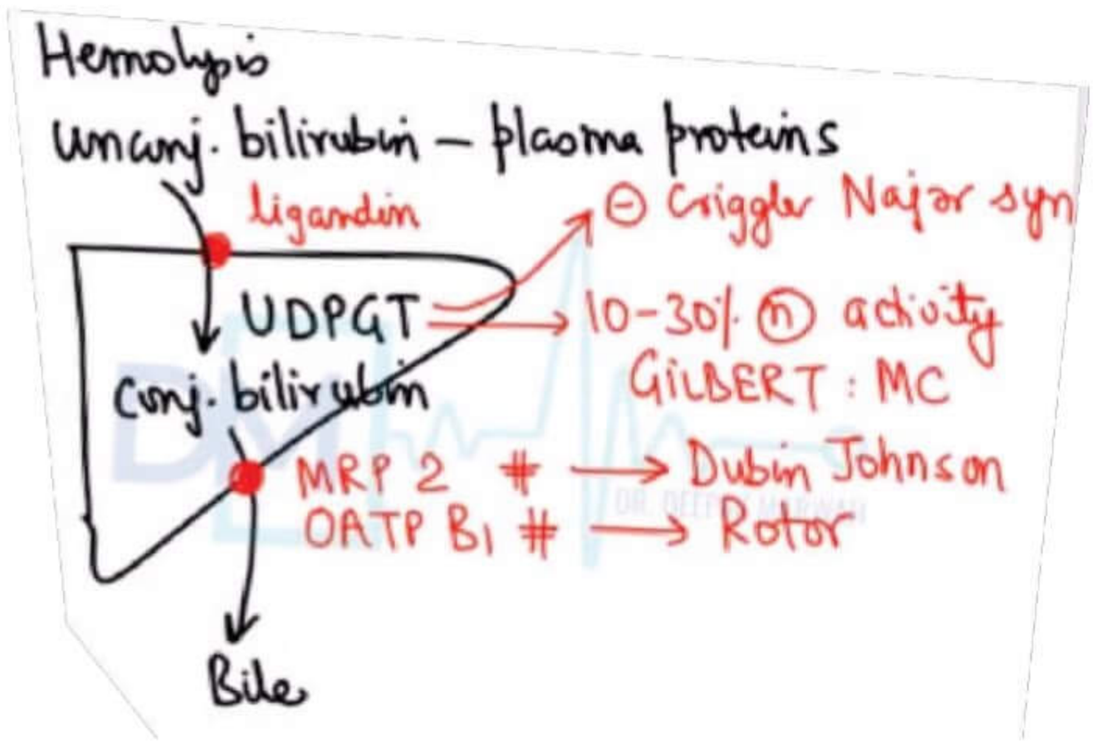
Hereditary Hyperbilirubinemia

Hereditary Hyperbilirubinemia

- Hemolysis → Unconjugated Bilirubin is produced and to prevent the drastic effects of unconjugated bilirubin – Plasma proteins bind to Unconjugated bilirubin.



GILBERT →

- If , Promoter molecule mutation is present – **Autosomal Recessive**
- If Missense Mutation is present - **Autosomal Dominant**
- UDPGT **(UDP-glucuronosyltransferase)** activity as compare to normal person is 10-30%
- Elevated Unconjugated Bilirubin ↑↑ - most of the times it is Incidental diagnosis
- **Phenobarbitone- Enzyme inducer activity** is used to promote the enzyme activity of UDP-glucuronosyltransferase → so that it can normalize the S. Bilirubin levels.

Note:- It can be used as diagnostic challenge test to diagnose the GILBERT disease because as such we can't rule out the disease by biopsy and any other modality.

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CRIGGLER NAJAR TYPE I

- Complete absence of UDP-glucuronosyl transferase enzyme activity leading to KERNICTERUS.

C/F→ Neonate presents in first 24 hours → Pathological jaundice

Rx → In these patients in spite of giving Phototherapy and Exchange Transfusion, the levels of bilirubin remain high and tends to cause → Bilirubin encephalopathy and the bilirubin damages Putamen and it leads to sequelae called as **Athetoid cerebral palsy** later on in life.

Note:- There is no effect of phenobarbitone because there is complete absence of enzyme

DUBIN JONHSON:

- **Gene: - ABCCA**
- Protein: **MRP-2 (Multi drug resistance associated protein 2)** - Canalicular protein responsible for excretion of conjugated bilirubin.

PrepLadder

C/F:

- Obstructive jaundice occurs but here the bile acid handling is normal so pruritus is absent.
- ↑↑ conjugated bilirubin-Bilirubinuria → Mustard yellow urine (presenting complaint of patient

Triggering agents/conditions:-: Pregnancy, OCP, illness

Work up: -

- Conj. Bilirubin > 15% of Total serum bilirubin.
- **SAP (Serum alkaline phosphatase) and 5'nucleotidase → Normal**

- IOC:- **Bromsulphalein** (BSP)Test

Normally BSP is cleared, excreted into bile by MRP-2 protein but in DJS – as the defect lies in the transporter protein- BSP regurgitates back into blood stream and is not excreted into Bile after 90 minutes of giving the injection.

- **Urine total coproporphyrin value- Normal, but ratio of coproporphyrin is changed.**
  → In normal person the value of **Coproporphyrin III > I.**
  → In DJS values of **Coproporphyrin I > III.**
- **Oral cholecystography** - GB not visualized

Note:- Very particular finding with DJS is Black liver → it is due to epinephrine derivative that becomes elevated due to defect in MRP-2 protein.

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Rotor Syndrome

- AR, defect in **OAT P1 - organic anion transport protein 1**
- Liver Color- Normal, Echotexture also remain normal
- GB can be visualized because the cholecystography dye is excreted by MRP-2 and not excreted by OAT P1.
- Total coproporphyrin ↑↑↑ - significantly elevated
- Coproporphyrin I/III is more (I>III)

PrepLadder

PARACETAMOL TOXICITY/ ACETAMINOPHEN TOXICITY

- Toxicity causes → Centrilobular necrosis
- **Safe dose: 3gm/ day**
- **Safe dose with alcohol: 2 mg/day**
- PCM + Opioids tablets → May cause toxicity.

  To decrease risk to liver damage **max. dose of PCM as marketed is 325 mg** tablet
- **10 -15 gm → Liver injury**: Hospitalization required
- > 25g → fatal
- Antidotes (N-acetyl cysteine) started within 8 hrs (optimal time) of intake, can be given up to 24-36 hrs.
- Blood PCM **>300 µg/ml**: at 4 hrs of ingestion – High chance of liver damage

  < 150 µg/ml: at 4 hrs of ingestion – damage is unlikely

Metabolism of PCM

- Metabolized by phase 1 & 2 of metabolism

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In phase 1:

Cyt. P_{450}: Produces NAPQ I (N- acetyl-P-benzoquinone Imine)

↕

Glutathione

Low glutathione (In alcoholics: already reduced)

↓ (in starvation, consumption of anti TB drugs & Barbiturates)

Ability to cause more damage to liver

In Phase 2: Involves conjugation: Responsible for

- Sulfate
- Glucuronidation

Clinical features.

- At 4 – 12 hr: Nausea vomit / abdominal pain/ shock

PrepLadder

- At 24-48 hr: fulminant hepatic failure

Coagulopathy **Encephalopathy**

- Acute kidney injury
- Myocardial injury

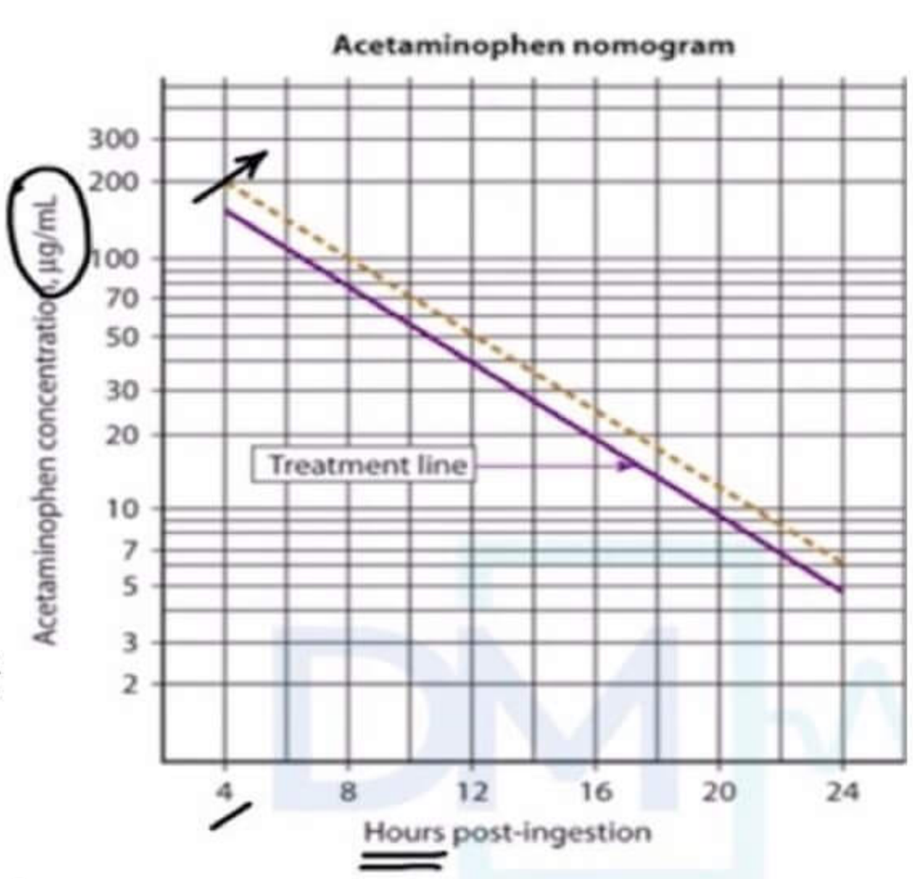
Rx:

Acetaminophen Nomogram

If at 4 hr. – level > 200 µg/ml or

At 8 hr. – level > 100 µg/ml

} Is indication of treatment



1. Gastric lavage } {not effective after half an hr of intake}
2. Cholestyramine }
3. N – Acetyl cysteine - <8 hr.

   MOA: replenish levels of glutathione which will neutralize NAPQ I
4. If fulminant hepatic failure ⊕ → Orthoptic liver transplant

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PrepLadder

BUDD CHIARI SYNDROME

Normally

Portal vein ammonia liver

$\downarrow NH_3 + CO_2 \rightarrow$ Urea

Urea Excreted

In BCS → Thrombus formation in hepatic veins → Backward pressure → centrilobular Necrosis formation

Etiology

Vaso-occlusive Thrombosis occurs in hepatic vein → spreads to C/L hepatic veins → then in IVC

Definition - Thrombus ≥ 2 in hepatic veins→ sinusoidal pressure → hepatomegaly → stretching of capsule → RUQ pain

- Usually Caudate lobe drains in IVC
- IF IVC thrombosis → Enlargement of caudate lobe (identified in color doppler) (Right upper quadrant Pain)
- Pressure in Portal vein ↑ → Portal hypertension

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Secondary BCS → BCS with tumoror a giant Hydatid cyst compressing on the hepatic vein.

Causes of B.C.S

1. Hematological disorder → Polycythemia vera (JAK 2 mutation)
   → Paroxysmal nocturnal Hemoglobinuria

(P.I.G.A gene)

↓

Flow Cytometry

Thrombotic diathesis

2. Protein C/S, AT III ↓→↑clotting tendency in body
3. Factor V Leiden mutation → defective binding with protein C→ extrinsic system activation
4. High estrogen leads to hypercoagulable state
5. Tumors – 2°, hepatocellular carcinoma, RCC, Wilm's tumor (TUMOR PRESSING HEPATIC Vn)
6. Infections → hydatid cyst
7. CTD → Behcet ds, Sarcoidosis, APLAS (Anti β2 glycoprotein) (intrinsic system activation)
8. Membranous defects in IVC / portal Vein
9. TPN → IVC catheter

PrepLadder

C/F of B.C.S–

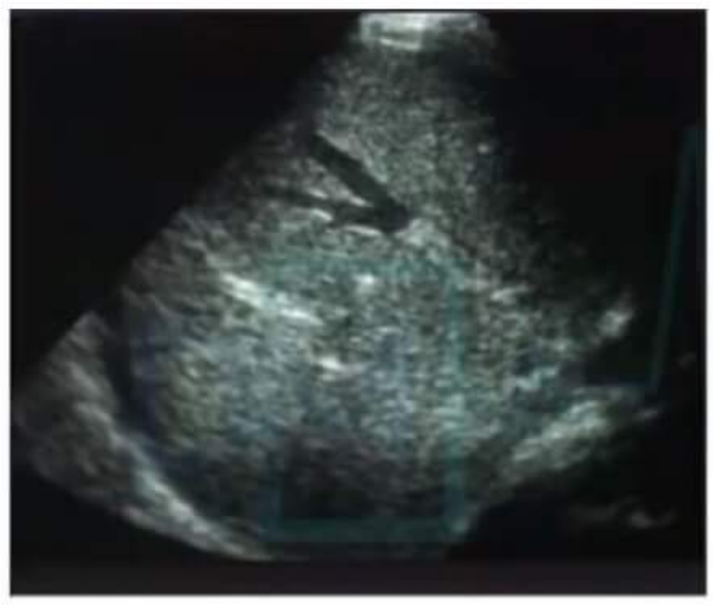
1. Triad – RUQ pain, Ascites (portal HTN), Hepatomegaly
2. Jaundice d/t necrosis in central part of liver d/t backward pressure. Not seen in chronic form.
3. Hepatorenal Syndrome
4. IVC blocked → decreased blood to right heart → Obstructive shock

↓

Causes are

- Cardiac tamponade
- Tension Pneumothorax
- BCS

5. Pedal edema
6. Collaterals + (Chronic)



Diagnosis

- Ultrasound (thrombus in hepatic vein)
- Color Doppler

Work up

1. Ultrasound
   - To rule out gall stone, cholecystitis, cholelithiasis
   - Caudate lobe enlargement seen in BCS on USG
2. Color doppler
3. Ascitic Tap → SAAG > 1.1
4. LFT → Enzymes ↑, bilirubin ↑
5. MRI of abdomen
6. IOC → Hepatic venography

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Treatment

- EASL Guidelines for acute–
  → Balloon angioplasty (Acute presentation BCS)
- Anticoagulation
- In chronic BCS – TIPS
- Spironolactone
- Liver Transplantation in ESLD (in nutmeg liver)

PrepLadder

CYSTIC FIBROSIS

→ Aka **mucoviscidosis**

- Because the secretions in body especially the one in relation with the Pancreas, are very thick and contribute to various manifestation

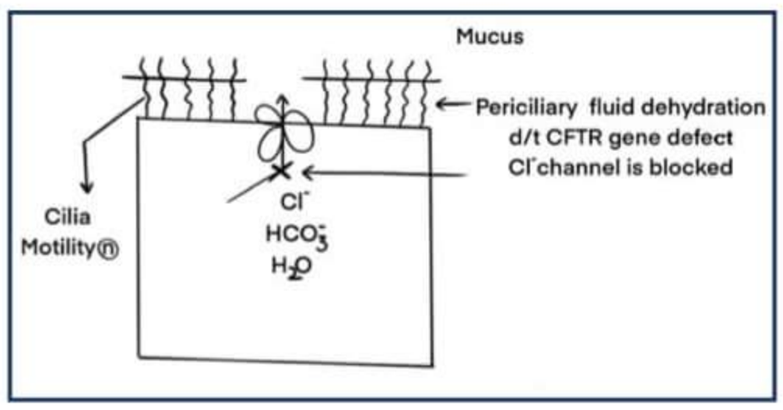
→ aka **Exocrinopathy**

- Because this condition is having the propensity to involve the exocrine glands.

PATHOGENESIS:

→ **AR, CH-7 # CFTR gene**: With 1480 AA sequence CFTR protein

[CFTR – Cystic Fibrosis Transmembrane Conductance Receptor]



→ In Cystic Fibrosis- phenyl alanine present at 508th position is deleted

→ So, mc mutation is F508 mutation

→ CFTR protein malfunction leads multiple manifestations.

→ kartagener syndrome - disease due to defect of dynin protein. So mucociliary clearance are poor.

→ Cl^- channel is defective, as a result of which $Cl^-/HCO_3/H_2O$ transport doesn't take place across it and due to this periciliary dehydration occurs and mucus becomes highly viscid

Important organs involved in this condition:

→ Lungs

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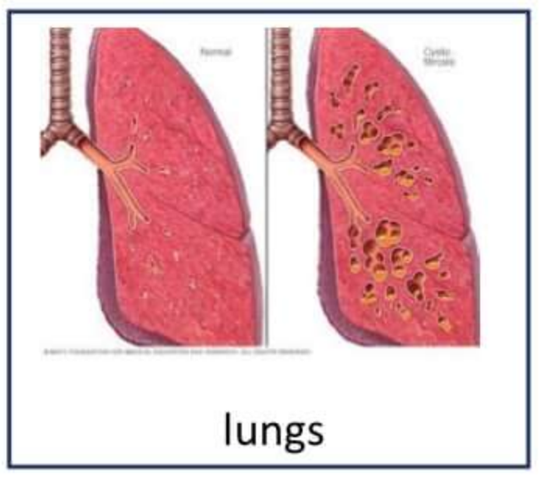
→ GIT

→ Pancreas - results in T2DM in future

→ Liver: Biliary stasis can cause liver damage.



lungs

Root cause of this condition:

1. Low H_2O content of PCL (Periciliary fluid)
2. Acidic Environment of Periciliary fluid d/t defect in HCO3 release.
3. Mucociliary clearance

↓ inhaled bacteria

S. Aureus, Pseudomonas, burkholderia undergoes mucoid transformation, can Forms Biofilm Impervious to antibiotics.

Pathologic features:

→ **1st Involved in Lungs**

- Bronchiolitis –(folicular pluging in airway by Thick Tenacious secretions)

↓

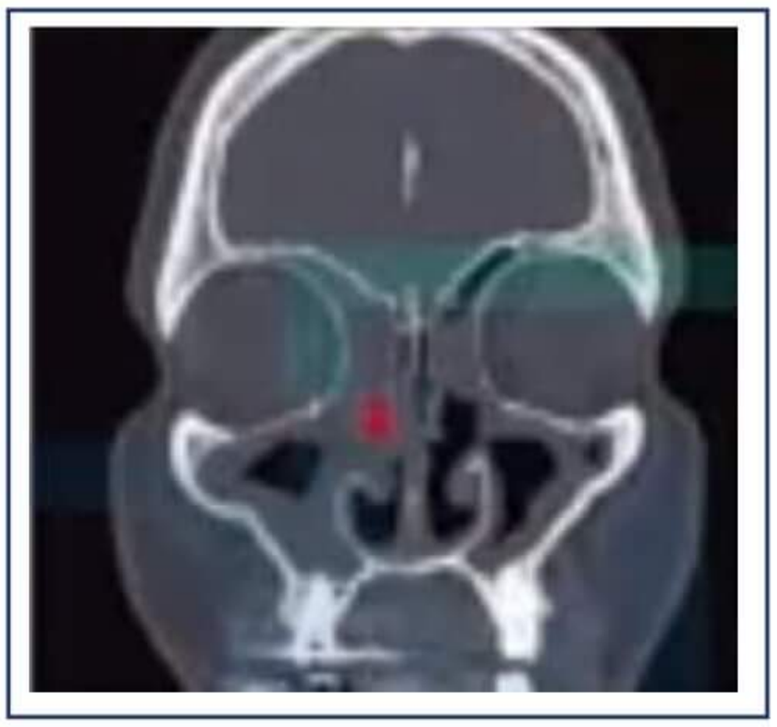
Bronchitis

↓

Bronchiectasis

(Large dilated airways filled with pus)

↓



SINOSITIS OF CYSTIC FIBROSIS

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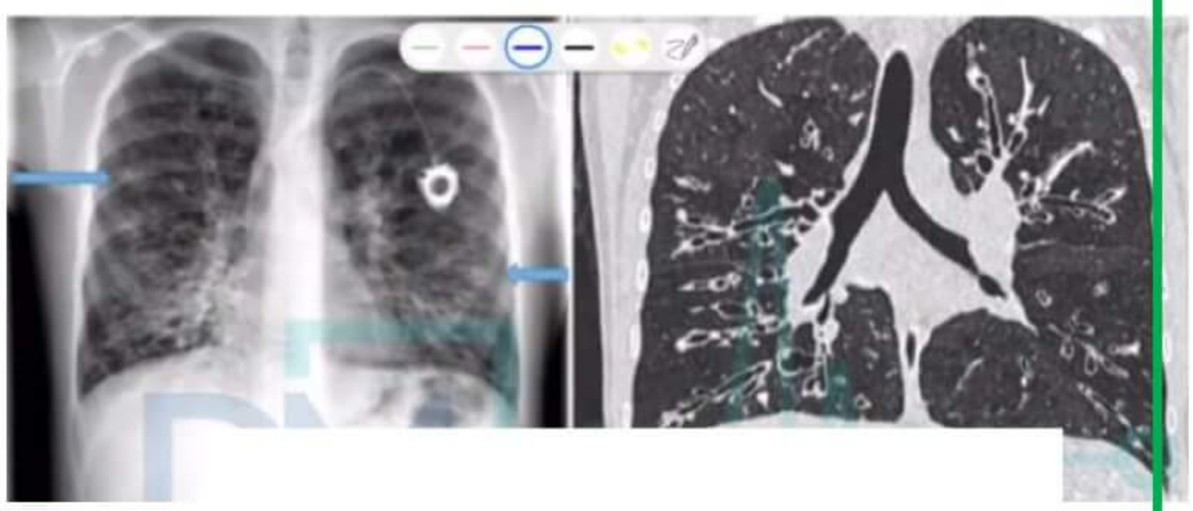
Ultimately leads to Recurrent Pneumonia & cause death of person (Before 1st yr of life in India)

→ **URT is also involved in form of**

- Nasal polyps
- Recurrent Sinusitis

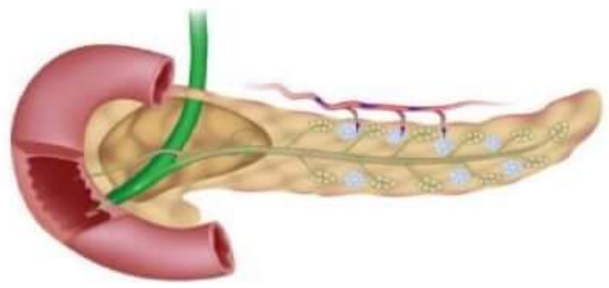


Bronchiectasis Tram track appearance

→ **GIT:-**

Pancreas: Size ↓

- pancreatic secretion become thick and viscid.
- Can be replaced by Fibro fatty tissue
- (In 2nd decade DM can also occur)
- Amylase ↓, Lipase ↓
- Malabsorption syndrome can occur - failure to thrive.



→ **Liver**

- Patient end up with **2° biliary cirrhosis**
- Obstructive jaundice/ prolongation of physiological jaundice

  [NOTE : **1° PBC** - (Autoimmune condition) AMA ab anti mitochondrial antibody]
- Absence of cystic duct

  (M/c overall organ involved in CF is Lungs>> Liver)
- **Rx:- Organ transplantation** is required in these pts.

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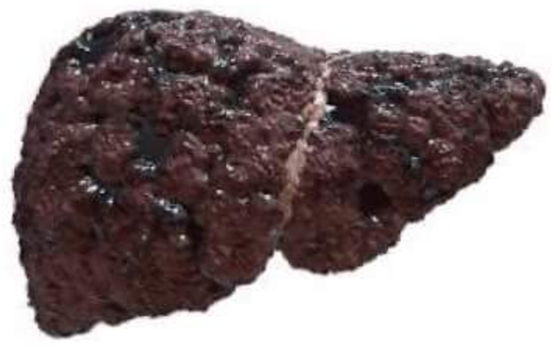


2° biliary cirrhosis

→ **Esophageal/ duodenal glands (Brunner's) filled with thick mucus, Unable to secrete their own secretions and acid from stomach will not be neutralized and leads to duodenal ulcers.**

→ **Genito urinary System**

In females

- Formation of Thick Cervical mucus plug causes Conception issues (Infertility)

  Rx : ART
- Pregnancy can happen or not depends upon on her lungs function status.

  (Shrunken lungs with decreased lung volume is c/I for pregnancy)

  Rx : Regular tobramycin nebulization.

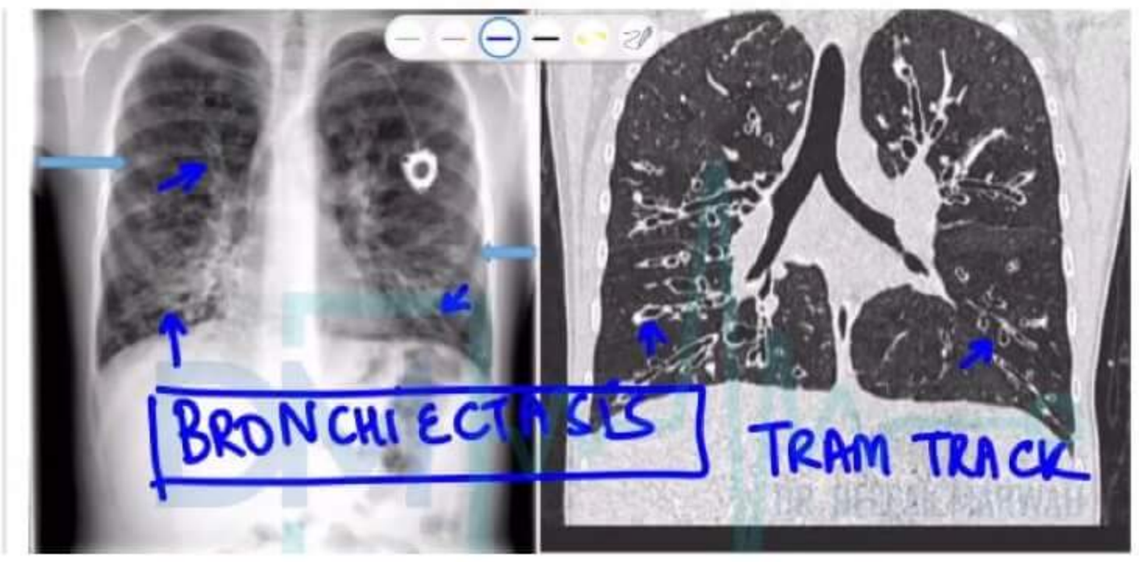
In males: Sexual function (Normal – ejaculation and erection)

- Agenesis of vas deferens and epididymis
- Azoospermia
- Infertility

PrepLadder

Clinical features

1. **Chronic cough** productive (Purulent)
   - Foul smelling pus present
   - Shortness of breath
   - Cor pulmonale: RVF – Non cardiogenic edema (Need for Lung Tx)
   - AP diameter ↑
   - Chest, Hyper resonance
   - Clubbing +
   - Sudden deterioration
     → Pneumothorax: R.D ++
     → Massive Hemoptysis : BP ↓↓ (cause severe hypotension)



2. **Nasal Stuffiness**

3. **Meconium ileus** -Q
   - Abdominal distension & Delayed passes of meconium (**Normal < 48 hrs**)

   IOC: GASTROGRAFFIN enema
   TOC:-GASTROGRAFFIN ENEMA
   → as it Softens the stool

Abdominal distension

Meconium ileus

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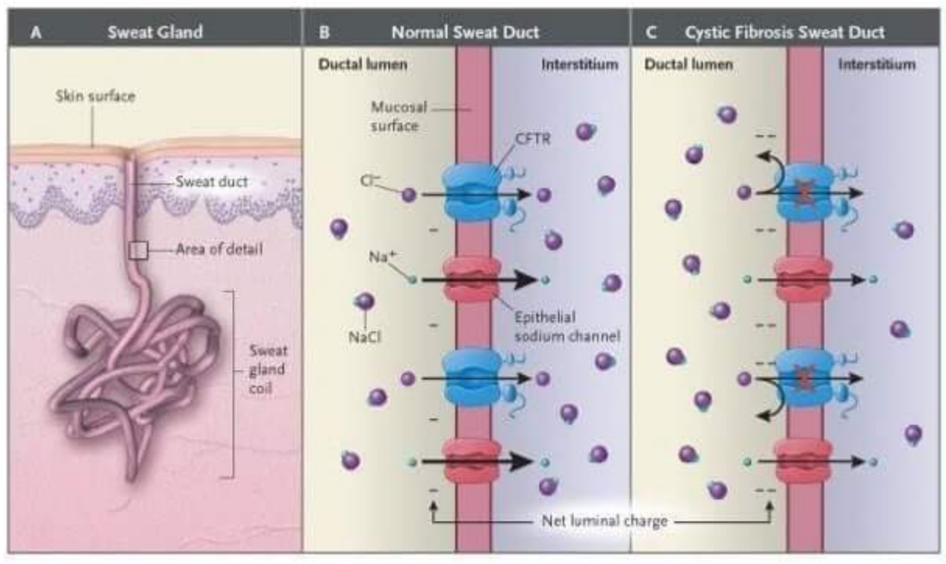
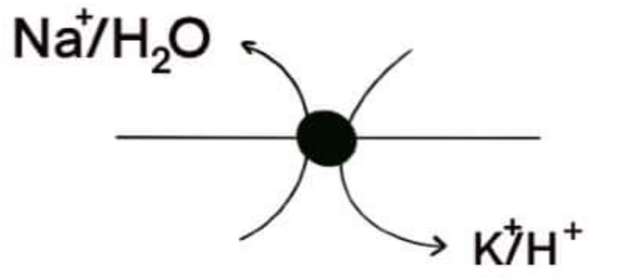
4. **GIT** → Osmotic diarrhea D/t absence of poor pancreatic secretions. (Sugar)
   - Steatorrhea
   - Failure to thrive/P.E.M
5. **Vit E ↓** → Hemolytic anemia (Acanthocytes formation occur)
   Vit K ↓ → Bleeding
6. **Liver cirrhosis** – ICTERUS
   Ascites/ Hypersplenism/ CAPUT medusae, Esophageal varices
7. **GU system:** INFERTILITY (Agenesis of vas deferens)
8. **Sweat gland**
   - Sodium and chloride Reabsorption both is inhibited in C/Fibrosis → also called as salty baby syndrome

Present in sweat { Na^{++}, Cl^{++}, H_2O^{++} ↓

RAAS ACTIVATED
↑ Aldosterone
↓
In kidney

Which leads to
→ Hypochloremic
→ Hypokalemic
→ Metabolic Alkalosis





Aldosterone action in kidney

Diagnostic criteria for cystic Fibrosis (CF)

→ Presence of typical clinical features

- Respiratory → COPD, Bronchiectasis
- Gastrointestinal → Meconium ileus, Malabsorption (osmotic diarrhea to steatorrhea)
- Genitourinary → Infertility

or

→ A history of CF in a sibling

or

→ A positive new born screening test

plus

→ Laboratory evidence for CFTR (CF transmembrane regulator)

→ **Dysfunction:**

1. Two elevated sweat chloride concentrations obtained on separate days

   >60 mEq/L

   or

2. Identification of two CF mutations by DNA sequencing

   or

3. An abnormal nasal potential difference measurement.

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Work up

1. **Sweat chloride test**

   Method used here is PILOCARPINE IONTOPHORESIS

   → > 60 mEq/L x twice

PILOCARPINE IONTOPHORESIS

→ False positive: Sweat Cl^- > 60

- Anorexia Nervosa
- Addison Disease
- Congenital Adrenal Hyperplasia
- Nephrogenic DI

→ False negative

- Malnutrition
- Edema

If equivocal report comes here i.e.

Report 1 → 50

Report 2 → 65

→ A non-confirmatory sweat chloride test. Then we do the 2nd test

PrepLadder

2. **TRANS EPITHELIAL NASAL POTENTIAL TEST**

→Done in case of equivocal test chloride report

TRANS EPITHELIAL NASAL POTENTIAL TEST

3. **DNA testing**

→ +ve of at least 2 mutation

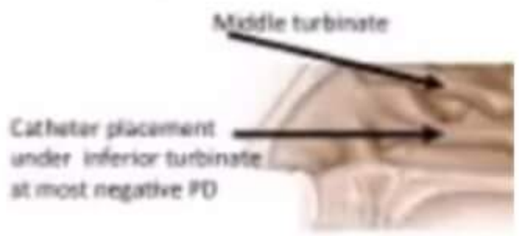
4. **Fecal Elastase level**

→ To identify malabsorption component of disease

5. **Pulmonary function Testing**

→ Obstructive manifestation earlier part of disease / Restrictive lung disease in later part of disease.

6. **HbA1C > 6.5% → 2° DM**



7. **CXR/ HRCT chest** – shows dilated airway.

8. **Sputum culture** – staph aures, pseudomonas infections can occur.

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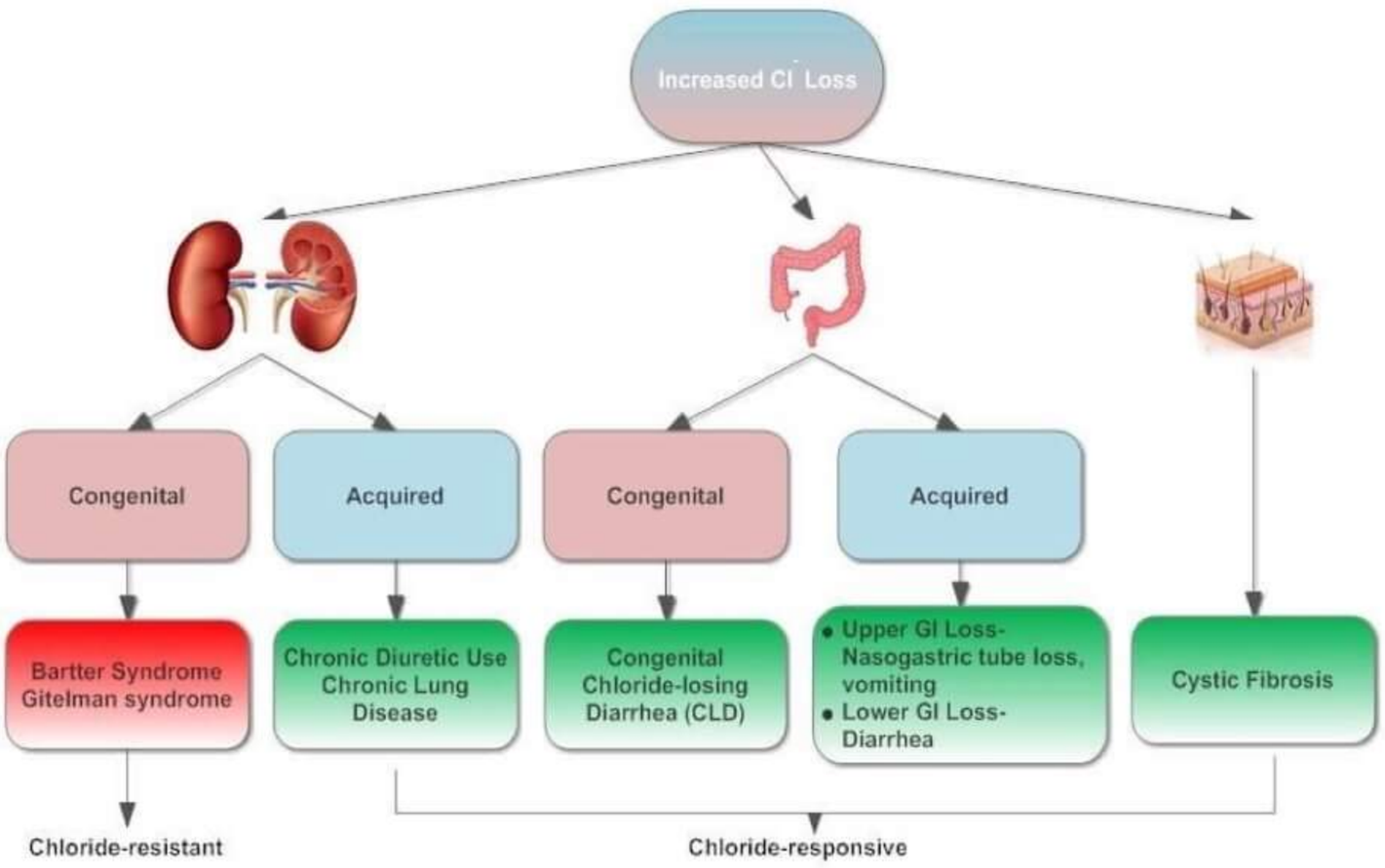
– Causes of Hypochloremic [Metabolic alkalosis (n) cl in our body is 96-106 mEq]

Equivocal test Chloride Report



Treatment :

1. Human recombinant DNA tech

→ DNA ase

→ DORN ase

→ It will ↓ viscosity of sputum so antibiotic penetration and cough out of sputum is relatively easy.

2. N- acetyl/ cysteine followed by β_2 agonist nebulization

(Causes vigorous cough and expectorate sputum out)

PrepLadder

3. Nebulized Hypertonic Saline 7% - can draw water in to perciliary mucus.
4. Nebulized TOBRAMYCIN/ AZTREONAM weekly (Reduces chances of colonization)
5. Chest PERCUSSION/ PHYSIOTHERAPY
6. Hand held Oscillometric devices (Vibrations help to mobilize secretions)
7. if BURKHOLDERIA CEPACIA infection present : Antibiotic of choice – MEROPENEM
8. Steroids: ABPA { CF, Asthma }

Because lot of patient might be having upper airway colonization by aspergillus with highlighted feature of **CENTRAL BRONCHIECTASIS** - serum precipitin antibody against aspergillosis has to be done

9. IVACAFTOR

[CFTR G551 Mutant proteins loss of Cl^- conductance]

→ 150 mg B/D **IVACAFTOR** will improve Cl^- conductance

So, advantage is FEV_1 ↑ → Pulmonary exacerbation ↓

[Prenatal Diagnosis of CF –with chorion villus sampling/ amniocentesis]

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OBSTRUCTIVE SLEEP APNEA

CLINICAL SCENERIO:

- ↑ day time drowsiness d/t recurrent cortical arousals at night time which are secondary to diseases – obstructive sleep apnea.
- Patient are morbidly obese/ obese with BMI > 30

- Normal Individual have normal pharyngeal dilator muscles which prevent tongue from falling backwards when we are in supine position, they promotes normal delivery of oxygen to lungs by keeping the airway patent.
- **In patient with obstructive sleep apnea, the normal sinusoidal inspiration & expiration will not occur.**

normal

- **REM phase:** Tone of muscles are least but to a level which its causing narrowing of airway which will in return contribute to development of hypoxia
  → which will cause cortical arousal.

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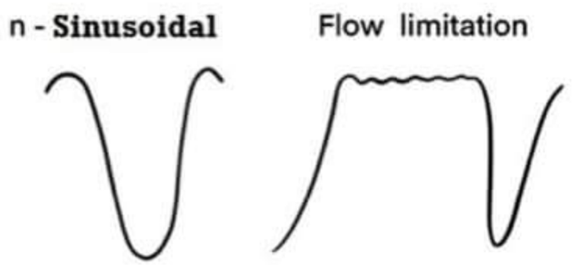
Tongue slightly fallina backwards

- Patient with OSA have sharp inspiratory uptake sequentially plateau wave then scooped out pattern of breathing seen on polysomnography which has flow limitation.



- Magnitude of obstruction increased even further, soft tissues are falling backwards (Secondary to obesity, or patient with smaller jaw – micrognathia)
- When air tries to goes through narrow airway, there is vibration of soft tissues/ esp. uvula → giving characteristic **loud snoring**. As airway progressively get narrowed intensity of snoring increases.

tongue partially covering airway

Shows development of apneic episode in an individual

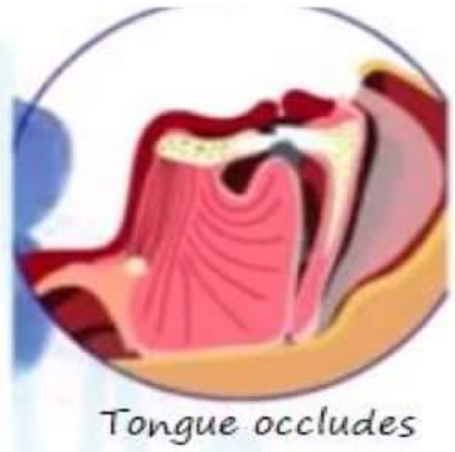
↓

Contributes to

- **Bradycardia**
- **Oxygen saturation falls**
- **Hypoxia**

↓

Cortical arousals



Tongue occludes the airway

- Continuous twisting & tossing in bed
- Grunting at end of apneic episode → Helps forceful opening of mouth → helps passage of air inside airways

↓

Oxygen saturation increases put tremendous load on heart

↓

Patient develop LVH/LV strain

Note: RV failure is least likely/ not seen.

Cortical arousal → Strain on LV → also other body systems not getting rest → causing extreme fatigue at night → never wake up fresh, body pain, thought process – "when will i get back to sleep".

→ Sleep apnea is one of the causes of 2° HTN.
→ Sleep apnea increases cardiovascular mortality
→ In some congenital CVS disorders, children have OSA by birth and might have some Behavioral issues
→ Increase in neck, abdominal circumference (Characteristic of obesity) are risk factor for obstructive sleep apnea.

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IOC: Polysomnography

For obstructive sleep apnea/ Hypopnea syndrome.

- **Polysomnography**: Records nasal air flow, chest expansion
- **Abdominal expansion:** When the person is not breathing/ having apnea – machine records a dip in oxygen saturation once the breathing resumes, on cortical arousal, increased efforts in inspiration – oxygen saturation increases

➢ If **oxygen saturation decreases > 3%** – **Dx: Obstructive sleep apnea.**

Apnea:

→ Absent breathing effort for > 10 sec
→ Associated with 3% decrease SaO_2
→ Cortical arousal (By checking on EEG)

Hypopnea:

→ > 30% ↓ airflow for > 10 sec
→ Associated with 3% decrease in SaO_2
→ Cortical arousal

PrepLadder

Obstructive Sleep Apnea Hypopnea Syndrome (OSAHS)

Diagnostic Criteria

1. Symptoms (Can also occur without symptom)
   - → Nocturnal: **Snoring/ grunting/ snorting /Breathing pauses** (Partner usually notices)
   - → ↑ day time sleepiness
2. When measuring polysomnography
   - → **> 5 episodes of apnea/ hours of sleep**
3. In Apnea Hypopnea Index (AHI)
   - → Calculated by → number of Apneic episodes /no. of hours of sleep
   - → If > 15 episodes/ hr of sleep **minus** symptoms

Risk Factors :

1. Centripetal obesity (MC)

Central obesity

→ Narrowing of pharyngeal inlet d/t Fat deposition.

→ Decreased chest wall compliance which decrease the Caudal Traction for Patency of Upper Airway

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Acromegaly

2. Micrognathia/ Retrognathia

→ Tongue disproportionate to the size of mandible

→ Tongue falls backwards during the REM phase of sleep

MICROGNATHIA: Mandibular hypoplasia

RETROGNATHIA: Abnormal mandibular alignment with respect to maxilla.

Micrognathia/ Retrognathia

3. Down syndrome

4. TREACHER COLLINS

5. Menopause (> 45 years - as decrease in estrogen is associated with development of OSA in post menopausal females)

6. Acromegaly

7. Hypothyroidism

8. High Nasal Resistance: DNS/ polyps

→ Development of mouth breathing in sleep causing The tongue to fall backwards leading to occlusion of airway.

Down Syndrome

Clinical Features

1. Snorting/ Gasping
2. Dyspnea (-)
   → Nocturnal dyspnea will be due to
   P.N.D, Nocturnal asthma or GERD
   → **Absent in OSAHS**
3. Frequent Awakening
4. Dozing off involuntary during task
5. Dry mouth, Halitosis, Mood swings
6. Erectile Dysfunction

O/E

1. BP ↑ (Can be pre-existing to the current symptoms)
2. Abdominal Girth ↑
3. Neck Circumference ↑
4. Tongue size ↑, mandible ↓
   Low lying palate with bulky uvula
5. Enlarged tonsils

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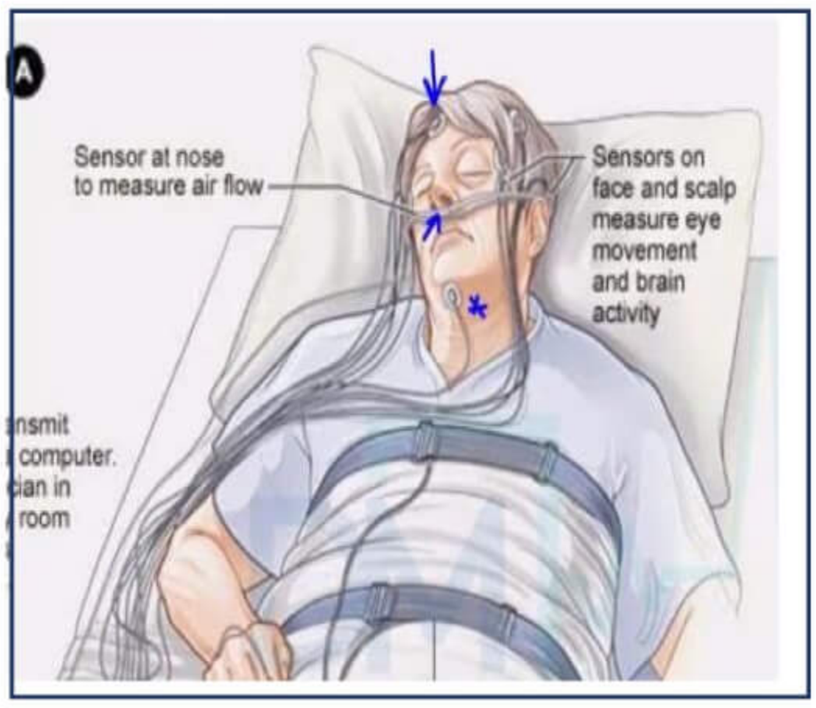
Work up

→ **Polysomnography**
- EEG, EOG, EMG (Chin), ECG, SpO_2, Nasal Airflow, Chest/ abdominal movements BP monitoring → **absence of nocturnal dip**
  ECHO – Chamber size **(RVF is not seen)**



Polysomnography

Whenever there is apneic episode

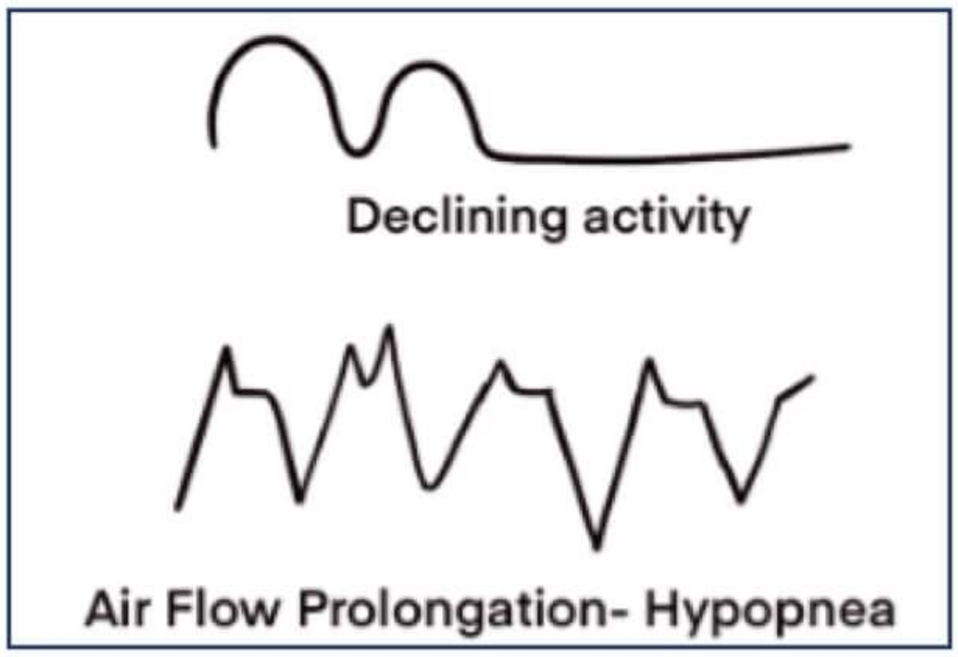
EEG: In REM

→ Cortical Arousal will be present
→ I.e. conversion to α wave from β

ECG: R-R interval will be prolonged (Bradycardia)

Naso-Pharyngeal Airflow sensor: Shows declining activity

PrepLadder



Snore flow:

Image Noting: Hypo apnea → apnea→ Hyper apnea

SaO_2: Dip in the SaO_2 at the time of episode

→ CHEYNE STOKES BREATHING

(hypopnea - apneic - hyperventilation)

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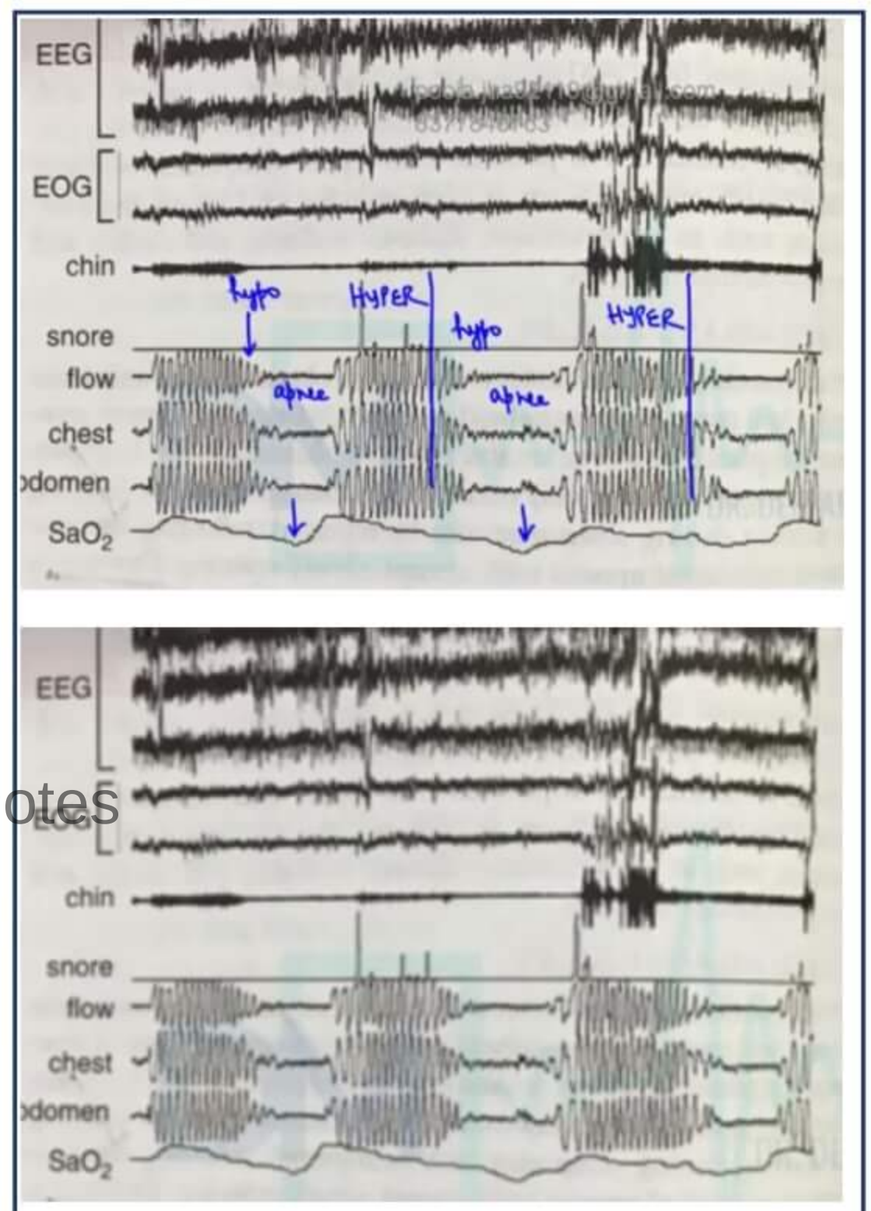

CHEYNE STOKES BREATHING

Note : There is a sinusoidal movements between chest and abdomen.

Treatment:

1. Weight loss

   [Weight 10% ↑ → 30% ↑ OSA incidence]

2. Avoid sleeping in supine position, try to sleep on later position.
3. Nasal allergy
4. Avoid alcohol (3hrs before sleep)
5. **C.P.A.P** (T.O.C) → > 15 Hypopneic episodes/ hr (or)

   >5 apneic episodes/ hr

   CPAP [Continuous positive airway Pressure] - Splint airway open

Continuous positive airway Pressure

6. Uvulo-Palato pharyngoplasty
7. Upper Airway Device: Sx implantation

   - Stimulates the hypoglossal Nerve

8. **Oral Devices**: Reposition of mandible (efficacy is very less)

PrepLadder

EPWORTH SLEEPINESS QUESTIONNAIRE

→ Fill up a Questionnaire and if score is > 8 medical advices is recommended and a polysomnography should be done.

Epworth Sleepiness Questionnaire For a Medicare subsidised sleep study a patient must score 8 or more.

How likely are you to doze off in the following situations?	No Chance	Slight Chance	Moderate Chance	High Chance
Sitting and reading	○0	○1	○2	○3
Watching television	○0	○1	○2	○3
Sitting inactive, in a public space	○0	○1	○2	○3
Lying down to rest in the afternoon when circumstances permit	○0	○1	○2	○3
Sitting and talking to someone	○0	○1	○2	○3
Sitting quietly after a lunch without alcohol	○0	○1	○2	○3
As a passenger in a car for an hour without a break	○0	○1	○2	○3
In a car, while stopped for a few minutes in traffic	○0	○1	○2	○3
			TOTAL SCORE:	

Central Hypo Ventilation Syndrome

→ As known as ONDINE curse

→ Genetic condition involving PHOX 2B gene

→ Patient have absent response to hypoxia/ hypercapnia

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Rx

→ NIPPV (No-invasive Positive pressure ventilation)

→ Phrenic nerve/ diaphragm pacing (New Technique) → not done for OSA

Obesity Hypoventilation Syndrome

1. BMI > 30
2. PCO_2 > 45 mm Hg:
   - → Patient have chronic day time hypoventilation
   - → Patient may/ may not have apneic episodes

PNEUMOMEDIASTINUM

Can occurs due to:

1. Alveolar Rupture → dissection of air
2. Perforation of Esophagus (Boerhaave syndrome)
3. Trauma to the Neck/ Neck tissues may get damaged leading to dissection of air

C/F

→ Substernal chest pain ± Radiation to arms

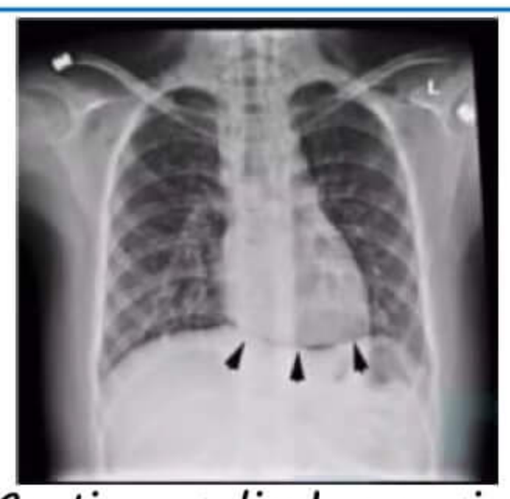
→ On Auscultation

- Hamman Crunch Sign
- Crunch synchronous with heart beat + better heard – lateral decubitus position

PrepLadder

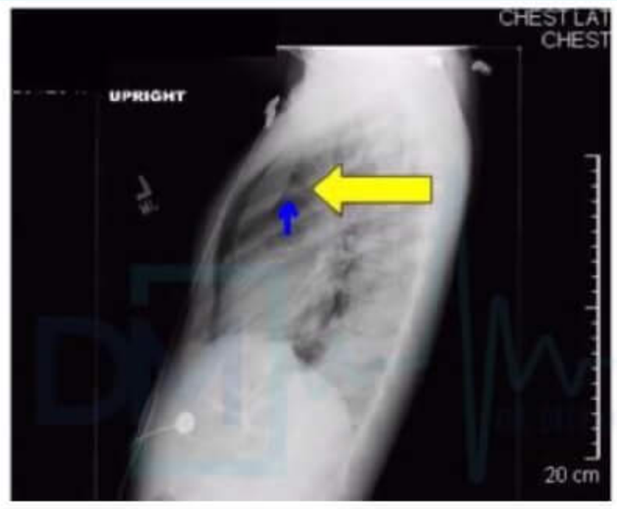
On CXR:-

- Air below the heart of patient (Image – pneumomediastinum CXR)
- **Continuous Diaphragm sign** - Q



Continuous diaphragm sign

- Air at heart borders
- Lateral view – air present in mediastinum. - **Spinnaker sail sign**
- Thymus pushed up



Spinnaker sail sign

- **Naclerio V Sign:**

Rx:

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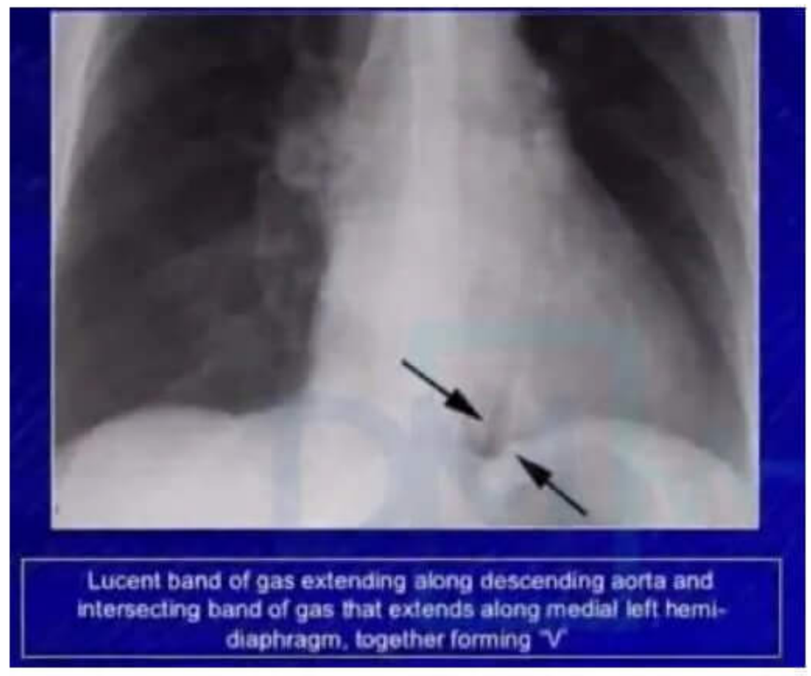
→ No treatment required (Self- reabsorption of air)

→ If high flow O_2 is given, rate of reabsorption is increased

→ If obstructive shock occurs then needle decompression will be required

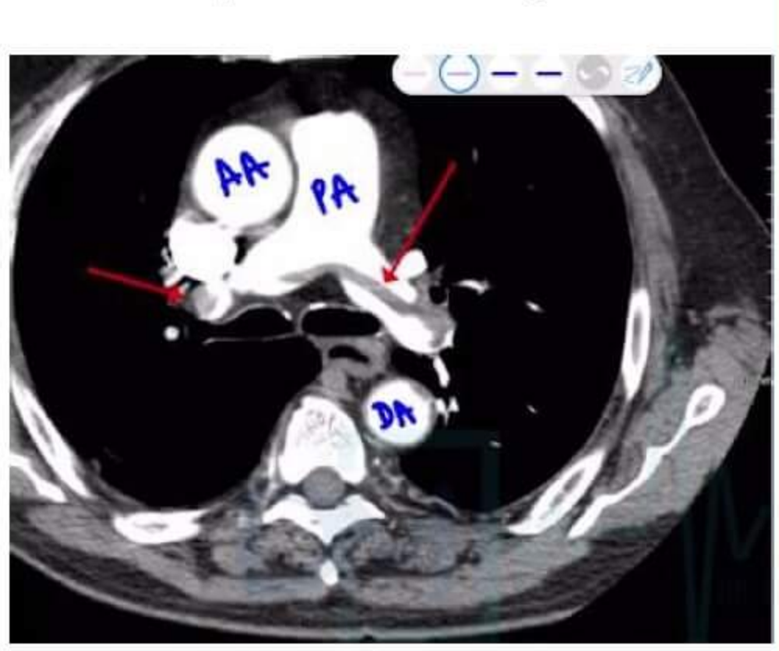


Naclerio's V sign

PrepLadder

PULMONARY EMBOLISM

- Pulmonary thromboembolism originated from DVT which is leading risk factor
- M/C/C of presentable death in hospitalized patients = **pulmonary thromboembolism** by treated with LMWH, Fondaparinux, and all post op patient can treated with pneumatic compression stocking.



Pulmonary thromboembolism

Etiology

1. Deep vein thrombosis: "Virchow Triad"
   - **Immobilization** > 72 hrs can cause thrombosis in

Mainly soleal vein and popliteal vein so piece of clot has broken and Pass through right side heart results in v/p mismatch.

- **Prothrombotic state**: 1. Autosomal dominant

Factors V Leiden mutation

Prothrombin Gene mutation

Note: M/C congenital hypercoagulable state → Factor V Leiden mutation.
Unopposed factor V leads to procoagulant state where protein-c cant Inhibit factor V

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Pneumatic compression stockings

2. Antiphospholipid syndrome
   - Anti β_2 glycoprotein antibody
     ↓
     Stimulate intrinsic pathway
3. Oral contraceptive
4. Hormone replacement therapy
5. Post menopausal female
6. Cancers surgery
7. Ortho implant surgery (Massive PE can develop on 3rd post op day which is results in V/P mismatch)

Physiological Basis of pulmonary thrombo embolism:-

In this condition increased ($PAO_2 - PaO_2$) because normal volume of air is inhaled so PAO_2 is normal but insufficient blood supply in pulmonary artery so PaO_2 is decreased leads to mismatch.

Normal A – a gradient = 5-15 mmHg
($PAO_2 - PaO_2$)

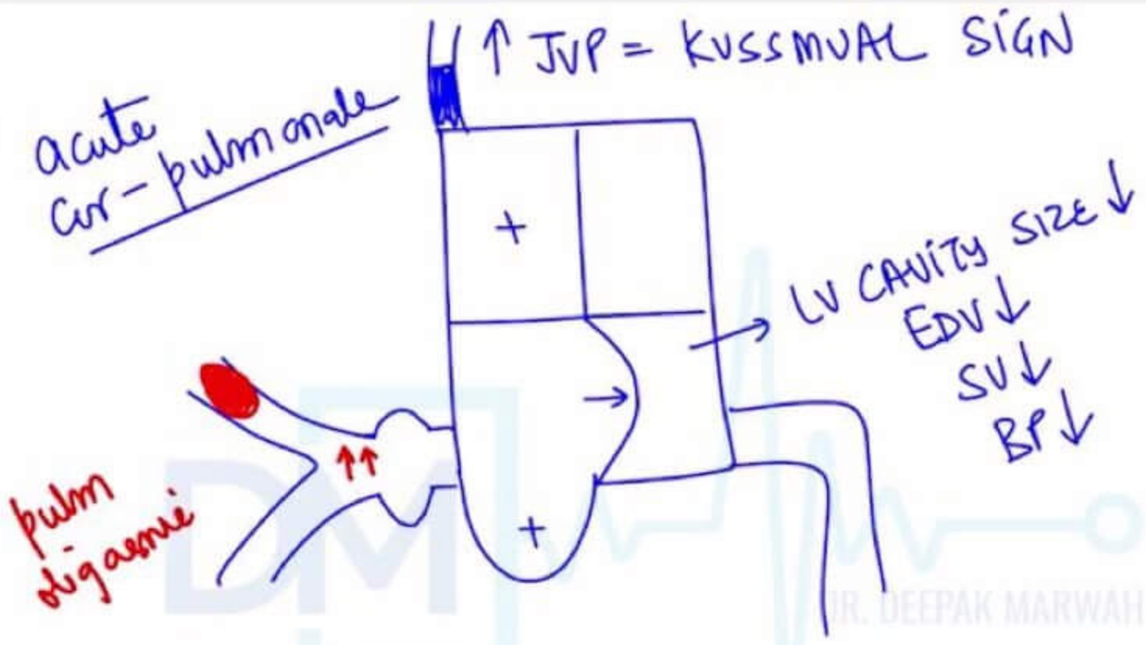
= ↑sed dead space ventilation
= Pulmonary vessel constriction increases dure to hypoxia.
= Alveolar Hyperventilation
= Decreased lung compliance

PrepLadder

MASSIVE PTE:

- Seen around 5 -10 % of cases
- **Pathophysiology**: There is block in one of the pul

Artery which increase the pulmonary artery pressure
And patient manifest with following presentation.



1. Pulmonary oligemia
2. P.A. HTN
3. Sudden Rt. Ventricular failure

   JVP ↑

   Echo = **Mc Connell Sign** -imp

   ↓

   Rt. Ventricular hypokinesia

   Rt. Ventricular apex hyperkinetic

4. Septal deviation
5. Left ventricular = End diastolic volᴹ ↓↓

   Stroke volume ↓↓

   Co ↓↓

   B.P. ↓↓

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Note: 3 + 4 +5 presentation together called as **acute cor pulmonale.**
COPD is the leading cause of the **Cor pulmonale**. Where acute cor pulmonale is associated with PTE

6. Rt. Coronary artery compression due to sudden dilatation of right ventricle.

   ↓

   Micro infarctions

C/F: **"GREAT MASEQUEDER"** – mimics MI by chest pain but here the pain is due to pleural infarction where pulmonary artery blood supply compromised.

Q. 75 yrs old man underwent total Hip replacement B/L on day 3. at 8 pm c/o dyspnea with chest pain.

O/E = HR = 120/min BP 90/60 mmHg

JVP elevated

Kussmaul sign +ve

S_1 Loud

S_2 wide split because P2 closure takes more than 30 msec. } Heard with diaphragm

S_3 ⊕

Lungs = B/L clear

NOTE: Based on C/F we need to do ECG, CXR, ECHO but as time concerned there is criteria to diagnose PTE

Well's criteria

PrepLadder

B – Blood in sputum

D – Deep vein thrombosis sign and symptoms + → Homan Sign (Pain on the calf while dorsiflexion of the ankle.)

C – Cancers

H – HR>100 /min on 3rd or 4th day is suggesting atelectasis or PTE.

I – Immobilization > 3 days, surgery < 4 weeks

P – Prior pulmonary embolism

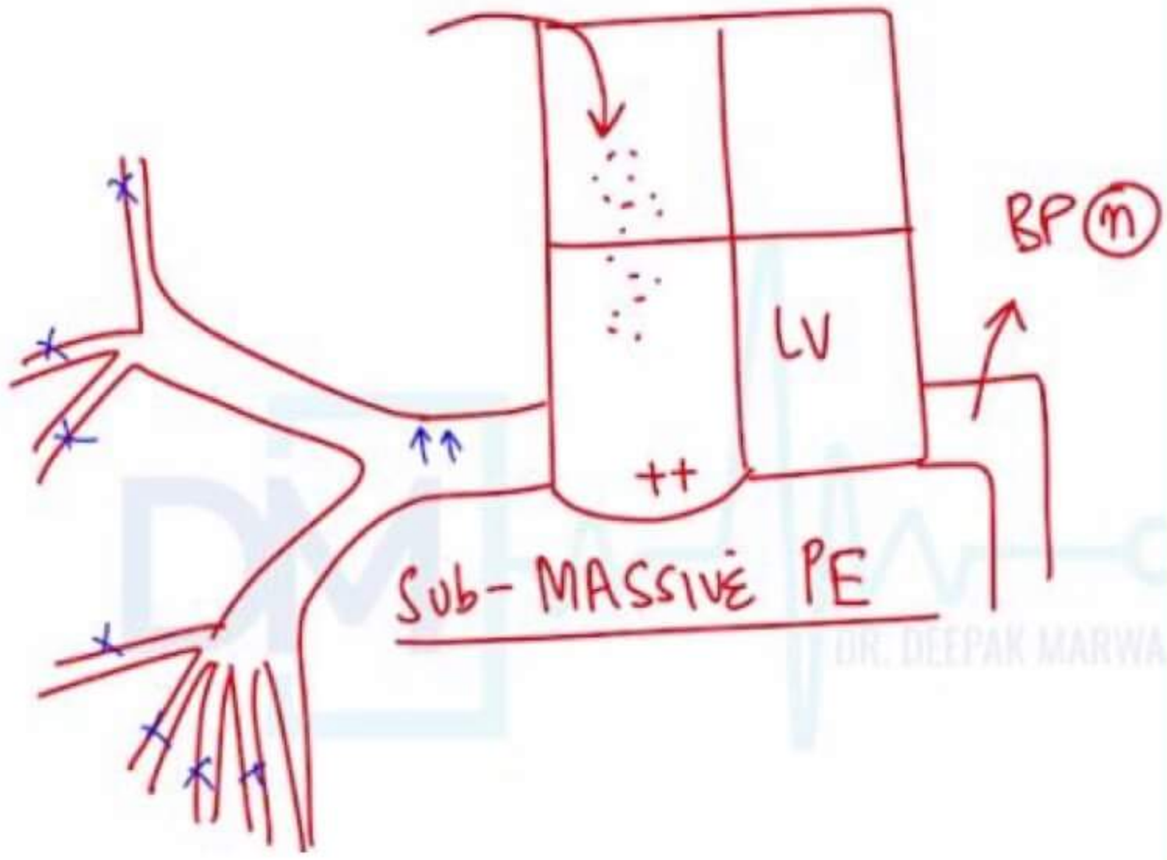
Or

Prior DVT

If Score > 4 = High probability

SUB- MASSIVE PTE:

- Multiple small pulmonary emboli enter into Right heart leads to block small arteries of Pulmonary artery that results in mild distension of right ventricle without affect left ventricle.
- Seen around 60 % of cases.



WORK -UP:

1. **E.C.G =** $S_1 Q_3 T_3$
   Deep S wave in lead I
   Deep Q wave in lead III
   Inverted T wave in lead III

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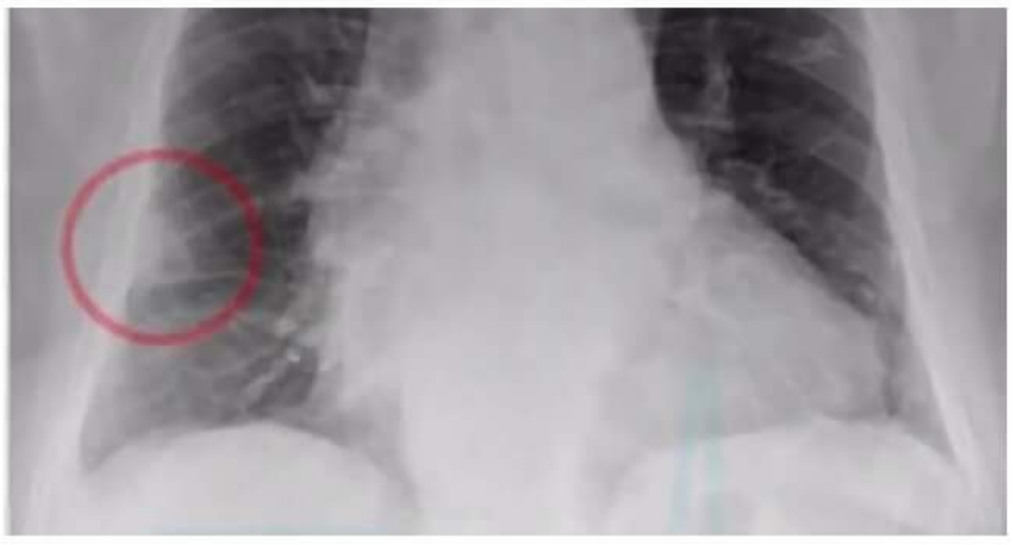
2. **Chest X ray:**
   - Palla sign
   - Hampton hump
   - Wester mark sign

Concepts: There is a block by dislodged emboli on pulmonary artery which presents dilated to the proximal emboli called Palla sign - commonly seen in Right descending pulmonary artery and wedge shaped infarction to the distal emboli called Hampton hump.

Wester mark sign – due to focal oligemia seen in only one lung where emboli lodged in to Right descending pulmonary artery.



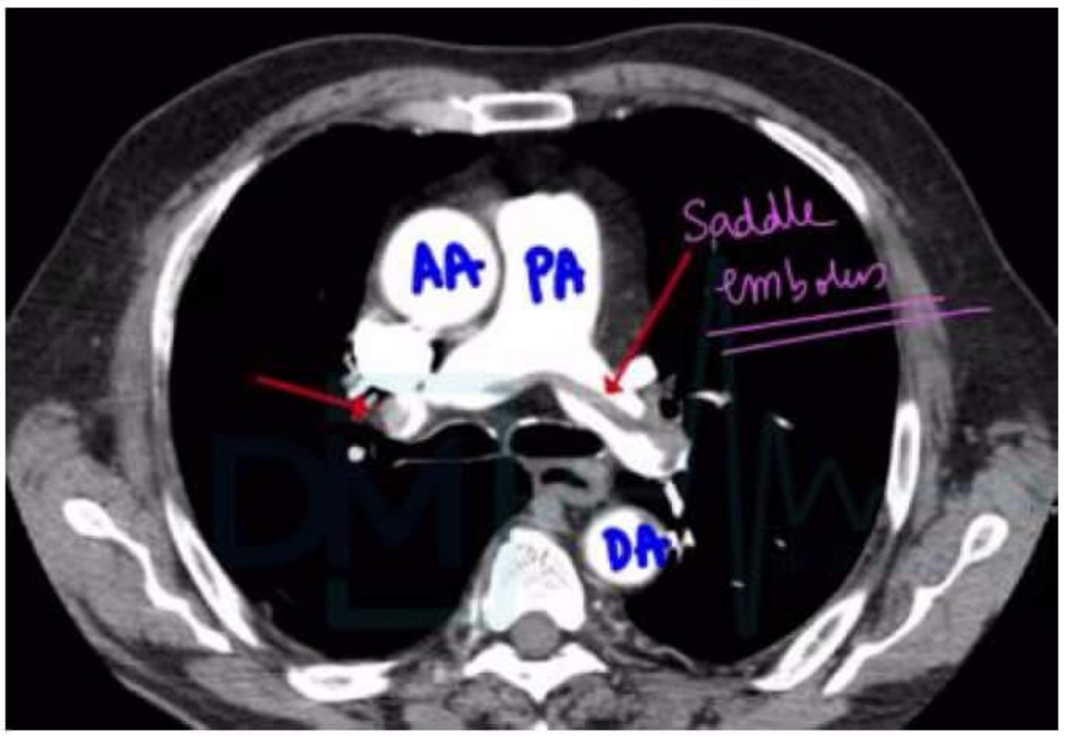
Hampton hump

3. Trop I / HFABP / B.N.P → Elevated due to R.V micro infarction
4. USG / Doppler of legs = Non compressibility of big veins normally these veins are compressed by placing the USG prob.
5. **Screening test** = D – Dimer assay = elevated
6. **I.O.C** = CT angiography

Triple rule out CT -imp- new technique

- Pulm. Embolism
- Acute aortic syndrome
- Acute coronary syndrome

7. Gold standard test: Pulmonary angiography
   → Not recommended nowadays
8. Echo = Mc Connell sign
   - R.V wall hypokinesia
   - R.V Apex hyperkinesia



SADDLE EMBOLUS

Management:-

Primary therapy: Pharma co mechanical approach

→ Alteplase 100 mg → given for Massive PE but this leads to S/e of bleeding.

To prevent bleeding the new approach was tried:

→ Catheters dissected thrombolysis = 25 mg alteplase then embolus fragments are removed by another device so that it can prevent dislodging of emboli into distal.

Secondary prevention:

→ Anticoagulation / I.V.C filters

CLINICAL SCENARIO:

Massive P.E	Submassive P.E
1. BP ↓↓ 2. R.V Hypokinesia 3. ECG = S_1 Q_3 T_3 4. CXR = Hampton Hump	1. BP normal 2. R.V dilatation 3. E.C.G sinus tachycardia 4. Chest x ray normal
5. Old age = Immobilization /malignancy Post-operative sudden onset respiratory distress on day 3 or day 4	
Screening test → D- Dimers assay **For diagnosis:** CT Angio	
T/t = Thrombolysis	**T/t** → Anticoagulation

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Drug used :

PrepLadder

1. Unfractionated heparin = Requires monitoring aPTT – 60 to 80msec has to be done (Normal value of aPTT: 30 - 40 msec)
   - U.F.H can cause H.I.T (Heparin induced thrombocytopenia)
   - To control H.I.T = bivalirudin is given
2. Enoxaparin
3. Fondaparinux

} Can be given OD, Subcutaneously, No Monitoring required

4. Warfarin → It will take at least 5 days to work so it can be bridging by any of above mentioned drugs. So for first 5 days UFH / Enoxaparin/ Fondaparinux can br given parenterally with warfarin.
   - Target INR = 2-3 = Requires monitoring
5. Noble oral anti coagulant = Start action within Hrs.
   = Dabigatran
   = Betrixaban

} Given for 1st six months.

Drug	Antidote
Dabigatran =	Idarucizumab
Betrixaban =	Andexanet

Indication of I.V. C Filters:

1. Recurrent prevention of pulm. Embolism
2. Bleeding with anticoagulation

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- Pharmaco mechanical catheter dissected treatment
  = New intervention
- Pulmonary thrombo – embolectomy.

PrepLadder

FAT EMBOLISM SYNDROME

CASE SCENARIO:

18 years old male had bike accident: # Shaft of Femur for which he was operated

Post op 12-72 hours: Sudden onset dyspnea

Cognitive defect

Petechiae: Axilla > rest of the body

D_x: Fat Embolism syndrome

*__Note__: Most of the time patient have predisposition for development of pulmonary embolism like hypercoagulable state or if pt. was immobilized for a long time then we can think of DVT and subsequently pulmonary thromboembolism

PATHOGENESIS:

Bone fracture

↓

Fat molecule come into circulation

↓

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Lipoprotein lipase

↓

Free fatty acid generation

↓

- Structural damage to pulmonary circulation esp. pulmonary endothelium
- Cytokines

↓

Ventilation perfusion imbalance/ resp. distress

- During intramedullary nailing → asymptomatic fat embolism syndrome

TRIGGERS:

→ Polytrauma
→ Acute pancreatitis
→ Joint reconstruction surgery
→ Liposuction
→ IV fat infusion (Pt. on TPN)
→ Decompression sickness = Caisson's disease

PrepLadder

In poly trauma: Incidence = 90% of Fat embolism

Long bone: Incidence = 2% of Fat Embolism Syndrome

*Note: Most of the times body's inbuilt system will neutralize the fat and pt. will not develop any symptoms

C/F: **Based on GURD CRITERIA:**

MAJOR

1. **Respiratory:** - Respiratory symptoms present → sudden onset breathlessness
   - Resp. insufficiency → fast breathing, accessory muscles. of respiration being used
   - Radiological evidence → diffuse infiltrates
2. **CNS:**
   → Cognition defect
   → Stupor
   → Coma (GCS <8)
3. **Petechiae:** Axilla
   Subconjunctival

MINOR

1. HR ↑
2. Temp ↑ >38°c
3. Retinal changes
4. Kidney dysfunction
5. Jaundice
6. Hb ↓↓, platelet ↓↓, ↑ ESR
7. Fat microglobulinemia: Urine/ sputum

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Fat globules in urine/oval fat bodies: Nephrotic syndrome
Chyluria
Fat embolism

1 major criteria + 4 minor criteria = D_x

Work up-

1. **Chest X Ray** = Normal or B/L diffuse infiltrates
   ↓
   Also seen in ARDS
   ARDS may be due to
   H1N1
   Sepsis
   Multiple BT (TRALI)

PrepLadder

2. **CT Head** = Normal / or diffuse white matter petechiae ±
3. **Transesophageal echo** = Patent Fossa Ovalis (20-30%)

   Right to left shunt so operates opposite to ASD

   Paradoxical embolism: Fat globules comes to right atria then goes to left atria then goes to brain circulation
4. **Doppler** = Rule out deep vein thrombosis
5. **Bronchoalveolar lavage** with staining for fat

T/t

1. High flow O_2
2. IV fluids: to prevent dehydration
3. Endotracheal tube + intermittent positive pressure ventilation
4. Steroids
5. Heparin = Anti lipemic effect
6. Prevent D.V.T and stress GI bleeding

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PrepLadder

BRONCHIECTASIS

→ **Destruction/ Dilatation of large airways** → airways are filled with results in the features of bronchorrhea.

Note: Bronchorrhea also seen in chronic bronchitis.

→ **Histopathological examination**

↓

Cylindrical / Tubular – m/c subtype → Represents airways are dilated and thick walled which filled with pus by the dangerous organisms like pseudomonas. This organism later will form the biofilm in the lung which results in antibiotic resistant. Expansion of pus filled cavity will erode the blood vessels of lungs which results in massive hemoptysis and death of the patient.

Cause of death → massive hemoptysis

Causes :-

a) **Focal** → Obstruction which subsequently cause infection in the airway and results in pus. Following condition can cause focal bronchiectasis.

→ **Foreign Body aspiration – Children**

→ **Pulmonary hamartoma**] Adults

→ **Bronchial carcinoid**]

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Note: Benign tumor in adults like pulmonary hamartoma and carcinoid tumor which encroached the bronchus and result in obstruction of airways and causes atelectasis. So the secretion of lungs become infective in atelectasis area.

b) **Diffuse** →

(A) Infection

i) Pseudomonas Aeruginosa

ii) Mycoplasma Pneumoniae –

- Resistant to beta lactams so macrolides should given

if any Doctors not aware of these results in bronchiectasis

iii) Bordetella Pertussis (100 day illness)

] Affects mucociliary clearance

(B) α1 Antitrypsin deficiency

(C) Cystic Fibrosis

(D) Kartagener syndrome

] Genetic causes

PrepLadder

(E) ↓↓ Immunity

→ HIV

→ Hypogammaglobulinemia

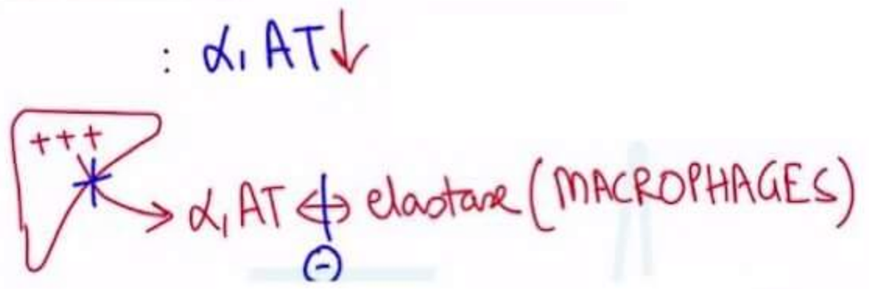
Genetic causes (BCD) :

1) α1 Antitrypsin deficiency :

It is produced by liver but the problem here is to release of α 1 antitrypsin from the liver. So main function of α 1antitrypsin is neutralization of elastase from macrophages. This function is impaired in this condition.

Effects

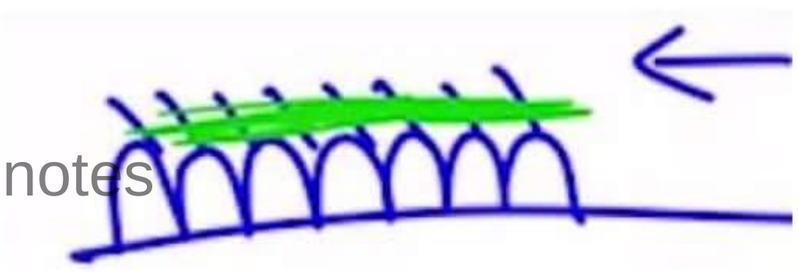
a) Panacinar Emphysema
b) Bronchiectasis
c) Cirrhosis



2) Cystic Fibrosis: (Mucoviscidosis)

→ AR

→ F508 mutation, defect in chromosome 7.



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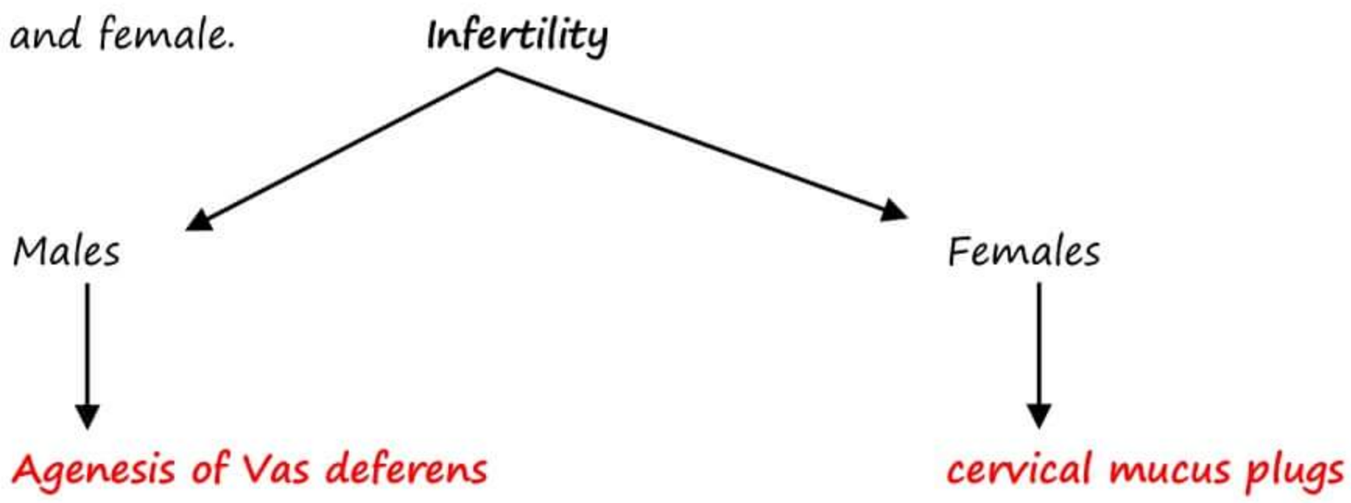
→ Mucus become thick and viscid, so there is stasis of mucus.

→ Infertility seen in both male and female.



c) Kartagener syndrome

Immotile cilia due to dynein arm defect.

Triad

a) Recurrent sinusitis
b) Bronchiectasis → due to recurrent lung infections.
c) Situs Inversus

Infertility – not a part of Triad

- **Male** → Seen due to defect of sperm motility
- **Female** → Not seen because movement of ova is depends on both peristalsis and cilia motility so even cilia motility is affected still ova can move in fallopian tube.
  So infertility is not included in triad.

PrepLadder

Approach of case Qn: Bronchorrhoea, clubbing → Suggestive of large Airway disease

f) Autoimmunity:

a) Rheumatoid Arthritis, Sjogren syndrome, IBD

- RA can develop inflammatory nodules which results in local airway damage and later It may leads to fibrosis which can distort the anatomy of the airway.

b) ABPA (Allergic Bronchopulmonary Aspergilloma) → it is not colonized by aspergillosis species but it can cause hypersensitivity reaction to fungus ASPERGILLUS FUMIGATUS and results in local damage of lungs.

- Predisposing factor here is asthmatic where patient present with **Brown to black sputum plugs.**

- **So diagnosis is made based on:**

1. CT Scan for central bronchiectasis → Presents with middle lobe involvement.

[ABPA] → Aspergillus fumigatus

↓

Asthmatic with black sputum plugs.

→ Middle lobe involvement → Central Bronchiectasis

→ Hypersensitivity

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- Serum Precipitins against Aspergillus - Checking for antibodies against aspergillus which can damage the middle lobe of the lungs.

↓

Test to diagnosis the aspergillus – imp

G) Recurrent Aspiration (Micro aspiration)

a) Scleroderma (Esophageal dysmotility) → aspiration of food particles taking place when patients is lying down.

b) Bulbar Palsy seen with stroke patients where vagus nuclei involved.

Upper lobe Bronchiectasis

→ Cystic fibrosis

→ Tuberculosis

→ Post Radiation Fibrosis → causes traction bronchiectasis because radiation can destruction of airway.

PrepLadder

Lower lobe Bronchiectasis → Usually seen in the people with aspiration.

→ Scleroderma

→ Repeated Infections

→ Hypo gamma globulinemia

Middle lobe Bronchiectasis

→ ABPA-*imp*

→ Kartagener syndrome -*imp*

→ Non Tuberculosis mycobacteria -*imp*

→ William Campbell syndrome

↓

Defect in cartilage so anatomy of the airway destructed.

Clinical features:

CASE SCENARIO: Young adult came to OPD presents with productive cough since long time and foul smelling sputum despite of consult with many doctors, having past history of cystic fibrosis.

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1) Productive cough

2) Bronchorrhoea

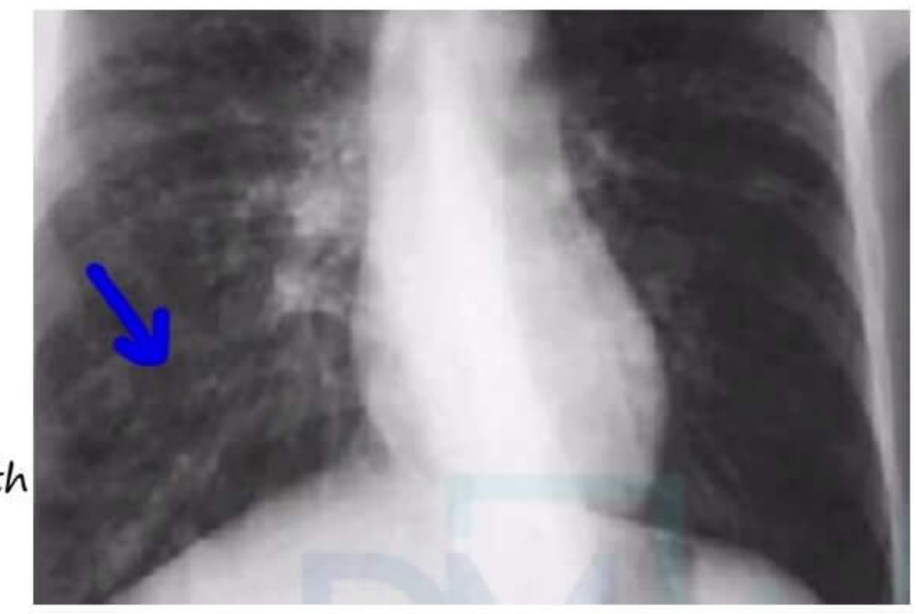
3) Dyspnea on exertion

4) Crept present (Rales)

5) Clubbing → Present because longer duration of illness

Work up:

1) CXR → mostly present with normal, if few cases presents with Tram track appearance on lower lobe.

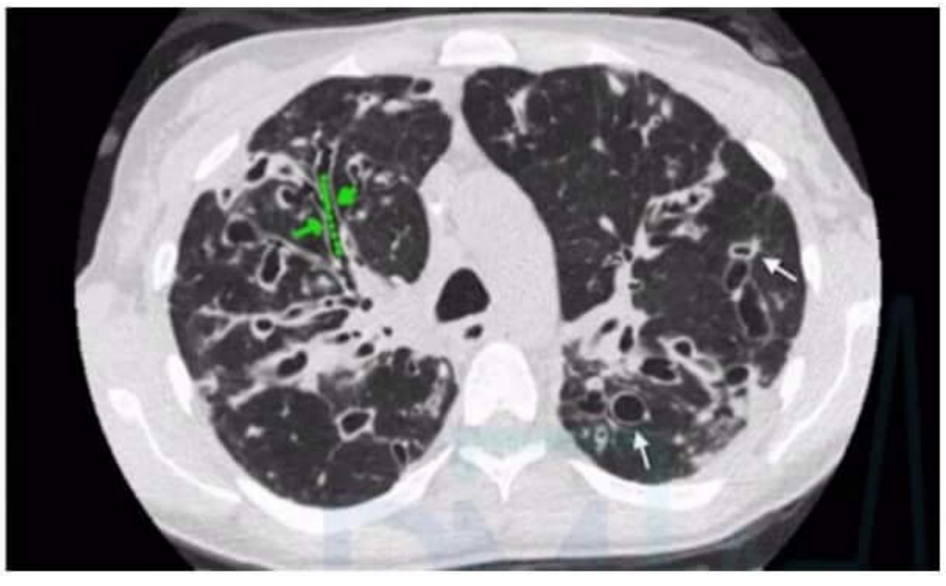


Tram track appearance on CXR

2) CT-scan (HRCT – *Investigation of choice*)

ON HRCT:

a) Tram track appearance
b) Signet ring
c) Tree in bud → seen in endobronchial TB, pneumocystis jiroveci, many other condition so its not specific.



Tram track appearance on HRCT

3) Pulmonary Function test → Obstructive Pattern

$\frac{FeV1}{FEC}$ ↓↓ → < 0.7

4) Sputum culture -imp

5) HIV – to test with ELISA

6) Genetic Studies – CFTR gene.

7) α1 Antitrypsin assay

8) Nasal/ lung Biopsy – test for Kartagener syndrome

9) Videomicroscopy of lung (Cilia)

10) RA factor

Treatment

1) Antibiotics x 14 days → initially with begins empirical antibiotics later can shifted to sensitive antibiotics.

2) Non TB Mycobacterium → Macrolide + Rifampicin or ethambutol

3) Mucolytics - Dornase, DNAase

4) **Percussion device**

↓

Helps in dislodgement of mucus

Chest Physiotherapy

Incentive spirometry

5) **Bronchial hygiene**

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PERCUSSION DEVICE

Complications:

Massive Hemoptysis (500 ml to 600 ml / day)

- IOC → Rigid Bronchoscopy
- TOC → Bronchial Artery Embolization

To prevent 1° exacerbation of Bronchiectasis

→ Ciprofloxacin BD x 2 weeks/ month

→ Macrolides OD

→ **Tobramycin Nebulization:** Weekly

↓

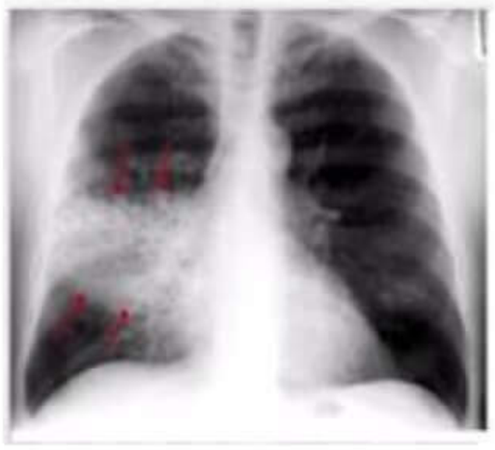
Anti pseudomonal

→ I.V Antibiotics "Cleans out" of lungs intermittently.

→ Vaccines/ gamma globulin – incase of hypogammaglobinemia.

PrepLadder

PNEUMONIA



Consolidation present in the right middle lobe with silhouette sign is seen because heart border is not visible, all these features suggested.

Labor pneumonia = community acquired pneumonia (CAP)

Associated with → pneumococcus / streptococcus pneumonia

EXTRA MILES: same pneumococcus is responsible for causing **acute bacterial meningitis** in both adults and children

- Diffuse infiltrates of B/L lung fields in the patients is presentation of **Ventilator associated pneumonia (VAP)** but without history this could be Miliary tuberculosis or ARDS as well. But the patient had intubated due to myasthenic crisis or diaphragmatic paralysis. So the **pseudomonas** can enter into contaminated intubation and results in VAP. Its not associated lobar predilection.

  a) **MDR** associated with Pseudomonas.

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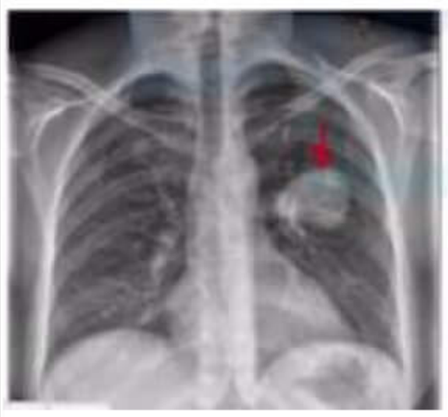
  Acinetobacter

  b) **Non MDR** associated with Pneumococcus



- Young female came with combination of breathlessness, productive cough, difficulty in speech, fever and CXR shows lung mass.

  ↓ **Characteristic features of round pneumonia**

  Round pneumonia caused by **Pneumococcus** in community acquired pneumonia.

Pathology:-

- Initially there is a inhalational of bacteria into the lungs results in phase of Edema → proteinaceous exudates develops in the alveoli. So there can be a crepitation, crackles of Bronchial breathing develops in the patient and subsequently patients enter into the following phases.
  - **Red hepatization** = RBC + Neutrophils (PMN)
  - **Grey Hepatization** = RBC lysis + PMN (Neutrophils) ⊕⊕ → it signifies successful containment of infection despite of given antibiotic might have expired.
  - **Resolution** = Here Macrophages predominantly present because these cells are restore the normal tissue.

PrepLadder

- **Community Acquired Pneumonia (OPD)** commonly associated with following organism:
  1. Pneumococcus
  2. Mycoplasma pneumoniae
  3. Hemophilus influenzae → highest incidence with COPD and SMOKERS.

Note: Azithromycin is the first line drug for community acquired pneumonia because it can active against both pneumococcus, mycoplasma pneumoniae (Can give if beta lactams are resistant to mycoplasma).

- **Community acquired pneumonia (ICU)**
  - Pneumococcus → because patient got infection from community but he is admitted to ICU only because of severity of the symptoms.
- **CAP (Routine wards/Non ICU)**
  - Pneumococcus

Note: In AIDS positive patient common cause of infection is still pneumococcus, but pneumocystis jiroveci present only when CD4 is < 200. While starts Antiretroviral therapy there is a progressive decrease of P. jiroveci still pneumococcus infection is present.

- **Atypical pneumonia (Walking pneumonia)**

-Here patient having symptoms of breathlessness, fever, cough still patient can walk so called as walking pneumonia. Even Patient having mild manifestation but Xray showing significant changes.

1. Mycoplasma pneumoniae → DOC → Azithromycin
2. Legionella pneumophila → pt have a history of ship crews and stayed in hotels.
3. Chlamydia pneumoniae
4. Influenza, RSV, adenovirus, Meta Pneumo virus

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- All these organisms are resistant to β lactam so following treatment were given.

Rx → **Macrolides / Fluoroquinolones**.

Note: Influenza A can superinfected / complicated with staph aures.: Q

Ribavirin nebulization can be given to RSV: Q

- **Anaerobes:** -
  - Are present in the oral cavity, in between tooth which aspirated into lungs and cause anaerobic pneumonia.

Causes :

- Aspiration lead to pneumonia
- Drug overdose/ overdose of alcohol results in inhalation of saliva .
- Impaired airway defenses
- Seizures episodes.

CASE SCENARIO: A 20 years old male on Holi festival, consumed alcohol excessively with his friends and took some drugs like charas, due to effect of intoxication, he was continuously slept for 2 days. While wake up patient have protective cough, fever, chills, rigors, bronchorrhea. And found bus in the sputum. On CXR finding shows air fluid levels. All these features are suggested of lung abscess. The organism is responsible for these features is anaerobic organisms. So **DOC for anaerobic organisms → Clindamycin:Q**

If a questions with following key words:

- Alcohol + Pneumonia → Pneumococcus pneumonia.
- Alcohol + **Red currant jelly sputum due to necrotizing pneumonia** + **On chest X-ray →** Bulging fissure sign } Klebsiella pneumoniae | Friedlander's pneumoniae
- Alcoholic and drug overdose manifest with decrease airway defense so patient end up with Anaerobic lung abscess
- **Lung abscess:-**

Primary lung abscess associated with	Secondary lung abscess associated with
↓	↓
Oral Anaerobes	**Staph. aureus**

- **Organism specific Approach to Pneumonia: -**
  - COPD & smokers end up with → H. influenzae
  - Structural lung disease, Eg. Cystic fibrosis were mucus plugs thickened present = Pseudomonas Aeruginosa

↓

Grows **in Cetrimide Agar**

* Burkholderia ceparia

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  - Dementia / stroke = **Oral Anaerobes**
  - Contact with Birds = **Chlamydia psittaci**
  - Contact with Bats = **Histoplasmosis**
  - Contact with Rabbits = **Francisella tularensis**
  - Contact with Goat/ sheep = **Coxiella burnetii can cause Q fever.**
  - Hotel/ cruise = **Legionella pneumophila**
    - Mild form of legionella pneumophila can cause Pontiac fever
    - Severe form of legionella pneumophila can cause legionnaires disease results in pneumonia

- **Clinical features**

CASE SCENARIO: 65 years old male having fever past 2-3 days and neglecting the symptom of breathlessness, suddenly breathlessness getting worsen so patient can talk only monosyllables. Patient is not specific to productive or non productive cough, and sometimes presents with hemoptysis and chest pain. On auscultation heard pleural friction rub.

  - Fever
  - Breathlessness
  - Cough
  - Hemoptysis → present only in the case of MRSA
  - Chest pain: due to pleuritis
  - Nausea and vomiting

PrepLadder

- Abdominal pain
- Headache
- Myalgia

Note: If person suddenly deteriorated with above mentioned symptom then there could be two possibilities:

1. Acute Non decompensating cardiac failure
2. Pneumonia

➢ **On examination:-**

- Respiratory rate = Increase
- Use of Accessory respiratory muscle
  - Scalenus
  - Sternocleidomastoid muscle
  - Alae nasi
- Trachea is central
- Vocal fremitus increased because lung has become solid so called as Bronchophony.
  - Sometimes vocal fremitus is lesser due to parapneumonic pleural effusion at bottom of one side of the lung.
- **On Percussion** = Dull due to consolidation (Usually finds resonant in normal lungs).
- **On auscultatory** findings in pneumonia is Breath sounds of bronchial breathing not
- crepitation or freckles. There is a gap between inspiration and expiration component.

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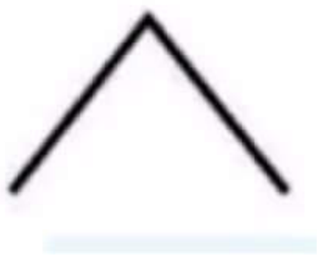
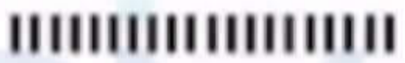
Breath sounds			
VESICULAR SOUNDS		Normal- heard over periphery Gentle rustling sound Fades on expiration	There is no gap present inbetween inspiration and expiration, while inspiration takes longer time than expiration.
BRONCHIAL SOUNDS		Normal – heard over substernal notch LOUDER – Expiratory lasts longer Silent internal	There is a audible gap in between 1/4th to 3/4th distance and here expiration takes longer time. If this sound heard in any other place consider as abnormal.
BRONCHOVESICULAR		Normal – heard 1st & 2nd inter coastal space anteriorly and between scapulae posteriorly intermediate intensity	Its difficult to distinguish between Bronchovesicular and vesicular , bronchial sounds.

FINE CRACKLES		Abnormal – discontinuous High pitched Popping quality	Crepitations Heard in ADCHF, ILD. But in ILD only basilar crepitation is heard.
COARSE CRACKLES		Abnormal – discontinuous Low pitched Louder & longer	
WHEEZE		Abnormal – continuous High pitched Musical quality	Heard with stethoscope in the asthma and chronic bronchitis cases.
RHONCHI		Abnormal – continuous Low pitched Gurgling quality	Heard with or without stethoscope also in the cases of asthma, chronic bronchitis.

- **Egophony** → Due to lung consolidation there is the modifications in the vocal sounds which heard through stethoscope **Eg: EE heard as AAAH**
- So the better term of egophony is **whispering pectoriloquy** where a patient turns back and sounds of patient is heard through stethoscope.

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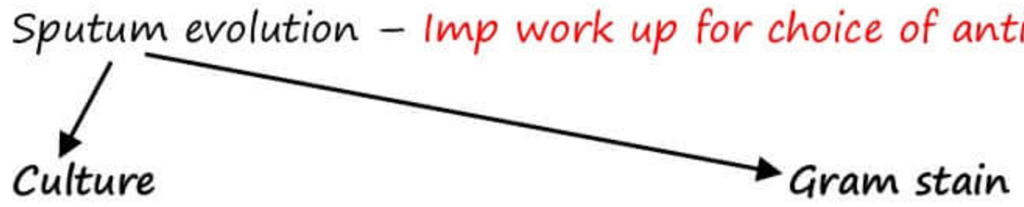
➢ Work – up of patient:-

- CBC = TLC increased (Neutrophils counts are increased)
- Sputum evolution – Imp work up for choice of antibiotics.



Adequacy of sputum sample:

On M/E: > 25 PMN

>10 epithelial cells

- Blood culture (**First step to done in the case of bacterial meningitis**)
- Urine antigen
  - Legionella pneumophilia
  - Pneumococcus
- PCR sputum / BAL
- Chest X-ray = Consolidation
  - Lobar

PrepLadder

- Round
- Bronchopneumonia
- Parapneumonic Effusion

- Biomarkers = CRP ⊕, Procalcitonin } Helps to identify infective process in the body

Treatment:-

CURB – 65 score - Parameters used for the need for hospitalization

Parameters →		
	Confusion	1 point
	BUN ↑	1 point
	Respiratory rate >30 /	1 point
	min BP <90/60 mm Hg	1 point
	Age ≥ 65 yrs	1 point

• **Note**: Old man with pneumonia discharged from the hospital after 15 days came to hospital again for MI

This is Because of pneumolysin the toxins released by pneumococcus which will activate platelet results platelet plug in coronary vessels and lead to MI.

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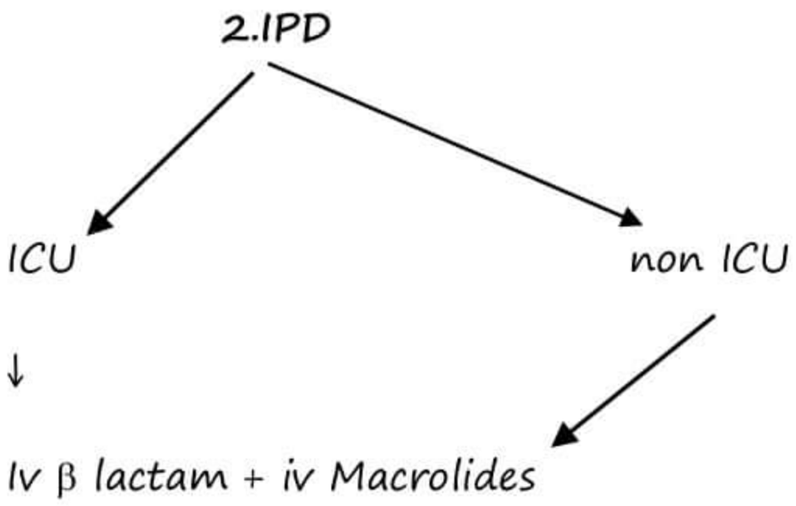
Score	mortality	Rx
0	1.5%	OPD Basis
1-2	9.2%	IPD basis
≥ 3	22%	ICU Basis

NOTE: If age alone > 65 and results in score 1 then patient can be treated in OPD basis.

➢ **Empirical treatment of CAP:-**

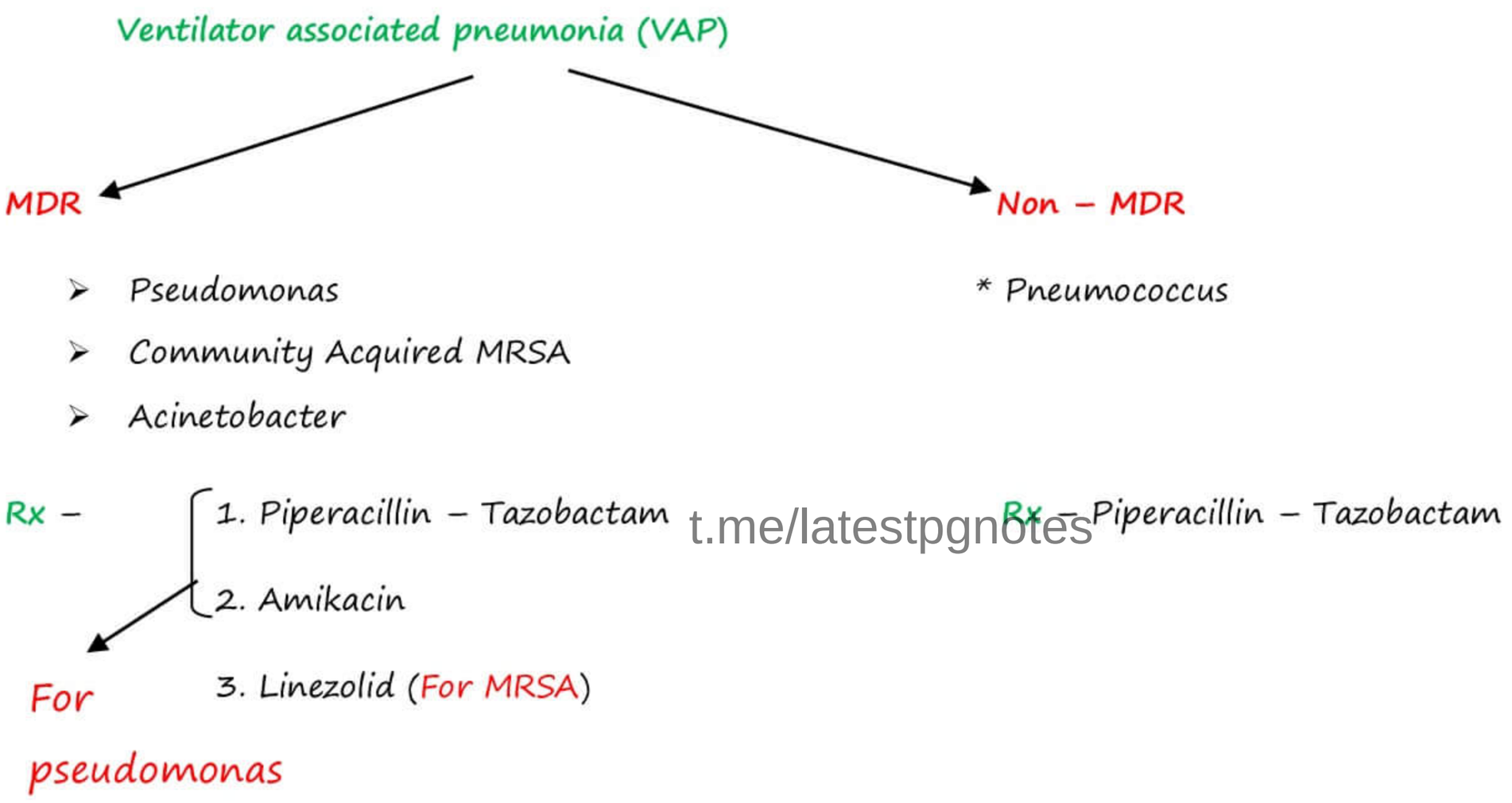
1.OPD treatment:- -Imp

Previous health	Co – morbid condition
Or	or
Not received antibiotic in last 3 months	Antibiotics in last 3 months ⊕
↓	↓
MACROLIDES (Clarithromycin / Azithromycin)	**Moxifloxacin** or
Or **Doxycycline (If macrolides is not available)**	**β lactam + macrolides**



If pseudomonas ⊕ → Add Meropenem

s. Aureus ⊕ → linezolid



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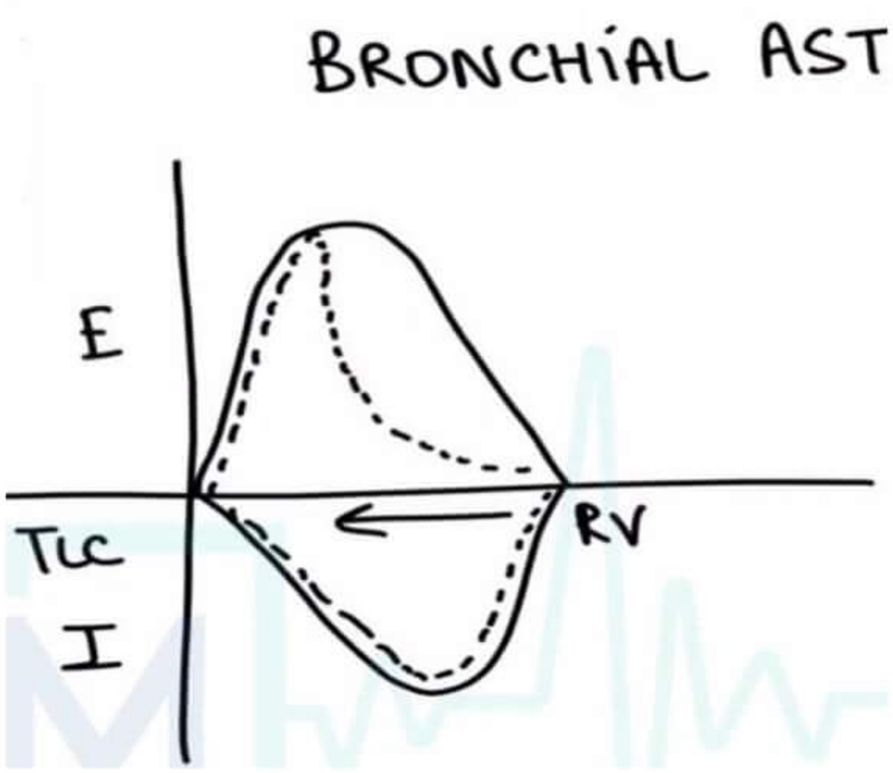
PrepLadder

BRONCHIAL ASTHMA

→ Main diagnostic criteria for bronchial Asthma is reversibility of airflow obstruction which is demonstrated by spirometry.

→ Patient is made to perform forceful inspiration and expiration and flow volume curves are obtained



→ Baseline curve for inspiration part remain same but in expiration part: Patient is not able to push out the air as Asthma is **disease of expiration** So, **marked concavity** in expiration part is present.

→ Now **salbutamol** is given and test is repeated in 10–15 min, **concavity will reduce significantly**

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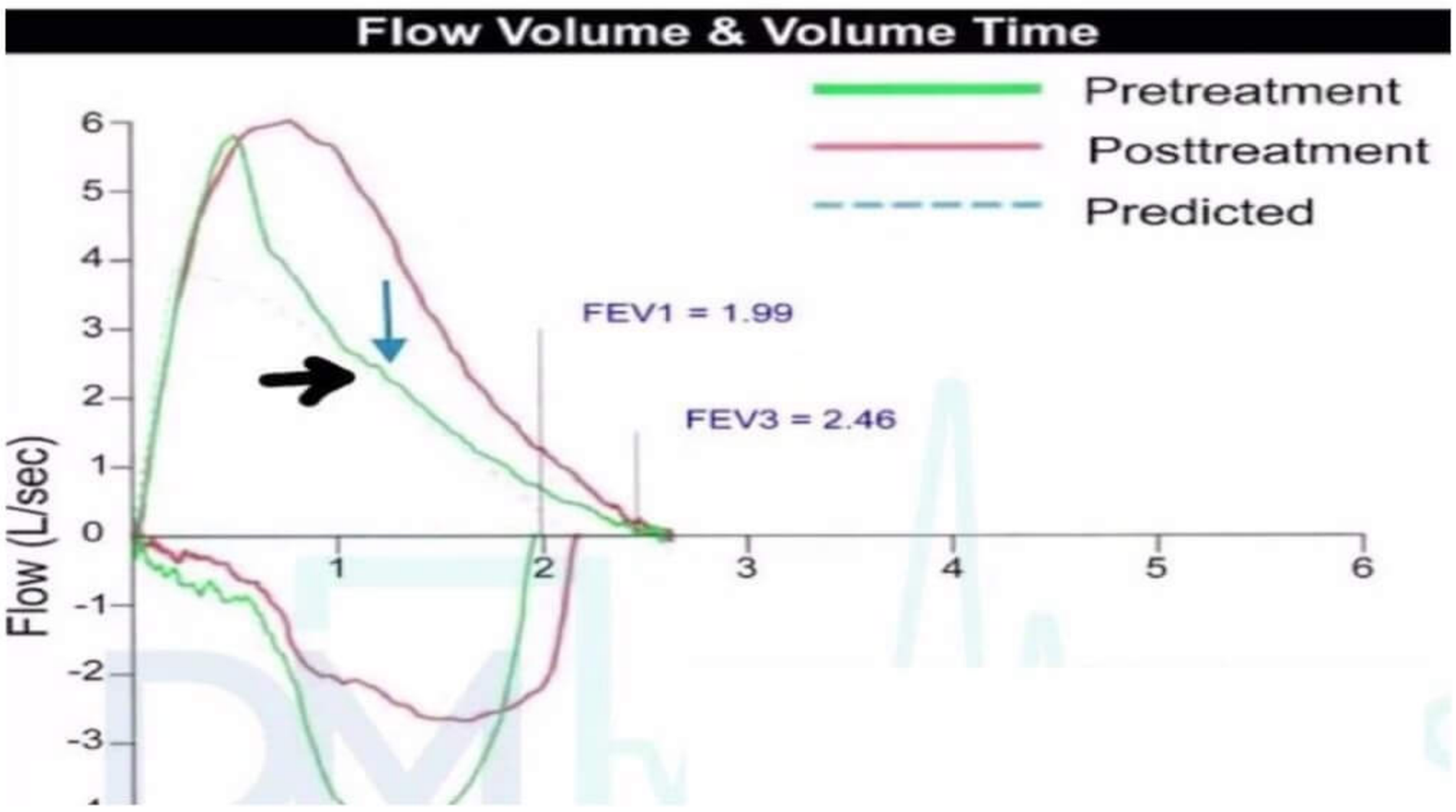

$FEV_1 \downarrow \xrightarrow{\text{S.A.B.A.}} FEV_1$ normal

Δ FEV1 > 12% or 200 mL increment over baseline value of FEV1 → to say that pt. is of bronchial asthma

Methacholine provocation test – It is of historical importance. Not done now as may lead to imminent respiratory failure

PrepLadder

- **Eucapnic hyperventilation test** – Person is made to breathe in cold air. Asthmatics has bronchial hyper reactivity to cold air and FEV1 will fall.

- Diagnostic criteria:

a) **Reversibility (Absolute criteria): Asthma** is **reversible airflow obstructive disease** whereas **COPD** is **non reversible** obstructive airflow disease.

b) Asthma is **episodic**

c) Most attacks are **nocturnal.** Possible explanation is that at night time air is cold

d) **Main test for diagnosis is** spirometry

e) Chest X- ray may show **hyperinflation** and **flattening of diaphragm** or it **can be normal also, so it has no role in diagnosing asthma**

f) No role of HRCT chest in diagnosis of Asthma

g) **Allergic bronchopulmonary aspergilloma**:- Hypersensitivity reaction to **A. fumigatus** which is associated with **central bronchiectasis**. **Steroids and itraconazole** are given for treatment

Update GINA 2019:-

New studies have suggested that patients treated only with salbutamol (SABA) are found to have higher asthma related death incidence.

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Controller – **prevention** – low dose inhaled **corticosteroid (ICS) with formoterol**

(Formoterol – Rapid acting LABA)

Reliever- low dose inhaled corticosteroid (ICS) with formoterol

Earlier SABA

Asthma medication options:

Adjust treatment up and down for individual patient needs

	STEP 1	Step 2	Step 3	Step 4	STEP 5
PREFERRED CONTROLLER to prevent exacerbations and control symptoms	As needed low dose ICS-formoterol	Daily low dose inhaled corticosteroid (ICS), or as needed low dose ICS-formoterol	Low dose ICS-LABA	Medium dose ICS-LABA	High dose ICS-LABA Refer for Phenotypic assessment add on therapy. e.g. tiotropium, anti-IgE, anti- IL5/5R, anti-IL4R
Other controlled options	Low dose ICS taken whenevee SABA is taken	Leukotriene Receptor Antagonists (LTRA) or low dose ICS taken whenever SABA taken	Medium dose ICS or low dose ICS + LTRA	High dose ICS, add-on Tiotropium or add-on LTRA	Add low dose OCS but consider side-effects
PREFERRED RELIEVER	As needed low dose ICS- formoterol		As needed low dose ICS-formoterol for patients prescribed maintenance ans reliever therapy		
Other reliever option	As needed short acting β_2-agonist (SABA)				

→ Steroids given in both conditions as it treat the disease by inhibiting enzyme **phospholipase A2** and **decreases release of Leukotrienes**

PrepLadder

Controller

	Symptoms	Interference	FEV1	Rx
Intermittent	< 2 d/week	None	N (>80%)	STEP 1
Mild persistent	> 2 d / week	None	Normal	STEP 2
Mod. Persistent	Daily	Some limitation	60-80%	STEP 3
Severe persistent	All Through day	Extreme Limitation	<60%	STEP 4 or 5

- STEP 1 – Low dose ICS (Budesonide) with formoterol: **As needed**. Patient advised to rinse his mouth with water to minimize risk of oropharyngeal candidiasis
- STEP -2 – Low dose ICS **(Daily)**→ Should be continued at least for next 3-6 months
- STEP -3 – Low dose ICS + LABA: **daily**
- STEP -4 – Medium dose ICS + LABA
- STEP-5- High dose ICS + LABA + add on therapies.
  - Sputum m/e = Eosinophils >3% indicates requirement of up-gradation of therapy
  - Sputum guided therapy is used to done standardization of therapy

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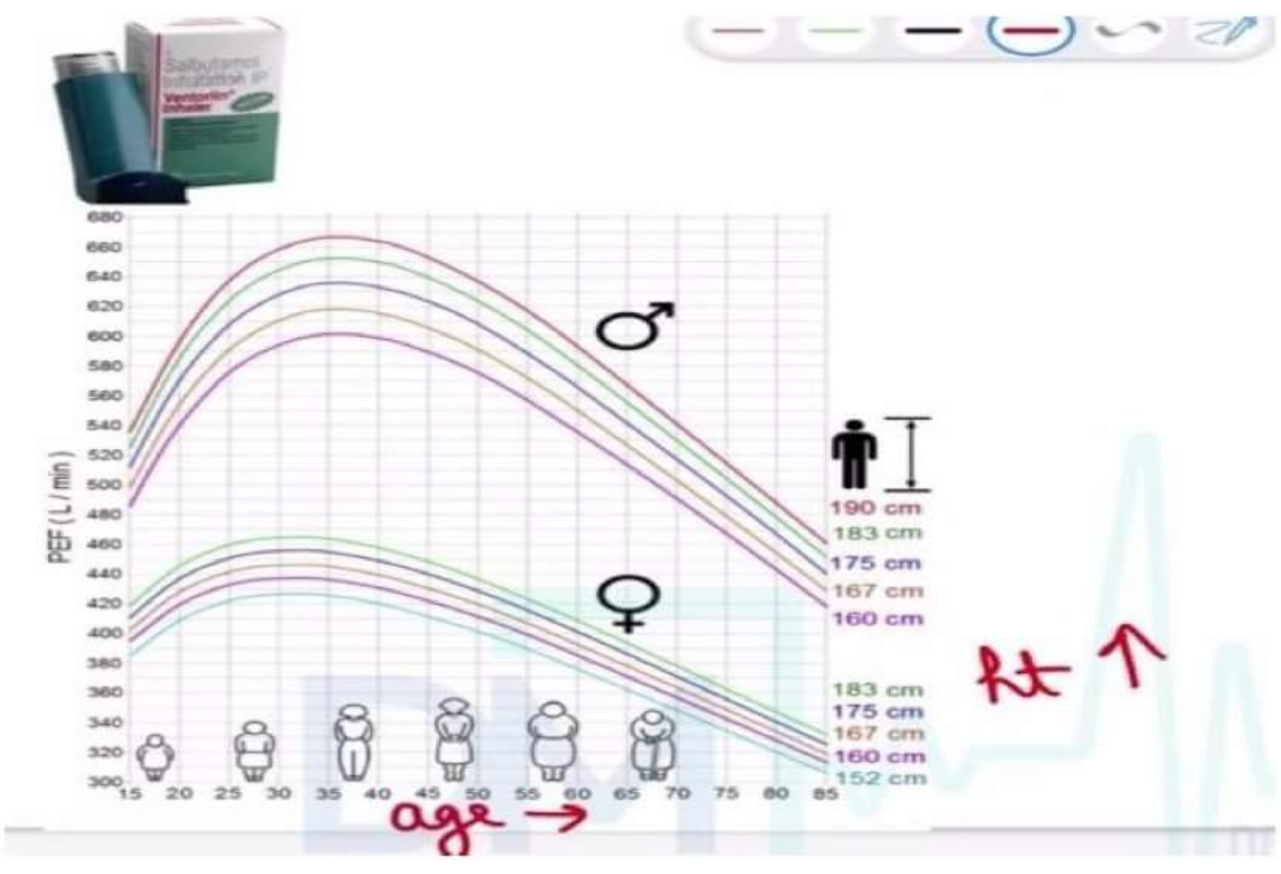
Add ons :-

- Tiotropium – Long acting muscarinic agent (LAMA) → anticholinergic
- Omalizumab – Anti IgE Given Subcutaneously.
- Mepolizumab - Anti IL-5/5R
- Dupilumab - Anti IL-4/4R (Useful in severe type 2 Asthma)

 # Acute asthma exacerbation:-

PEFR meter is advised



Flow rates can be observed according to age, sex & height

PrepLadder

Management of acute exacerbation:

1. Increase the dose of controller medication – can be increased up to 4 times of normal dose.

2. Add S.A.B.A (Salbutamol)

(Color coding of inhalers is done for easy recognition)

3. Add oral corticosteroids

Exacerbation	FEV1	PaO2
Mild	>70%	Normal
Moderate	40-69%	>60 mm of Hg
Severe	<40%	<60 mm of Hg

Indications of hospitalization:-

- Inability to lie flat in bed
- Cannot speak / talk
- Patient is drowsy and can't obey commands due to CO_2 narcosis
- FEV_1 <25% of predicted value (Personal best; pre-treatment)
- Post treatment FEV_1 <40%

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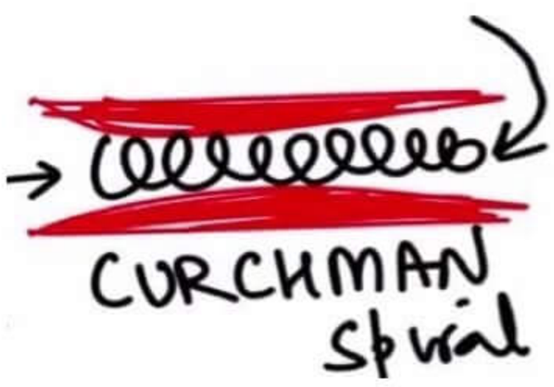
- **Severe acute Asthma**

1. Talks in words
2. Agitated
3. Tripod position
4. Accessory respiratory muscles used by patient
5. Resp. rate > 30 / min
6. Heart rate > 120/ min
7. Pulsus paradoxus ±
8. Loud Rhonchi

Treatment – Nebulization with salbutamol, O_2 driven (Humidified). Done every 20 min in first hour.

(Air driven nebulization can lead to ventilation perfusion mismatch)

- **Curschmann spirals** are casts of mucus plugs which can block the airways



- Disappearance of loud Rhonchi may be indicative of underlying blockage of airways

→ Inj. Terbutaline subcutaneous

PrepLadder

→ **I/V Hydrocortisone** (Can also potentiate effect of bronchodilators)

→ Consider **$MgSo_4$ I/V** → As Mg^{+2} antagonize effect of calcium mediated bronchoconstriction.

→ Aminophylline ± (Toxicity)

→ Ipratropium

Imminent Respiratory Arrest: -

1. Can't talk, silent
2. Drowsy due to CO_2 narcosis
3. >30/min resp. rate, bradycardia
4. Shallow rapid breathing
5. Cyanosis
6. Pulsus paradoxus disappears
7. Peak expiratory flow / FEV_1 <25%.

   PaO_2 <60, pco_2 > 45 mm of Hg.

Treatment:

1. **Hydration**: - As neuromuscular blockade for intubation causes vasodilation and severe fall in B.P. can occur so before intubation I/V fluids should be given to patient.
2. **Neuromuscular block + E.T. tube + Assisted contracted mechanical ventilation** (ACMV)

   Barotrauma can occur if inspiratory pressure is increased to decrease the pCO_2
3. To minimize risk of barotrauma, permissive hypercapnia is allowed pH=7.3; pCO_2 = 50 mm Hg

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Controller / prevention = Low dose inhaled corticosteroids (ICS) + formoterol

Acute Asthma = Low dose ICS + formoterol + SABA

Severe Acute Asthma = Nebulization with salbutamol + I/V hydrocortisone

Brittle Asthma

Diurnal variation of PEFR > 40%

Epi – PEN is advised to keep along and injected subcutaneously when patient feels attack.

→ Permissive hypercapnia is **contraindicated** in patient with **raised ICT** as it may cause vasodilation and worsen cerebral edema.

→ It is allowed in patient of **Imminent Resp. arrest, Severe acute exacerbation of COPD**

→ Brittle Asthma

diurnal variation of PEFR > 40%

Epi – PEN is advised to keep along and injected subcutaneously when patient feels a attack.

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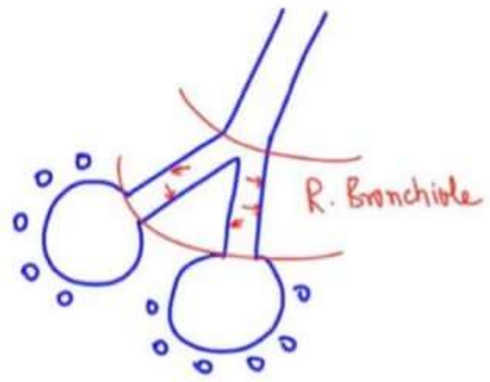
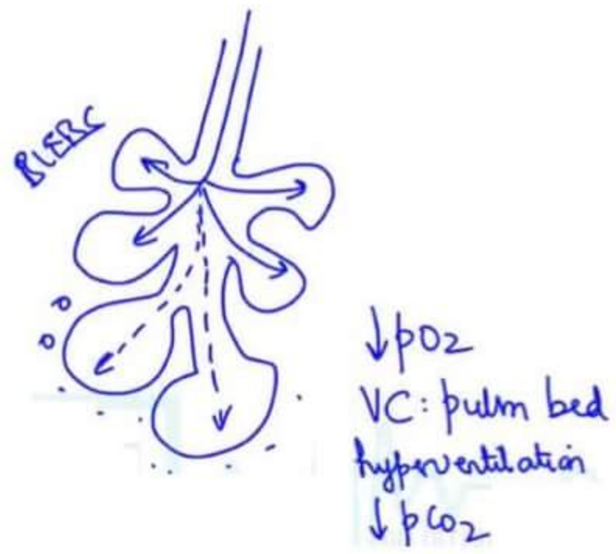
COPD



In a heavy smoker -

- Tar → Macrophages → elastase → elastin damage.
- Maximum damage → Respiratory Bronchiole → Hypoxia
  → Vasoconstriction of Pulmonary bed →
  Hyperventilation → Decreased pO2, decreased pCO2



Emphysema

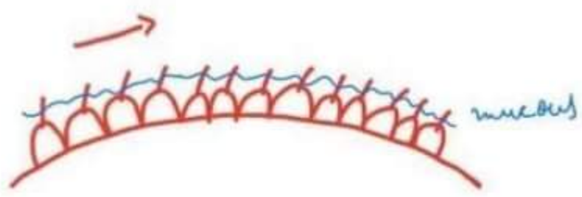
- Blebs in respiratory airways
- Type I respiratory failure
- Respiratory alkalosis
- Air trapping on exhalation and amount of air going out is lesser.
- So FEV_1 less than normal. Also RV and TLC increase
- On giving salbutamol, no change in FEV_1

So it is a Non Reversible Air flow obstruction

IOC – HRCT - Blebs / bulla

MC Complication - Cor pulmonale

Patient Suddenly turned blue → Spontaneous pneumothorax



Chronic Bronchitis – Muco-ciliary escalator

- In heavy smoker → Tar

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↓

Ciliary damage

↓

Failure of muco-ciliary escalator

↓

Stasis of secretion

↓

Infection

↓

Pus

↓

Occlusion of respiratory bronchiole
Leading to underventilation of alveoli

↓

Very severe hypoxia → central cyanosis (↓↓ pO2)
Increased pCO2 → Narcosis, sleeping period increase, weight gain
→ 'BLUE BLOATERS'

Chronic Bronchitis

C/F -

- Wheel chair bound patients
- Type 2 Respiratory failure
- Respiratory acidosis
- Bronchorrhea
- central cyanosis

PrepLadder

Emphysema Patient presentation ->

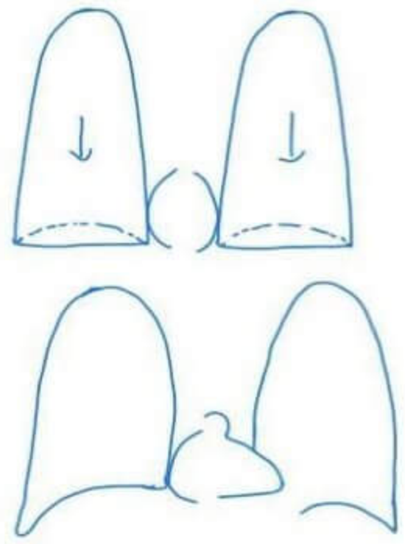
- Tall Thin smoker, exercise Intolerance, breathlessness

O / E –

- Tachypnoea
- Accessory Muscle (+) working excessively
- Barrel shaped chest (AP diameter > Transverse diameter)
- Liver Palpable (d/t Hyperinflation of lungs)

Work up –

1. Spirometry
2. HRCT (IOC) -> Blebs
3. ABG -> Type I R. failure (Resp. Alkalosis)
4. **DLco** -> diffusion capacity of Lung for CO -> **decreased**
5. CXR
   - Flattening of diaphragm
   - Tubular heart
   - Lungs appear more Black than normal
   - Vascular Markings present



Emphysema

Treatment – Quit smoking - Nicotine buccal spray / varenicline ($\alpha_4\beta_2$ Partial Agonist of nicotine R)

- Video assisted Thoracoscopic surgery

↓

Bullectomy

TOC – Lung Transplantation

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Chronic Bronchitis

- Fat smoker with severe dyspnoea on minimal activity grade III, Halitosis Bronchorrhea

O / E –

- increased Resp Rate, accessory muscles overactivity, subcostal recession
- pursed lips, Central Cyanosis (blue bloater)
- Bronchorrhea
- Halitosis
- Clubbing absent
- Both inspiratory and expiratory Ronchi
- Haemoptysis is absent

Bronchiectasis

- Bronchorrhea
- Smoker
- Clubbing
- Haemoptysis
- Basal crepts L >> R

Work up

1. Spirometry
2. Chest X ray – increased Broncho vascular markings (dirty lungs)
3. IOC - HRCT
4. ABG -> Type 2 Respiratory failure Respiratory acidosis

PrepLadder

Treatment

Antibiotics + mucolytics

Ipratropium Bromide, Theophylline

Mainstay of treatment: - Portable oxygen cylinder -> Low flow O2 with a Nasal Cannula (1L / min or 16 hrs / day)

It will Increase dissolved O2 -> increased work capacity of patient

For severity of COPD

- GOLD Classification

1.	Mild COPD	FEV1 / FVC < 0.7	FEV1 = ≥ 80% predicted
2.	Moderate COPD	FEV1 / FVC < 0.7	FEV1 = 50-80% predicted
3.	Severe COPD	FEV1 / FVC < 0.7	FEV1 = 30-50% predicted
4.	Very Severe COPD	FEV1 / FVC < 0.7	FEV1 < 30% predicted

Asthma

Mild	FEV1 = 50-80%
Moderate	FEV1 = 30-50%
Severe	FEV1 = < 30%

COPD – UPDATE

→ In **mMRC (Modified Medical Research Council)** grading for **dyspnea**:

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→ GRADE 1: Incline (Breathlessness on going upstairs)

→ GRADE 2: Slow walk than peers (Breathlessness on walking in straight surface)

→ GRADE 3: Stops (Keep on stops walking in between)

→ GRADE 4: Too Breathless to go out of his house

COPD severity index:

mMRC: 0-1 (1st patient)	**mMRC** ≥ 2 (More severe)
Exacerbation: 0-1 (No hospitalization)	**Exacerbation** ≥ 2 or Hospitalized once)

A – **Low risk, Low symptoms** (No hospitalization in recent 6 months to 1 year)

B – **Low risk, high symptoms** (No hospitalization in recent with high mMRC grading)

C – **High risk, low symptoms** (No hospitalization in recent with low mMRC grading

D – **High risk, High symptoms** (Hospitalized in recent with high mMRC grading)

High risk means → Patient has had hospitalization

High symptom means → mMRC more than 2

Treatment:

A – Bronchodilators

B – LABA or LAMA → if fails - LABA + LAMA

C – LABA + LAMA + ICS - **imp**

D – LABA + LAMA + ICS + Roflumilast, PDE -4 inhibition - **IMP**

(LAMA - Tiotropium)

PrepLadder

RESPIRATORY FAILURE

→ Respiratory failures further divide in to 4 types

Type 4:

- Due to ↓ perfusion of respiratory muscles

Cause : shock

Rx:

1. E tube + intermittent positive pressure ventilation – first line management.
2. Tt of shock

Type 3:

Cause : due to Post – op – atelectasis

Rx:

- Supplemental O_2
- Chest physiotherapy

Type I	Type II
- ↓ pO_2 - pCO (n) / ↓ - **Hyperventilation** 1. ARDS 2. Fat embolism syndrome 3. Acute asthma 4. Pneumonia 5. Spontaneous pneumothorax	- ↓ pO_2 - ↑ pCO_2 **Hypoventilation** - Diaphragm paralysis: 1. GBS 2. Polio 3. T. Myelitis 4. Botulinum **Cervical cord injury**: $C_3 - C_5$ A. Chronic bronchitis B. Tension pneumothorax C. Status asthmatics D. Foreign body glottis E. OSA F. Pickwickian syndrome

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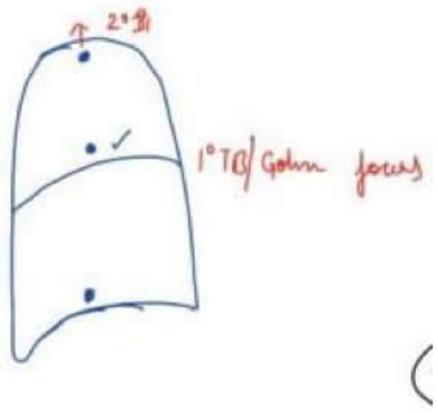
Respiratory failure Type I	Example: ARDS	Mx Low volume ventilation
Type II	Status asthmaticus COPD exacerbation	• Tight fitting face mask • Non Invasive Ventilation pCO_2 ↑ > 60 mm Hg • E. tube + I.P.P.V
Type III	Post – op – atelectasis	• O_2 + chest physiotherapy
Type IV	↓ perfusion of respiratory muscle	E. Tube + I.P.P.V

PrepLadder

TUBERCULOSIS

- **M/c site primary TB / Ghon focus:** Lower part of upper lobe.
- Apex is site for 2° **TB or reactivation TB**
- Most common presentation of extra pulmonary TB is development of **cervical Lymphadenopathy.**

- **Ghon focus** site: Tonsils
- Within few days after infection



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Immunity will react

↓

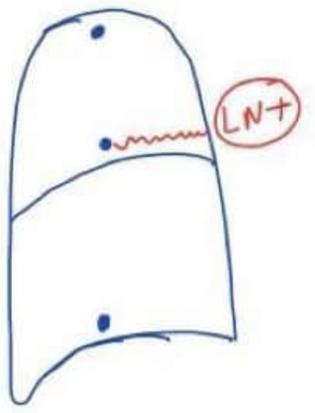
Development of lymphangitis + unilateral hilar lymphadenopathy

↓

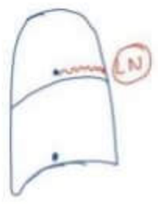
LN + Mycobacterium tuberculosis bacteria

↓

Ghon's complex (Asymptomatic -> MC presentation)



- Ghon's complex is subpleural, can erupt and cause pleural effusion.
- Fever, chest pain worsen on inspiration called as Pleuritic chest pain.
- Erythema nodosum
- Phlyctenular conjunctivitis



* Two possibilities of ghon's focus in the body

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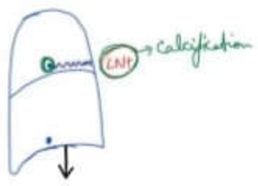
Body will try to limit it



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By calcification around focus / LN

↓

Ranke Complex

Good immunity (+)

If CMI decreased

1) Pleural effusion

2) Cavity formation called as Primary progressive pulm TB

3) L.N enlargement : exhibit Ball valve effect & Lobar Hyperinflation, Segmental Collapse

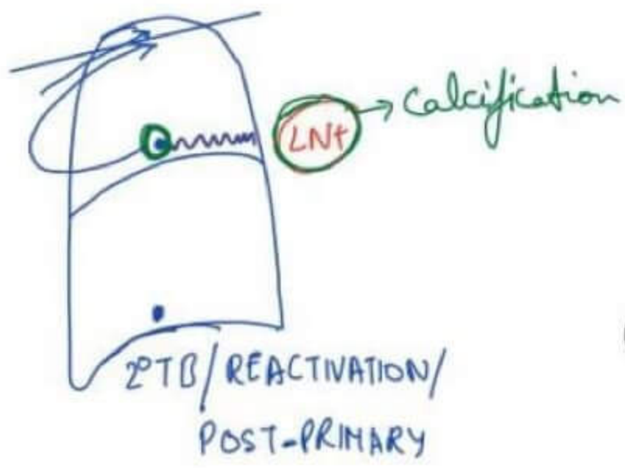
4) Tubercular pneumonia can cause Bronchiectasis by pus formation

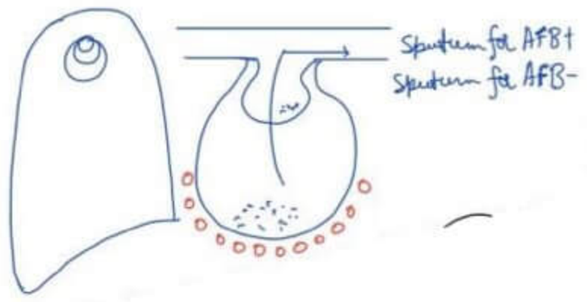
5) Disseminated

If CMI decreased after calcification formed so bacteria can be disseminated To following sites:

- PUHL Lesion = **Supraclavicular**
- Assmann focus = **Infraclavicular**
- Weigert focus = **Pulmonary vein**
- Rich focus = **CNS**
- Simmonds focus = **Liver**
- Simon focus = **Supraclavicular**

} Related to dissemination of disease





Secondary TB / Reactivation / Post-Primary TB:

- Cavity formation which keep on increase in size results in damage And eroded into bronchus. So the sputum presented with bacteria.
If person with sputum negative does not mean negative TB, Because Small cavity may have small quantity of bacteria which turns to be negative sputum test.

Clinical presentation:

- Fever : Diurnal Variation
- Night Sweats
- Wt. loss, decreased appetite
- Purulent sputum
- Hemoptysis massive d/t erosion of bronchial artery (MC cause of hemoptysis in India / USA - TB)
  Massive = > 500 ml / day → Rigid bronchoscopy has to be done.
- Clubbing ±, SIADH ±

- Rassmussen aneurysm present in the pulmonary artery
  Commonly seen in Bronchial TB.

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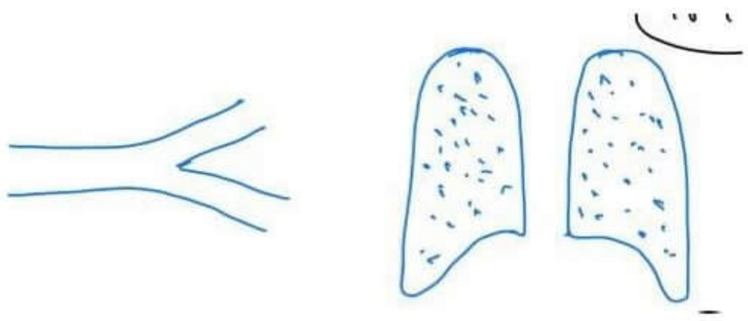

Snow storm appearance on x ray

Disseminated TB:

- if dissemination involves pulmonary artery can cause snow storm app

- If dissemination occurs via Bronchial A / vein
  ↓
  Heart
  ↓
  All over body

Hallmark presentation

On fundus examination: Choroid Tubercles

M / C extra pulm. TB: LN > Pleura > GU tract LPG

Diagnosis -> FNAC / excision Bx

- **Pleural Biopsy** -> XPERT MTB / RFF

Pleural fluid -> XPERT MTB / RFF

Snow storm appearance

1. TB
2. Silicosis
3. Hemosiderosis
4. Varicella zoster pneumonia
5. Pulmonary alveolar proteinosis.

Pleural TB:

- It can be 1°, 2° TB, extra plum. TB

Presentation:
Fever, chest pain (Pleurisy)

* **On Thoracocentesis**: Straw colored fluid.
  In CSF: Lymphocytes + / Sugar decreased / Protein increased
* **Screening test for diagnosis of Pleural TB**: Adenosine deaminase levels

IOC: Pleural Biopsy gene XPERT

PrepLadder

INDICATIONS OF GENE Xpert :

Gene Expert : It is used for detection of TB and finding the Rif-Resistance.
→ WHO-recommends to use this as initial Dx test for adults and children presumed to have MDR-TB or HIV associated TB.
→ MTB/RIF → should be the initial test for CSF examination of patients presumed to have TB.

HIV + TB (Decreased immunity):

- Cavity size: Small
- Sputum for AFB negative
- Montoux test: -ve
- CXR -> Normal
- **IOC**: Gene XPERT
- Chances of dissemination increased

Treatment:

→ **Combine Anti Retroviral Therapy + ATT**

Protease inhibitors <-> Rifampicin

- There is a drug interaction between these two drugs.

Drug which **Contraindicated in HIV + TB**: Rifampicin
Indicated: Rifabutin

If CART therapy given first → high grade fever, chills, rigors, worsening of symptoms.

IRIS → Immune Reconstitution inflammatory syndrome

ATT should given first (Decreased load of Bacteria)

After 2 weeks ↓

CART should be initiated -**imp**

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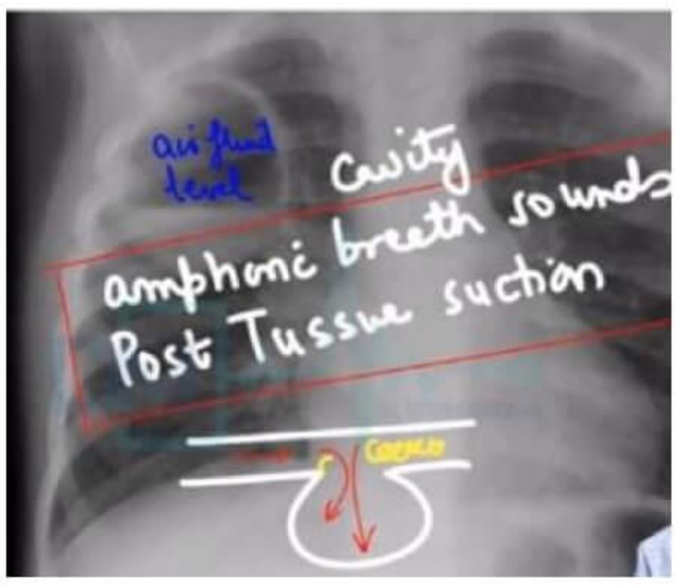
SUMMARY:

- 1°: Lungs: **Lower part of upper lobe**
- 2°: **Reactivation on the APEX**
- Extrapulmonary TB: **Cervical group of LN**
- HIV + TB: **dissemination**
- Site of Congenital TB -> **liver**

M/C opportunistic infection on AIDS (+ve): TB
M/C opportunistic infection on AIDS (+ve) with CD4 < 200: P. Jiroveci

Sites of Ghon focus: Ileum, Liver, Tonsil, Lungs.

Lung calcification



Cavity formation :
↓
Amphoric breath sound

PrepLadder

INTERSTITIAL LUNG DISEASE

Etiology:

- Alveolitis, interstitial fibrosis:

Asbestosis
Drugs
Radiation
Desquamative interstitial pneumonitis:- Smoking
Langerhans cell histiocytosis
Usual interstitial pneumonia Idiopathic
Pulmonary fibrosis Cryptogenic
Organizing pneumonia
Connective tissue disorders:- SLE, dermatomyositis, pulmonary alveolar proteinosis

- Granulomatous response:

1. Hypersensitivity pneumonitis organic dust
2. Berylliosis
3. Silicosis
4. Sarcoidosis, Wegener's Churg-Strauss

Clinical Features

1. **Acute:-** Hypersensitivity Pneumonitis
   Acute interstitial pneumoniae (**Mimic A.R.D.S**) / Hamman Rich Syndrome

Extra Mile:

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Hamman CRUNCH sign: Pneumomediastinum

Hamman sign: Subcutaneous emphysema

Homan sign: Deep vein Thrombosis

3. **Subacute:-** Sarcoidosis

2. **Chronic:-** Idiopathic Pulmonary fibrosis

4. **Smoking** ± - Pulmonary alveolar proteinosis / Pulmonary lymphangioleiomyomatosis, Desquamative-interstitial pneumonitis, Good –pasture syndrome

5. Occupational H/O-
   - Dyspnea
   - Fatigue
   - Weight loss
   - R. Rate ↑
   - Bi-basilar crepitations
   - End- inspiratory Rhonchi

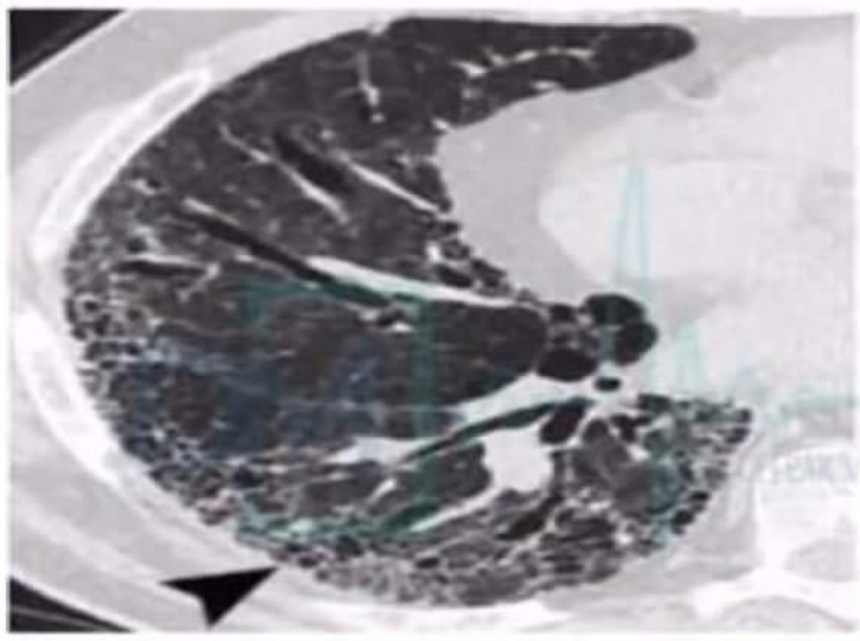
   } Present / Absent

6. Clubbing, Hemoptysis

Work up:-

1. Serum ACE Levels ↑: Sarcoidosis
2. LDH↑
3. ANA
4. CXR→ Bibasilar reticular pattern
5. HRCT

7. Cor pulmonale
   Pedal edema JVP↑ loud P_2



1. Subpleural reticular opacities
2. Traction Bronchiectasis

6. Spirometry – FEV1/ FVC /↑

Obstruction pattern in ILD

Sarcoidosis HP, LAM

7. **D.L.Co** ↓ (Pneumonia, emphysema, PAH)
8. **B.A.L.** → CD 4 / CD8 Ratio → 3.5; Sarcoidosis

CD4 / CD8 Ratio ↓: organizing pneumoniae

9. **Gold standard**: - Transbronchial lung Biopsy Disease activation

Investigation of choice:- HRCT

Rx:- Steroids, Cyclophosphamide

Azathioprine

For I.P.F Thalidomide + P.P.I and Lung transplantation

Pulmonary lymphangiomyomatosis:

- Common in pre-menopausal women
- ↑ with pregnancy, abates with oophorectomy

1. Emphysema
2. R. pneumothorax
3. Chylous pleural effusion

Idiopathic pulmonary fibrosis:- Most common sub type of idiopathic interstitial lung disease.

Extra Mile

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- Leading cause of lung Transplantation is idiopathic pulmonary fibrosis.
- Coal Worker's pneumoconiosis is not associated with development of I.L.D. and has obstructive pattern of emphysema on spirometry.

PrepLadder

PULMONARY ALVEOLAR PROTEINOSIS

Type 2 Pneumocyte

↓

DPPC (Dipalmitoyl phosphatidylcholine) + Surfactant Proteins

↓

GM - CSF (Granulocyte – Macrophage colony stimulating factor) bioactivity ↓

Alveolar macrophages ↓

↓

Clearance of surfactant ↓

Accumulation of surfactant in alveioli

Causes:-

1. Congenital = AR
2. Acquired = Silicosis
   - Inhalation dusts
   - Lysinuric acid protein intolerance
   - BM malignancies

C/F → 30-50 year male

1. Dyspnea (Exertional)
2. Fatigue
3. Wt. loss
4. Fever
5. Chunky gelatinous material: expectoration

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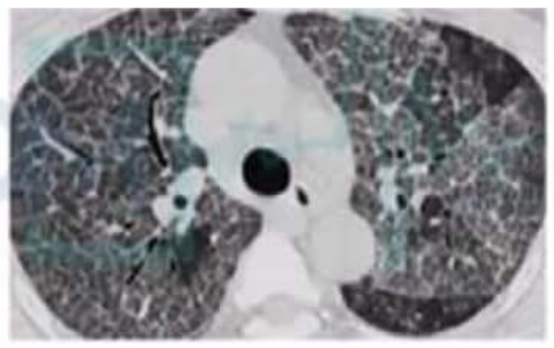
Work Up:-

1. PFT (Pulmonary function test): **Restrictive pattern FEV_1 / FVC n /↑**
2. Chest x - **Ray: snow storm / "Bat wing" appearance**
3. HRCT: **"Crazy pavement" pattern**



"Crazy pavement" pattern on HRCT ↑

IOC → BAL (Bronchoalveolar lavage)

↓

PAS +

↓

Presence of lipo proteinaceous material

Rx:- Whole lung lavage

PrepLadder

PLEURAL EFFUSION

Pleural Effusion

- Normal amount of fluid in Pleural space → **5-15 ml**
- Pleural fluid **secreted** by → **Parietal Pleura**
- Rate of synthesis of pleural fluid → 0.01/ml/kg/hr
  (Some of this secreted fluid is **reabsorbed by lymphatics**)

→ Minimal Amount of fluid present in pleural cavity for **Clinical Detection** → **300ml.**

→ **IOC** for Minimal Pleural Effusion → **CT chest > USG chest**

- Minimal Amount of fluid that should be present to confirm pleural effusion on **CXR** in **Upright position**
  - CXR Upright → Lateral view > 100ml
  - CXR Upright → Frontal view > 200ml
  - CXR Upright → Frontal view
    → Amount of fluid needed for obliteration of Hemi-diaphragm > **500 ml**

→ **Characteristic of Pleural effusion on CXR**
  → **Obliteration /Blunting of CP angle**
  → **Meniscus sign**
(CP Angle → Costophrenic Angle)

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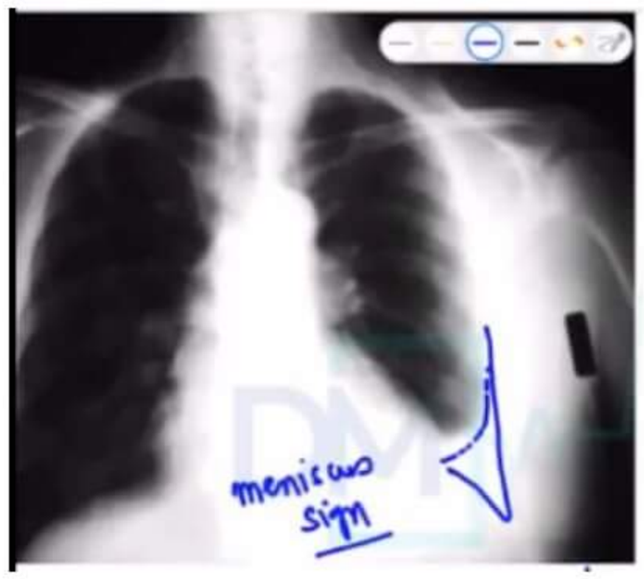
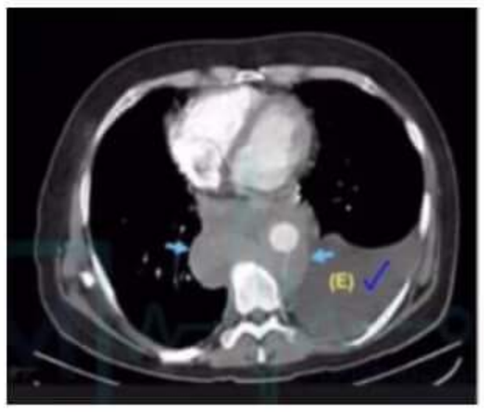


Meniscus sign



B/L Pleural Effusion (Hydrothorax)

Hydro pneumothorax

CT chest showing Left sided Pleural Effusion

→ **Etiology**

2 types of PE
- Transudative
- Exudative

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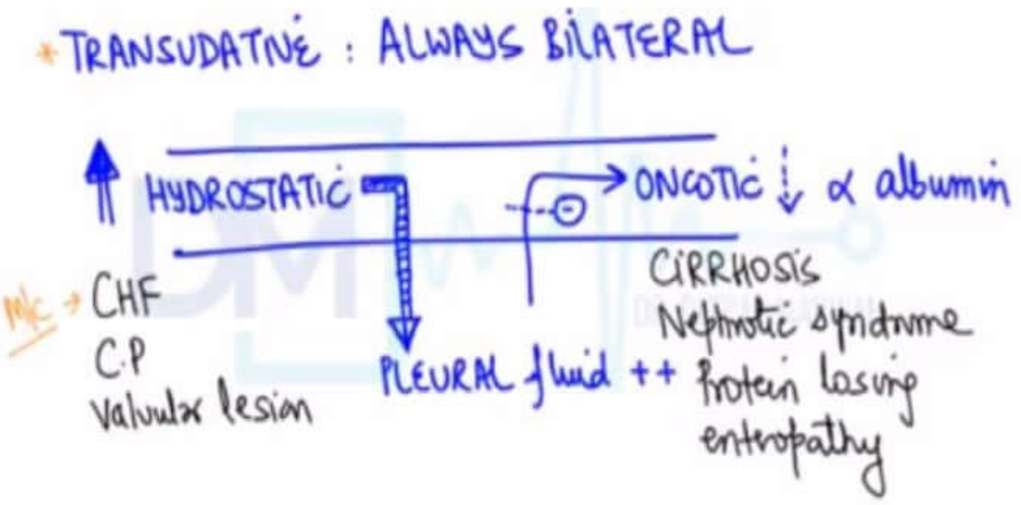

1. **Transudative Variety**

- **Hydrostatic Pressure** will drive the fluid **out of vascular space/capillaries** While **Oncotic pressure** will drive the fluid **back into Intravascular compartment**

- **Any condition causing**
  ↑ in Hydrostatic Pressure
  Or
  ↓ in Oncotic pressure

→ **Would lead to Excess of Pleural fluid accumulation in Pleural space of patient**

➢ **Conditions causing ↑ in Hydrostatic Pressure:**

- CHF (MC)
- Constrictive Pericarditis
- Valvular lesions

➢ **Conditions causing ↓ in Oncotic pressure:**

- Oncotic Pressure ∝ Blood Albumin
- ↓ Blood Albumin (Hypo Albuminemia) → ↓ Oncotic Pressure

Hypoalbuminemia is seen in conditions like:
- Cirrhosis
- Nephrotic Syndrome
- Protein Losing enteropathy

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- **Transudative Pleural Effusion** is **always B/L** as pressure is distributed equally to left & Right Side.
- Leading cause of B/L Pleural effusion → **Heart Failure**
- **Exudative Pleural effusion** can be **U/L** or **B/L**

2. **Exudative Variety:**

- **Causes of Exudative Pleural Effusion:-**
  1. Parapneumonic Effusion (**Pleural Effusion + Pneumonia**)
  2. Malignancy
  3. TB

Note: Leading cause of Malignant Pleural Effusion → **Adenocarcinoma Lung**
- Adenocarcinoma lung is peripherally located so it would keep on causing Irritation of pleural surface resulting in Exudative pleural Effusion.

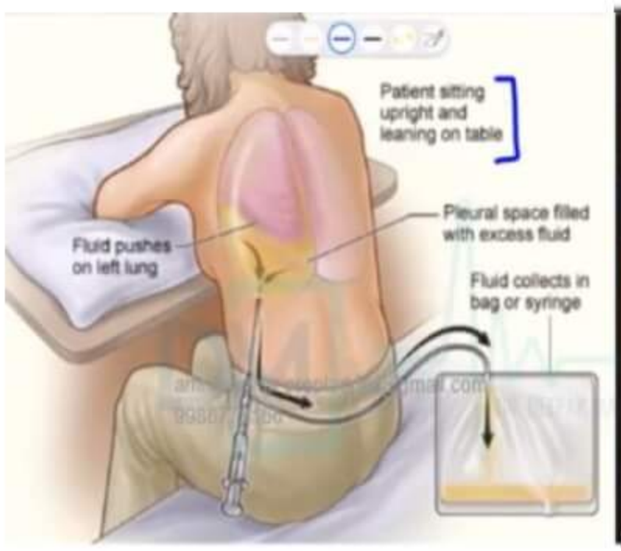
  4. Rheumatoid Effusion
  5. Meigs Syndrome

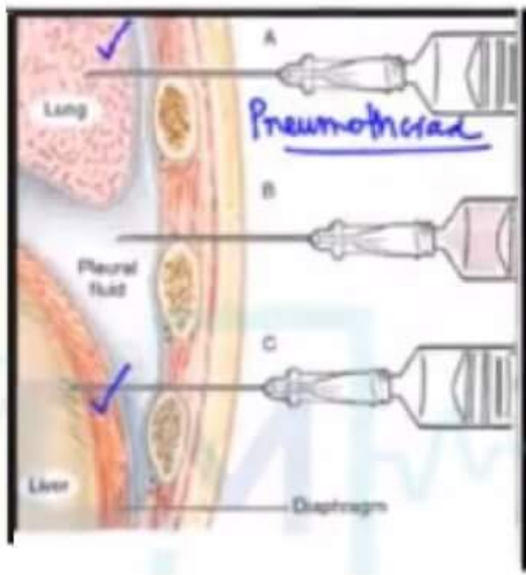
On Thoracocentesis:
- Fluid **Clots** on standing in **Exudate**
- Fluid is transparent like water and **Never Clots** in Case of **Transudate**

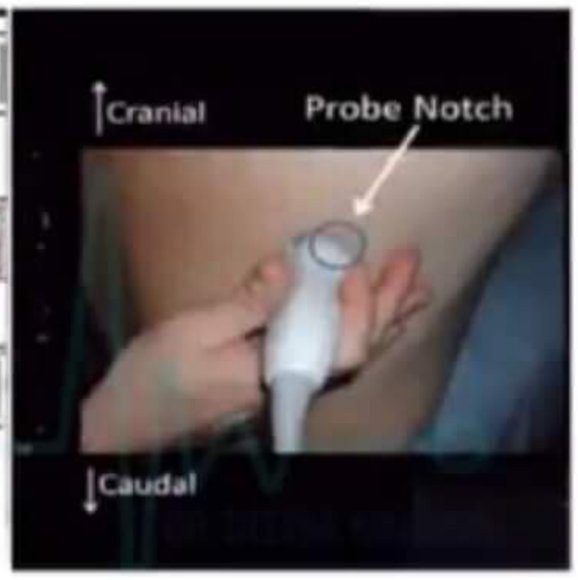
PrepLadder

Thoracocentesis

- Thoracocentesis is always done **USG guided**
- **>1 cm** distance b/w Pleural surface & lung border (i.e. **1 cm** of Fluid separating Lung border from Pleural Surface) on CXR is an Indication of Doing Thoracocentesis







Preferred site of Thoracocentesis → 7th ICS (Inter Coastal Space) Scapular line

→ Different Varieties of Pleural effusion:

a. **Pleural Effusion related to Malignancy**

- Usually there is occurs **Massive** Pleural Effusion in Malignancy

NOTE:

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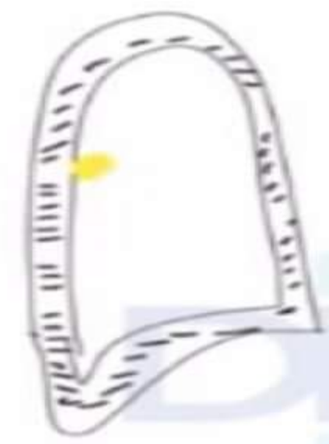
- Leading cause of Malignant Ascites → Ca Ovary
- Leading cause of Malignant Pleural Effusion → Ca Lung (Adenocarcinoma)



Symptoms → Pt. C/O

→ **TREPEPNEA** → Dyspnea of Patient is **Increasing** on **Lateral Decubitus position.**

Management:

a) **Diagnostic Thoracocentesis**
   - Send the fluid to laboratory to confirm the **Exudate** based on **LIGHT's Criteria**

b) **Check for**
   - Pleural Fluid Protein
   - Pleural Fluid LDH

LIGHT's Criteria

- Pleural Fluid Protein > 0.5 time of serum protein
- Pleural Fluid LDH > 0.6 time of serum LDH
- Pleural Fluid LDH > $\frac{2}{3}$ time upper Reference limit of serum LDH

- Ideally **any 1 of 3** present is sufficient for Diagnosis of Exudative Pleural Effusion. However in about 25% of cases light's criteria may **misdiagnose Transudate as Exudate.**

Therefore we also check

PrepLadder

- Pleural fluid Sugar < 60 mg%
- Cytology → **Microscopic examination** → Cancer Cells + nt
- Pleural effusion in these cases of Malignancies recur a lot after Thoraco-centesis. To prevent these, we **inject a sclerosing agent in pleural space** which causes obliteration of pleural cavity and the fluid doesn't reaccumulate.
  This procedure is k/as **Pleurodesis**

Note: Maximum Amount of fluid that can be removed per episode of Thoraco centesis

↓

< 1500 ml

(As per BTS Guidelines) (BTS – British Thoracic Society Guidelines)

- We don't remove fluid > 1500 ml due to risk of development of **Re-expansion pulmonary edema.**
- Stop the procedure of Thoraco-centesis immediately if the patient develops **persistent Hiccups or chest pain** as his/her **Phrenic Nerve** is getting irritated.

Pleurodesis

Rx → After Removing the fluid from pleural space can give following drugs:

A) Injection Doxycycline Into pleural space via chest tube

↓

Leads to formation of **Adhesions** in various layers of pleura ultimately causing **Pleurodesis**

Procedure of choice for Mx of patients C Malignant pleural effusion → Pleurodesis

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EXTRA MILES:

Orthopnea → Breathlessness ↑ing in **supine** position
→ Seen in **Acute CHF**

Platypnea → ↑ in Breathlessness in **sitting** position
→ Seen in

- **Atrial Myxoma**
- **Hepato pulmonary syndrome**

B) Parapneumonic Effusion

↓

If Diagnosed later or failed to Diagnose

↓

Can lead to **Empyema** which then is managed by **Chest tube insertion in 5th ICS, Mid Axillary line.**

C) Tubercular Pleural Effusion

- Classified as **Extra-pulmonary TB**

→ Adenosine Deaminase Levels ↑ in Pleural fluid

→ **IOC** – Pleural Biopsy gene Xpert / CBNAAT
(Not Pleural Fluid gene Xpert)

D) Rheumatoid Pleural Effusion

PrepLadder

- Inflammatory nodules in Lungs, Heart
- Skin in Extensor Distribution

→ Inflammatory nodules undergo Breakdown that results in development of Exudates

→ **On Microscopic Examination**

- **Cholesterol crystals** +nt in Pleural Fluid

Low pleural Fluid Sugar:

Seen in

- Infection
- Malignancy
- Rheumatic Arthritis associated Pleural Effusion

E) Meigs syndrome

Associated with

1. **Ovarian Tumors**
   - Fibroma / Thecoma
2. **Ascites**
3. **Rt. sided Pleural effusion**

Left Sided Pleural Effusion:-

Usually Encountered after surgical aspects t.me/latestpgnotes

1. Acute Pancreatitis (Involving Tail of Pancreas)
   - Sympathetic Pleural Effusion
2. Boerhaave Syndrome (Rupture of Esophagus)
3. Esophageal Malignancy

Note: B/L Pleural Effusion → CHF

Hemorrhagic Pleural Effusion →

- Has Hematocrit Value **0.5 times** that of blood
- Seen with TB / Ca lung / Mesothelioma / Trauma

Mesothelioma → A/w **Asbestosis**

1. Pleural Plaque Calcification
2. Hemorrhagic Pleural Effusion

Normal Pleural Fluid has the following characteristics:-

- Clear Ultrafiltrate of plasma that originates from the Parietal pleura
- A **pH** of 7.60-7.64
- Protein content of less than **2%** (1-2 g/dL)
- Fewer than 1000 white blood cells (WBCs) per Cu MM.
- Glucose content similar to that of plasma
- Lactate dehydrogenase (LDH) less than 50% of plasma

Indications of ICD tube insertion:

PrepLadder

a. Loculated Pleural Fluid / Emphysema
b. Pleural fluid PH < 7.20
c. Pleural Fluid glucose < 3.3 mmol/L (< 6mg / dl)
d. + ve Gram stain or culture of pleural fluid
e. Presence of Gross pus in the pleural Space

Characteristics of important Exudative Pleural Effusion:-

Etiology or Type of Effusion	Gross appearance	White Blood Cell Count (cells/mcL)	Red Blood Cell Count (cells/mcL)	Glucose	Comments
Malignancy	Turbid to bloody: occasionally serous	1000 to < 100,000 M	100 to several hundred thousand	Equal to serum levels: < 60 mg/dl. In 15 % of cases	Eosinophilia uncommon; postive result on cytologic exmiantion
Uncomplicated parapneuimonic	Clear to turbid	5000-25,000P	< 5000	Equal to serum levels	Tube thoracostomy unnecessary
Empyema	Turbid to purulent	25,000-100,000 P	< 5000	Less than Serum levels: often very low	Drainage necessary; putrid odor suggests anaerobic infection
Tuberculosis	Seroud to serosanguineous	5000-10,000M	< 10,000	Equal to serum levels: occasionally < 60 mg/dL.	Protein > 4.0 g/dL (may exceed 5 g/dL); eosinophils cells (> 10%) or mesothelial cells (>5%) make diagnosis unlikely: see text for additional diagnostic tests
Rheumatoid	Tubrid; greenish yellow	1000-20,000 M or P	< 1000	< 40 mg/dl	Secondary empyema common; high LD, low complement, high rheumatoid factor, cholesterol crystal are

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					characteristic
Pulmonary infarction	Seroud to grossly bloody	1000-50,000 M or P	100 to > 100,000	Equal to serum levels	Variable findings: no pathognomonic features
Esophageal rupture	Turbid to purulent red-brown	< 5000 to > 50,000 P	1000-10,000	Usually low	High amylase level (salivary origin); pneumothorax in 25% cases; effusion usually on left side: pH < 6.0 strongly suggests diagnosis
Pancreatitis	Turbid to serosanguineous	1000-50,000 P	1000-10,000	Equal to serum levels	Usually left-sided; high amylase level

LD- Lactate dehydrogenase

M- Monoculear cell predominance

P- Polymorphonuclear leaukocyte predominance

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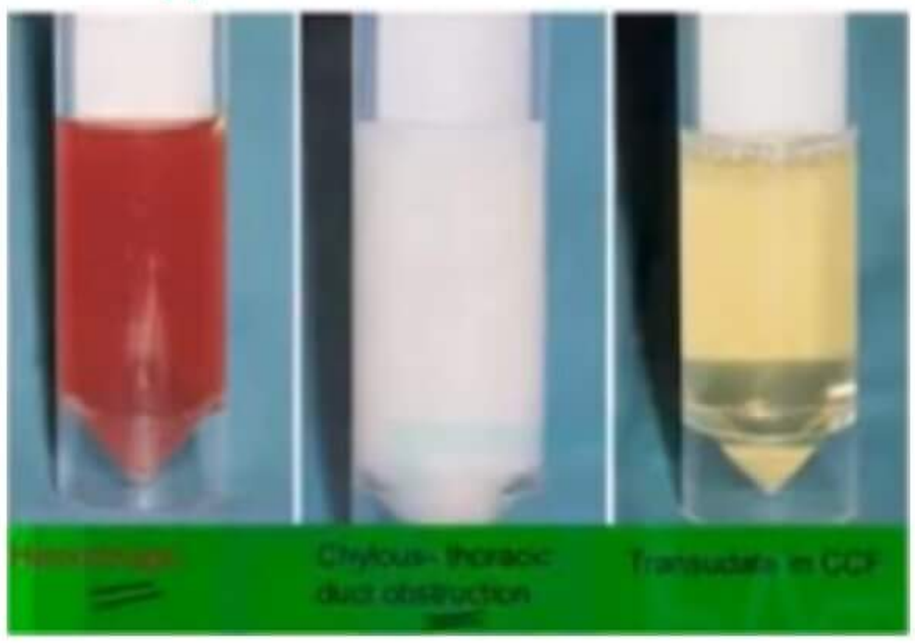
Gross Appearance of Pleural Fluid:



Chylous Thoracic duct obstruction leads to **Chylothorax**

→ Pleural Fluid Characters

- Milky White Colored
- ↑ Triglycerides

Cause of Chylothorax → Damage to lymphatics by Conditions such as **Filariasis**

Empyema

↓

Drainage of Pus via chest tube.

Normal chest tube placement

HIGH ALTITUDE & PULMONARY EDEMA

- High Altitude: **> 2500m**
- High altitude pulmonary edema usually develops on 2nd day and high altitude always causes hypoxia.
- If a persons is staying in high altitude for a longer time may feel head ache due to low partial pressure of oxygen that results in cerebral vasodilation. So that if a person going for a trekking over a mount Everest without oxygen is not possible due to less inspiratory partial pressure of oxygen: 43mmhg where maintaining partial pressure of oxygen is not attainable.

Acute mountain sickness: (HAPE/HACE) High Altitude Pulmonary/ Cerebral edema.

Acute Mountain sickness

- Nausea
- vomiting
- Flatulence
- Abdominal pain/ distension

Note: Vomiting leads to Dehydration of the person and also person is having tachypnea on altitude that may worsen the dehydration by heat vaporization from the body.

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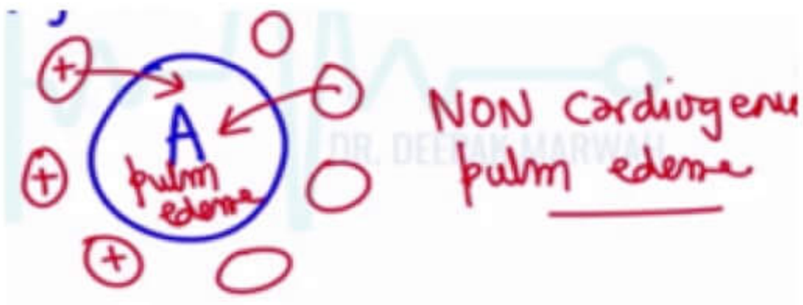
- **Acute mountain sickness is Prevented by**
- Acetazolamide

1 atm = 760 mm of Hg

Ascent ↑ ipo_2 ↓ → **Hypobaric hypoxia**

- 1. Cerebral Blood vessel dilatation will stretch the Dura mater which is pain sensitive → **Headache**
- 2. Pulmonary Blood vessel vasoconstriction ↑ hydraulic stress on basement membrane of Blood vessel so this will result in pulmonary artery hypertension.

CASE SCENARIO: a person went to trekking in a mountain, his family physician advice him to do not take part any exercise on the first day of mountain trekking due to acclimatization of body for mountain, but this young enthusiastic person involved in active exercise on the first day and end up with breathlessness and blood tinged sputum. So here the cause of hemoptysis is due to non cardiogenic pulmonary edema. Where low pressure of partial pressure can increase hydrostatic pressure of microcirculation of lungs so person develops **non cardiogenic pulmonary edema.**

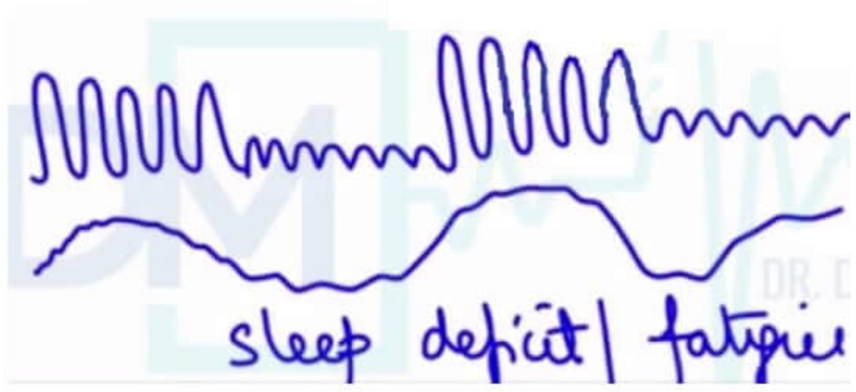


PrepLadder

→ Treatment of choice → Immediate descent:Q

Periodic Rhythm:

Most person went to high altitude cant sleep properly due to periodic rhythm of both hyper and hypoventilation simultaneously so oxygen saturation keeps on fluctuating so persons never feel fresh.



→ Acetazolamide – Carbonic Anhydrase inhibitor

- Urinary loss of HCO_3^-
- Metabolic Acidosis
- Hyperventilation

→ **Used to prevent Acute mountain sickness** and helps to maintain bodies oxygen saturation by maintaining hyperventilation.

→ Acetazolamide – No role in prevention of HAPE/HACE

→ **BAL (Bronchoalveolar Lavage) → ↑ RBC/↑ Proteins** → represents integrity of blood vessels is lost.

→ **BAL in ARDS (Adult Respiratory Distress syndrome)**

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↓

Neutrophils ↑↑

→ Unacclimatised – Risk factor of HAPE

HAPE (Non cardiogenic Pulmonary edema)

C/F: **Young adult** begins to deteriorate between **Day 2 to Day 4** when he arrived at height **2000-2500 m** after day 4 to day 5 its unlikely to cause pulmonary edema. Rapid ascend on First time may results in HAPE / while Reclimbing after 2 – 3 years the severity can be same or increase of HAPE. So HAPE is lethal or fatal.

→ **↓↓ Exercise intolerance** – Person felt breathlessness.

→ **Non productive cough**

→ **Frank Hemoptysis** – Person can be saved by this time if there is medical support available.

→ Cyanosis

- **↑↑ Heart Rate**
- **↑↑ Respiratory rate** – Person should drink water continuously to prevent dehydration.
- **Crackles in the chest** – Mostly involved middle zone of lungs.

PrepLadder

Work up:

1) CXR → **Pulmonary edema on left and right middle zone**, but there is no batwing edema, no cardiomegaly

2) ABG → **Respiratory Alkalosis CO_2 ↓↓**

Note: if PH is more than 7.7 then person won't survive.

3) **Echocardiography → RV strain**

4) **PCWP → Normal**, because this is an example of non cardio genic edema.

Treatment of HAPE:

1) **DOC: Nifedipine 60 mg** sustained release Tablet: Dilates pulmonary vessels which will decrease pulmonary artery hypertension and pulmonary edema component.

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2) **Immediate descent if not possible then Gamow bag can help.**

→ **Gamow bag** → provide Stimulated descent above 2000 m. there is a hyperbaric oxygen available in this bag. This oxygen can shifted to oxygen tang then

Will provided to patients.

Gamow bag

3) **Supplemental oxygen (4-6 L/min): sPo_2 > 90%**

4) **Salmeterol / salbutamol with 40% alcohol nebulization**

/Tadalafil (PDF – 5 Inhibitor)

SUMMARY:

HACE → Dexamethasone

Acetazolamide	Nifedipine	Dexamethasone
↓	↓	↓
Acute mountain sickness	HAPE	HACE

PrepLadder

PNEUMOTHORAX

TENSION PNEUMOTHORAX:-

* Type II respiratory failure

1. Sudden onset respiratory distress

C/F:- 2. Kinking of great veins (SVC / IVC)
Decreased Venous return
SBP decreased
} OBSTRUCTIVE SHOCK

* Causes of Obstructive Shock:-
1. Cardiac Tamponade
2. Tension pneumothorax
3. Budd Chiari Syndrome

Examination findings:-
1. Trachea shift C / L
2 Apex Beat displacement C / L
3 On Percussion: HYPER RESONANT NOTE
4 HAMMAN CRUNCH SIGN
(Sounds like walking on snow with Leather boots)
5. Air Entry : Absent
Breath sounds : Absent

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Rx:-

1) Wide Bore Needle at 2nd inter costal space near MCL, into chest of patient
↓
This system creates an exit mechanism of air, thus reducing severity of obstructive shock.

2) I.C.D 5th I / C space, MAL, connected to under water seal, creating (-) suction.
3) **Volume resuscitation**

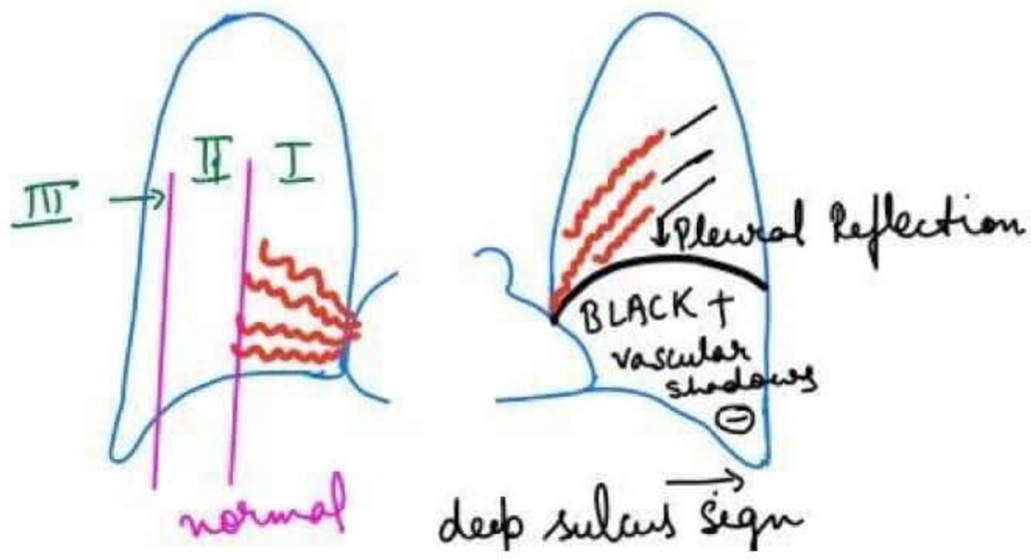
4) **Emergency Thoracotomy:**
* Hemostasis

SPONTANEOUS PNEUMOTHORAX:

EMPHYSEMA:- RUPTURE of BULLA

Clinical presentation:-
60 yrs, smoker, coughing Bout (+)
Turned blue, Sudden Respiratory Distress.

O /E:-
1. R. rate increased 30/ min
2. S.C.M / Scalenus / Alae Nasi Usage
Trachea C / L displacement
4. Hyper-Resonant on Percussion
5. Absent Air-Entry / Absent Breath sound



Chest X-ray:- Deep sulcus sign

: Absent Vascular Shadows

: Pleural Reflection

Rx :-

- <25% lung collapsed = **Supply O_2**
- 25%-50% lung collapsed = **Needle aspiration**
- >50% lung collapse => **I.C.D 5^{th} I / C space MAL with under water seal**
  Or central cyanosis (-) suction

In Pedo cases Pneumatocele rupture => Spontaneous pneumothorax

C/f :- 6 month old body with pneumonia on Vancomycin X 2 days, child taking feeds
But there is sudden onset cyanosis, Respiratory Distress
CXR => Deep sulcus sign

Diagnosis

Sudden rupture of Pneumatocele resulting in Spontaneous Pneumothorax.

Causes or Features of S.P Pneumothorax:-

1 Tall thin smoker: COPD
2 Tall thin Arm span > height Fibrillin Defect: Marfan Syndrome
3 EHLER DANLOS SYNDROME
4 Pneumatocele Rupture

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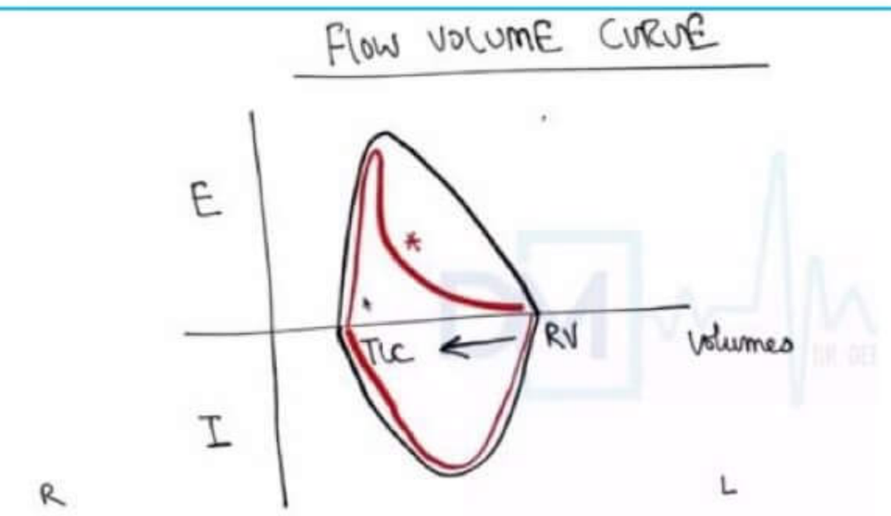
PrepLadder

FLOW VOLUME CURVE, SPIROMETRY AND DLCO

FLOW VOLUME CURVE

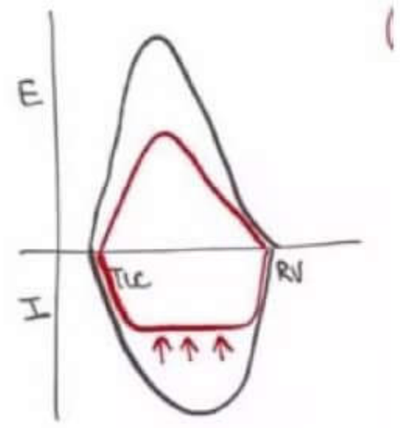
Asthma – Prolonged expiration
– Obstructive parenchymal ds.



Retrosternal Goiter

On Inspiration
- (–) Pressure
- Downward displacement of Goiter
- Compression of airway

On Expiration
- Displacement of Goiter upwards
- Relief of air compression



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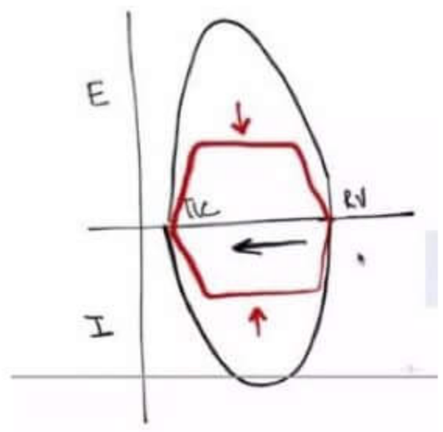
Extra thoracic airway obstruction – obstruction is not uniform both in expiration and inspiration phase

↓

So K|A extra thoracic variable airway obstruction

Tracheal stenosis – prolonged intubation



Intra thoracic fixed obstruction:-

Restrictive Airway Disorder/ Disease:

IPF
ILD
RV↓
TLC↓

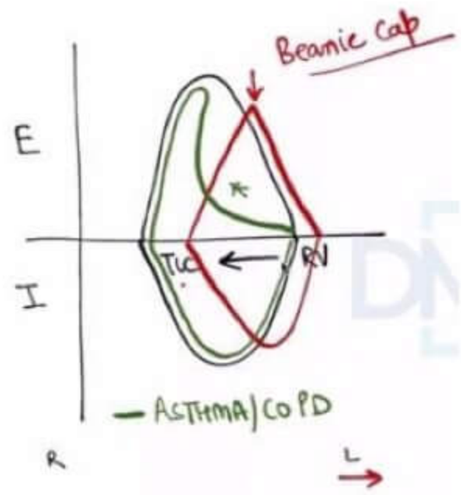
– Best spirometric parameter to evaluate Airflow obstruction

↓

FEV1

↓

F.E.F 25-75% - for small airway disease. Eg. Emphysema



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– Asthma – $FEV_{1}\downarrow$ Salbutamol (15 min) → FEV_1 (N)

$FEV_{1}\downarrow$ 50–80% (Mild asthma)

$FEV_{1}\downarrow$ 30–50 % (Moderate asthma)

$FEEV_{1}\downarrow$ >30 % (Severe asthma)

- A change in FEV_1: > 12% after salbutamol or 200 ml difference b/w FEV_1 before and after salbutamol: Bronchial asthma
- **REVERSIBLE Airway obstruction**

3 Diagnostic criteria for Asthma

- Reversibility
- Nocturnal attacks
- Episodic

Obstructive	Restrictive
1. Asthma 2. $FEV1\downarrow$ 3. TLC (n)↑ 4. (Timed Vital capacity) $FeV1/TLC\downarrow$ $FEV_{1}\downarrow$ 5. $\frac{\quad}{FVC}$	1. -ILD 2. $FEV1\downarrow$ 3. TLC ↓↓ 4. FeV1/TLC n/↑ 5. (N)|↑

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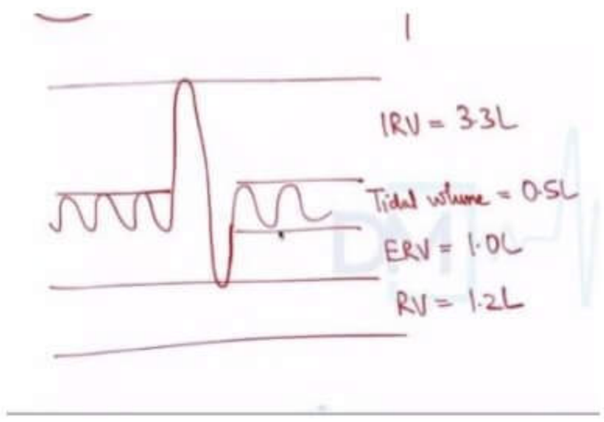
- TV = 0.5L
- ERV = 1.0 L
- RV = 1.2 L

- TLC = IRV + TV + ERV + RV – 6L
- VC = IRV + TV + ERV – 4.8L
- IC = IRV + TV – 3.8L
- FRC = ERV + RV – 2.2L



I.P.F | Asbestosis	Asthma
1 TLC↓	TLC↑
2 FRC ↓	FRC↑
3 RV ↓	RV ↑
4 Timed vital capacity ↑	Timed vital capacity↓

Methods to measure Residual volume:

1 Body plethysmography

2 Helium dilution test

3 N_2 washout test

PrepLadder

ANKYLOSING SPONDYLITIS

↓

Costochondral joint stiffness

↓

Residual Volume↑

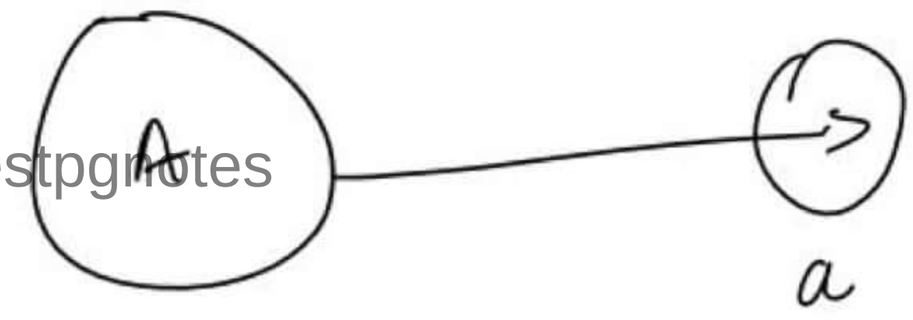
* Extra parenchymal restrictive lung dis –RV
* Parenchymal restrictive lung disease – RV ↓

RV

1) ILD|IPF	1) Asthma
2) UIP	2) COPD (Blebs)
3) DIP desquamative	3) Ankylosing Spondylitis (HLA B_{27}+)
4) BOOP	
5) Asbestosis	

Alveolar Arteriolar Gradient:

A-a gradient = 5-15 mmHg



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Status Asthmaticus:

- Airway closure

A - a = unaffected value

↓ ↓

- Type 2 Respiratory failure
  - Po_2↓
  - PCO_2↑
  - A-a gradient (n)

Congenital cyanotic Heart disease:

TOF
POF
TAPVC

↓

-Mixing defect
- ↑ A-a gradient
- MC cyanotic heart ds – TOF > POF

POF = TOF + ASD

$pAO_2 - paO_2$ = 5-15 mmHg

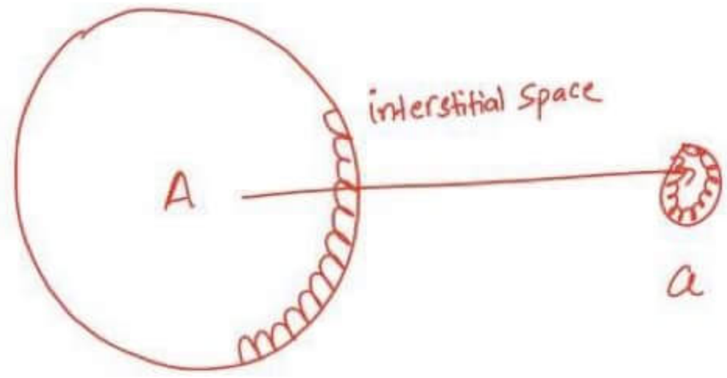
↓

(N) (Lesser < (n))

PrepLadder

Dlco:

- Diffusion capacity of lung for Carbon mm oxide



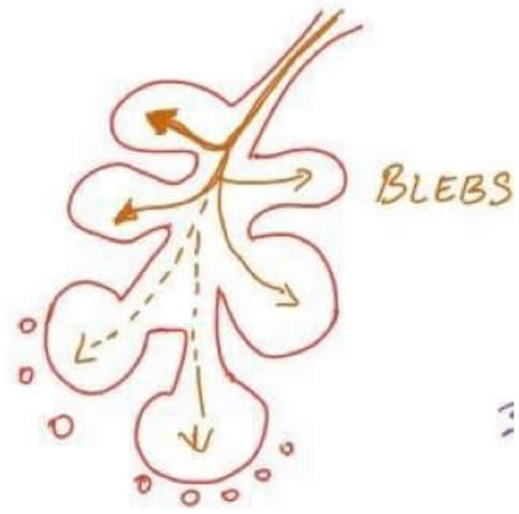
Causes for ↓ DLCO:

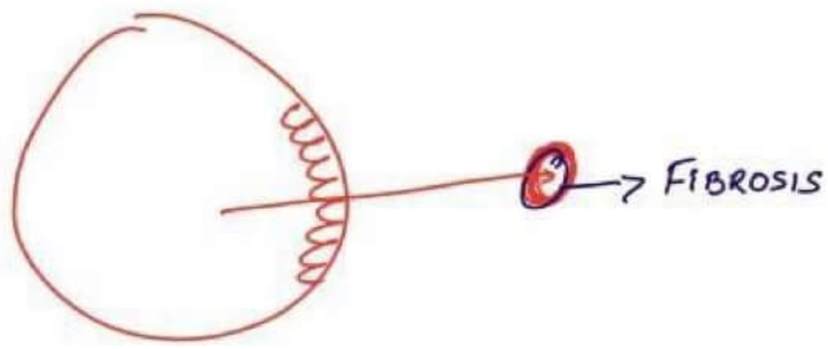
1 ILD – IPF| UIP

2 Interstitial pneumonia: P. Jiroveci| Mycoplasma Psittacosis

3 Emphysema |COPD

4 PAH





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PrepLadder

ABG ANALYSIS PART 1

Respiratory Acidosis

$CO_2 + H_2O \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$

$\uparrow Co2 \longrightarrow \uparrow H_2CO_3 \longrightarrow \uparrow H+$

In Respiratory Acidosis

↓

↑ CO2

↓

↑ H+

↓

↑ HCO_3^- (To neutralize)

By PCT reabsorption

→So HCO_3^- reabsorption compensate ↑ H+

→In acute acidosis

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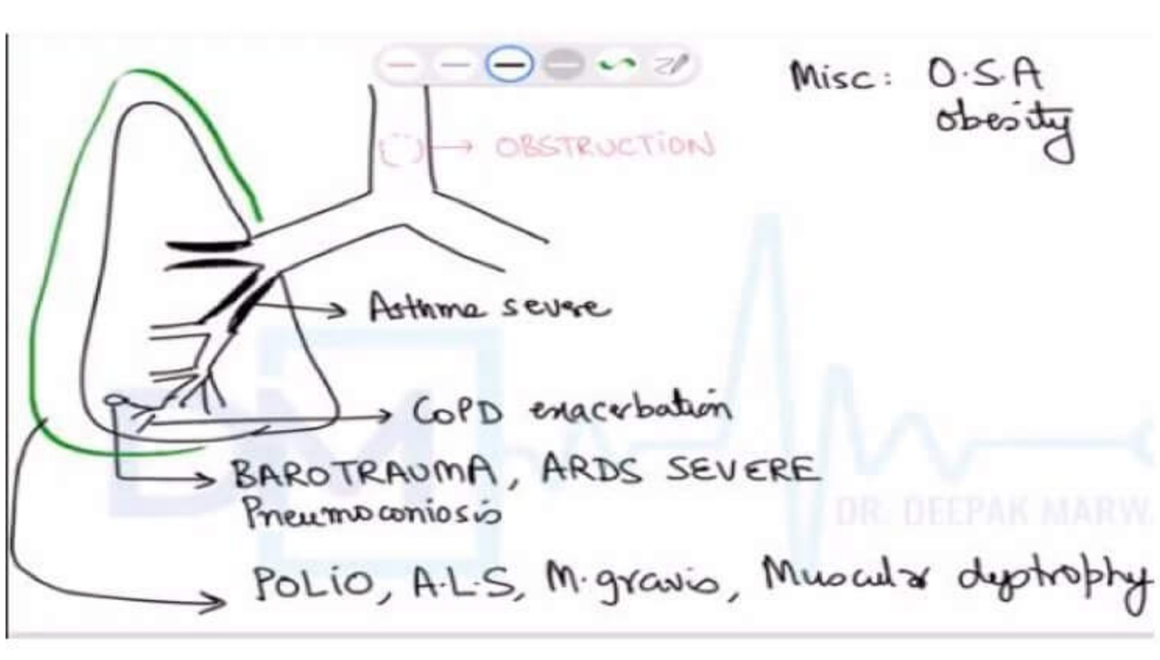
10 mm ↑ in Co_2 → 1 mEq ↑in HCO_3^-

→In chronic acidosis

10 mm ↑ in Co_2 → 4 meq ↑in HCO_3^-

Causes:-

1. Central causes
   - CVA
   - Drugs, Morphine, sedates, Anaesthesia
   - CNS Infection
2. Respiratory Causes



PrepLadder

Mnemonic: **DEPRES**

- Drugs
- Disease of NMJ
- Edema
- Pneumoconiosis
- Respiratory center depression

HIGH Co_2

↙ ↘

Co_2 Necrosis ↑ICT

Rx-

1. Elective Intubation
2. IPPV

- Aggressive treatment do not recommended

↓

If given Co_2 washout

↓

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↓ Cerebral perfusion

↓

Seizures (Due to under perfusion)

→ Co_2 vasodilatory effect on CEREBRAL VESSELS

RESPIRATORY ALKALOSIS

$CO_2 + H2o \rightleftharpoons H_2CO_3 \rightleftharpoons H^+ + HCO_3^-$

In respiratory alkalosis

↓

↓ Co_2

↓

↓ $H+$

↓

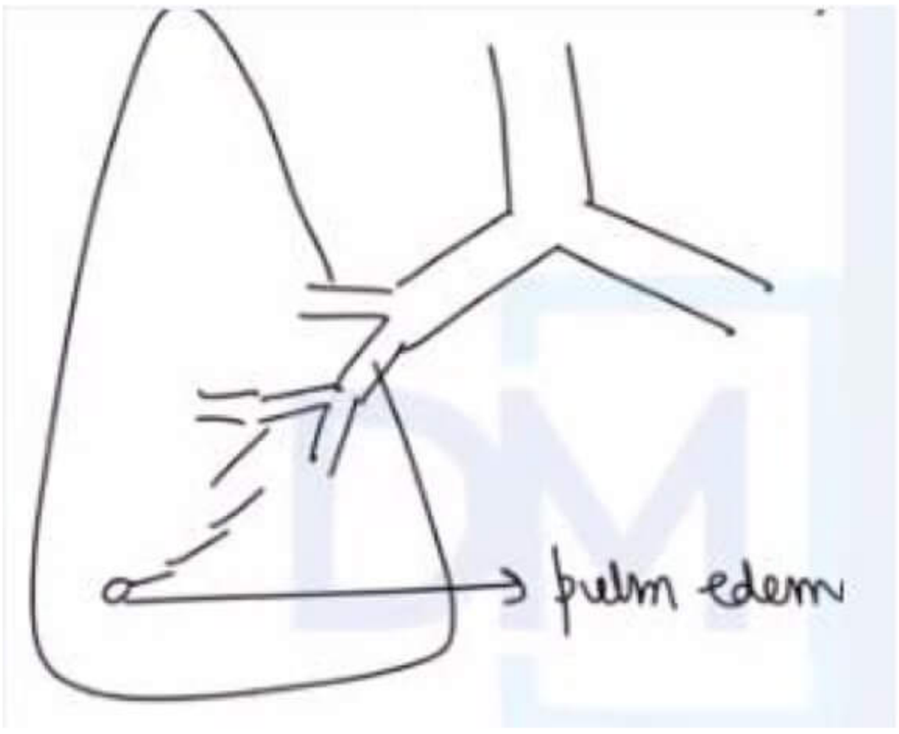
↑ HCO_3^- loss from PCT

PrepLadder

→ Acute: For 10 mm Co_2 ↓ → HCO_3 ↓ by 2 mEq

→ In chronic: 10 mm Co_2 ↓ → HCO_3 ↓ by 4 mEq

CAUSES-



- Pulm edema CHF
- High altitude pulmonary edema
- Pulmonary embolism
- Flail chest

MISC:-

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- Sepsis
- Heat exposure

C/F: ↓ Co2

Cerebral hypoperfusion

- Dizziness, vertigo
- Intracellular shift Na+ K+ po_4^{2-}

So arrhythmia can occur

- ↑ protein binding of Ca++

↓

↓ ionized Ca++

↓

Tetany

PrepLadder

→ MC ABG disorders in chronic ill patient in ICU

Rx – Paper–bag breathing

Procedural aspects

→ Modified Allen test – to check integrity of palmar arch

Steps:-

- Obliterate both Arteries
- Ask patient to form fist
- Entire palm became pale
- Release arteries simultaneously
- If collaterals present whole hand will have a gush from release of either arteries.

NUMERICALS

1. A 24 year old beggar is found unconscious at the gate of Metro station Green park. In the ER, room air arterial blood gas is performed and reveals: pH 7.25, PCO2 60, PO2 65, HCO3 26, Base Excess 1. On the chemistry panel, the sodium is 137, chloride is 100, bicarbonate is 27. What is the diagnosis?

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Solution:

→ pH. 7.25

PCO_2 – 60

HCO_3 – 26 – N

Respiratory acidosis

→So respiratory uncompensated

2. A 60 year old man with amyotrophic lateral sclerosis is brought to the clinic by his family who are concerned that he is more somnolent than normal. On further history, they report that he has been having morning headaches and does not feel very refereshed when he wakes up. An arterial blood gas is performed and reveals: pH 7.37, PCO2 57, PO2 70, HCO3 34. What is the diagnosis?

pH – 7.37

Pco_2 – 57

Hco_3 – 34

- As patient is suffering from ALS

PrepLadder

- So $Co_2 \uparrow$ is ~ 20 mm Hg
- HCo_3 to be increased by 2 x 4 = 8 mEq
- HCo_3 – 34 mEq
- So it is **Fully compensated as pH- Normal**

3. **A patient has readings of pH 7.3, PaCO2 68 mmHg, HCO3 28 mmol/L, and Pao2 60 mm Hg. How would you interpret this?**

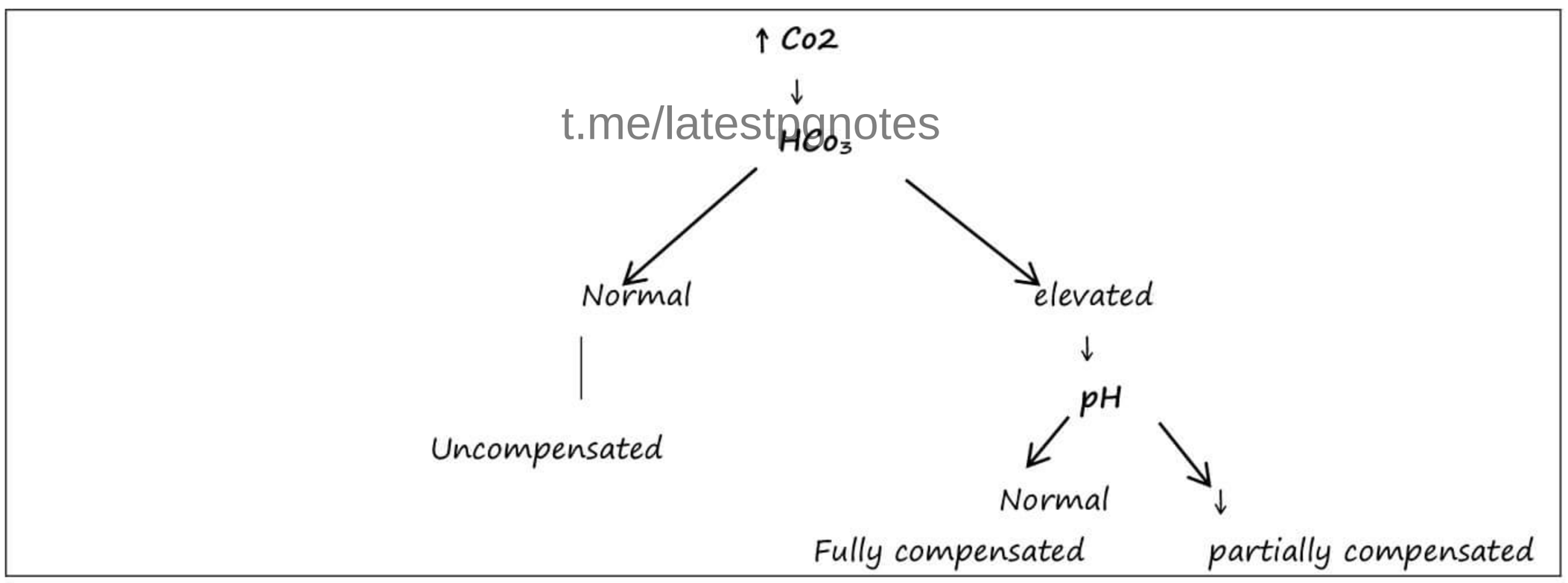
pH – 7.3 - acidic

$paCo^2$ – 38 mm Hg – respiratory acidosis

HCo_3 – 28 mm / L – elevated

- As pH acidic

→ So **partially compensated**



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4. **A 68 year old man with a history of very severe COPD (FEV1~1.0L, <25% predicted) presents to the ER complaining of worsening dyspnea and an increase in the frequency and purulence of his sputum production over the past 2 days. His oxygen saturation is 78% on room air. Before he is placed on supplemental oxygen, a room air arterial blood gas is drawn and reveals: pH 7.25, PCO2 68, PO2 48, HCO3 31.**

- pH- 7.25 (Acidic)
- PCo_2 – 68 mm Hg (Respiratory acidosis)
- HCo_3 – 31 mm Hg (Elevated)

PrepLadder

→So pH acidic – **So partially compensated**

5. **A 15 year old juvenile with a history of inhalant abuse presents to the emergency room complaining of dyspnea. He has a SpO2 of 99% on room air and is tachypneic. A room air arterial blood gas is performed and reveals: pH 7.25, PCO2 17, PO2 128, HCO3 2. A chemistry panel revealed sodium of 130, chloride 98, HCO3 2. What is the diagnosis?**

- pH – 7.25 (Acidotic)
- PCo_2 – 17 mm Hg (Low)
- HCo_3 – 2 mm Hg (Very low)

→ So **metabolic acidosis**

→ PH – acidic

→ **So partially compensated**

→ AG – 130 – (98+2)

30 - ↑ A.G

So, Dx **HAGMA**

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→ Predicted PCo_2 = HCo_3 + 15 → for both **metabolic acidosis + alkalosis**

= 2+15

=17

So actual value = Predicted value

→ So **compensated**

6. **A three year old child is admitted to the hospital with a diagnosis of severe asthma exacerbation. The mother of the child reports to the nurse on duty that she has witnessed slight tremors and behavioural changes in her child over the past four days. The attending physician orders routine ABGs following an assessment of the ABCs. The ABG results are pH 7.35, PaCO2 72 mm Hg and HCO3 38 mEq/L What acid-base disorder is shown?**

PH – 7.35 (N /Acidotic)

PCo_2 – 72 mm Hg (Elevated)

PrepLadder

HCo_3 – 38 meq (Elevated)

→ So respiratory acidosis

→ As pH - Normal

→ So **fully compensated respiratory acidosis**

7. A resident working in the ER decides to draw a room air arterial blood gas from a sick patient, which reveals: pH 7.46, PCO2 49, PO2 68, HCO3 34. On his chemistry panel, the sodium is 139, chlorides 95, HCO3 34. What is the diagnosis?

pH – 7.46 (Alkaline)

PCo_2 – 68 (Elevated)

HCo_3 – 34 (Elevated)

→ So **metabolic alkalosis**

8. A climber is coming down from the summit of Mt. Everest. At an altitude of 8,400m, he has a blood gas drawn while breathing ambient air as part of a research project. The blood gas reveals pH 7.55, PCO2 12, PO2 30 and HCO3 20. What does it demonstrate?

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pH – 7.55 (Alkaline)

PCo_2 – 12 (Low)

HCo_3 – 20 (Low)

→ **Respiratory alkalosis**

- For every 10 mm ↓ in Co2
- HCo_3 to be ↓ by 2 meq.
- So PCo_2 ↓ ~ 30 mm Hg
- HCo_3 to be ↓ by 2x3=6
- So 26-6 = 20
- But pH - ↑
- So **partially compensated**

PrepLadder

9. A 57 year old woman presents with 2 days of fever, dyspnea and a cough productive of rust-colored sputum. Her room air oxygen saturation in the emergency room is found to be 85% and the intern decides to obtain a room air arterial blood gas while they are waiting for the CXR to be done. The blood gas reveals: pH 7.54, PCO2 25, PO2 65, HCO3 22, Base excess-1. What is the diagnosis?

   pH – 7.54 ↑

   PCo_2 – 25 (Low)

   HCo_3 – 22 (N)

→ So uncompensated Respiratory alkalosis as HCo_3 (Normal)

10. A patient has pH 7.6, PaO2 120 mm Hg, PaCO2 31 mm Hg, and HCO3 25 mmol/L. What does this mean?

    pH – 7.6 (Alkaline)

    Co_2 – 31 (Low)

    HCo_3 – (N)

→ So uncompensated

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11. Patient X is admitted to the hospital and is to undergo brain surgery. He is very anxious and scared of the upcoming surgery. He begins to hyperventilate and becomes very dizzy. STAT ABGs reveal pH 7.51, PaCO2 22 mm Hg and HCO3 25 mEw/L. What is the ABG interpretation based on the findings?

    pH – 7.51 (Alkaline)

    Co_2 – 22 (Low)

    HCo_3 – 25 (N)

    - As hyperventilated & HCo_3 – N
    - So uncompensated respiratory alkalosis

12. Lab values: pH 7.42, paCO2 25, HCO3 18
    A. Metabolic acidosis, partially compensated
    B. Respiratory acidosis, partially compensated
    C. Respiratory acidosis, fully compensated
    D. Respiratory alkalosis, fully compensated

PrepLadder

pH – 7.42 (N)

$PaCo_2$ – 25 (Low)

HCo_3 – 18 (Low)

- Chronic
- So respiratory alkalosis
- ↓ in Co_2 = 40-25 = 15
- For chronic change for every 10-↓ by 4 mEq.
    - HCo_3 to be ↓ by

$4 \times 1\frac{1}{2} = 6$

HCo3 – (22-26) – 6

So (16-20)

HCo_3 = 18

→ So fully compensated

13. Lab values: pH 7.56, paCO2 20, HCO3 20

a. Respiratory alkalosis, uncompensated
b. Respiratory alkalosis, uncompensated
c. Respiratory alkalosis, partially compensated
d. Metabolic alkalosis, partially compensated

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pH – 7.56 (Alkaline)

$PaCo_2$ – 20 (Low)

HCo_3 – 20 (Low)

- So this is Respiratory alkalosis
- $PaCo_2$ ↓ by 20 mm Hg
- So HCo_3 to be ↓ by 4x2=8
- HCo_3 to be b/w (14 -18)
- HCo_3 in question 20
- & PH-alkaline

→ So respiratory alkalosis but partially compensated

PrepLadder

ABG ANALYSIS PART 2

14. A 47 year old man with a history of heavy alcohol use presents with a two day history of severe abdominal pain, nausea and vomiting. On examination, his blood pressure is 90/50 and he is markedly tender in his epigastrium. His initial laboratory studies reveal a sodium of 132, chloride 92, HCO3 16, creatinine 1.5, amylase 400 and lipase 250. A room air arterial blood gas is drawn and reveals pH 7.28, PCO2 31, PO2 88, HCO3 16.

What is the diagnosis?

Solution:

- Alcohol & severe abdominal pain

  ↓

  Point towards possibility of acute pancreatitis
- BP of 90/50 means patient is having shock probably of distributive etiology
- From lab studies; quickly calculate Anion gap

i.e. Na + – (cl + Hco3)

= 132 – (92+16)

= 24 meq. Which is elevated [(N) = 10 mEq]

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Therefore, high anion gap

→ Then look at pH of 7.28 reflecting an acidotic pH [(N) pH = 7.35-7.45]

→ PCO_2= 31 which is low [Normal 38-42 (average – 40)]

→ This low PCO2 cannot explain acidotic pH also → HCo3 = 16 which is low (Normal 22-28)

- This explains acidotic pH

Therefore, acidic pH is due to metabolic problem i.e. metabolic acidosis

In this case a compensatory process is also going on which is Hyperventilation leading to Co2 washout thus low Co2

Since pH is still not normalized, meaning compensation is partial.

Final answer would be: HAGMA (High anion gap metabolic acidosis)

Also calculate the expected PCO2 using formula.

Expected Pco2 = HCO3 +15

Since expected pCo2 = actual pCO2 in this case implies compensation process is going fine.

PrepLadder

15. pH = 7.27, PCO2 = 33 and HCO3 = 17 what is the Dx?

Solution:-

Acidotic pH

Low PCO2 (Cannot explain acidotic pH)

Low HCO3 (Can explain acidotic pH)

Therefore, metabolic acidosis.

Accompanied by hyperventilation (Kussmaul breathing)

Since pH still not normalized, compensation is partial.

If PCO2 would be 38 – uncompensated M.A

If PCO2 would be 60 - M. acidosis + R. acidosis (Mixed disorder)

↓

This is seen in cardio respiratory arrest.

16. lab values: pH 7.37, paCO2 33, HCO3 17

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a. Metabolic acidosis, fully compensated

b. Metabolic acidosis, partially compensated

c. Respiratory acidosis, fully compensated

d. Respiratory alkalosis, uncompensated

Solution:-

pH – normal

PCO_2 – low meaning Co2 washout is occurring

HCO_3 – low

M. acidosis.

Along with compensatory hyperventilation respiratory alkalosis

Since pH is normal, means it is fully compensated

Therefore Ans. (A) M. acidosis fully compensated

PrepLadder

17. Lab values: pH 7.23, PaCO2 37, HCO3 18

a. Respiratory alkalosis, partially compensated

b. Respiratory alkalosis, uncompensated

c. Metabolic acidosis, uncompensated

d. Metabolic alkalosis, partially compensated

Solution:-

pH – acidotic

pCO_2 – normal (38-42)

HCo_3 – low

↓

M. acidosis

Since pCO_2 is normal means – compensatory process has not started

Therefore uncompensated

Answer – (C) metabolic acidosis, uncompensated

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18. Lab values: pH – 7.30, PCo2 – 36, HCO3 – 16

Solution:

pH – 7.3 – acidotic pH

pCo2 – 36 – normal – means compensatory process not started

HCO3 – 16-low – Dx is M. Acidosis

Since pH is not normal it is uncompensated

19. An 8 month female baby presented with 1 day h/o lethargy. She had vomited several times. Her drug addict mother said she appeared "intoxicated"

O/E: baby was obtunded but she was easily reusable and muscle bone was normal.

RR = 60/min. pupils are normal. No dehydration BP was 112/62. Heart & chest examination was normal planter response was normal.

PrepLadder

Ix:

Na += 135

K + = 4.2 Glucose 5.9 mmol/l

Cl^- = 116

$HCO3^-$ = 6

Urinalysis: pH = 5.0; negative for glucose & ketones, positive for calcium oxalate crystals

ABG:

pH = 7.19

pCO_2 = 16

PO_2 = 100

HCO_3 = 6.2

Solution:-

Important points in history:

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- Drug addict mother
- Tachypnea
- Pupils normal – no CNS depression by opioids
- Calcium oxalate crystal – d/t ethylene glycol poisoning

Calc: Anion gap: Na+ (Cl^- + HCO_3)

= 135-(116+6)

= 135-122 = 13

Ethylene glycol poisoning – leads to – acute tubular necrosis

From ABG: Metabolic acidosis partially compensated

METABOLIC ALKALOSIS

20. Mr. Sharma, who underwent post-abdominal surgery, has a nasogastric tube In-situ. The nurse on duty notes that the nasogastric tube is draining a large amount (900 cc in 2 hours) of coffee ground secretions. The patient is not oriented to person, place, or time and hence STAT ABGs are ordered. The results from the ABGs show pH 7.57, PaCO2 37 mmHg and HCO3 30 mEq/L. What is your assessment?

PrepLadder

Solution:-

pH = 7.57 – Alkalotic pH

pCO_2 = 37 – Normal

HCO_3 = 30 – Elevated – explains M. alkalosis

Compensatory mechanism in M. alkalosis is ↑ in CO2 i.e. Respiratory acidosis but in this case, CO2 is not raised, so Dx is uncompensated M. alkalosis.

Excessive secretion from NG tube

↓

Dehydration

↓

↓ GFR

RAAS +

↓

Aldosterone ↑

↓

Loss of K+ and H+

Hypokalemia Metabolic alkalosis

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Expected pCO_2 = 15+HCO_3^-

= 15+30

= 45

But actual = 37 – not equal to 45 thus, compensatory process not started

21.

Lab values: pH 7.52; PCO_2 = 48, HCO_3^-=28

Alkalotic pH; ↑ pCO_2; slightly elevated HCO3$^-$

PrepLadder

Primary problem → M. alkalosis with partial compensation expected pCO2 =15+28 = 43 which is not equal to 48, therefore partial compensation

22. You are reviewing the latest arterial blood gas results for a sick Cushing's Syndrome patient. Which result indicates that the ABG derangement is compensated?

a) pH 7.32
b) PaCO2 18 mmHg
c) HCO3 8 mEq/L
d) PaCO2 48 mmHg

Solution:-

Cushing syndrome patient

↓

↑ Cortisol

↓

Stimulate ENaC

↓

↑ Na+ & H2O absorption

loss of K+ & H+

↓

M. Alkalosis

↓

Compensation by ↑ CO2

Ans. d.) pCO2 48mmHg

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23. A patient is post-op from knee surgery. The patient has been receiving analgesia 47 mg IV every 2 hours. You notice the patient is exhibiting a respiratory rate of 8 and is extremely drowsy. Which of the following condition is the patient at risk of?

a. Respiratory acidosis

b. Respiratory alkalosis

c. Hypokalemia

PrepLadder

d. Metabolic acidosis

Solution:

analgesia → CNS depression → CO2 narcosis

↓

Respiratory acidosis

If there is inadequate analgesia

↓

Patient will hyperventilate

↓

Respiratory alkalosis

24. A patient attempted to commit suicide by ingesting a bottle of Aspirin. Which of the following conditions is this patient at risk for?

a. Hyperkalemia

b. Hypercalcemia

c. Respiratory alkalosis

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d. Respiratory acidosis

Solution:

Aspirin toxicity

↓

Metabolic acidosis

↓

Stimulates Respiratory center

↓

CO2 ↓

↓

Respiratory alkalosis

→ intracellular shift of Na+ /K+/Po4

→ ↑ protein binding of calcium, ↓ ionized Ca2+ leading to tetany

PrepLadder

25. Respiratory alkalosis can affect which electrolyte levels in the body?

a. Calcium and sodium levels

b. Potassium and sodium levels

c. Calcium and potassium levels

d. Potassium and phosphate levels

Solution:

respiratory alkalosis affects Ca^{2+} & PO_4^{3-}

↓

Tetany and hypokalemia

26. A Patients is experiencing respiratory alkalosis. What is the most classic sign seen ?

a. Bradypnea

b. Chvostek sign

c. Bradycardia

d. Hoover sign.

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↓

Solution: CHVOSTEK sign + → sign of tetany which present in respiratory alkalosis

Hoover sign: Rule out hysterical leg weakness

27. A patient has the following blood gases: PaCO2 25, pH 7.50, HCO3- 19. Which of the following could not be the cause of this condition?

a. Anxiety attack

b. paO_2/Fi O2 ratio <100

c. Hysteria

d. Aspirin toxicity

Solution:

First read pH always

- Alkalotic pH
- Low pCO_2

PrepLadder

- Low $HCO3^-$

Respiratory alkalosis partially compensated

Caused by:-

- Anxiety attack
- Hysteria
- Aspirin toxicity - + respiratory center → R.R ↑

Severe ARDS

↓

Blood vessel collapse

↓

V/P imbalance

↓

CO_2 build up

↓

Respiratory acidosis

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28. A patient on mechanical ventilation has the following blood gases: $PaCO_2$ 29, pH 7.56, HCO_3 23. Which of the following conditions is the patient experiencing?

a. Respiratory alkalosis not compensated

b. Respiratory alkalosis partially compensated

c. Respiratory alkalosis fully compensated

d. Respiratory acidosis partially compensated

Solutions:

Alkalotic pH

Low CO_2 } - Respiratory alkalosis uncompensated

HCO_3 normal

PrepLadder

29. A patient is experiencing respiratory acidosis due to brain trauma. Which of the following lab values correlates with this acid imbalance?

a. Potassium level of 6.0

b. Potassium level of 2.5

c. Potassium level of 5.0

d. Potassium level of 3.5

Solutions:

Respiratory alkalosis – I/C shift Na+ K+ PO_4^{2+} inside

Respiratory acidosis – I/C shift Na+ K+ PO_4^{2+} outside

Therefore K+ ↑ ans. is (A)

30. Which of these patients is experiencing partially compensated respiratory acidosis?

a. $PaCO_2$ 30, pH 7.35, HCO_3 26

b. $PaCO_2$ 53, pH 7.23, HCO_3 28

c. $PaCO_2$ 45, pH 7.49, HCO_3 21

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d. $PaCO_2$ 50, pH 7.30, HCO_3 23

Solution:

pH = Acidotic

pCO_2 = Elevated

HCO_3 = Elevated

} (B) option

31. Which of the following is not a cause of respiratory acidosis?

a. Pulmonary emboli

b. Asthma

c. Chronic obstructive pulmonary disease (COPD)

d. Hyperventilation

Ans: Hyperventilation cause Respiratory alkalosis

PrepLadder

32. A patient with COPD has the following blood gases; PCO2 59, pH 7.26, HCO3 32. Which of the following conditions is presenting?

a. Respiratory alkalosis

b. Respiratory acidosis

c. Metabolic alkalosis

d. Metabolic acidosis

Solutions: Acidotic pH

Elevated pCO_2

Elevated HCO_3

} Respiratory acidosis partially compensated

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PrepLadder

MIXED DISORDERS

33. A 28 year old woman was admitted electively to a HDU (high dependency unit) following a caesarian section. A diagnosis of 'fatty liver of pregnancy' had been made preoperatively. She was commenced on a continuous morphine infusion at 5 mg/hr and received oxygen by mask. This was continued overnight and she was noted to be quite drowsy the next day. Arterial blood gases were.

pH 7.16

pCO2 61.9 mmHg

pO2 115 mmHg

HCO3 21.2 mmol/l

Solution: Acidotic pH

Elevated CO2 } Respiratory acidosis

Low HCO3 } Metabolic acidosis

34. Comment on the diagnosis:-

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pH 7.31

pCO_2 56 mmHg

pO_2 87 mmHg

HCO_3 13 mmol/L

Solution: Acidotic pH

↑CO2 } Respiratory acidosis

↓HCO3 } Metabolic acidosis

35. A 70 year old man was admitted with severe congestive cardiac failure. He has been unwell for about a week and has been vomiting for the previous 5 days. He was on no medication. He was hyperventilating and was very distressed. Admission biochemistry is listed below. He was on high concentration oxygen by mask.

Biochemistry results: Na+, 127, K+5.2, Cl: 79, HCO3 20, urea 50.5, creatinine 0.38 & glucose 9.5 mmol/l. Anion gas 33 mmol/l

Arterial blood gases

PrepLadder

pH 7.58

pCO_2 21 mmHg

pO_2 154 mmHg

HCO_3 32 mmol/L

Vomiting –> dehydration –> RAAS –> M. alkalosis

Hyperventilating –> Respiratory alkalosis

Anion gap = 127 – (79+20)

= 28 (elevated)

Alkalotic pH

Low CO_2

Elevated HCO_3

Respiratory alkalosis

+

Metabolic alkalosis (Lactic acidosis)

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PrepLadder

FEVER OF UNKNOWN ORIGIN

- Diurnal variation in body

- Max Temp → Evening
- Min Temp → Morning
- Normal Diurnal Variation < 0.9 F

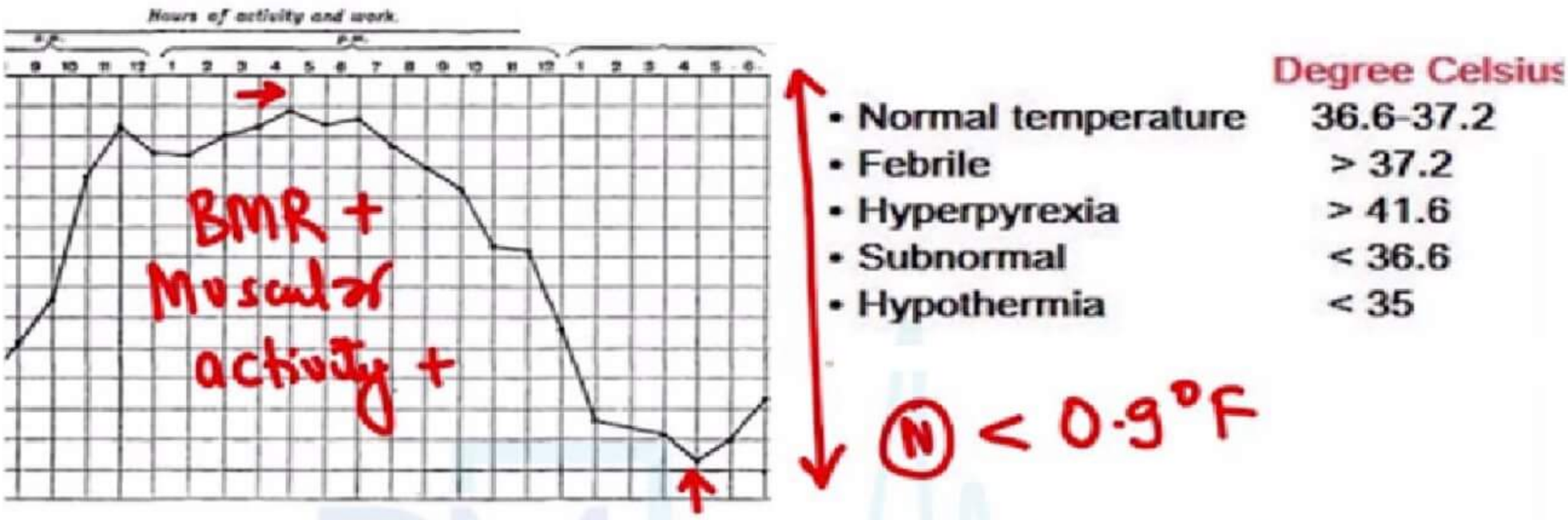

Chart showing diurnal variation in body temperature, ranging from about 37.5 °C from 10 a.m. to 6 p.m., and falling to about 36.3 °C from 2 a.m. to 6 a.m.

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Note: Reason for Increase in Temperature in Evening

- BMR
- Muscular Activity

Fever/Temperature

AM > 98.9° F (Because of circadian rhythm)

PM > 99.9° F

Hyperpyrexia > 107° F → associated with heat stroke

Cause

1. Hyperpyrexia → > 107 ° F
2. Hypothermia: → < 35° c
   - Mild → 32 - 35° c
   - Moderate → 28 - 32° c
   - Severe → < 28 ° c

ECG changes in Hypothermia → J wave/ Osborne wave

PrepLadder

To measure core temperature

Ideal Site → Pulmonary Artery

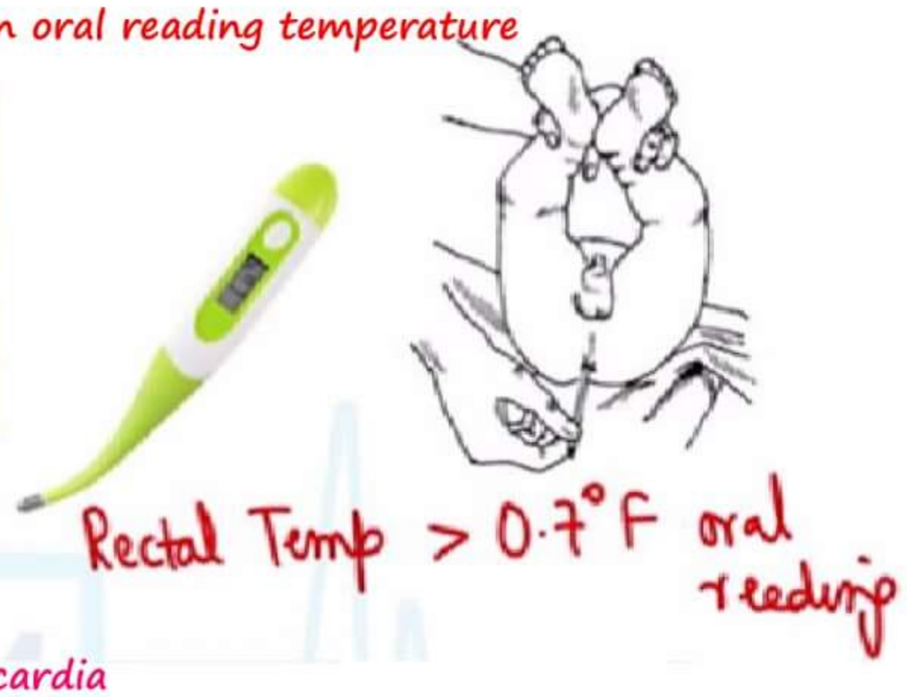
Preferred site → Lower esophagus

In fever → Pulse Rate is increased

If Temp Increase > 100° F

For every 1°F rise of temperature above 100° F PR increases >10 bpm

Note: Rectal Temp > 0.7° F than oral reading temperature



Faget's Disease/ Relative Bradycardia

- Disease manifested hyperthermia with bradycardia which More common with gram –ve bacteria and infections of bacteria that are transmitted by Ticks.

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Mnemonic

T → Typhoid/ Tularemia/ Typhus Scrub.

B → Brucellosis/ Babesia

M → Mycoplasma pneumoniae/ Malaria

C → Coxiella Brunetti (Q fever)/ Corynebacterium Diphtheria

L → Legionella pneumophila/ Leptospira

R → Rickettsiae

All are gram negative or Tick Born Infections

Tularemia → Caused by Ticks (Living on Body of Rabbit, Deer)

- Person Hunter by Profession, shot a rabbit or deer while handling the meat, the tick entered the body of hunter so he developed Axillary Lymphadenopathy

Typhus Scrub → Transmitted by baby mites (Shiggers)

Brucella → Caused by consumption of Raw milk.

Babesia → D/D of malaria [On **Peripheral smear** → Maltese cross appearance]

PrepLadder

Coxiella Brunetti/ Q fever (Query fever) → Spread by animals
- can cause subacute bacterial endocarditis in rheumatic fever cases.

L. Pneumophila → Spread by inhalation of water Droplet.

Viruses causes of faget's disease → Dengue, Yellow fever

Other causes → Drug fever/ Factitious Fever/ CNS Lesions

Drug fever → Allopurinol [h/o postmenopausal women with gout], β Blocker, Sulfa Drugs
→ Non-Hodgkin Lymphoma

Factitious Fever

→ Seen in Health care worker or access to Health care services.

→ Mostly Female

→ Due to Injection of Infected Distilled water

CNS Lesions :

1. Pontine Hemorrhage (Parabrachial nucleus- present at junction of mid brain & PONS. It is in direct connection with hypothalamus. It regulates body temp) → expanding hematoma will press nucleus → resetting hypothalamus → **central fever**

2. Non Hodkins lymphoma.

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PATTERNS OF FEVER :

1. Continuous Fever

→ Never touch Baseline

→ Diurnal Fluctuation < 1°F

2. Remittent Fever

→ Fever never touch baseline

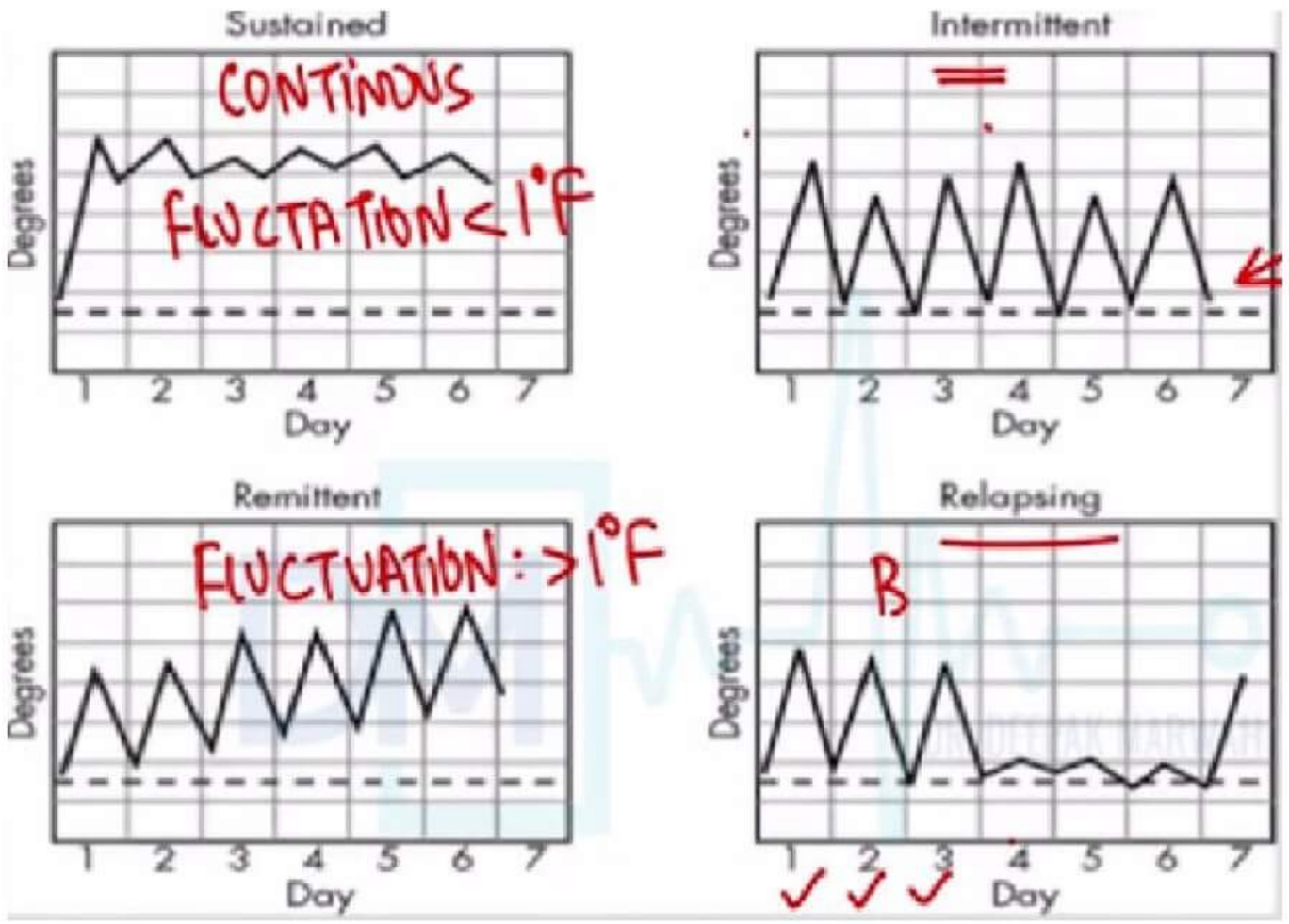
→ Diurnal Fluctuation > 1°F

3. Intermittent

→ It touches baseline

→ Diurnal variation >1°F

e.g. Malaria



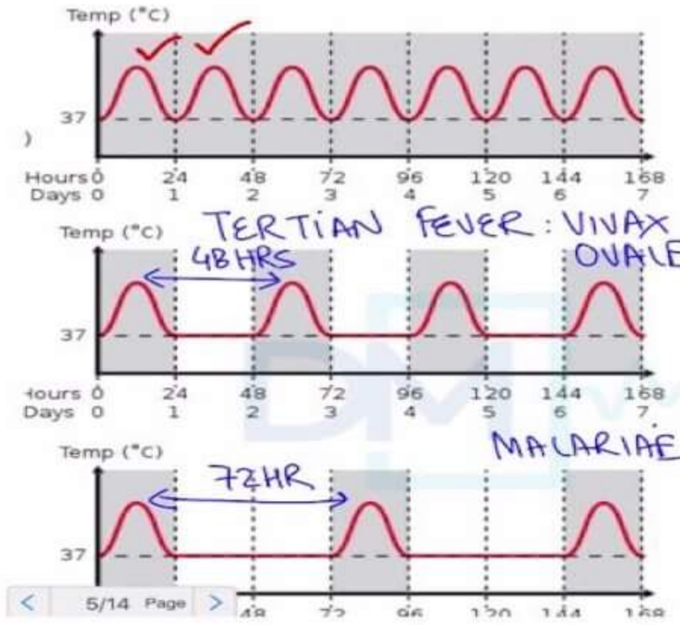
PrepLadder

4. Relapsing Fever

Fever can be develop in a interval of 3 days.

E.g. → Borrelia Recurrentis,

Rat Bite Fever



QUOTODIAN FEVER
INTERMITTENT FEVER
24 HR : FALCIPARUM KNOWLESI
double QUOTODIAN FEVER = adult onset STILL disease

Pattern of Fever in malaria

- **Quotidian Fever** → Fever will be occurring once every day. Example of Intermittent fever

E.g. → Falciparum infection

P. Knowlesi

- **Double Quotidian fever** → Fever will be spiking Twice per day i.e. Fever will be touching baseline and again spike in a single day. i.e. Two spikes of fever in single day.

E.g. → Adult onset STILL disease, juvenile rheumatoid arthritis.

- **Tertian Fever** → Fever is occurring every 48 hours or fever is occurring every 3rd day.

E.g. → P. Vivax, P. Ovale

- **Quartan Fever** → Fever will be occurring after every 72 hours or every 4th day

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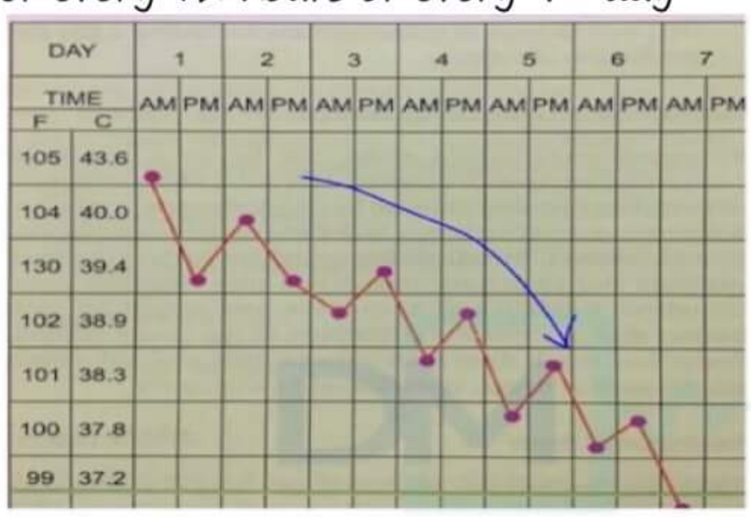
Fever Resolution with Lysis

→ Fever is resolving in person with lysis

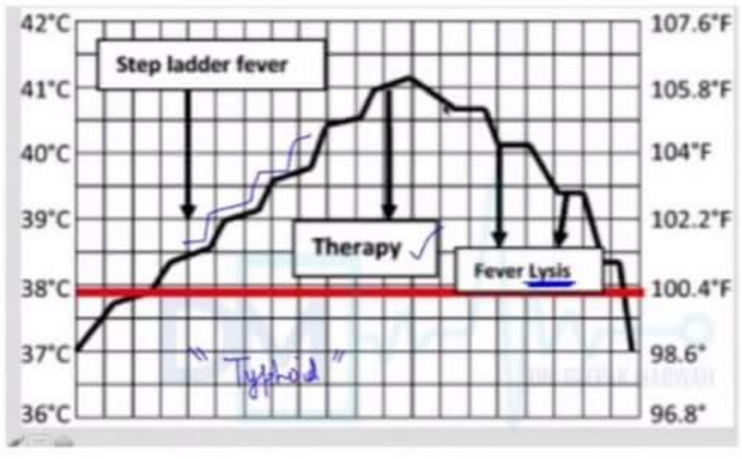
→ Gradual step ladder pattern of decrease of fever seen mostly post antibiotics.



FEVER RESOLUTION ⊂ LYSIS

Step ladder pattern of fever

→ Seen in Typhoid.



PrepLadder

Fever Resolution by Crisis

→ Fever is suddenly falling

e.g. → Acute Tonsillitis

→ Resolving case of Pneumonia

FEVER Resolution by CRISIS

Katayama Fever

→ Associated with Schistosomiasis

Q Fever → Coxiella Burnetii

Parrot Fever → Chlamydia psittaci

Pyrexia of unknown origin

DIAGNOSTIC CRITERIA

1. Fever > 101 ° F : > 2 occasions
2. Duration > 3 weeks
3. Absence of Immuno compromised state
4. Uncertain Diagnosis in spite of

→ Thorough history taking

→ Physical examination

→ Obligatory Investigations

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- **Obligatory Investigations: -**
  1. Hb, TLC, DLC, Platelet count, ESR → to rule out hematological illness
  2. CRP, Elevated LDH, Elevated Ferritin → to rule out inflammatory illness
  3. KFT with serum electrolytes
  4. LFT– SGOT, SGPT, Serum Alkaline Phosphatase, With total serum protein→ Albumin
     → Globulin
  5. Serum Electrophoresis gammopathy → To identify monoclonal gammopathy [multiple myeloma]
  6. For Autoimmunity → Creatine Kinase
     → RA factor
     → ANA (Anti-nuclear Antibody)
  7. Urine Microscopic Examination & culture → Only 1 culture with Mid Stream Urine
  8. Blood culture – not more than 3 times.
  9. Imaging → CXR for Diagnosis of Miliary Tuberculosis
     USG for → Liver Abscess

PrepLadder

→ Pyogenic Liver Abscess

→ Hydatid Cyst

10. Tuberculin skin test, IGRA

CAUSES

→ Infection > Inflammation

→ Atypical presentation of Infection

→ **SAPHO/ PAPA/ SCHINTZLER SYNDROMES**

In PUO

→ Exclude Thermometer manipulation

After this → Stop all medications if still fever is present >72hrs

Then do

→ Fundus examination

- To rule out SABE
- For Roth spot

→ Cryoglobulins

→ FDG PET/ CT → To rule out

1. Malignancy of Bone marrow
2. Lymphoreticular malignancy
3. Any occult cancer
4. Vasculitis

But, FDG PET/ CT cannot differentiate between infection and Inflammation.

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FDG PET/CT > Scintigraphy

Scintigraphy done by

- Gallium 67
- Indium –III
- ^{99}Tc labelled RBC

→Chest CT/ Abdominal CT

→ Temporal Artery Biopsy: To rule out Temporal arteritis

PDC [Potential Diagnostic clue]

1. **Fever associated with Headache**. (GCS is in Lower side or Neurological deficit)

Therefor Lumber puncture can be done and CSF examination to rule out

1. TBM
2. Cryptococcal meningitis
3. Mollaret meningitis

PrepLadder

2. **Fever + cytopenia / HSM/ LN enlargement**

Then do bone marrow aspiration/ BM biopsy / BM culture.

3. **Fever + Feature of T.B** (e.g. Matted Lymph nodes Disseminated T.B)

IOC → Liver Biopsy (by CBNAAT)

Algorithm to be followed in PUO

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PrepLadder

Obligatory Investigations

ESR and CRP, hemoglobin, platelet count, leukocyte count and differential, electrolytes, creatinine, total protein, protein electrophoresis, alkaline phosphatase, AST, ALT, LDH, creatine kinase, antinuclear antibodies, rheumatoid factor, urinalysis, blood cultures (n-3), urine culture, chest x-ray, abdominal ultrasonography, and tuberculin skin test

↓

Exclude manipulation with thermometer

↓

Stop or replace medication to exclude drug fever

↓

PDCs present

↓

Guided diagnostic tests

↓

DIAGNOSIS

NO DIAGNOSIS

PDCs absent or misleading

↓

Cryoglobulin and funduscopy

↓

FDG-PET/CT (or labeled leukocyte scintigraphy or gallium scan)

↓

Scintigraphy abnormal

↓

Confirmation of abnormality (e.g. biopsy, culture)

↓

DIAGNOSIS

NO DIAGNOSIS

Scintigraphy normal

↓

Repeated history and physical examination perform PDC – driven invasive testing

↓

DIAGNOSIS

NO DIAGNOSIS

↓

Chest and abdominal CT Temporal artery biopsy (≥ 55 years)

DIAGNOSIS

NO DIAGNOSIS

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PrepLadder

SAPHO syndrome

→ Synovitis Acne pustulosis Hyperostosis osteomyelitis

PAPA syndrome

Pa → Pyrogenic sterile Arthritis

P → Pyoderma gangrenosum

A → Acne

Schnitzler syndrome

→ Urticaria

→ Bone pain

→ Monoclonal gammopathy

Infections

1. **T.B**
2. **Endocarditis**
   - → Culture negative by HACEK Group
   - → Q fever (valve Lesion)
   - → Bartonella
   - → Sterile Endocarditis aka Marantic endocarditis → Adeno carcinoma.
   - → SLE, APLAS (Antiphospholipid Antibody Syndrome)

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HACEK

H → Hemophilus Aphrophilus

A → Aggregati bacter

C → Cardiobacterium

E → Eikenella

K → Kingella

3. **GIT Cause** → Diverticulitis (In long standing constipation)
4. **Vertebral Osteomyelitis**
5. **Q fever**
6. **Whipple Disease** → By Treponema Whippelii
7. **Travel History**
   - → MALARIA
   - → KALA AZAR
   - → HISTOPLASMOSIS
   - → COCCIDIOMYCOSIS

PrepLadder

NIID (Noninfectious inflammatory Disorder)

1. Large Vessel vasculitis (mc in India → Takayasu Arteritis, mc in central asia →BEHCET disease)
2. Sarcoidosis

→ (Breathlessness in young female)

→ Hilar Lymphadenopathy developing in a patient

3. Adult onset Still disease (Adult onset Juvenile Arthritis)
4. Polymyalgia Rheumatica

Note : if infectious and inflammatory causes ruled out then consider about tumor, drug

Tumor

1. Malignant Lymphoma (mc)
2. Leukemia

Drugs

1. Allopurinol
2. Antiepileptic Drugs - a) Lamotrigine b) Phenytoin
3. Sulfa drugs
4. Furosemide
5. Quinidine

Note :-

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- **Factitious Fever**

→ Manipulation of Thermometer by patient

- **Fraudulent fever**

→ Health care worker

→ Patient is injecting contaminated distilled water into her body.

Summary of PUO

1. **History**

→ Pattern/ duration of fever

→ Medical History: Medication

→ Sexual History

→ Travel History

→ Contact with Animal/ Pets

2. **Examination –**

→ Eyes- Fundus Examination

→ Lymph nodes

→ Temporal Arteritis

→ Liver/ Spleen

→ Surgical Scar

PrepLadder

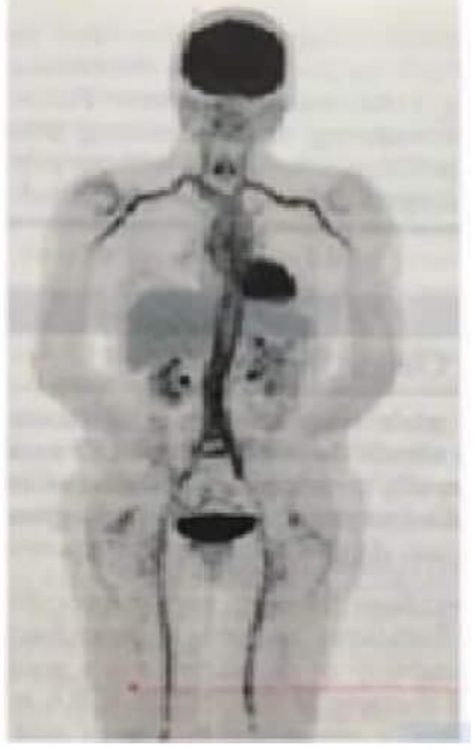
→ Skin/ mucosal examination

3. PDC (Potential Diagnostic clue)

1. Headache → CSF
2. T.B dissemination → Liver Bx.
3. Cytopenia/ HSM → Bone marrow Biopsy with culture

Q- 72 Years female with low grade fever, fatigue for 3 month/ No drugs/ History/ No travel History/ No pet history/ No abnormality in Temporal Artery. Diagnosis?

Obligatory → CRP ⊕nt, Normocytic normochromic anemia +



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FDG PET CT → Increased uptake in subclavian Arteries

Diagnosis is Takayasu Arteritis

Rx- steroids

Treatment of PUO

1. **Empirical ATT**
   - → IN CNS findings
   - → BP is falling
   - → Sickness Increasing
2. **NSAIDS** → Still disease
3. **Colchicine** → Familial Mediterranean Fever
4. **Anakinra** → IL -1 Receptor Antagonist

Best Treatment → Causes specific treatment

PrepLadder

DENGUE FEVER

- M/c arthropod/ Arbovirus infecting human beings

Incidence

> 50% of world population exposed to the virus infecting human being including developed countries and about 3 billion people in 112 countries are exposed to dengue virus.

Dengue Virus

→ Has 4 serotypes 1,2,3,4

→ Transmitted by Aedes mosquito

→ Mortality: usually < 1%

If severe dengue ~ 5%

Undiagnosed dengue : 20%

→ I.P = 3-14 days

→ Person infective to mosquito – for 4-5 days [12 days]

7 Warning signs

→ Restlessness / obtundation [under perfusion of brain]

→ Mucosal bleeding [epistaxis is concerning]

→ Vomiting: dehydration

→ Pleural effusion: massive/ B/L: Dyspnea

→ Hepatomegaly (2 cm below costal margin)

→ Ascites

→ Hematocrit rise/ Platelet decline → D/t capillaritis

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C/F: Living or Travelled in endemic area.

[Dx: Fever and any 2/ 6 features +]

1. Retro orbital pain/ myalgia/ Break bone fever
2. Protracted Nausea/ vomiting : dehydration.
3. Rash (during illness)

4. Warning Signs
5. Positive Tourniquet Test: > 20 Petechiae/ sq. inch.

   [BP cuff in arm of Pt. → Inflate it to mean arterial pressure and keep it for 5 mins → appearance of petechiae]

6. Leucopenia (TLC low)

PrepLadder

POSITIVE tourniquet test

During Defervescence

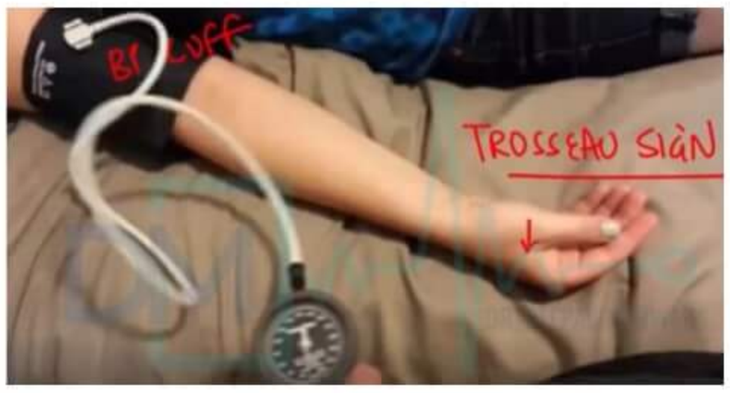
→ When Fever comes down i.e. after 2-7 days.

It is critical period.

Look for

- Dengue shock syndrome: Hematocrit ↑
- dengue hemorrhagic fever: Platelet ↓

Differential diagnosis:



Also, in patient,

- undergone massive blood transfusion.
- Post thyroid surgery.

Which would contribute to cytotoxicity → Tetanus

→ Trousseau Sign - Carpopedal Spasm

→ No petechiae

Differential diagnosis:

melasma

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→ if Question also mentions about H/O viral infection/ joint pain

→ Recovery 2 weeks: hyperpigmentation **'CHIK sign'**

Dx : chikungunya

	Category	Intervention
Dengue w/o warning signs	A	OPD
Dengue with warning signs	B	IPD
Dengue with risk factors [infants/ > 65 year/DM/ Pregnancy/ CRF/ steroid]	B	
Plasma leakage with fluid loss = BP ↓↓	C	IPD + Fluid Resuscitation
Fluid accumulation with RD ++	C	
Bleeding severe → instability of CVS	C	
Organ failure	C	

PrepLadder

Shock

- **Compensated:** Thready pulse (radial/femoral) with postural hypotension
  - Rx- Fluids to patient
- **Hypotensive:** absent pulse with BP unrecordable
  - Rx- Aggressive treatment in the form of fluids and colloids are given to the pt.

Dengue ± Warning signs	Severe dengue
Without with warning sign	1. Severe plasma leakage 2. Severe hemorrhage 3. Severe organ impairment

Criteria for dengue ± warning signs		Criteria for severe dengue
Probable dengue Live in/ travel to dengue endemic area. Fever and 2 of the following criteria: → Nausea, vomiting → Rash → Acnes and pains → Tourniquet test positive → Leucopenia → Any warning signs Laboratory confirmed dengue (important when no sign of plasma leakage)	**Warning signs** → Abdominal pain or tenderness → Persistent vomiting → Clinical fluid accumulation → Mucosal bleed → Lethargy, restlessness → Liver enlargement > 2 cm → laboratory: increase in HCT concurrent with rapid decrease in platelet count (Requiring strict observation and medical intervention)	1. **Severe plasma leakage, leading to:** → Shock (DSS) → Fluid accumulation with respiratory distress 2. Severe bleeding as evaluated by clinician 3. Severe organ involvement → Liver: AST or ALT >=100 → CNS: Impaired consciousness → Heart and other organs

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PrepLadder

Group A outpatient management	Group B inpatient management	Group C inpatient management
No warning signs	For Patients with warning signs of severe dengue OR co-existing conditions → Pregnancy → Infancy → Diabetes mellitus → Poor social situation → Old age → Renal failure	For patients with any of → Severe plasma leakage with shock and/ or fluid accumulation with respiratory distress → Severe bleeding → severe organ impairment

- **Don't use corticosteroids.** They are not indicated and increase the risk of GI bleeding, hyperglycemia, and immunosuppression.
- **Don't give platelet transfusions for a low platelet count.** Platelet transfusions do not decrease the risk of severe bleeding and may instead lead to fluid overload and prolonged hospitalization.
- **Don't give half normal (0.45%) saline.** Half normal saline should not be given, even as a maintenance fluid, because it leaks into third spaces and may lead to worsening of ascites and pleural effusions.
- **Don't assume that IV fluids are necessary.** First check if the patient can take fluids orally. Use only the minimum amount of IV fluid to keep the patient well-perfused. Decrease IV fluid rate as hemodynamic status improves or urine output increases.

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Rx:

DSS: Normal saline/ Ringer lactate.

C/I : ½ normal / N_2 saline not given, as it is hypotonic fluid which worsens the third space loss.

- N/2 saline is not given in → ↑ ICT
  → Patient of DSS

PrepLadder

Management

Group A: Dengue Fever

1. Awareness of critical period
2. Dehydration: Sunken anterior ante-fontanelle / eye balls dry, oral mucosa, cold clammy extremities, urine output ↓
3. Fever: PCM 6 hourly
   Tepid sponging
4. Cox 1 inhibitors are C/I as they interfere with the function of platelets
5. Insect repellent on patient

On arrival monitor patient's CCTV-R

1. Color of patient: PALLOR
2. Capillary refill time ((n) <3 sec)
3. Temperature (cold clammy limbs)
4. Volume of pulse
5. Rate of pulse

- Would help to decide if patient requires aggressive fluid Resuscitation or not

Group B patient management

→ Patient with presence of warning sign

→ Patient with presence of risk factors

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1. Vital monitoring (4 hourly)
2. Input-output monitoring

Crystalloids: Normal saline / Ringer lactate: 5-7 ml/kg/hr: 2 hr
3-5 ml/kg / hr for next 2 hrs

Hematocrit improving C/F improving 3 ml/kg/hr x 4 hours	Hematocrit ↑↑ C/F worsening IVF: 10 ml/kg/hr x 2 hr
↓	↓
Switch to oral fluids Keep for next 48 hours	Revaluate
	HCT ↑↑↑ **Bolus1:** 10 ml/kg /hr/ x 1 hours ↓ no improvement **Bolus2:** 10 ml/kg /hr/ x 15 mins ↓ no improvement Colloids: Albumin/dextran
	HCT ↓↓ Bleeding ↓ packed RBC Blood Transfusion

Group C
For monitoring

Platelets given: only if platelet count: < 50,000 with bleeding
OR < 10,000 without bleeding

PrepLadder

Group B: Dengue with warning signs (not in shock)- Inpatient fluid management

(Obtain Reference HCT before starting IVF therapy) (Started with isotonic crystalloids 5-7 ml/kg/hr for 1-2 hours) ↓ REASSESS ↓ Improved ↓ IV isotonic crystalloids 3-5 ml/kg/hr for 2-4 hours ↓ IV isotonic crystalloids 2-3 mL/kg/hr for 2-4 hours ↓ Clinical improvement or improved oral intake, reduced IVF accordingly ↓ Stop IVF therapy within 24-48 hours	**Reassess hemodynamic state** 1. Vital Signs 2. "5-in-1 magic touch": CCTV-R Colour Capillary refill time Temperature Volume of pulse Rate 3. Urine volume **If improvement in oral intake, HCT remains same or minimal high:** 1. Step-wise reduction in IVF 2. Consider glucose-electrolyte for children → Continue to monitor patient until out of critical period → Stop IVF within 24-48 hours

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- **IgM antibody captures asked Immunosorbent Assay (MAC-ELISA)**

  What is the test?

  → The dengue MAC-ELISA is used for the qualitative detection of dengue virus IgM antibodies.

  → The MAC-ELISA is based on capturing human IgM antibodies on a microtiter plate using anti-human-IgM antibody followed by the addition of dengue virus antigens. The antigens used for this assay are derived from the envelope proteins of the four dengue virus serotypes (DENV-1-4).

- **How should it be used and at what time during infection?**

  → As the immune system fights the infection, IgM antibodies against dengue virus are detectable starting 4-5 days after onset of symptoms and are reliably detectable for approximately 12 weeks. → Combined testing with a nucleic acid amplification test

PrepLadder

(NAAT) and MAC-ELISA usually provides a diagnostic result during the first 1-7 days of illness. A convalescent phase specimen is needed to make a diagnosis of dengue virus infection when results are negative on both tests from the acute specimen.
→ IgM antibody detection is not useful for dengue virus serotype determination.

Dx:

1. Ig m Dengue Virus: 4x ↑↑
2. NAAT
3. NS-1 Ab (IgG).

- **Specimen types**

→ Serum
→ Cerebrospinal fluid
Some IgM tests can be performed on plasma and whole blood but these tests have not been extensively evaluated for these specimen types.

- **Interpretation of results**

→ **Positive IgM:** Patients with a positive IgM test result are classified as presumptive, recent dengue virus infections.
→ **Negative IgM:** Patients with negative IgM results before day 8 of illness and absent or negative NAAT or NS1 results are considered unconfirmed cases. For these cases, a second sample should be obtained after day 7 of symptoms for additional serologic testing.

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  - Patients with negative IgM results after 7 days of symptoms, and absent or negative NAAT or NS1 (dengue virus antigen detection) are classified as negative for recent infection.
  - Patients with a change from negative to positive IgM results in paired samples (first sample collected during the first 7 days of illness, and second sample collected after symptoms subside) are classified as current dengue infections.

→ Due to cross-reaction with other flaviviruses and possible nonspecific reactivity, results may be difficult to interpret. Consequently, presumed positive, indeterminate, and equivocal, IgM antibody test results may be forwarded for confirmation by plaque reduction neutralization testing

Characteristics of selected Blood components			
COMPONENTS	VOLUME, ML	CONTENT	CLINICAL RESPONSE
PRBC	250-300 ml (including	RBCs with variable leukocyte content	Increase hemoglobin 10 g/L and hematocrit 3%

PrepLadder

	additive solution)	and small amount of plasma	
Platelets (from whole blood)	50-70/ RD unit pool of 4 to 6 RD unit	5.5 x 10^{10} / RD unit	Increase platelet count 5000-10,000/µL/ RD unit
Platelets (from apheresis)	200-400ml	≥2 x 10^{11} / SDAP product	For pooled RD and SDAP: CCI ≥ 10 x 10^{9} / L within 1 hour and ≥ 7.5 x 10^{9}/L within 24-hour posttransfusion
FFP	200-250ml	Plasma proteins - Coagulation	Increases coagulation factors about 2%

- ❖ 1unit PRP – increases platelet count by 10^{10}
- ❖ Whenever fluids reduced, reduce it slowly and increase oral intake.

➢ **Indication for Discharge**

Patients who are resuscitated from shock rapidly recover. Patient with dengue hemorrhagic fever or dengue shock syndrome may be discharged from the hospital when they meet the following criteria:

1. Afebrile for 24 hours without antipyretics
2. Good appetite, clinically improved condition
3. Adequate urine output → 1ml/kg/hr
4. Stable hematocrit level
5. At least 48 hours since recovery from shock
6. No respiratory distress
7. Platelet count greater than 50,000 cell/µL

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(Input)

[1 ml/kg/hr 60 kg = 60 ml/hr]

X 24

= 1500 ml

➢ **Vaccine**

CYD-TDV is a tetravalent, live attenuated, chimeric dengue vaccine in a yellow fever 170 D backbone developed by Sanofi Pasteur. The schedule that has been evaluated in Phase III clinical trials include 3 doses of vaccine (at 0, 6 and 12 months).

Philippines – banded dengue vaccine. It was found that people who got vaccine and then if come in contact with dengue virus – severity of dengue is more as compared to people who don't get vaccinated.

PrepLadder

NIPAH VIRUS & ZIKA VIRUS

NIPAH VIRUS → Initial report of Nipah virus from a village in Malaysia and then spreading to other parts of World, India, Bangladesh etc.

Incidence:

→ Paramyxovirus

→ related to Hendra virus (Hev)

→ 1st case was reported in Malaysia, mainly in people who worked in Pig farms.

→ **HOST**- MAN

INTERMEDIATE HOST- PIG

SOURCE- Fruits contaminated with dropping/ saliva of PTEROPUS/ Flying Fox [BAT]

→ 1st case reported in India was Siliguri in 2001

→ In Bangladesh & Kerala source were date palm sap, Which were contaminated with saliva/ droppings of PTEROPUS.

→ (Contact with salivary of infected) person → Person transmission is seen or anybody secretions

Modes of Transmission: Sap date palm
Fruits
Closed personal contact

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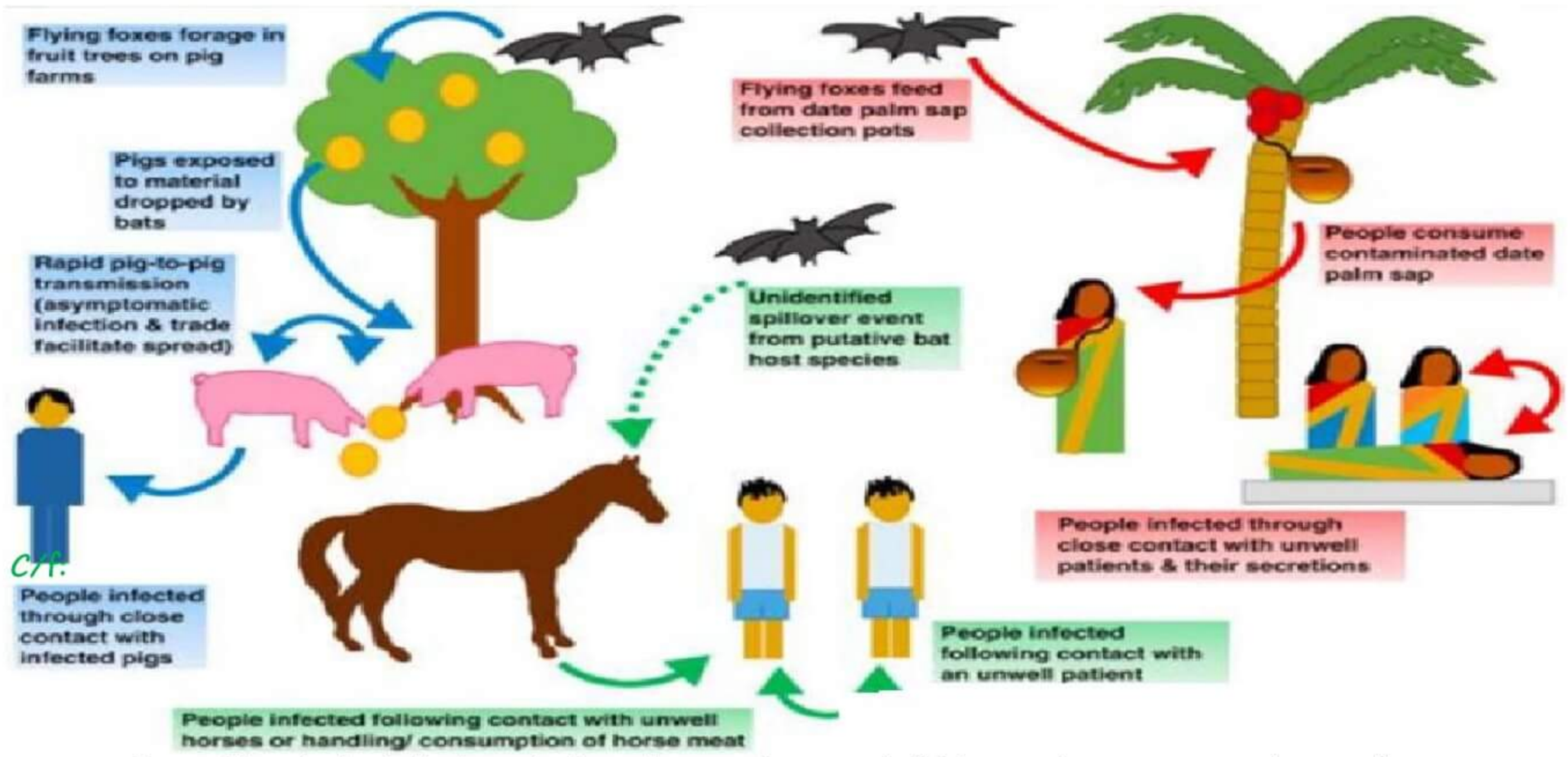
→ Nipah Virus occurs naturally in bats/ Horses/ Pig / Dog (natural reservoir)



→ Fever/ headache/ dizziness/ altered sensorium are Initial symptoms seen on day 1 of illness.

→ Mortality seen with patients suffering with encephalitis & ARDS and might die with in span of 4 days.

PrepLadder

→ Other symptoms reported: Myoclonic jerk/ Seizures/ Hallucinations/ abnormal doll eye Reflexes

→ Respiratory symptoms: ARDS

→ Neurological illness – GCS <8.

Work Up:

1. Serum IgM capture E.I.A from Nipah virus/ Hendra virus
   IgG indirect E.I.A for Nipah virus/ Hendra virus
2. CSF Reverse Transcriptase PCR
3. MRI head: **Punctuate hyperdensities** [d/t vasculitis manifestation of disease microinfarction in brain.]

Rx:

- No vaccine
- No treatment

→ It is a potential **category 3 Bioweapon (Bioterrorism)**

ZIKA VIRUS

→ It is a single stranded RNA virus

→ Family – Flavivirus

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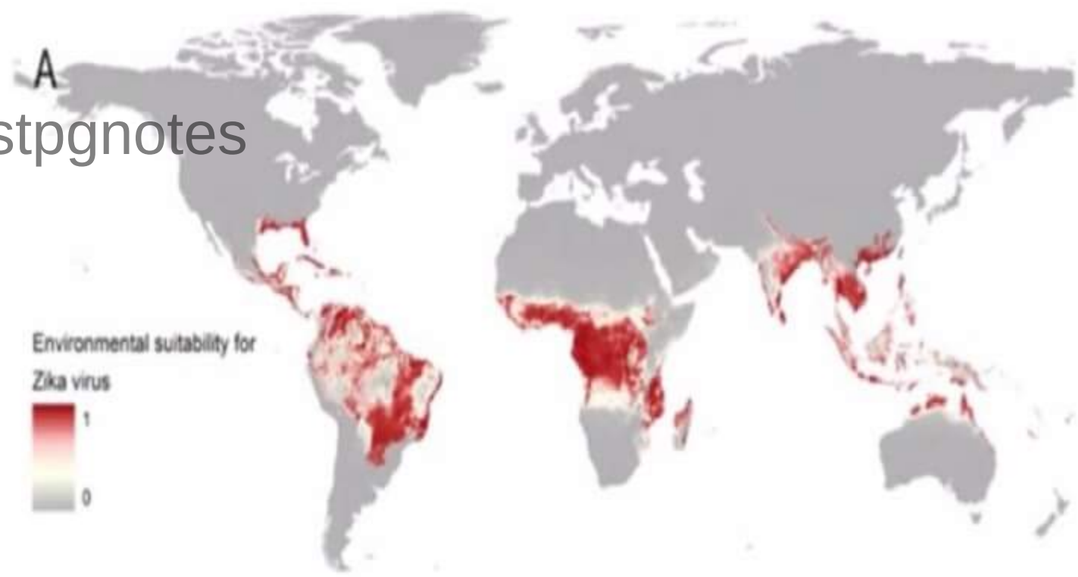

→ more prevalent in areas with height **< 2000 m** Where Aedes can survive [SE Asia, India (costal) Tamilnadu, west Bengal]

→ Cases reported first in 2016,
It was reported In Rio (Brazil) children born in 2016 had **microcephaly** which is neurological sequel which implies that the mother must suffer with Zika Virus infection.

→ IP = 3-12 days

→ Fever lasts b/w 2-7 days.

PrepLadder

Transmission – Aedes Aegyptiacus

- Sexual Transmission
- (man → man)

→ Zika virus contributes to incidence of **Guillain Barre Syndrome**

→ Pregnant Female with Zika virus infection delivers babies with **microcephaly**

C/F:

→ Fever/ Retro orbital pain/ arthralgia (mainly small joints of hands)

→ Rash (Palms, chest, ant. -abdominal wall) throughout fever

→ Conjunctivitis

→ It is self-limiting illness

C/F in infant:

- Microcephaly → HC = < -2 SD
- Abnormal/ absent foveal reflex
- Macular atrophy
- Hypoplasia of optic nerve head
- Incidence of GBS ↑

Microcephaly seen with:

→ Fetal alcohol syndrome

→ TORCH group infection

→ ZIKA virus infection

Brighton Criteria :

Diagnostic Criteria	Level of diagnostic certainty		
	1	2	3
Bilateral and flaccid weakness of limbs	+	+	+
Decreased or absent deep tendon reflexes in week limbs	+	+	+
Monophasic course and time between onset-nadir 12 h to 28 days	+	+	+
CSF cell count < 50/ml	+	+/-[a]	-
CSF protein concentration > normal value	+	+/-[a]	-
NCS findings consistent with one of the subtypes of GBS	+	+/-	-
Absence of alternative diagnosis of weakness	+	+	+
NCS nerve conduction studies, CSF cerebro-spinal fluid If CSF is not collected or results not available, nerve electrophysiology results must be consistent with the diagnosis Guillain-Barre Syndrome			

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PrepLadder

GBS Dx by Brighton Criteria

Flaccid Paralysis in below upward direction.

1. LMN paralysis: with B/L Flaccid paraplegia
2. Distal areflexia
3. Illness < 28 days (manifestation of progression of disease is < 28 days)

[If progression > 9 weeks known as CIDP (chronic inflammatory demyelinating neuropathy)]

4. Hallmark - Albuminocytological dissociation
   CSF cell count normal (to slightly elevated)
   Protein always elevated
5. Nerve conduction velocity study: demyelination

Work-up:

1. IOC: Urine Assay: Urine Triplex PCR (rRT – PCR)
   (Real time + Reverse Transcriptase PCR)
2. Blood sample: RT – PCR
3. ELISA IgM Zika [demonstrated only if > 7 days]
4. Pregnant Female - 1. Serial USG: microcephaly
   2. Amniocentesis

Treatment:

→ No definite Rx.

→ No Vaccine

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PrepLadder

PNEUMOCYSTIS JIROVECI

- It is common opportunistic organism causing infection in AIDS/ HIV+ patient or any immunocompromised patient on steroids, child with nephrotic syndrome on steroid or Ankylosing spondylitis patient on infliximab or person undergone kidney/ bone marrow transplantation (Hemopoietic stem cell transport)

- This organism has tropism for lungs.
  R.O.T → person to person via respiratory droplets infection or
  d/t reactivation of latent infection.
- It is important cause of pneumonia in AIDS patient.

- **Leading cause of pneumonia in AIDS +ve pt. → Pneumococcus**
  ↓
  As more common & prevalent in community

- **In AIDS +ve pt. with CD count < 200 → Pneumocystis jiroveci**
- For AIDS patient prophylactic Rx → **Cotrimoxazole**

Neutrophilic infiltration
Alveolar exudate

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Gomori methenamine stain (fungal stain)
Black color-cysts
[Other stain used Giemsa or IFA can also Be used]

C/F: Shortness of breath/ Dyspnea
Fever a/w chills & rigors
Nonproductive cough

PrepLadder

Workup

→ **CXR chest**: initially (N), in later part of illness: **Perihilar diffuse infiltrate**

→ **HRCT**: **Ground glass opacities** which might have cysts present in them so pneumothorax can also develop in these patients which may cause sudden deterioration

→ **Open lung biopsy**: done earlier

→ **β 1,3 glucan test**: pan fungal antigen to identify the infection

β 1,3 glucan test can also Dx.

- Candida
- Aspergillus
- Can't identify mucormycosis in DM patient.

→ **Real time PCR** → Can't distinguish colonization of airways

So, we can`t say whether it is infection or colonization

→ **IOC**: **Broncho alveolar lavage**

Then specimen is stained with **Giemsa/Gomori methenamine stain.**

Doesn't show entire parenchymal involvement but mainly B/L perihilar involvement.

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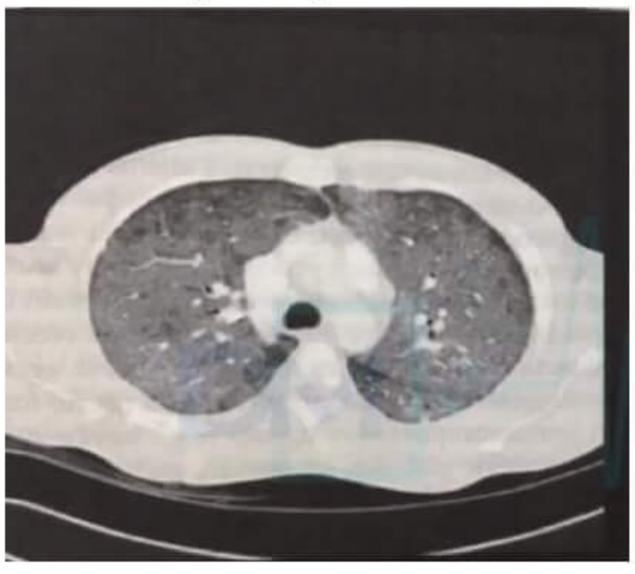
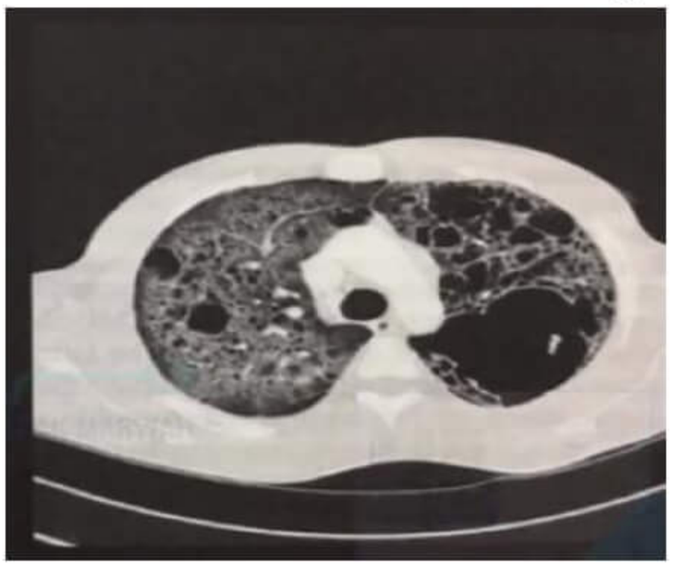
Gradual deterioration with further involvement of lower lobe of lung.





HRCT: Ground Glass opacities with cysts

PrepLadder

Diagnosis: Non-Invasive Tests

- **LDH**
  → Not specific
  → Prognostic

- **PCR**
  → can't differentiate b/w Infection and colonization
  → Not commercially available

- **Beta-1,3 Glucan test**
  → Sensitivity 92.8%
  → Specificity 75%
  → PPV 96.3%
  → NPV 60.0%

- **IFA**: can be done with BAL specimen to identify the infection

Diagnosis

LDH ↑, ↑ A-a gradient in PFT [(n) 5-15 mmHg]

SpO_2 ↓

PCR can't distinguish between colonization

R_x OC

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- DOC -IV Cotrimoxazole [Trimethoprim & Sulfamethoxazole] →also used for prophylaxis
- given for 21 days.
- MOA: inhibit folate metabolism
- IV pentamidine: for prophylaxis as well as Rx
- clindamycin
- Primaquine
- Atovaquone
- **Steroids are also useful here** [Cytokines produced on destruction of organism so steroids will help reduce symptoms of inflammation when organism die]

Prophylaxis of Pneumocystosis		
Drug(s)	Dose, Route	Comments
First choice Agent		
TMP-SMX	1 Tablet (double or single strength) qd PO	Incidence of hypersensitivity is high. Rechallenge for non-life-threatening hypersensitivity; consider dose-escalation protocol.

PrepLadder

Alternative Agents

Dapsone	50 mg bid or 100 mg qd PO	Hemolysis is associated with G6PD deficiency.
Dapsone + **Pyrimethamine** + **Leucovorin**	50 mg qd PO 50 mg weekly PO 25 mg weekly PO	Leucovorin ameliorates Cytopenias due to pyrimethamine.
Dapsone + **Pyrimethamine** + **Leucovorin**	200 mg weekly PO 75 mg weekly PO 25 mg weekly PO	Leucovorin ameliorates cytopenias due to pyrimethamine.
Pentamidine (inhaled)	300 mg monthly via Respigard II nebulizer	Aerosol may cause bronchospasm. Pentamidine is probably less effective than TM² SMX or dapsone regimens.
Atovaquone	1500 mg qd PO	Requires fatty meal for optimal absorption

- There has been considerable interest in serologic tests such as assay for (1,3)-β-D-glucan, levels of which are frequently elevated in patients with PCP. However, no serological assays developed to date offer both substantial sensitivity and specificity.

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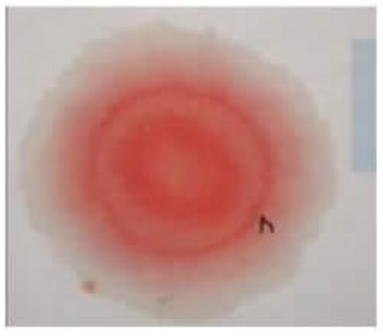
ASPERGILLOSIS

→ Aspergillosis has many subtypes like Niger, fumigatus etc.

→ Aspergillosis on CT chest: characteristic appearance

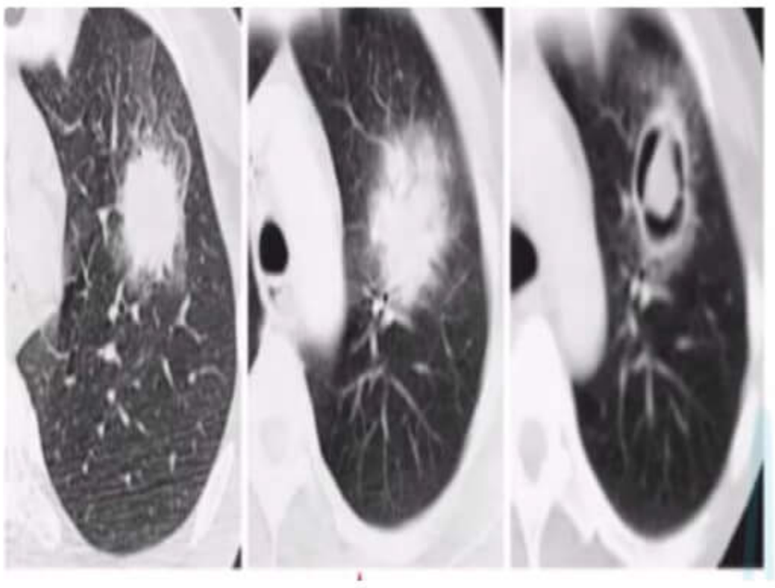
-Lesion where fungus present k/a "Halo sign"



Halo sign

→ CSF rhinorrhea w.r.t ant. cranial fossa fracture

→ CSF otorrhea w.r.t middle cranial fossa fracture



↓ Halo sign ↓ Air crescent sign

PrepLadder

→ As Aspergillosis progresses destruction of air parenchyma shows another characteristic sign "Air crescent sign" {i.e. air around actual fungal lesion}

Subtypes

→ **A. fumigatus**: causes **ABPA** [Allergic Broncho Pulmonary Aspergilloma]

Thermophilic Actinomycetes: seen in bagassosis

→ **A. Niger**: causes angioinvasive infection in diabetic patient which results in cavity formation and it can also contribute to massive hemoptysis.

→ **A. flavus**:

- Sinusitis
- Aflatoxin → Hepato cellular cancer

Risk factors

→ Neutropenia

→ AIDS

→ Leukemia

→ Steroids, infusions of Infliximab

→ TB

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→ COPD

→ Cystic fibrosis Q/ Asthma Q are condition with higher risk of developing **ABPA.**

- **Invasive Aspergillosis**: 100% mortality
- **Chronic Aspergillosis**: 50% mortality
- **Allergic Aspergilloma**: < 1% mortality

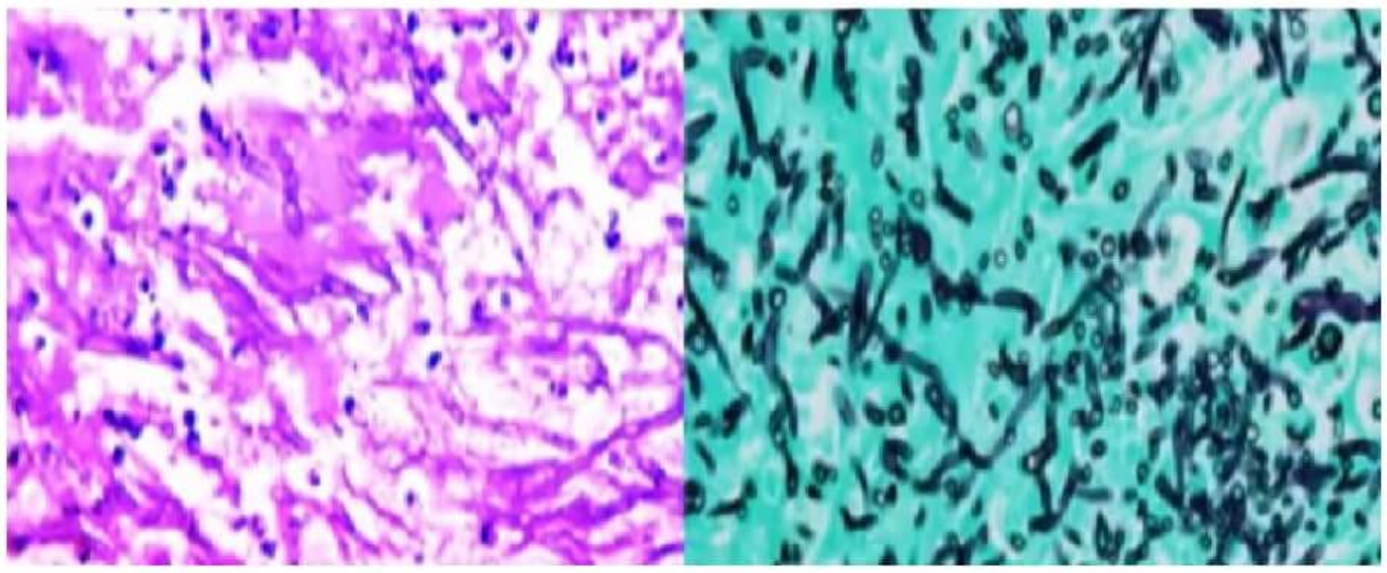
Etiology:

Inhalation of dust consisting of conidia of this fungus by severely immunocompromised patient.

PrepLadder

Diagnosis

By lung Bx: Shows hyphae branching at 45°, relatively thin.



Aspergillosis: Hyphae branching at 45°

Gomori Methenamine Stain

Hyphae is thicker; ribbon like hyphae branching occurs at right angle (90°)

Dx: Rhinocerebral mucormycosis

→Infection seen in DM patient & is invasive affecting frontal lobe of brain contributing to aggressive behavior

Acute pulmonary aspergilloma	Chronic pulmonary aspergilloma
→ Respiratory distress ++, Hemoptysis → **Dx:** with sputum: Antigen detection: **RTPCR** RTPCR (better) >Fungal Culture Because fungal culture accuracy may not be so high and report will take longer time **Histopathological Examⁿ**: Hyphae branch at 45° **HRCT**: Halo sign & air crescent sign **Rx:** Voriconazole **1° prophylaxis**: Posconazole	→ Usually misdiagnosed as TB/ Sarcoidosis/ atypical mycobacterial infection → Fungal ball may be seen in cavity [coughed out sometimes]

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ABPA (Allergic Bronchopulmonary Aspergilloma)

→ associated with A. fumigatus

→ Mostly seen in Asthma/ Cystic fibrosis [mucoviscidosis] →autosomal recessive with a mutation in CFTR gene

- in India death in cystic fibrosis occurs d/t recurrent pneumonia

C/F

1. Coughing bouts
2. Thick tenacious sputum
3. Shortness of breath/ Dyspnea on exertion

PrepLadder

Work up

→ Eosinophilia → 40 – 400 eosinophil

→ HRCT: Central Bronchiectasis Q → hyper attenuation of mucous ++

→ IgE for aspergillus
→ Total IgE > 1000 IU/mL } Confirm Dx for ABPA
→ Positive skin prick test

Rx: Itraconazole

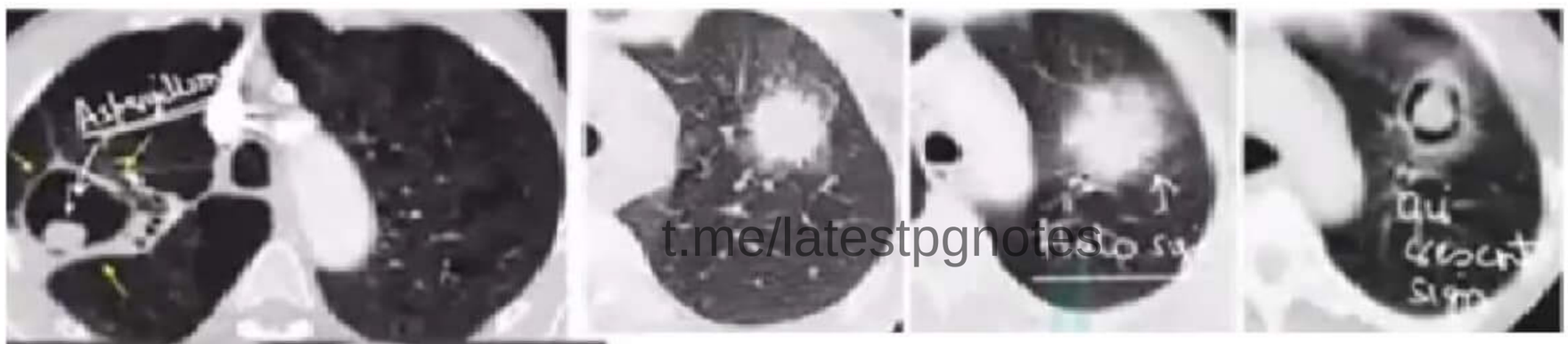
If above criteria are not met then Dx is **Severe Asthma with Fungal Sensitization** [SAFS]

Fungal asthma → ABPA or SAFS

↓

Hypersensitivity reaction to the fungus occurring in lung

Rx: Itraconazole



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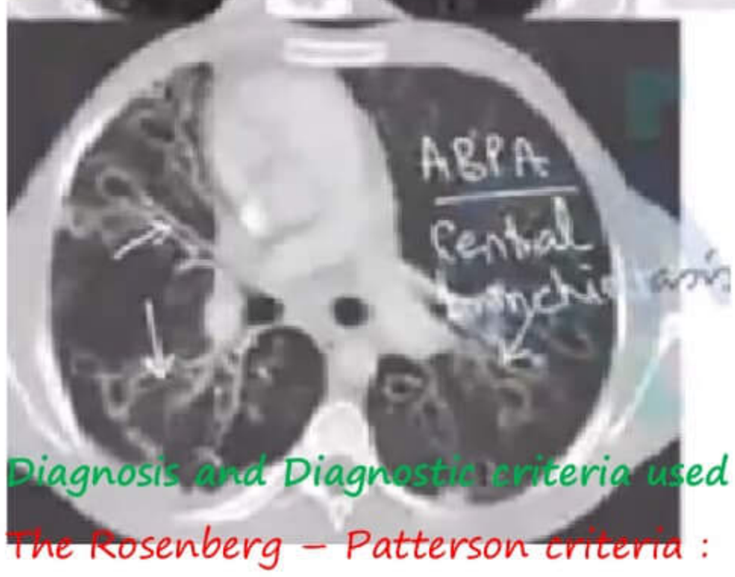

On CT :

- HALO SIGN
- Air crescent sign
- Dilated airway → ABPA → Bronchiectasis

Diagnosis and Diagnostic criteria used earlier

The Rosenberg – Patterson criteria :

Major criteria (Mnemonic ARTEPICS)

A – Asthma

R – Radiographic fleeting pulmonary opacities (Not used as it can be seen with drugs, parasite, fat embolism, tropical pulmonary eosinophilia.)

T – Skin test positive for aspergillus (Type, HSN Rx immediate cutaneous HSN)

E – Eosinophilia

P – Precipitating antibodies (IgG) in Serum

I – IgE in Serum elevated (1000 IU/Ml)

C – Central bronchiectasis

PrepLadder

S – Serum A fumigatus specific IgG & Ig E (> twice the value of pooled serum sample from patient with asthma who have aspergillus HSN by skin test.

Rx of Aspergillosis

- **Acute exacerbation ABPA:** Steroids (as it is a hypersensitivity rxn)
- **ABPA:** Itraconazole
- **Invasive pulmonary aspergilloma acute/ chronic:** Voriconazole
- **1° prophylaxis:** Posconazole

For Dx of Invasive fungal infection

- **Pan fungal test = β 1,3 glucan test**

  To detect invasive fungal infections like:

  C: Candida, Cryptococcosis

  A: Aspergillosis

  P: Pneumocystis jiroveci

- **Not able to Dx/ identify Mucormycosis**

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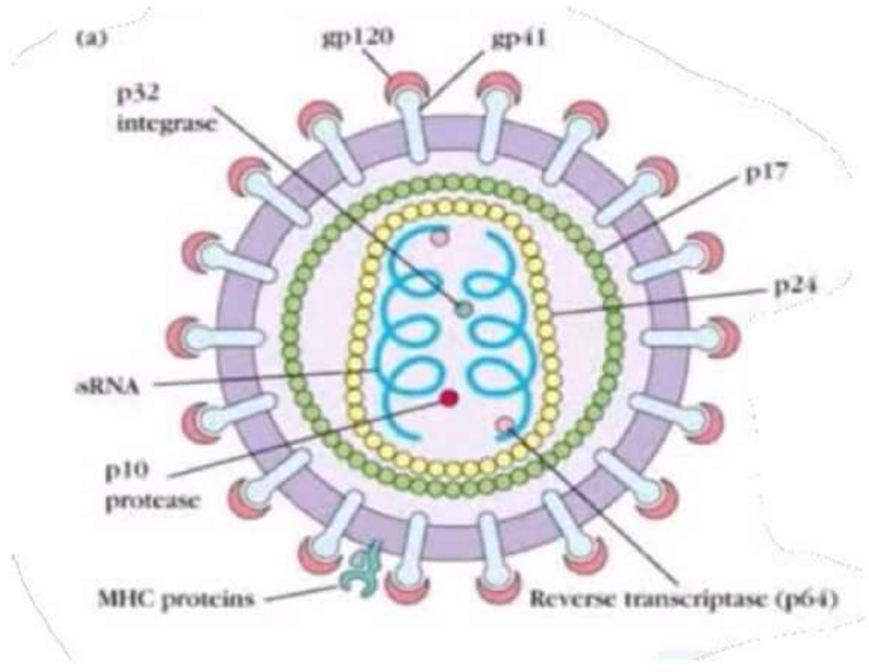
PrepLadder

AIDS



Acquired immunodeficiency syndrome

HIV Serology (+) & CD_4 Count < 200 cells/cu. mm or CD_4 count <14% (Normal CD_4 count → 800-1200 / cu.mm.)

- It belongs to **lentivirus genus & it's a retrovirus**
- Enveloped & it's a single standard RNA virus
- It has enzyme called Reverse transcriptase, which converts RNA to DNA and an enzyme called Integrase Which helps to integrate with host genome.
- The HIV or AIDS epidemic in India began in 1986-1987 with the detection of the first HIV infection in Chennai and first AIDS case was detected in Mumbai.

CASE LOAD

- 37 Million people living with HIV in the world
- Max. prevalence: 27% in Swaziland
- 2.4 million in India

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High Prevalence State

- Mizoram > Manipur
- 4 states with maximum numbers 55% of cases –
  1. Maharashtra
  2. Andhra Pradesh
  3. Tamil Nadu
  4. Karnataka
- 83% of total cases – 15-49 years of age
- 39% of total cases – Female
- **HIV-1 takes 10 years to get converted to AIDS.**
- **HIV-2 takes 15-20 years to get converted to AIDS.**
- HIV-2 is common in Africa
- HIV-1 group M-Subtype C → common in india

90-90-90

- 90% of patient should be aware of their HIV (+) status.
- 90% who are aware of their status should be on combination antiretroviral therapy (CART).

PrepLadder

- 90% who are on CART should have sustained viral remission. (<40 copies of viral RNA /ml on PCR)

ROUTE OF TRANSMISSION

- Sexual Contact > Blood transfusion
- Heterosexual
- Unprotected Receptive Anal Intercourse (URAI)= 1:30
- Unprotected Vaginal Intercourse = 1:10,000
- Insertive Anal act = 1:1000
- Fellatio/ ejaculation = 1:1000
- Needle Stick Injury = 1:300
- Needle Sharing = 1:150
- Blood transfusion infected blood = 95% chance.

TRANSMISSION INCIDENCE

- Hepatitis B – 1:300,000
- HIV-1,2 – 0.1–1:1,000,000

Highest incidence of transmission – **HBV > HCV > HIV**
Leading cause of transfusion association Hepatitis – **HBV**

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- Blood transfusion can be associated with transmission of dengue, zika virus, west Nile virus, Parvo virus B19, Trypanosoma, Ehrlichia, Syphilis, HHV8.

Pathology

When CD4 Count ↓:

After Sexual Contact →

- Dendritic cells (Antigen presenting cells) → in Anal Mucosa / Vaginal Mucosa are the first cells to be affected.

- CD_4 Counts ↓ (both infected and non-infected cells are dying)
  -Apoptosis increased
  -Pyroptosis increased

Stages

I : < 500 cell / <26%
II : 200-499 Cells / 14-25%
III : < 200 / <14%

These values are valid for children older than 6yrs and adults

PrepLadder

< 1 Year:

Stage I: < 1500 / < 34 %

Stage II: 750-1499 / 26-33%

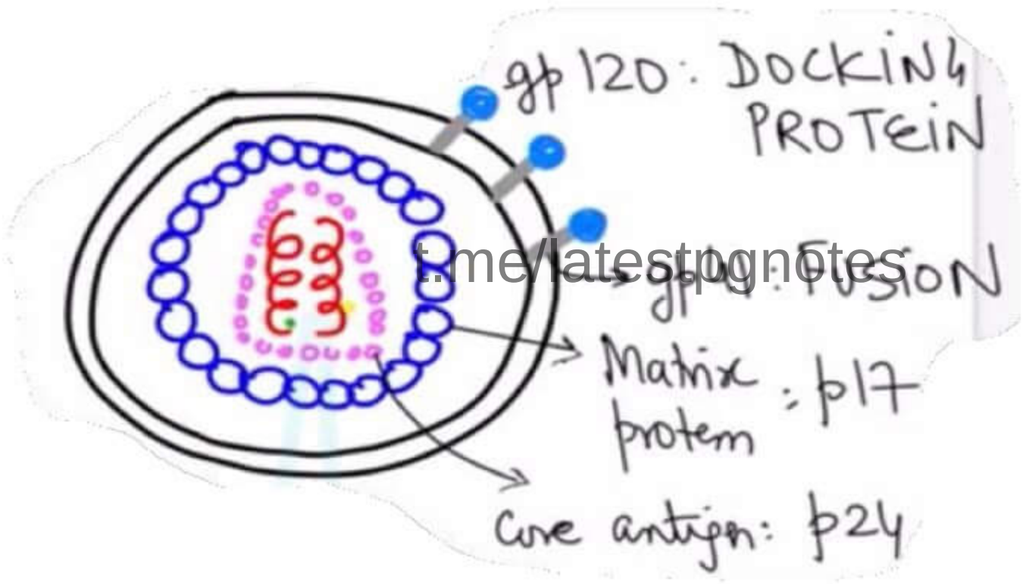
Stage III: < 750 / <26%

AIDS DEFINING MALIGNANCIES:

1. Kaposi Sarcoma
2. Non-Hodgkin's Lymphoma
3. Invasive Cervical Cancer

- Autoimmunity ↑ - Lymphocytic Interatrial Pneumonitis (LIP)

Viral Structure



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gp 120 – Docking protein: by which CD4 cells attach to its CD4 receptors

gp 41 – Fusion

p 17 – Matrix Protein

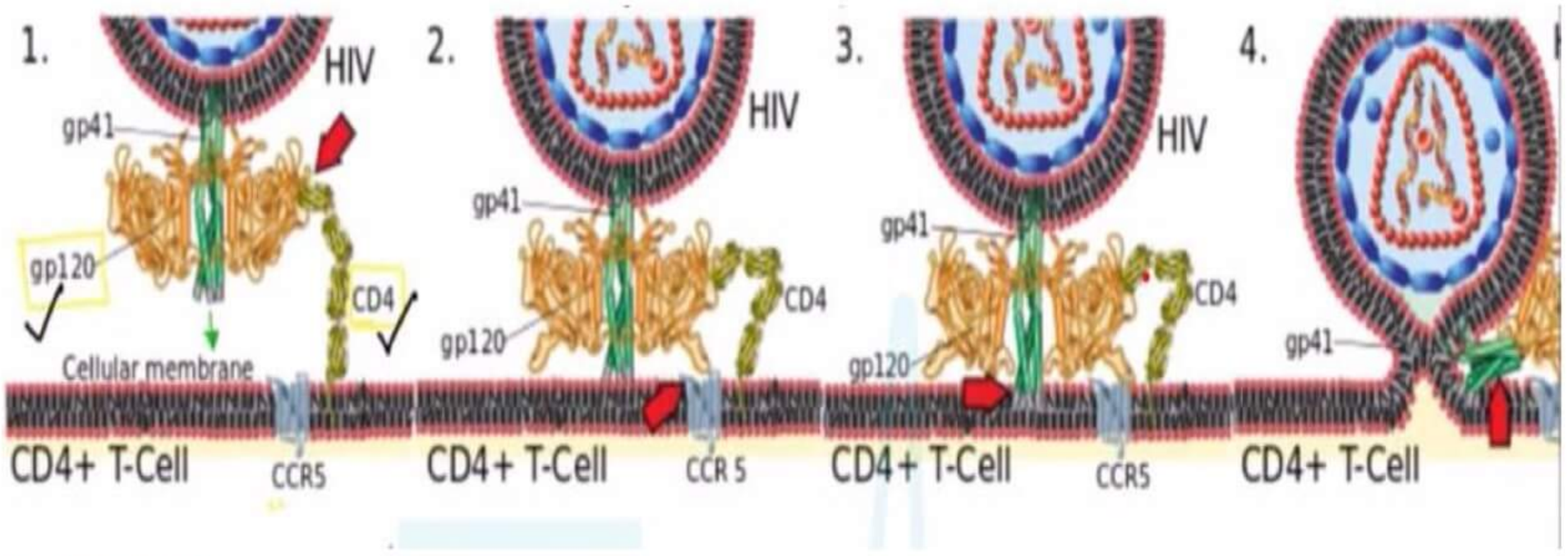
p 24 – Core antigen

- Vertical Transmission – 30%
- Best test to identify vertical transmission

↓

HIV PCR DNA > p24 antigen assay

PrepLadder



1. DOCKING

gp 120 is attaching to CD4 receptors on cell

Co receptor – CCR5, CXCR4] present on CD4 cells

↓

Conformational change

↓

virus comes closer to cell wall of CD4 which will further help in fusion

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2. FUSION

Virus ready to inject RNA into cell

↓

RNA Converted to double Standard DNA

Double standard DNA with help of Integrase gets integrated into host domain

- CCR5 delta 32 mutation – Patient will not express CCR5

↓

(Virus will be present in blood but does not attack the target cells)

↓

Called as Hampering the infiltrative ability of virus.

CDC AIDS DEFINITION WITH/WITHOUT HIV SEROLOGY (11 – 6C 2P HKM)

1. Candida: involving esophagus, trachea, bronchus
2. Cryptococcus neoformans meningitis (extrapulmonary cryptococcus)
3. Cryptosporidium parvum, chronic diarrhea > 1 month.
4. CMV colitis /esophagitis (serpiginous ulcers)

PrepLadder

5. Cerebral toxoplasmosis
   ↓
   Seizure (+) in AIDS pt.
6. (Primary) CNS lymphoma
7. Pneumocystis jiroveci: CD4 < 200.
8. Progressive multifocal leuco-encephalopathy
   (JC virus)
9. HSV esophagitis, mucocutaneous ulcer > 1 months
10. Kaposi Sarcoma < 60 years
11. Mycobacterium Avium Inter cellular (MAI)
    ↓
    CD4 < 50

- CD4 < 500 = TB
  < 200 = P. jiroveci
  < 100 = Cerebral Toxoplasmosis
  < 50 = CMV Retinitis or MAI

CEREBRAL TOXOPLASMOSIS

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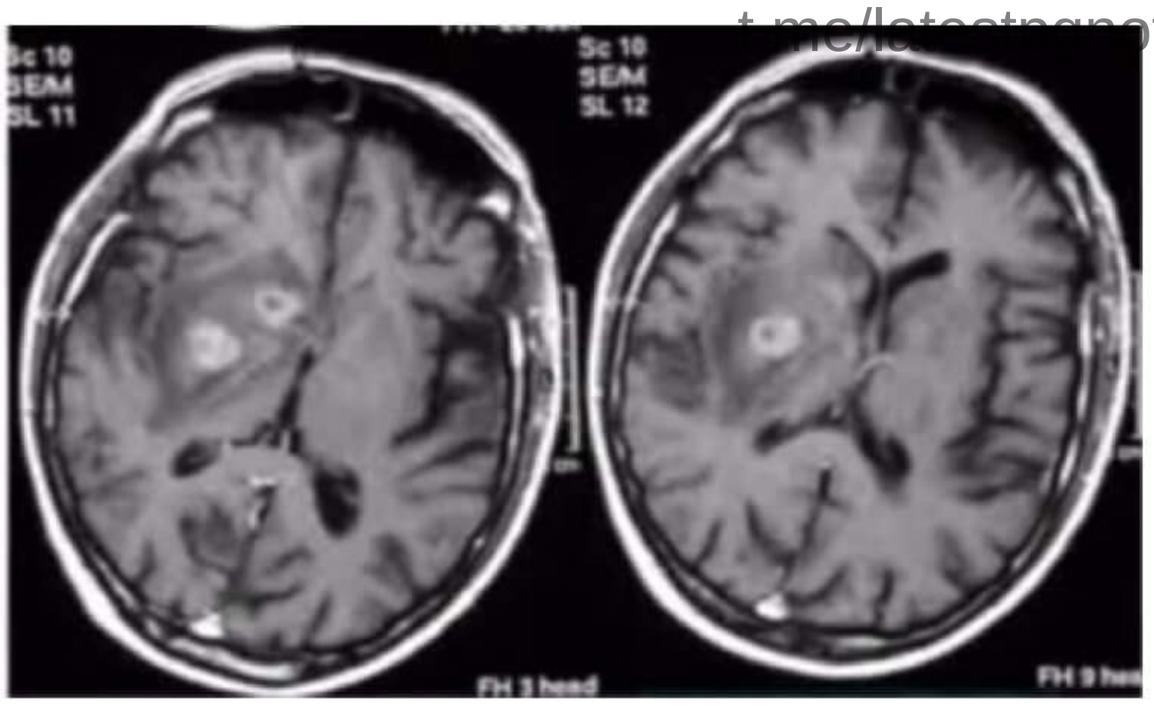


Eccentric dot Sign or Ring enhancing Sign

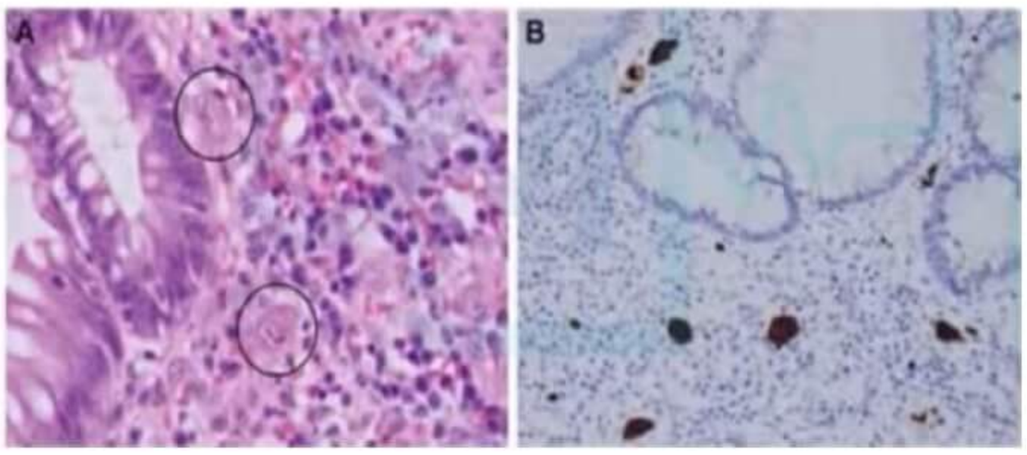
Multiple lesion can be seen

Mostly basal ganglia area is involved

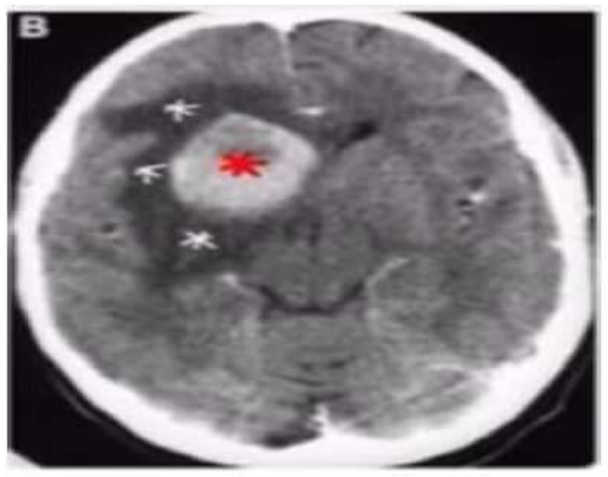
Note : In Neurocysticercosis scolex of worm can be seen inside the ring enhancing lesion in NCC.

PrepLadder

CMV (Cytomegalovirus): basophilic intracytoplasmic, Intranuclear inclusion bodies (+)



Primary CNS lymphoma



In this NCCT, Single lesion with extensive cerebral edema

↓

explains Seizures (+)

Cerebral Toxoplasmosis	Primary CNS Lymphoma
Multiple lesion (+) mostly in basal ganglia • Eccentric dot sign • Ring enhancing sign	• Single lesion (+) • Cerebral edema (+) Which cause seizures

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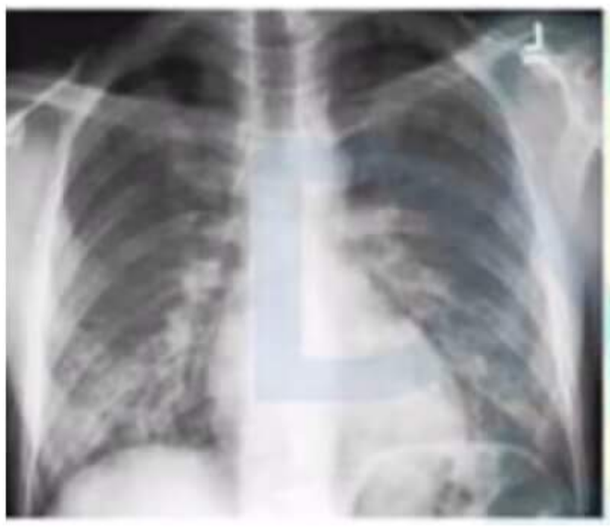
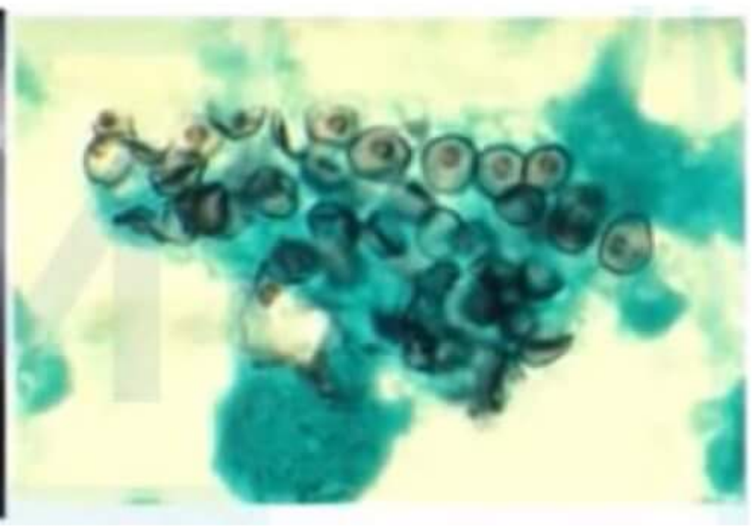
Pneumocystis jiroveci:





AIDS (+) patient with history of cough for 2 weeks & O_2 saturation of pt. is disproportionately low

In this X-ray Perihilar Shadows (+) bilaterally

Broncho alveolar lavage (BAL)

↓

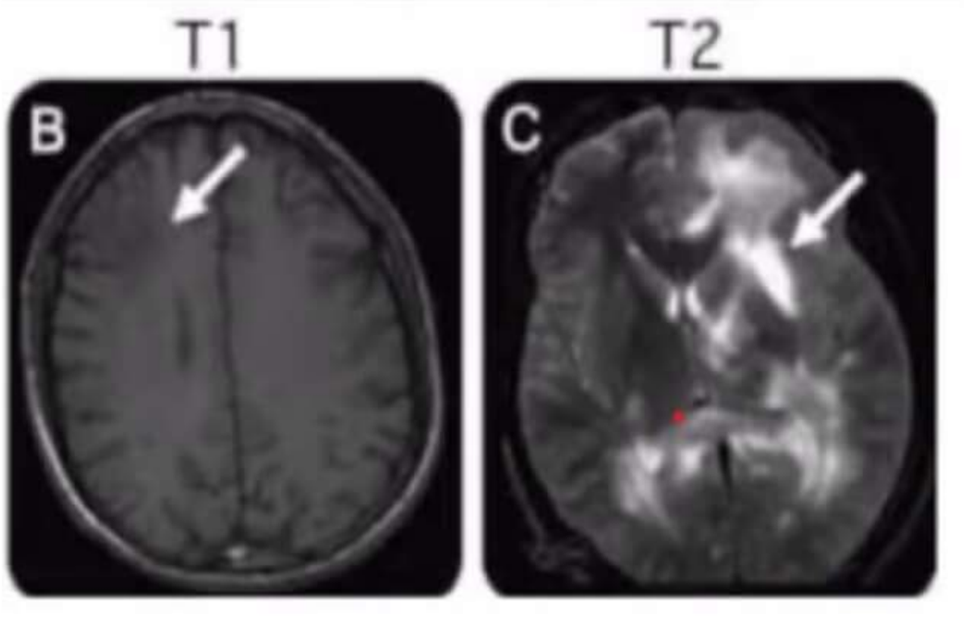
Gomori methenamine silver stain

↓

Dx: Pneumocystis jiroveci

PrepLadder

Progressive Multifocal Leuco-encephalopathy



In MRI – Subcortical white matter lesions (+)

mostly in parietal or temporal lobe of brain (+)

HSV esophagitis:

Solitary large ulcer in esophagus or

Punched out ulcer can also be seen sometimes

↓

cause odynophagia

HSV esophagitis

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Kaposi sarcoma

- Vascular tumor present in oral cavity or anywhere else in body
- < 60 years of age included in AIDS criteria
- Differential diagnosis – Bacillary angiomatosis caused by Bartonella henselae
- Reddish brown lesion (+) all over the body which may bleed on touch

Kaposi sarcoma

Life cycle of HIV

Whenever docking occurs conformational change receptor and co-receptor occurs

↓

Integration of virus with CD4 cell

↓

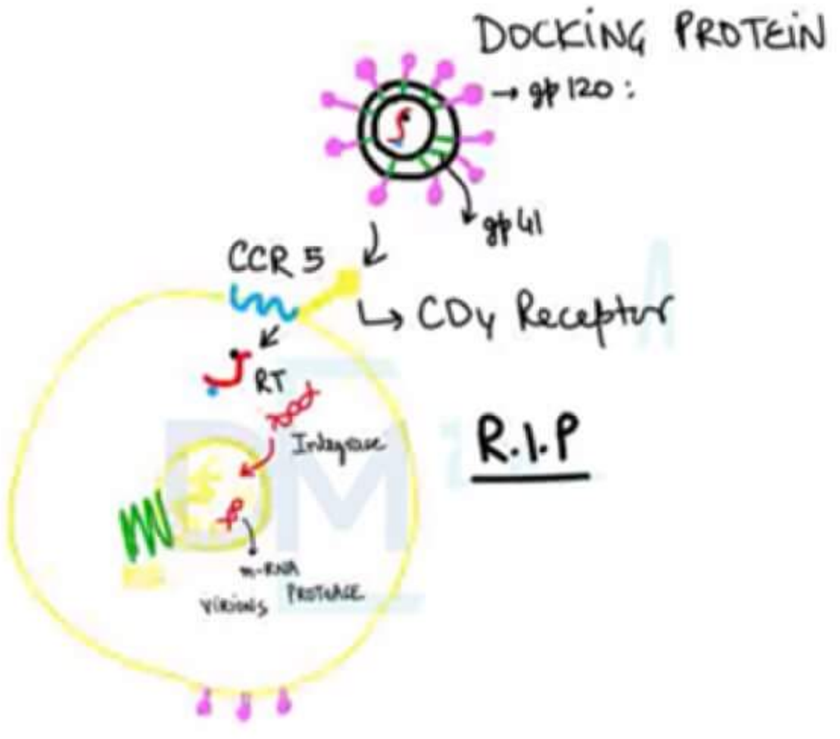
Single stranded RNA comes inside CD4 cell

↓ **[Reverse transcriptase]**

Double stranded DNA

↓ **[Integrase]**

splice up host DNA



PrepLadder

↓

HIV virus DNA integrated

↓

Produce messenger RNA which utilize host's rough Endoplasmic Reticulum

↓ **[Protease]**

Forms new virions

RIP enzymes → Reverse transcriptase

Integrase

Protease

To diagnose AIDS:

→ Histoplasmosis + HIV serology (+)

→ Coccidioidomycosis + HIV serology (+)

→ HIV wasting + HIV serology (+)

→ HIV Encephalopathy + HIV serology (+)

→ TB/Extrapulmonary TB + HIV serology (+)

LABORATORY DIAGNOSIS OF HIV

4th generation Enzyme immunoassay (EIA)

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It is able to identify:

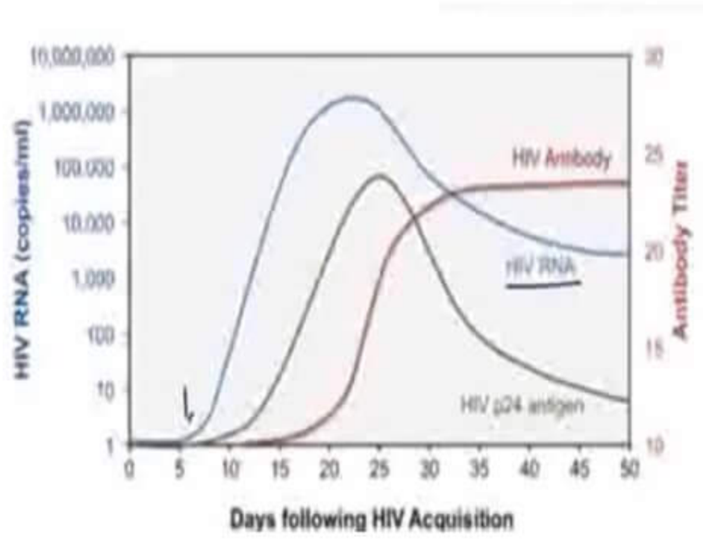
Antibody against HIV – 1

Antibody against HIV – 2

Antibody against P24 antigen

→ Sensitivity → 99.5%

→ 3rd generation EIA → turns positive by day 22 after unprotected intercourse with HIV pt.



→ **Window period for HIV infection**: 3 weeks (50%) - 6 weeks (80%)

→for early diagnosis - HIV-RNA starts appearing in blood as early as in 1st week

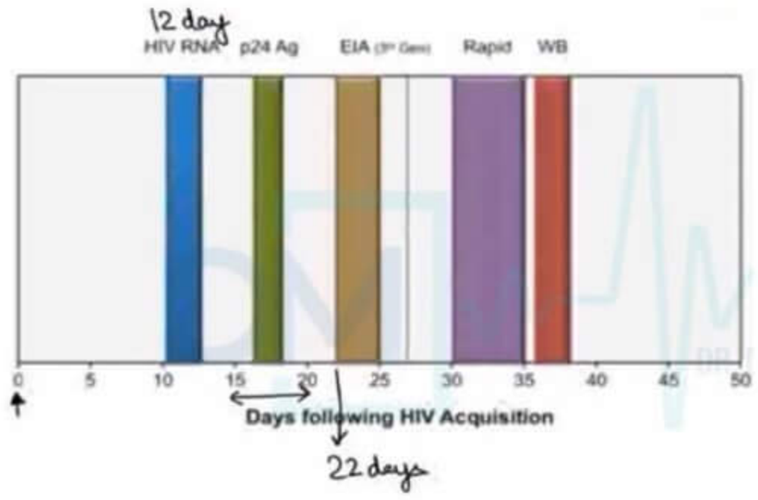
→ **Best test for early diagnosis** → Nucleic Acid Amplification technology (NAAT)

→ HIV RNA will be (+) by day 12 after exposure

→ P24 antigen will be (+) between 15 to 20 days

→ other tests include EIA on day 22

→Western blot will start turning (+) in around 30 days



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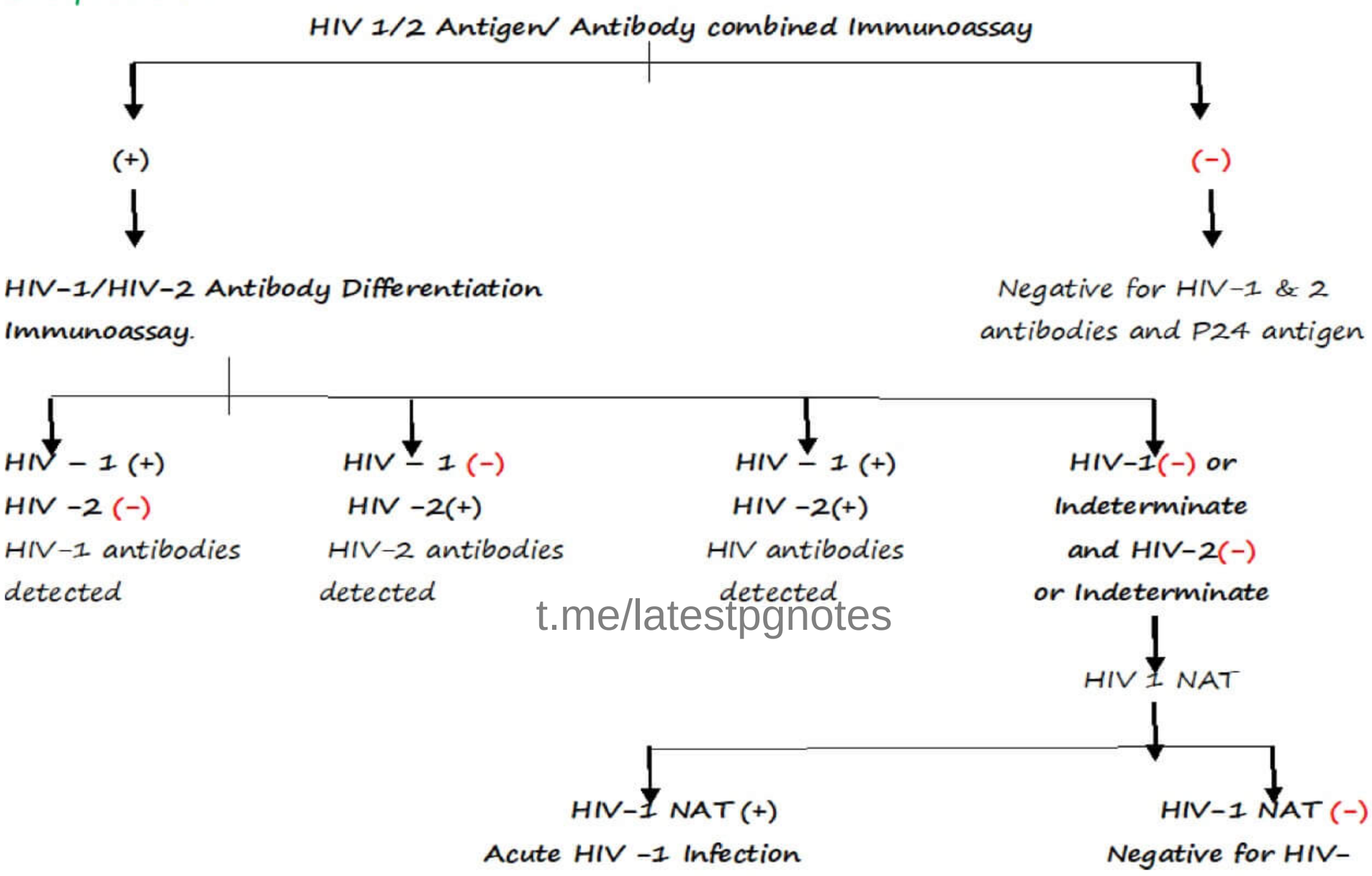
FALSE (+) ELISA HIV CONDITIONS :

1. Pregnancy
2. Influenza
3. Vaccination
4. Blood transfusion
5. Autoimmune disorders like SLE, scleroderma
6. Liver disease

CDC protocol :



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TESTS

1. EIA 4th generation combined immunoassay
2. Differentiation Immunoassay

↓ If both Indeterminate

N.A.T/ PCR

According to NACO or Government of India

Most sensitive test → EIA

Most specific test → Western Blot

↓

Picks up antibody against all these antigens-group 160,120, p17, p24

↓

Which are encoded by 3 gene gag, pol, env

PrepLadder

OTHER TESTS

→ CD 4 count

→ Liver function test

→ Lipid profile

→ HIV RNA – tells about viral load Q.

→ HIV DNA – Vertical Transmission of HIV

→ VDRL – Coinfection (+) in patient

→ Hepatitis B/C/D/G

With Hep G – progression of HIV is slower Q.

→ Purified Protein Derivative (PPD) → for LTB

→ Anti Toxoplasma Antibody: IgG.

→ MMSE (Mini Mental Score Examination)

ORAQUICK → New test for HIV done with saliva or blood at home

Diagnostic accuracy:

Saliva → 98%

Blood → 99%

ORAQUICK

Prophylactic drugs for HIV patients to ↑ longevity of life span

1. P. jiroveci → Cotrimoxazole [DOC & Prevention]
2. Toxoplasma → Cotrimoxazole [Prevention]
3. Toxoplasmosis with encephalitis → Pyrimethamine + Sulfadiazine + Leucovorin
4. MTB + PPD > 5 mm (in 48 to 72hrs) or
IGRA (Interferon Gamma Release Assay) (+) or
Contact with active case of TB → Latent TB infection (LTBI)

↓

Isoniazid (INH) + Pyridoxine x 9 months

5. Mycobacterium Avium Intercellular (MAI) → Clarithromycin + Ethambutol ± Rifabutin
6. HIV (+) patient exposed to chicken pox pt → Varicella zoster immunoglobulin (VZIg)
7. Cryptococcus Coccidioides → Fluconazole
8. Histoplasmosis → Itraconazole
9. Salmonella → Ciprofloxacin
10. Bartonella henselae → Doxycycline
11. CMV → Valcyclovir/ acyclovir

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PrepLadder

If TB diagnosed in HIV patients

↓

Treat TB 1st to decrease bacterial load in the body

↓

Chances of high risk that is Immune reconstitution inflammatory syndrome will be less.

↓

Then HIV treatment should be given.

Vaccines for HIV (+) patients

HAV, HBV, PCV 13 (pneumococcus), HPV vaccine.

Respiratory diseases in AIDS patients

Pneumococcal pneumonia > TB > P. jiroveci

Pneumococcal pneumonia → Consolidation or patch in one lobe of lungs

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→ P. Jiroveci → Bilateral perihilar opacities

Multiple spots (+) in both lung fields

↓

Miliary TB

History given by patients of P. jiroveci

→ Fever

→ Shortness of breath

→ Chest pain

→ Weight loss

→ Chest X-ray can be normal at early stages in all the above 3 conditions.

→ if perihilar opacities (+) → P. Jiroveci

→ LDH ↑

→ β 1, 3 glucan test (+)

→ Diffusion capacity of lungs for carbon monoxide (DLCO) ↓

PrepLadder

BAL: Wright Giemsa
Methenamine Silver

Treatment for P. jiroveci

→ Co-trimoxazole

→ IV Pentamidine if allergic to cotrimoxazole

Steroids given if:

→ paO_2 < 70 mm Hg

→ A – a gradient > 35 mm hg (N-15mmHg)

Extrapulmonary manifestations

→ Otic mass on external meatus

→ Lymph nodes enlargement

→ Hepatosplenomegaly

→ Lesion in choroid

Mycobacterial TB

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MTB + HIV → Cavity size smaller & dissemination chances are more

Treatment → ATT —(2 WEEKS)→ CART

LTBI →based on Mantoux test >5mm

Rx: Isoniazid + Vit. B 6 x 9 months

MAI → CD4 < 50 cells/ cu.mm

→ Entry: Lungs / GIT

→ CXR → Bilateral infiltrate

IOC → Culture BAL/ Bone Marrow biopsy/ Blood

Treatment

Clarithromycin + Ethambutol ± Rifabutin

PrepLadder

Lymphatic Interstitial Pneumonitis (LIP)

→ Antibody mediated damage to lungs

→ Hazy B/L lung field, but no organism has been isolated.

→ Due to B cell dysregulation in HIV (+) patients

→ **Invasive Aspergillosis → Not seen in AIDS (+) patients**

Cardiovascular association in HIV patients

1. MI
2. Cardiomyopathy

GIT disease in AIDS

1. Oropharyngeal Candida/ Oral thrush

Clinical presentation: HIV +ve truck driver presents with odynophagia

Dx: Esophageal candida: Rx IV Fluconazole

2. **Black hairy tongue: EBV**

Enlargement of filiform papillae of tongue

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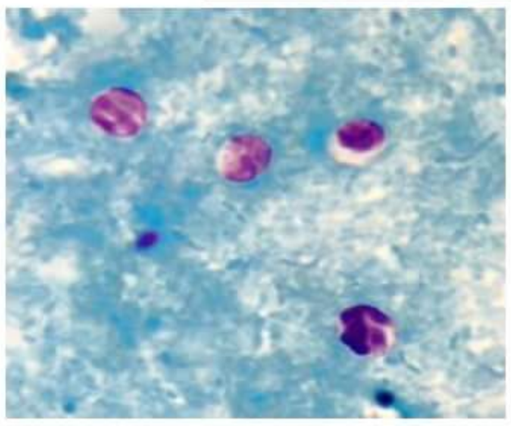
3. Chronic diarrhea

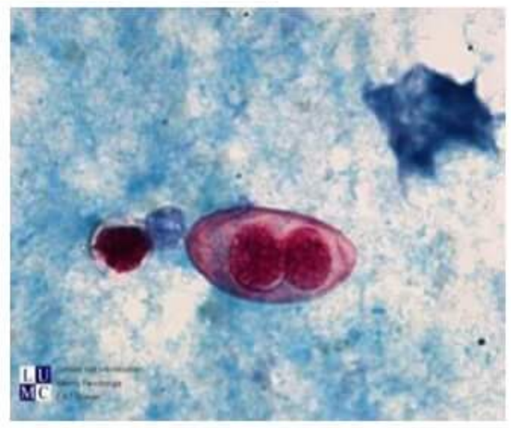
On ZN staining:

If cyst <10µm- **Cryptosporidium**

If size is bigger- **Isospora belli**



Cryptosporidium



Isospora belli

Rx

DOC for Cryptosporidium diarrhea → Nitazoxanide

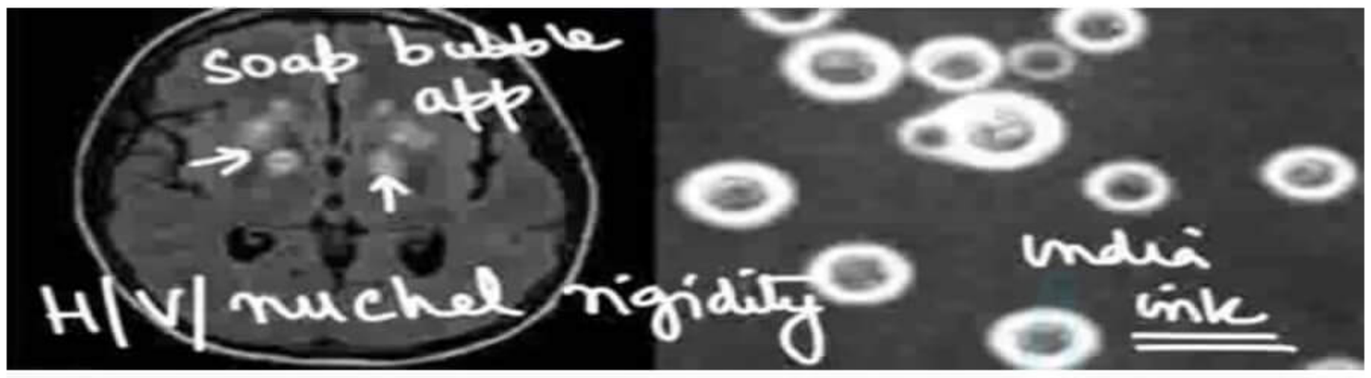
DOC for Isospora belli diarrhea → Cotrimoxazole

Cotrimoxazole uses:

P. jiroveci, Toxoplasmosis & Isospora belli

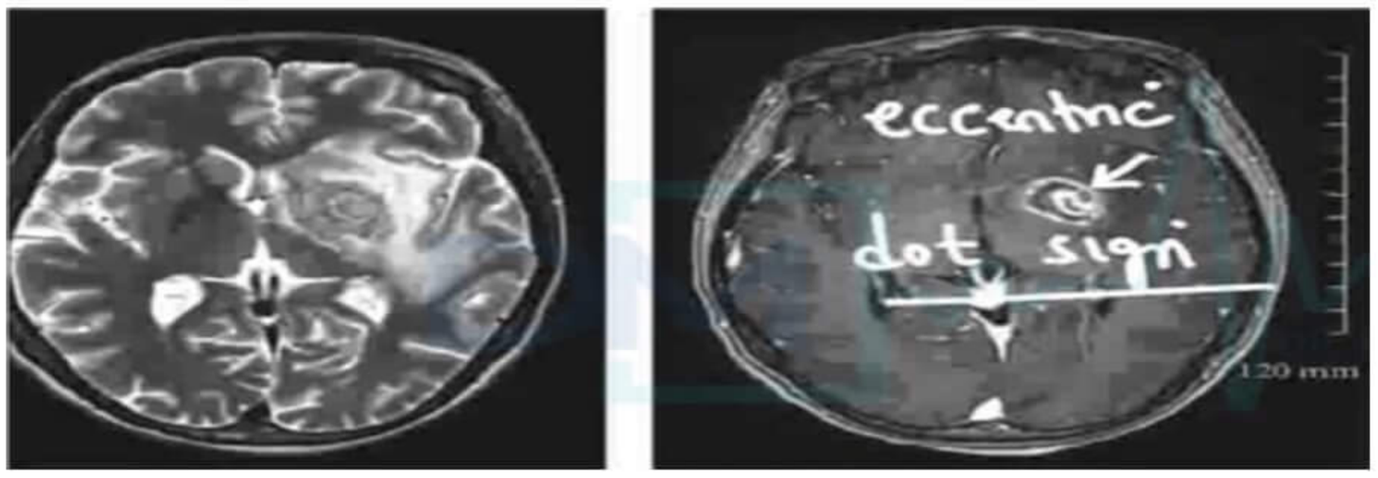
PrepLadder

CNS manifestations in AIDS (+) patients



Q. Patient presents with headache, projectile vomiting with nuchal rigidity. MRI shows **soap bubble appearance.**

Dx: Cryptococcal meningitis



Q. AIDS+ rickshaw puller with recurrent episodes of seizure and MRI shows Eccentric dot sign in basal ganglia.

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Dx: Cerebral toxoplasmosis

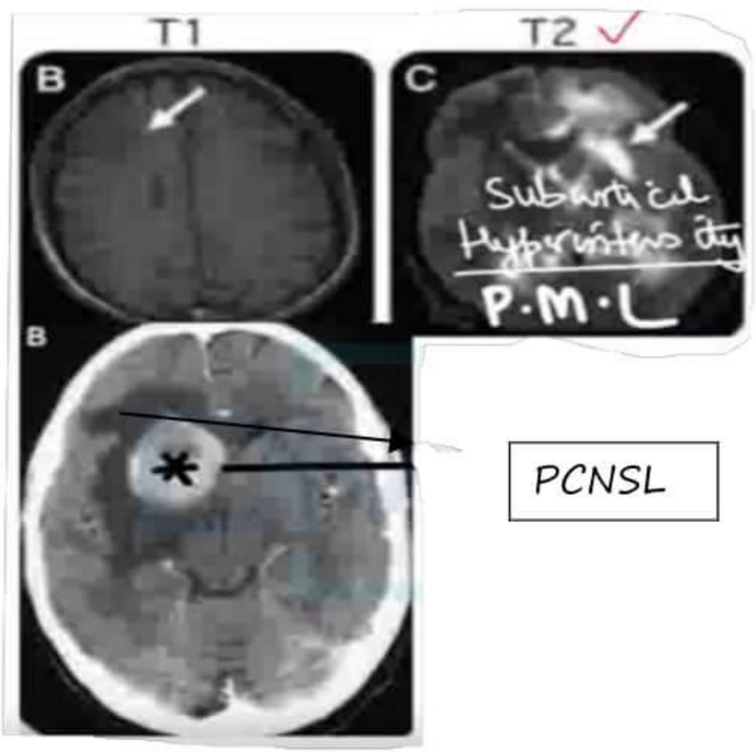
If test for Abs against toxoplasma is positive: Rx. Pyrimethamine – Sulfadiazine

→ in T2 image:

Subcortical hyperintensity

Seen with JC virus

Dx: Progressive Multifocal Leukoencephalopathy



PCNSL: Primary CNS Lymphoma →

Single large lesion assoc. with perilesional edema

→ Soap bubble appearance anywhere in body → Cryptococcus

→ Eccentric dot sign especially in basal ganglia → Toxoplasmosis

1. Cryptococcal Meningitis →**Best test**: CSF ELISA for Cryptococcal antigen

Rx:

→ Liposomal Amphotericin B + 5 Flucytosine x 2 weeks

→ Oral Fluconazole x 8 weeks

PrepLadder

2. Seizures → HIV Dementia > Cerebral Toxoplasmosis

↓

Tests- IgG anti toxoplasmosis + Eccentric dot sign on MRI mostly in basal ganglia

Rx: Pyrimethamine + Sulfadiazine + Leucovorin

3. Progressive multifocal leukoencephalopathy

Tests

→ PCR CSF for JC virus

→ MRI – subcortical hyperintensity in T2 images

3. Primary CNS lymphoma – Tests → Stereotactic or guided biopsy

CART REGIMENS

→ Start trail: Early initiation of t/t ↓ mortality to 50%

→ **Acute opportunistic infection (+) – start CART simultaneously**

Note: TB patients with HIV → Start ATT first

↓ Then after 2 weeks

CART

→ if CART given 1st → Immune reconstitution Inflammatory syndrome (IRIS)

IRIS leads to production of cytokines which reset the thermostat of hypothalamus so pt. will have fever after medication. So, drop out rate will be higher d/t worsening of symptoms

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→ Resistance testing (K103N): NNRTI

Same kind of mutation (+) in CML → T315L: **Rx → Ponatinib**

Nucleoside Reverse Transcriptase Inhibitors (NRTI)

1. Didanosine → Peripheral Neuropathy, pancreatitis, hepatitis or Fulminant hepatic failure
2. Stavudine → Peripheral Neuropathy, pancreatitis, hepatitis, Lipoatrophy.
3. Zidovudine/ AZT → Anemia and neutropenia
4. Abacavir → HLA B5701 testing necessary as it can cause rash, anaphylaxis
5. Emtricitabine, Lamivudine → Safe, It can be used in patient who have coinfection with HBV.

Non-Nucleoside Reverse Transcriptase Inhibitors (NNRTI)

1. Delavirdine → Rarely used d/t Inconvenient dosing : S/e. elevated transaminase.
2. Efavirenz → Neuropsychiatric symptoms, suicidality
3. Etavirine → Second generation NNRTI can be used in case if resistance (+).
4. Nevirapine →on long term use: Rash, Hepatotoxicity [↓ vertical transmission of HIV]
5. Rilpivirine

PrepLadder

Nucleotide Reverse transcriptase inhibitors

→ Tenofovir Alafenamide (TAF)
→ Tenofovir Disoproxil Fumarate (TDF)
Adv. Effective against HBV

} S/E → Kidney damage, Bone matrix damage

Protease Inhibitors

	Booster		S/E
Atazanavir	-Cobicistat	→	liver damage, jaundice and rash
Darunavir	-Ritonavir (inhibits Cyt P450 and reduces the metabolism of protease inhibitors)		
Indinavir		→	kidney stones
Fosamprenavir			
Lopinavir			
Nelfinavir		→	GIT complaints
Saquinavir			

→ Lipodystrophy is a common S/E for all the protease inhibitors

Entry Inhibitors

Enfuvirtide → given subcutaneously twice a day.
Maraviroc → CCR5 is affected

Integrase inhibitors

Elvitegravir
Raltegravir
Dolutegravir

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Once a day pill: AIDS

1. Dolutegravir + Abacavir + lamivudine → integrase inhibitor + nucleotide reverse transcriptase inhibitor
2. Dolutegravir + Emtricitabine + TAF
3. Elvitegravir + Emtricitabine + TAF
4. Raltegravir (twice a day) + emtricitabine + TAF

If patient cannot take integrase inhibitor

↓

[Efavirenz + Emtricitabine + TDF] – Atripla with longest clinical experience.

Accidental Needle stick injury → incidence of infection upto 0.3%

→ Post exposure prophylaxis – PEP should be administered ideally within 2 hours (but certainly within the first 72 hours) of exposure and the risk evaluated as soon as possible.

According to NACO guidelines

Tenofovir (TDF) 300 mg + Lamivudine (3TC) 300 mg. (mostly 3 drugs are preferred)

According to CMDT

Tenofovir 300 mg + Emtricitabine 200 mg daily with Raltegravir 400 mg twice a day.

PrepLadder