CVS

RHEUMATOLOGY

RESPIRATORY

ACID - BASE BALANCE

CVS

Examination

Non Auscultatory
- Pulse
- JVP
- Apex

Auscultatory : S_1-S_4
- clicks
- opening snap
- murmurs

Specific Disease.

Endocardial Disorders
- ARF, Valvular Heart Ds.
- Infective Endocarditis

Myocardial Ds
- Cardiomyopathy
- CHF

Pericardial Ds
- Acute pericarditis
- Tamponade
- Constrictive Pericarditis

Vacular Disorders
- HTN,
- IHD,
- Aortic Dissec^{n}

PULSE

(I) Pulse Rate

(N) 60 - 100/min

Ab (N)

1) **Bradycardia** - <60/min.

Causes

Physiological

1) Elderly
(age related SA node degeneration)

2) Sleep
(↓ in sympathetic activity)

3) Athletes
(Basal ↑ in vagal D/c)

(N) Thyroid hormone
↑ No. + ↑ func° of β_1 receptors

To perfuse brain systemic BP ↑ → stimulate baro receptors in carotid → release ↓ vagal D/c

Pathological

I) **CVS Cause**

1a) Brady arrhythmias
(AV Block)

2) MI [inf. wall]

SA node also supplied by (R) coronary artery

due to stimulation of vagal n/v nearby

II **Non-CVS Causes**

1) Hypothyroidism

2) Hypothermia
(directly affects SA Node)

3) Drugs
a) β blocker
b) non DHP CCB [cause AV Block]
c) ~~Digoxin~~ Digoxin effect

4) ↑ ICP
Cushing's reflex = BP ↑, HR ↓, irregular resp

↑ Bile ⇒ ⊖ SA node

⑤ Obstructive jaundice

2) **Tachycardia** > 100/min

CAUSES

Physiological

1) Infants (↑ SA node activity)

2) Anxiety (↑ sympathetic activity)

3) Exercise (↑ demand)

Sympathetic system ← Thoracic n/vs [thoracolumbar]

Pathological

I CVS Causes

1) Tachy ~~arrhythmias~~ arrythmias.

a) PSVT

b) AF

2) MI (ant. wall) [stimulation of nearby sympathetic n/vs]

II Non-CVS causes.

1) Hyperthyroidism.

2) Fever. 3) Beri-Beri

4) Drugs

a) β agonist

b) short acting DHPs [reflex tachycardia due to compensation]

c) Digoxin toxicity

d) Theophyllin

e) Thyroxin.

③ **Relative Bradycardia / FAGET'S SIGN** Q,

HR doesn't ↑ in proportion to body temperature.

(N) For every 1°c from 37°c.

↓

HR ↑ by 15-20/min from baseline

For every 1°F from 98°F → HR ↑ by 10/min.

e.g. if Body Temp is 40°c. HR = 112/min (baseline = 80/min)

min expected HR = 80 + 45

= 125.

CAUSES

Infectious
(also ⊖SA node)

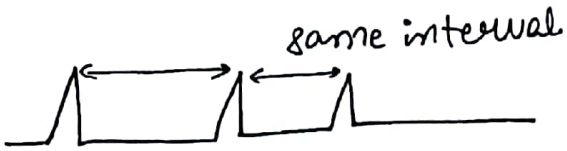
1) Typhoid fever
2) Brucella
3) Legionalla
   (Sputum AFB +ve)
4) Viral

Non-Infectious

1) Drug induced fever
2) Self induced fever or Factitous Fever. Q.
3) Fraudulent Fever
   (thermometer only).

(II) Rhythm :-

(N) → Regular = Fixed interval b/w any 2 consecutive pulses



Ab (N)

Physiological

Pathological.

Sinus arrhythmia

HR changes ↕ inspiration & Expiration.

During Inspiratory Phase

(-ve) Intrathoracic Pressure

↓

↑ Blood flow into (R) side of heart

↓

Pulmonary vessels dilatation (blood pooling)

↓

↓ blood flow into (L) side of heart

↓

CO will ↓

↓

SBP will ↓

↓

Baroreceptor stimulation ↓

↓

Vagal release ↓

↓

HR (↓)(↑)

During Expiratory Phase.

⊕ Intrathoracic Pressure

↓

↓ blood flow into Ⓡ side of heart

+

Pulmonary vessels are squeezed

↓

↑ blood flow into Ⓛ side of heart

↓

CO will ↑

↓

SBP ↑

↓

Baroreceptor ⊕↑

↓

Vagal ↑

↓

HR ↓

Pathological

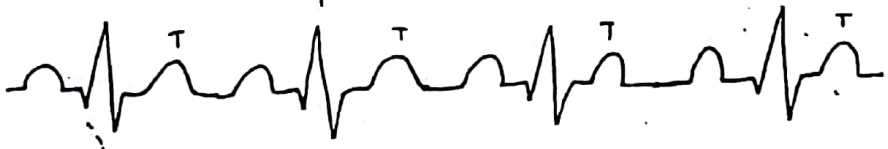
I) Regularly irregular rhythm

↓ predictable ↓ variable.

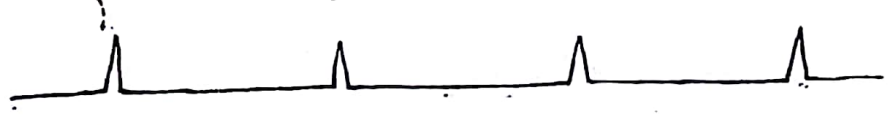
CAUSE :- 1) Bigeminy rhythm ← Digoxin Toxicity

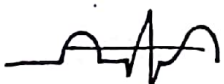
every alternate ventricle contrac° + depolarisate is due to premature ventricle ectopic

Ⓝ ECG.



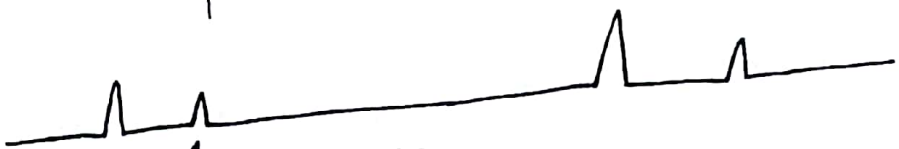
Pulse





Bigeny 

premature ventricular ectopic [hide p. QRS prolonged, inverted T. due to abnormal depolarization]

Pulsus Bigeminus 

↑ due to ectopic.

↓ amplitude due to ↓ ventricle filling time hence ↓ stroke volume

II Irregularly Irregular rhythm

↓ no predictable ↓ variation in intervals.

CAUSE = Atrial fibrillation. ∴ variable HR

(III) PULSE PRESSURE.

How well a pulse is felt

(N) : SBP - DBP [30 - 60 mm Hg].

AB (N)

I) ↓ PP. / Thready Pulse.

Mech. if SBP ↓ & DBP ↑

if CO ↓.

↓

Stimulate sympathetic activity

↓

arteriolar constrictⁿ → PVR ↑

CAUSE = Shock [Hypovolemic, Shock].
not found in septic or neurogenic shock.

II) ↑ PP / Bounding Pulse.

Mech - if SBP ↑ or DBP ↓

occur. if COT

to ↓ LV strain ⟶ PVR ↓

CO is inversely related to PVR

CAUSE : 1) **↑ CO state**

CVS

1) AR
2) MR.
3) PDA

Non- CVS

Physiological → ♀ when plasma vol ↑.

Pathological →

1) Hyperthyroidism

β_1 rec ⊕

ionotropic ⇓ ↑SV

chronotropic ⇓ HR ↑

COTT = ↑SV X HR ↑

2) Anaemia
3) Beri- Beri

Ⓝ vit B_1 ⊖ NO synthase

if Def of Vit B_1
↳ vasodilatation
↓ PVR ↓ → COT

PVR ↓ as arteriole are bypased
↳ COT

4) A-V fistula

5) Paget's Disease
[A-V fistula in Bone]

Q. ⊆ low CO state will cause bounding Pulse ?

Ans. severe bradycardia ⊆ complete AV Block

SV ↑ × HR ↓↓ → CO ↓

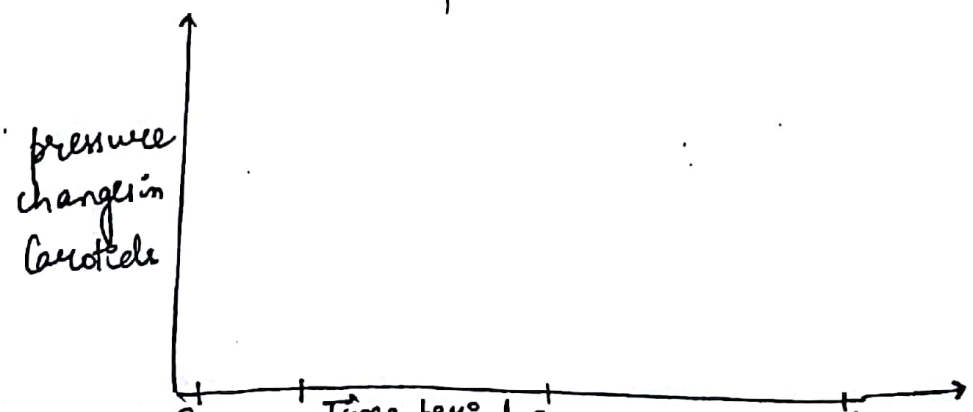
AV Block → ↓ depolarisation of ~~purkinje~~ purkinjee fibres
↓
rate is ↓ [firing speed is less in AVN]
↓
But EDV ↑
↓
SV ↑

(W) CHARACTER

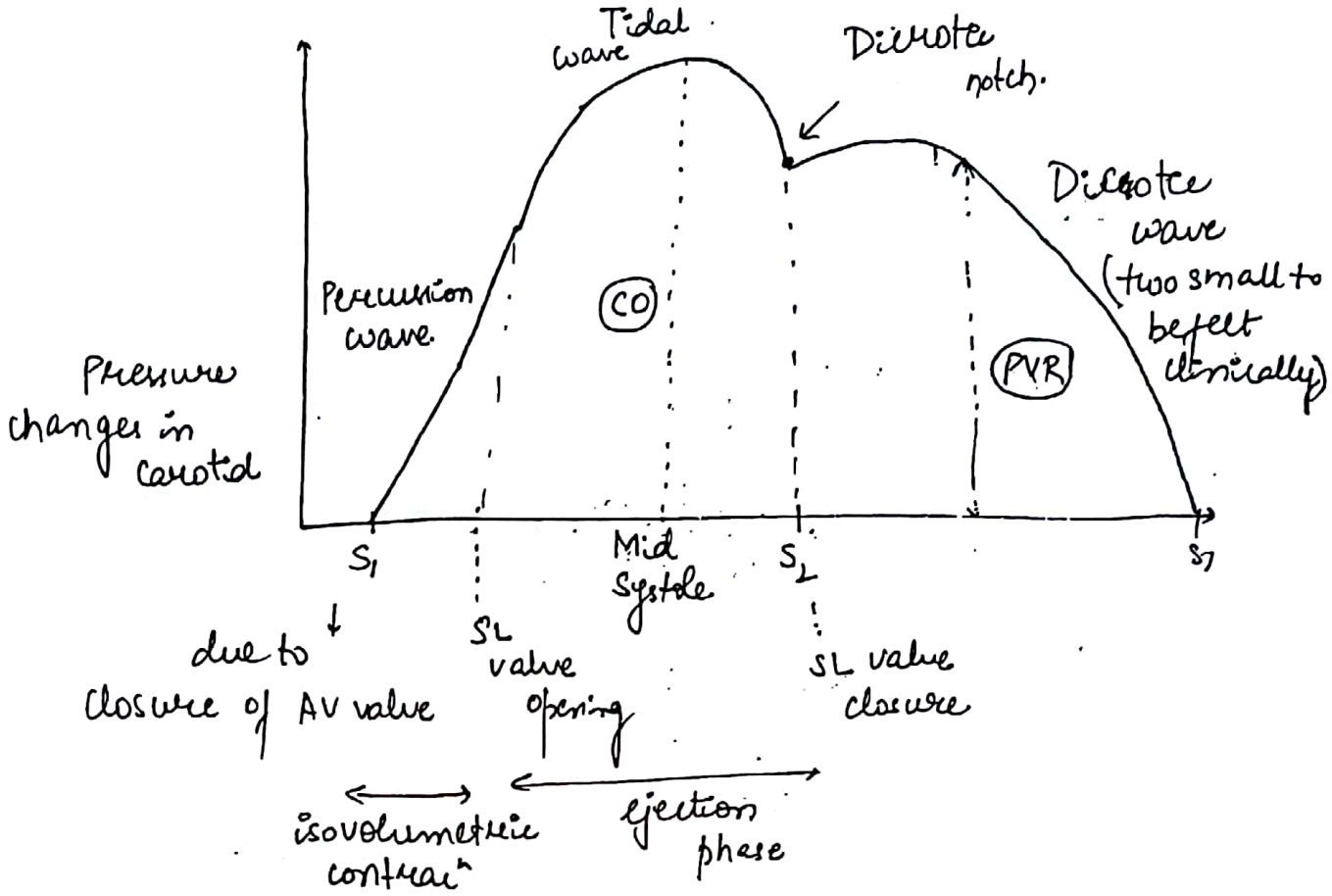
Rate Rhythm best anised in Radial artery

Character /contour " " " Carotid artery

(N) waveforms of carotid.

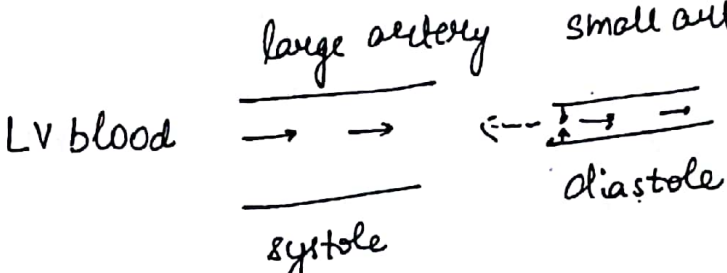


S_1 is due to closure of AV valves

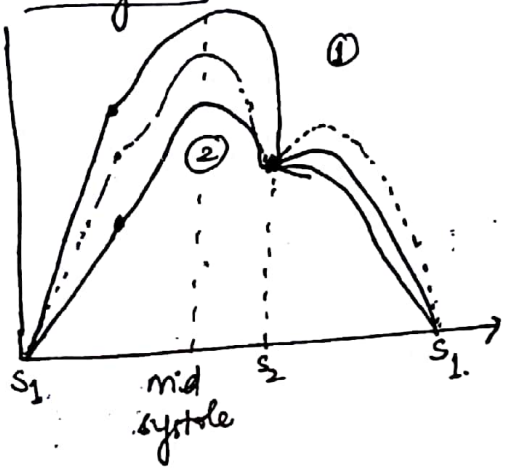
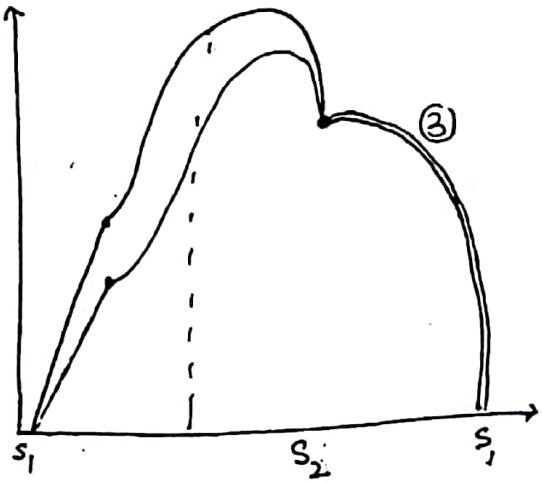


WAVE	MECH
① Percussion wave	It is due to pressure transmission by isovolumetric LV contrac" onto carotids
② Tidal wave	Beginning of blood ejec" into carotid ↑ing its pressure further.
③ Dicrotic wave	Due to back pressure reflection from small vessels

Dicrotic notch represents closure of aorta & pulmonary valve (S_2)

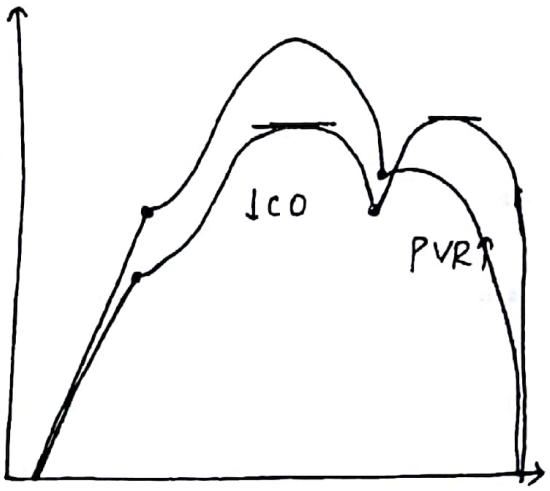


Recoil of small vessel lead to +ve pressure impulse

Ab (N)	Diagram	Cause
1) Hyperkinetic Pulse ⇒ ↑ amplitude		↑ CO state
2) Hypokinetic Pulse ⇒ ↓ amplitude	though dicrotic wave in ① but still not felt not felt clinically.	↓ CO state
3) ↓ amplitude = Parvus Late peak = et tardus		most specific pulse of severe AS.

④ Dicrotic Pulse

= 2 peaks
one in systole
other in diastole



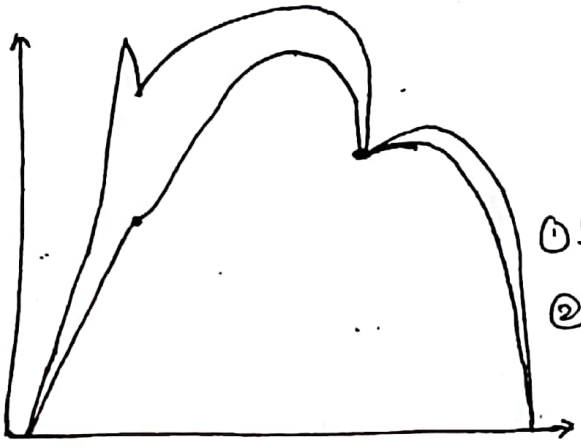
Dicrotic pulse is felt.

Shock
(Hypovolemic
Cardiogenic)

⑤ Bifferiens Pulse

= 2 peaks
(B) in systole

Best assessed in
Peripheral artery



Most specific pulse
of
① Severe AR.
② Severe AR + AS

Brisk isovolumetric (L) ventricular contraction.
(↑ LV vol. + ↑ stretching)
↓
Percussion wave will shift to (L) (as duration is less)
↓
gets separated from tidal wave

It will make tidal wave to come late.

③ HOCM ---?

V MISCELLANEOUS POINTS IN PULSE.

1) PULSUS ALTERNANS - Best assessed in Radial.
Regular alteration of pulse amplitude.

only amplitude changes, interval remain same

CAUSE → LV (Systolic) Dysfunc^{n}. ← most specific pulse.

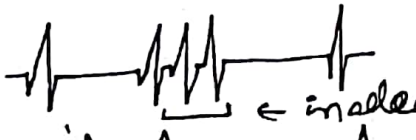
2) PULCE DEFICIT :-

(N) HR - PR ← due to adequate SV = 0
↳ arterial pulsation is felt
↓
due to ventricle contract

Ab (N) if HR - PR = (+ve) ⇒ PULSE DEFICIT.

CAUSES

1) AF ∴ variable heart rate



← inadequate ventricular filling ⇒ No pulse

Pulse ↑ adequate ventricle filling

Here 5 HR but 3 PR

2) Premature Ventricle Ectopics
less filling time → pulse not felt

If pulse Deficit > +10/min ⇒ AF only

3) PULSUS PARADOXUSES :-

(N) SBP_{exp} & SBP_{insp} = 0 to 10 mm Hg.

If this difference is > +10 ⇒ Pulsus Paradoxus.

Exaggeration of Normal Phenomenon. hence paradoxical word is wrong.

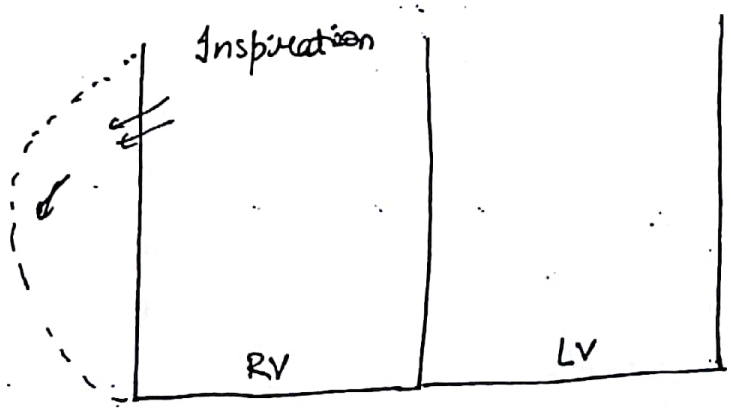
Mech ↓ in SBP_{insp} more than physio limits.

CAUSES

(I) CVS :- 1) H/c CVS cause = Cardiac Tamponade.

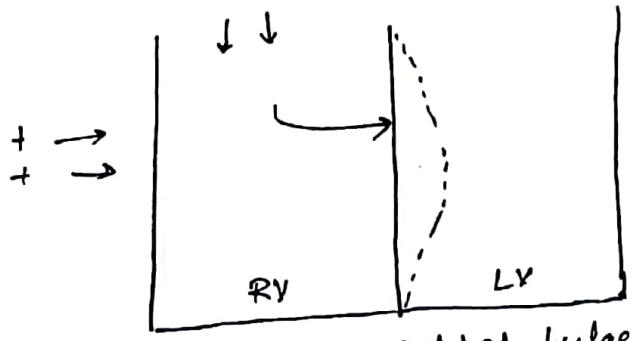
"Compression" of heart due to pericardial effusion.

(N) During Inspiration,
Blood flow is more in (R) ventricles
↓
RV wall dilates to accomodate extra blood.



In Tamponade.

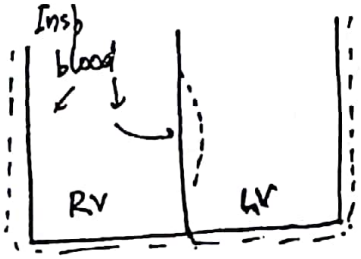
Inspiration
blood.



RV wall can't dilate due to ~~pleural~~ pericardial fluid. → septal bulge in LV → ↓ LV filling further → ↓ CO (↓) → SBP (↓) during inspiration than physiological limits.

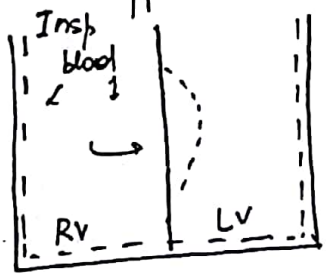
2) Constrictive Pericarditis

Failure of relaxation of heart due to stiff pericardium



3) Restrictive Cardiomyopathy

Failure of relaxation of heart due to stiff endomyocardium.



Septum should be spared from stiffness to cause this ~~side~~ sign

II) Non CVS Cause

H/c overall cause → 1) Acute Exacerbation of Asthma or COPD.

2) Pulmonary embolism
3) Kussmaul breathing [due to met-acidosis]
4) Obesity
5) SVC Obstruction [reason not known].

Deep Inspiratory efforts.

↓ Large -ve intrathoracic pressure

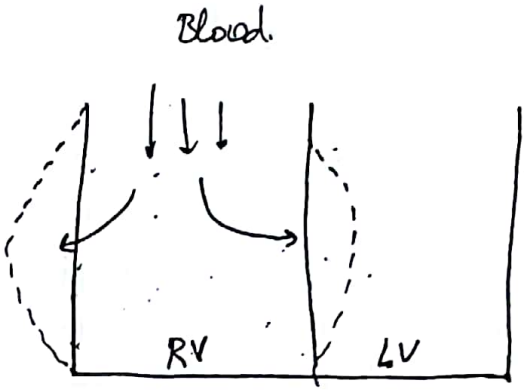
↑↑↑ venous return to the right side

↓

Septal bulge.

↓

Pulsus Paradoxus



Due to extra blood septal bulge occurs.

JVP

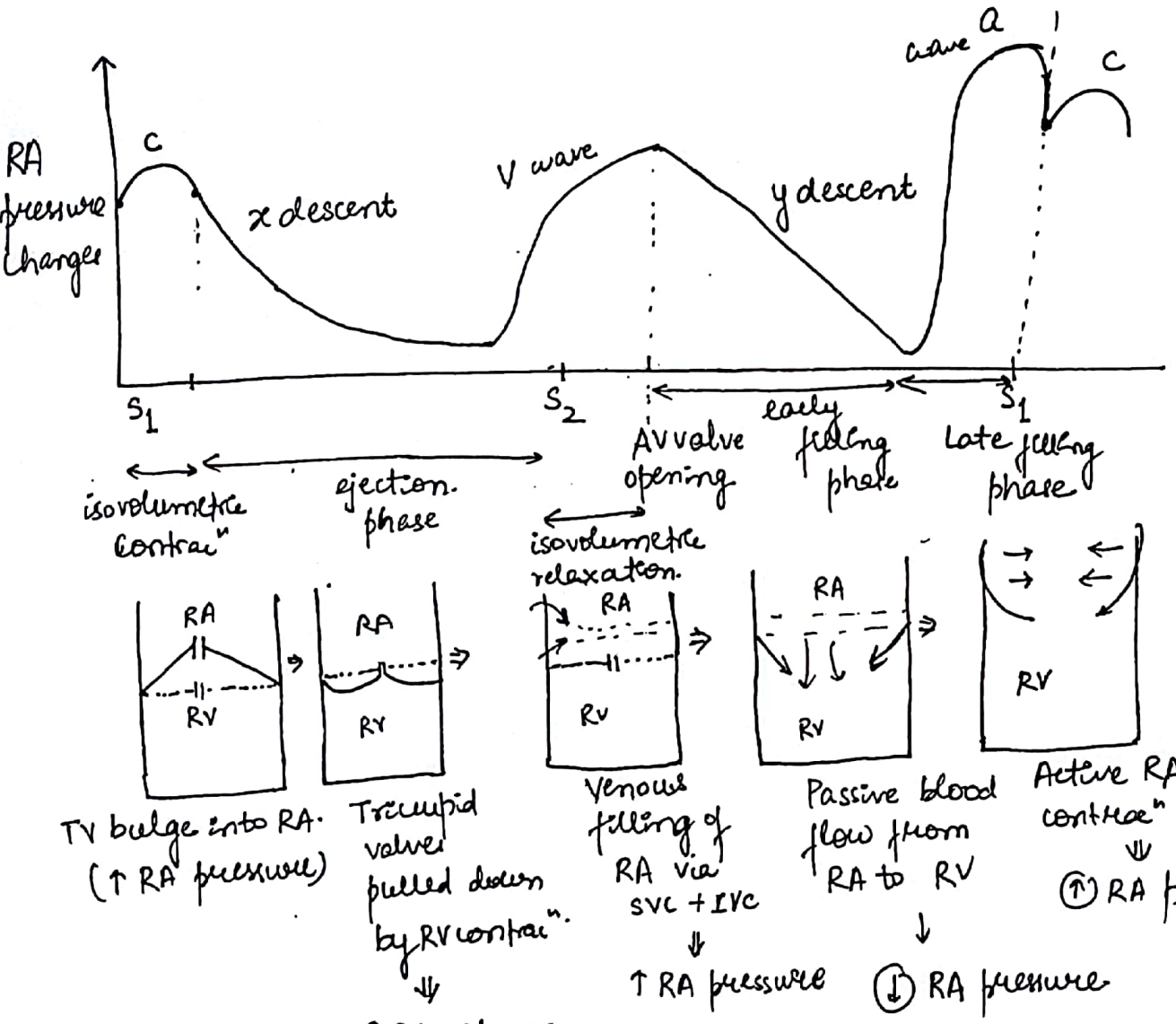
(N) - measure of (R) atrial pressure seen in (R) IJV

(N) Height → 0-3cm from sternal angle

↓ 5cm below

RA activity.

= 5-8cm from RV activity.



Q ∠ wave ; (B) syst + diastolic

⇒ V wave

Q. ∠ wave will be more prominent?

⇒ a wave.

Q. ∠ descent will be more prominent?

⇒ x ~~wave~~ descent

Ab (N) JVP

(I) **a wave** = due to (R) atrial contraction

1> **Absent a wave** = if ineffective atrial contraction

↓

AF

2> **Large a wave** = if (R) atria contracting against more resistance

(Diastolic wave)

If (R) atria is contracting → 1) Tricuspid valve gives resistance
2) RV also gives resistance

cause-

a> **Tricuspid stenosis**

b> RV pressure ↑

- ↓ RVH (concentric) ↑ due to (PS) → **PAH**
- ↓ RV failure (systolic) → RV blood retention. ↑
  1) Pulmonary embolism
  2) RV ~~ex~~ MI
  3)
- ↓ "Compression of RV" ↓ **Cardiac Tamponad**

5> **Canon a wave** = if RA contracting against closed T. valve.
(Systolic event)

occur if RA & RV are contracting simultaneously → cause TV closure

causes → ① **Junctional rhythm.**

SA node arrest → AV node becomes pacemaker & impulse reach (B) atria & ventricle simultaneously

Rate of cannon a wave = 50/min, **Regular**

② **Complete AV Block**

SA node will depolarise atria.
Purkinje fibres will depolarise ventricle independently.

So occasionally atria & ventricle can depolarise simultaneously

Canon a wave is = **intermittent**

(II) X Descent

(N) due to tricuspid ring pulled down by RV contrac. during ejec. phase.

+

(R) atria is free of significant blood (during this phase)

Ab (N)

1> Absent x Descent

if (R) atrial pressure doesn't fall as it contains

significant Blood or Clot

Significant blood → TR

Clot → AF

② Deep x Descent

occur if tricuspid ring pulled more downward due to

↑

» Increased RV contract

(?) 1) Cardiac tamponade

2) Constrictive Pericarditis.

III V Wave

(N) due to venous filling of (R) atrea

Ab(N)

1) Absent or Low V wave :-

occur if venous filling of RA (↓)

cause - a) obstruc" SVC

2) Large V wave :-

If RA pressure ↑ during venous filling

↓

if venous filling ↑

SVC → IVC → RV ↑ TR

or ↓ compliance of (E) atrea

[failure of relaxation]

1) constrictive pericarditis

2) Restrictive cardiomyopathy

(IV) Y Descent

(N) due to passive blood flow from (R) atrea to (R) ventricle ab(N)

1) **Rapid Y Descent** :- / FREIDRICH'S SIGN.
Will occur if (R) atrial blood moves very fast into (R) ventricle as soon as Tricuspid valve opens.

All causes of large v = Rapid y

2) **Slow y Descent** :-
If (R) atrial blood moves into (R) ventricle slowly.

cause - 1) Tricuspid stenosis
2) ↑ RV pressure

Causes of Large a = Slow y

y descent absent - if RA blood doesn't move into RV during passive filling phase

↑

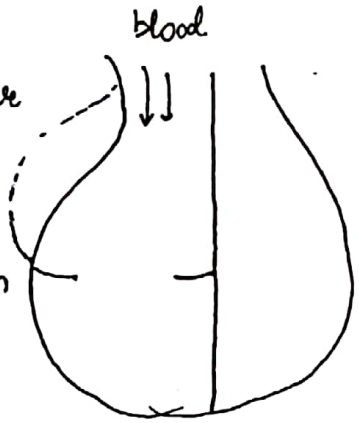
occurs if (R) ventricle is fully "compressed"

⇕

Cardiac Tamponade.

Signs of JVP	Description	Causes
① Abdomino Jugular reflex [abdomen compressed for 30 sec]	if JVP remain elevated by more than 3cm even after release of compression for >15 sec	Latent RVF. / no RVF in basal state + RVF is manifested if RV workload ↑
② Kaussmaul's sign	↑ in JVP during inspiratory phase [Ⓝ JVP ↓ during inspiration]	if Ⓡ atria fail to relax Ⓝ ↓ Constrictive pericarditis Restrictive cardiomyopathy

RA relaxes further
[RA Ⓟ doesn't ↑]
+
Diaphragm goes down
⇓
Ⓡ atria goes down
↓
JVP falls



If basal RA Ⓟ if = TS RVF

Basal atrial 'P' ↑ due to
↙ if AV valve Stenosis
↘ ventricle failure

Kussmaul's sign is absent in tamponade. --- ?

Q. Δ of etiology :-

Ⓝ

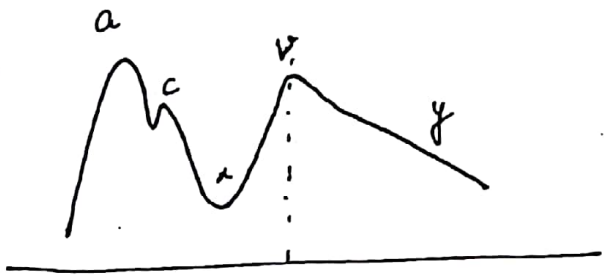
Ab (N)

(1)

y is absent

a) TS b) constrictive Pericarditis c) Tamponade d) TR.

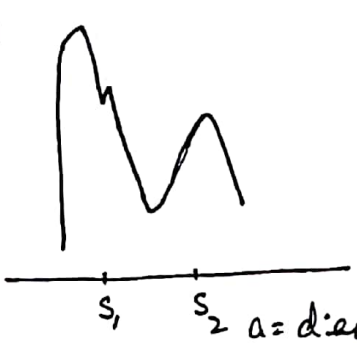
(2)



Δ = slow y descent

ans (a) → TS

(3)



a = diastolic a

(A)

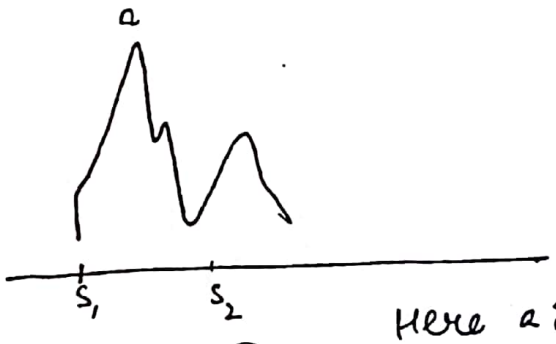
Δ = large a

TS

Options

(1) TS

(2) Junctional rhythm



(B)

Here a is systolic

↓

Δ = canon A wave

↓

Junctional rhythm

APEX BEAT

(N). due to isovolumetric (L) ventricular contrac^{n}.

⇓

LV apex displaced superiorly

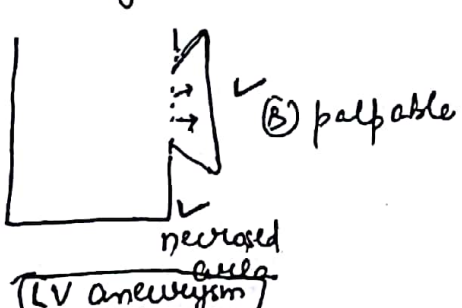
Nature → Tapping.

Site → (L) 5th ICS; just medial to mid-clavicular line

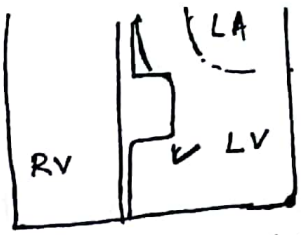
Area → < 2.5 cm^2 [localised].

Ab (N) of Apex

Ab(N)	Description	Cause
(1) Hyperdynamic	Palpable for upto $\frac{2}{3}^{rd}$ of systole	(L) ventricular volume overload. [↑ CO state]
(2) Sustained	Palpable for > $\frac{2}{3}^{rd}$ of systole	(L) ventricle pressure overload. eg. AS.
(3) Diffuse	area > 2.5 cm^2	Dilated cardiomyopathy
(4) Double	2 impulses palpable in systole	LV aneurysm (complication of MI)



Asymmetrical Septal hypetrophy



= HOCM / Subvalvular Aortic Stenosis

If hypertrophy is anterior then palpable

↳ it obstruct LV outflow

⑤ Triple — 3 impulses palpable in systole

HOCM.

⑥ Absent — non-palpable

Pericardial effusion
Emphysema
Obesity
Dextrocardia Q
↳ apex goes posteriorly hence not palpable

Q. Double Apex seen in

~~① AS~~ [HOCM is subvalvular AS]

② TS

③ MS

④ AR.

AUSCULTATORY FINDINGS

* S_1.

due to closure of AV valve.

(N) = $M_1 T_1$ [mainly contributed by mitral valve].

Split < 20msec.

Site : Apex

* Pitch : moderate

Any mitral valve sound/ murmur.
Best area = Apex

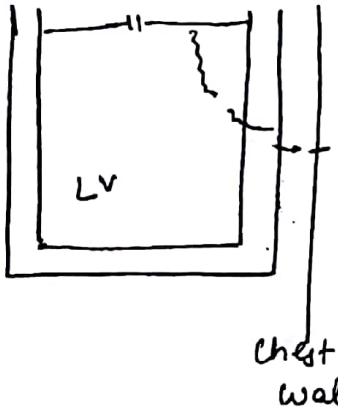
Ab(N)

Factors affecting the intensity	soft S_1	Loud S_1
1) Force of isovolumetric ventricle contraction	if weak force ↑ eg. Dilated CMP, LVF, RVF, VSD &	Strong force eg MS, TS (if atrial (P) is high)
2) Cond^n of A-V leaflets	if fail to strecke each other eg. MR, TR, calification of leaflet	–

3) The presence of fluid, mls air fat between AV leaflet & stethoscope

- if ventricle blood vol. ↑
  - AR
  - PR
- if ventricle wall thickness ↑
  - LVH ← AS
  - RVH ← PS

thin, lean.

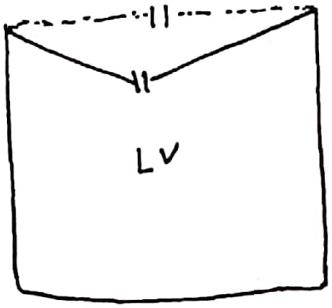


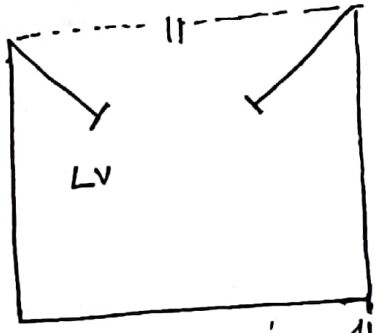
LMR

All valvular Lesions cause Soft S_1 except MS . TS

4) Most imp factor

Position of AV leaflets at onset of ventricle contrac^n.





If impulse reaches ventricle late + ventricular blood filling fully complete

↓

AV leaflets pushed to close position.

- Bradycardia
- PR interval ↑

If impulse reaches ventricle fast + ventricle blood filling incomplete

↓

AV leaflets fully open.

Tachycardia

Short PR interval

Q. In Hypothyeroidism, S_1 is soft-

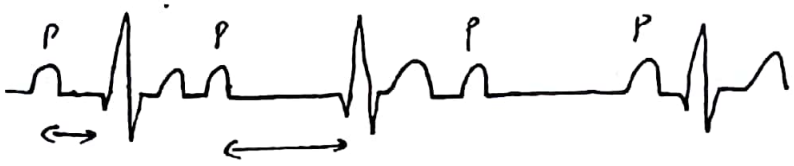
Q. In Digoxin effect, S_1 is soft ans AV Block → PR ↑ interval

Q Cond^n causing variable S_1 intensity :-

If variable HR = AF

Q If variable PR interval = 2° AV Block

→ Mobitz -I. Q.Q.



Progressively PR interval ↑ till atrial impulse fails to conduct to ventricle

= Wenkebach's phenomenon.

* S_2

It is due to closure of Semilunar Valves.

(N) - A_2 P_2

Aortic valve closes earlier than Pulmonary valve

↓

LV ejec^n time is less than RV

Site = For A_2 — aortic area — (R) 2nd ICS

For P_2 — Pulmonary area — (L) 2nd ICS

Best for S_2 → Pulmonary area. [as both sound heard]

Split = 30-60msec.

During Inspiration → split Increase

LV blood vol ↓
LV ejec" time ↓
A_2 early

RV blood vol ↑
RV ejec" time ↑
P_2 → Late

During Expiration → split Decreases. or Expired

LV blood vol. ↑
A_2 late.

RV blood vol ↓
P_2 early

Ab (N) of S_2 split

1. **Wide split**

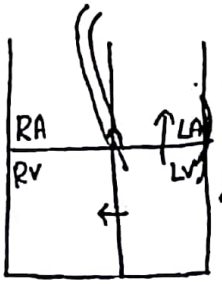
CAUSES

I) **Early A_2.** (earlier than physio limit)

↓ If LV ejec" time ↓
- VSD
- MR

or

↓ If LV early depolarisation.



accessory pathway from LA to LV will depolarise LV early.
(Bundle of Kent)

- WPW Syndrome
- M/cSite → (L) Q.

→ Type A WPW syndrome

WPW SYNDROME

1) ♂ > ♀
2) (L) side more common
3) short PR interval
4) S_1 will be Soft Q. ... ?

II) P_2 is Late [Later than physio Limit]

RV ejec" time ↑ or RV late depolarisation

eg PS
RVF

eg. RBBB

(2) REVERSE SPLIT or PARADOXICAL SPLIT

P_2 A_2.

CAUSES

(I) P_2 is early (earlier than A_2)

RV ejec" time ↓ or RV early depolarisation.

- TR
- VSD ± R to L shunt
  (Eisenmenger Syndrome)

WPW type (B)

(II) **A_2 is Late** (later than P_2)

- LV ejec" time ↑
  - AS
  - LVF
- LV Late depolarisation
  - LBBB

Q. How to differentiate bet" Split & Reverse Split.

During Inspiration.

Reverse split will Decrease RV vol ↑

LV vol ↓

Split Decrease [against (N) rule].

During Expiration

Rever split will Increase

RV vol ↓

LV vol ↑

Split Increase

Q. In. Pulmonary artery HTN, S_2 Split

(a) (I)

(b) ↑

(c) No change

→ P_2 comes early ----?

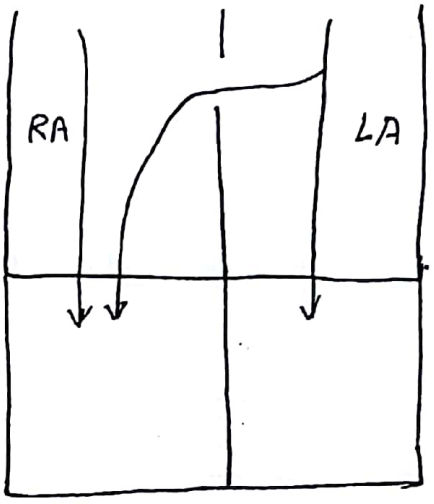
Hint - Pulmonary hang out interval

(3) WIDE + FIXED SPLIT

doesn't vary ∵ resp. phases.

cause → ASD.

RV blood ↑ → P_2 late
LV blood ↓ → A_2 early
} Wide



Split is fixed
= ventricle blood vol remain constant during Insp. + Exp.

⇓

RV blood → Insp. = ↑ + ↓
→ Exp. = ↓ + ↑
⇒ Fixed.

Intensity of S_2

Factors	Soft	Loud
1) Pressure of aorta/ Pulmonary to close SL valves.	Hypotension	Systemic HTN → A_2 P. HTN → P_2
2) Cond^n of SL valves Leaflets.	calcified AR PR	x

* Single S_2 seen in - AR [A_2 is absent]
PR [P_2 absent]
AS/PS [valves get severely calcified]

S_3 / Ventricle Gallop

It is due to ↑ in ventricle blood volume during early filling phase.

↓

ventricle vibrations

Causes:-

Systolic dysfunc^n [↑ end systolic volume]

↓

(L) VF.
RVF
DCMP
MI
LV aneurysm

Site → LV S_3 → Apex
RV S_3 → Tricuspid area. [(L) lower parasternal]

Pitch → Low pitch.

Atrial venous filling ↑

↓ early filling phase

↑ blood will enter ventricles from atria

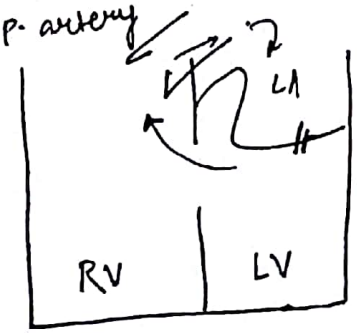
↓

eg. high CO state
MR . TR

Q. In atrial septal defect ⊆ side S_3 → RV S_3 / LV S_3 ?

ans → RV S_3.

Q. In VSD, ⊆ side S_3 = LV S_3



Pulmonary valve is open in systole so blood from VSD goes into

P. artery

↓

P. vein

↓

(L) atrium

MV is closed in systole & blood is collected in it
1st chamber to enlarge is (L) atria.

Q. In PDA ⊆ side S_3 = LVS_3

S_4 / Atrial Gallop

It is due to atria contracting against stiff ventricles → ventricle vibrate

Causes-

1) Restrictive CMP
2) HOCM
3) LVH due to AS
4) RVH due to PS
5) Acute MI.

In acute MI Both S_3 & S_4.

↓ relaxation
↑
↓ ATP due to ischaemia.

Site- LVS_4 → Apex
RVS_4 → Tricuspid area

Pitch - Low pitch.

Q. S_3 can be physiological (= True) / False

Ans → ♀ . young children & athletes

Q. S_4 can be physio - True (False)

Q. S_3 represents systolic failure

Q. S_4 represents Diastolic failure

Q. S_4 seen in all except

a) AS [LVH]

b) Constrictive Pericarditis [ventricles are trapped → can't vibrate]

c) AR → extreme (L) ventricle dilatation → making it stiff

d) Amyloidosis [RCMP]

Constrictive Pericarditis doesn't produce S_3 & S_4.

ADDITIONAL HEART SOUNDS

Name	Cause	Timing	Pitch
1) Ejection click	due to sudden cessation of opening of SL valves at it open i high pressure	S_1 ——— S_2 early systole	High.

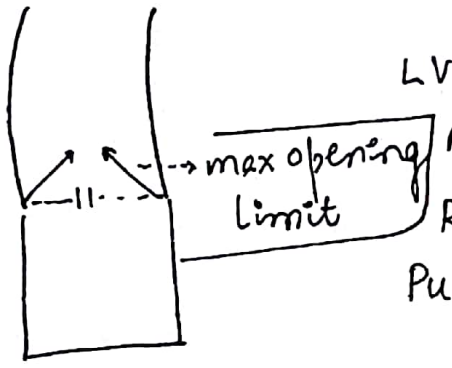
↑

LV 'P' (↑) = AS

Aorta 'P' (↓) = aortic aneurysm

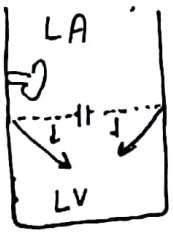
RV 'P' (↑) = PS

Pulm. artery 'P' (↓) = P. artery aneurysm.



Ejection click ↓ in calcified lesions.

2. Opening Snap

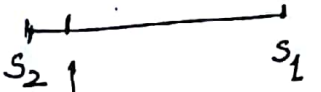


Sudden cessation of opening of AV valve as it opens ∵ high Pressure

↓

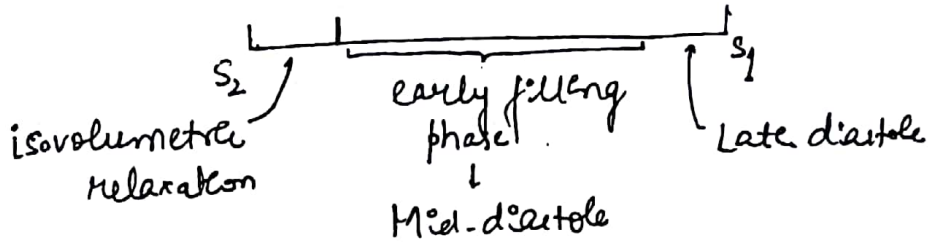
LA ↑ pressure ↑ = MS, LA myxoma

RA pressure ↑ = TS



early diastole phase

High



↓

Mid-diastole

③ Tumour Polyp

Ⓛ atrial myxoma striking mitral valve

Early diastole

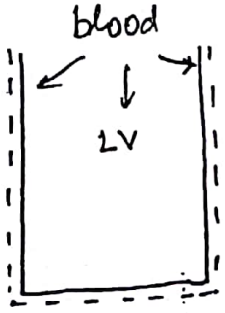
Low

④ Pericardial Knock

ventricle wall strike [knock] on stiff pericardium

Early filling phase

High.



Most Specific sign of

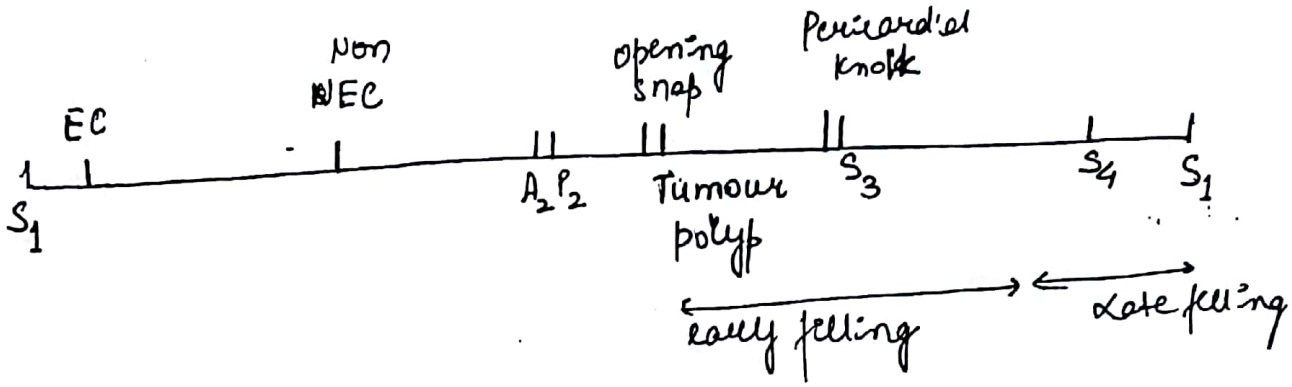
Constrictive Pericarditis.

⑤ Non-ejection Click

MVP rolapse

≥ mid systole

High



In AF. JVP = a wave absent

Hs = S_4 ⊖ [if previously present]

MURMURS

Due to turbulence of blood flow ~~in the~~

If ab Ⓝ ↑ pressure gradient during normal direc^n of blood flow

↓

due to stenotic Lesions

If ab Ⓝ direc^n of blood flow

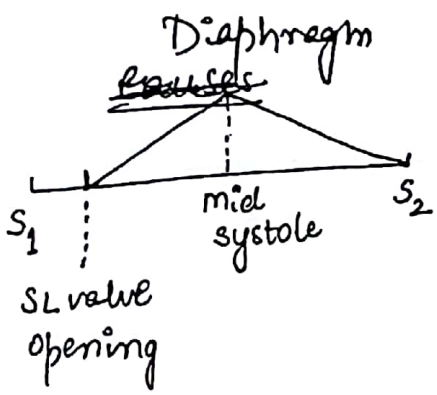
↓

due to Regurgitant Lesions or VSD

TYPES

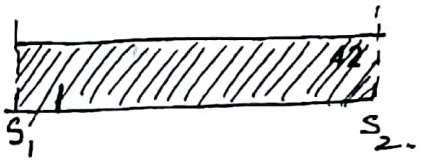
(I) SYSTOLIC MURMURS

Name	M/c murmur overall	Causes
① Ejection systolic murmur or Mid-systolic murmur or crescendo-Decrescendo	due to turbulence of blood flow due to ejection phase	AS, PS ↑CO states. → [⊙]. (↑ blood flow across SL valves)



② Pansystolic Murmur
No peak.

VSD
[LV pressure remain > RVP throughout systole]



chr MR
[LV 'P' remain > LA 'P' throughout systole]
Chr. TR.

QQ.
③ Early systolic murmur

If defect closes before mid-systole
eg. Small muscular VSD

or

If pressure gradient becomes zero (≤ mid-systole)
ⓑ Acute MR.
[MI or IE].

LA is not dilated unlike chr. MR.

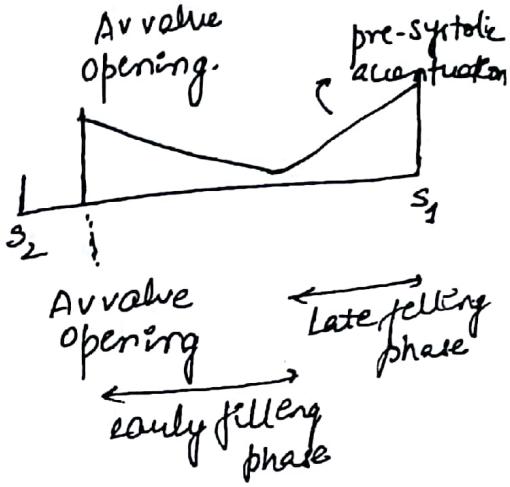
During early systole, Ⓛ ventricle blood enters LA
⇓
LA 'P' will ↑ rapidly
⇓
during mid systole Ⓛ atrial 'P' = Ⓛ ventricle 'P'
⇓
murmur will stop

ⓒ Acute TR.

④ Late systolic murmur

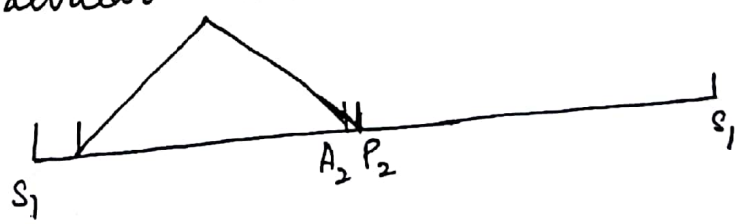
MV Prolapse

(II) DIASTOLIC MURMURS

Name	Causes	Diagram
1) Early Diastolic murmur. or Decrescendo Murmur	AR, PR	
2) Mid-Diastolic murmur	Turbulence of blood flow from atria to ventricles. MS, TS	

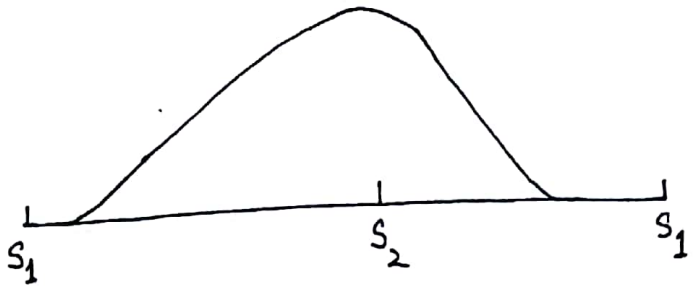
Q. Early Systolic murmur seen in all except
a) TR (acute)
b) VSD (small muscular)
c) papillary m/s necrosis (MI → acute MR)
d) AS

Q. Identify the valvular lesion



a) MS
b) TS
c) PS
d) PS

(III) CONTINUOUS MURMUR



- Starts in systole
- Peaks around S_2
- Ends in Diastole

Origin - single site

Mechanisms :-

If Ab (N) pressure gradient is maintained throughout systole & Diastole

&

If Defect remains open throughout Systole & Diastole

Continuous murmurs are never due to valvular Lesions

CAUSES :-

1) Ab (N) communication b/w artery to vein

eg : A-V fistula

Ruptured sinus of valsalva (aorta to (R) atria connection)

2) Ab (N) communication b/w systemic to Pulm.

eg. PDA

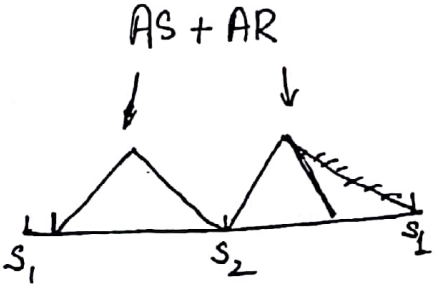
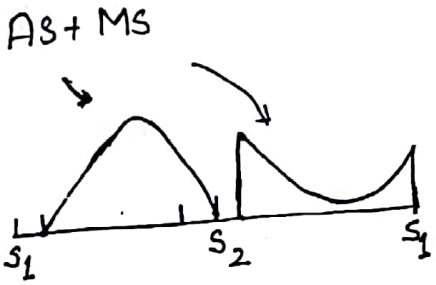
(3) ↑ blood flow into blood vessels
mammary artery souffle (lactation)
uterine artery souffle. (♀)

(4) Severe arterial stenosis [>70% narrowing of diameter]
Renal artery stenosis → 'bruit'

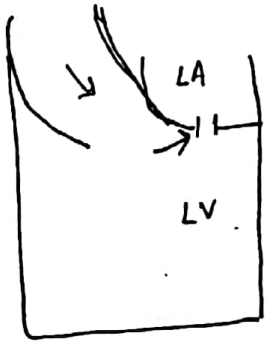
Q. Continuous murmur can be physiological - True/false
↳ ♀, Lactation

Q. All causes continuous murmur except
a) Pt. of CKD on heamodialysis [A-V fistula]
b) Severe atherosclerosis [carotid or renal artery stenosis]
c) AR + AS
d) Lactation.

D/D of Continuous Murmur.

	Continuous murmur ✓	To & Fro ✓	Systolic-diastolic ✓
Systole + Diastole			
Origin	single site	single site	Different sites
Peak around S_2	✓	×	×
Eg.	✓	AS + AR 	AS + MS 

Name	Cause	Type	Site
1) Gibson's murmur	PDA	continuous	(L) upper parasternal area
2) Key Hodgkin's murmur	AR	early diastolic	(L) 3rd ICS = Erb's area = Neo-aortic area
3) Graham-Steel's murmur	PR	early diastolic	(L) 2nd ICS Pulmonary area
4) Austin flint murmur	AR Regurgitant jet of AR striking mitral valve.	mid-diastolic to late	Apex
5) Carey Coomb's murmur	ARF Turbulence of blood flow over inflammed rough mitral valve	mid-diastolic murmur.	Apex
6) Dock's murmur	Severe stenosis of LAD artery (widow's artery)	continuous murmur.	3rd (L) ICS 4cm from sternal margin



⑦ Still's murmur — young children — Ejection systolic murmur — Pulmonary area

- Innocent murmur

(Relatively ↑ blood flow across Pulm. valve)

⑧ Rytand's murmur — complete AV Block. ⇓ ↑ Blood flow across AV valve — mid-diastolic — apex.

FACTORS AFFECTING MURMURS:-

If blood flow ↑ → all murmur will ↑ **except** ⇓ MVP, HOCM.

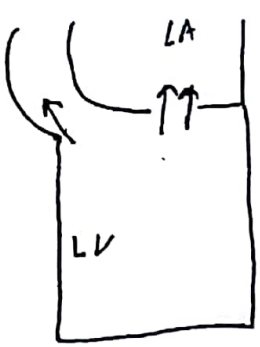
	Blood flow	Murmur
1) Respiratory variation.		
a) Inspiration	↑ blood on ® side	↑ TS, TR, PS, PR exception Pulmonary ejection click ↓ in inspiration
b) Expiration	↑ blood on Ⓛ side	↑ MS, MR, AS, AR [except HOCM, MVP]
c) Valsalva effect (Persistent expiration)	~~Persistent expiratory~~ ↓ blood on ® side followed by Ⓛ side.	All murmur will ↓ [except HOCM, MVP].

II Postural :- Valiation

a) Standing	↓ blood flow into R+L side	all murmur will ↓ except HOCM, MVP
b) squatting (immediate effect)	↑ blood flow into R+L side	all murmur will ↑ except HOCM, MVP

III Effects of Afterload changes :-

Lesion	Afterload ↓ (aorta 'P' ↓)	Afterload ↑ (aorta 'P' ↑)
AS	murmur ↑	murmur ↓
Pressure gradient = LV 'P' - aorta 'P'		
AR	murmur ↓	murmur ↑
Pressure gradient = aorta 'P' - LV 'P'		
MR	murmur ↓	murmur ↑



Regurgitant Lesions behave similar

MVP

Cause- Deficiency of type III collagen in MV leaflets (posterior)

⇓

↑ leaflet flexibility

↓

surface area of MV leaflet ↑

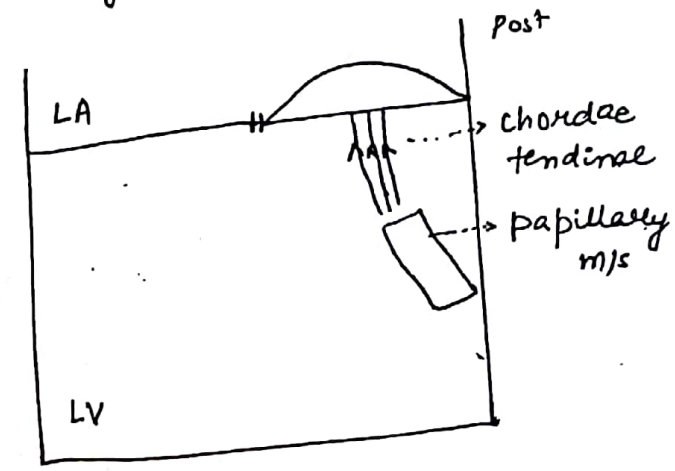
↓

too big for LV cavity

C/F

Symptoms:-

1) chest pain
   M/c symptom
   Due to papillary m/s stretching

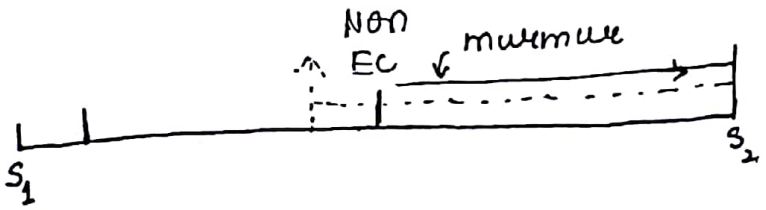


2) Palpitations
   Ventricle fibre stretching
   ↓
   produce ventricle ectopic

Sign:-

▷ M/c sign → **Non-ejection click.**
due to doming of MV
↳ occurs when LV cavity size ↓ significantly

2) Late systolic murmur (MR)
   occur when post. leaflet looses contract & ant. leaflet



If LV cavity blood vol. ↓ → Prolapse will occur early
[standing position
inspiratory phase]

↓

Non-Ejec^n click earlier.

↓

murmur will start earlier

Inv

1) 2D Echo
if prolapse is **> 2mm** into LA

T/t

1) Reassurance. (mostly benign)

2) β blockers (if palpitations) DOC

3) S_x repair ← NYHA symp ≥ II
+
Severe MR on ECHO.

HOCM

Cause - AD
mutation of β-myosin heavy chain.
["Private mutations"]
⇓
Assymetrical Proliferation of septum.
near the LV outflow tract
⇓
Free wall hypertrophy

→ Diastolic func' ↓ as filling is impaired

→ LV systolic function ↑ to overcome obstruc"

C/F

Symptom :-

1) Earliest → Dyspnoea ← LA P' ↑ ← LV P' ↑

2) Angina ← ↑ LV workload.
+
Coronary vessels compressed by hypertrophied myocytes

3) Syncope ← Fixed CO [CO will not ↑ during demand]

4) * **Sudden cardiac death**

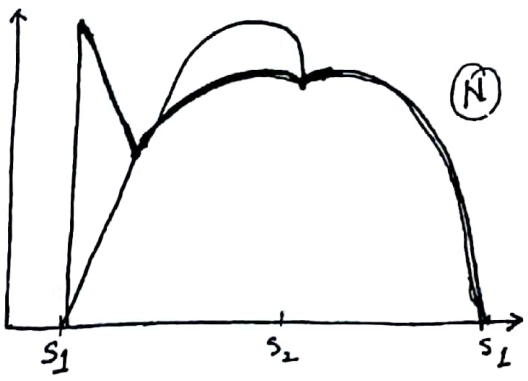
→ Irreversible loss of cardiac func"
c in 1 hour of symptoms

→ HOCM is M/cc.

- SCD is due to ventricular arrhythmias due to ischaemia
↓
Na⁺/K⁺ atpase.

Signs:-

1) Pulse = Bifid
or
Pointed finger pulse



2) JVP :

If hypertrophied septum bulge into (R) atrium

Bernheim's effect → RV 'P' T

- a ↑
- y slow

Systolic func" ↑ - Brisk ventricular contrac" → Percussion wave will be early + Tidal wave low due to obstruc" of blood flow

3) Apex = Double / Triple

4) S_1 = Intensity soft

S_2 = Split Reverse

S_3 = Rare

S_4 = LV S_4 ++

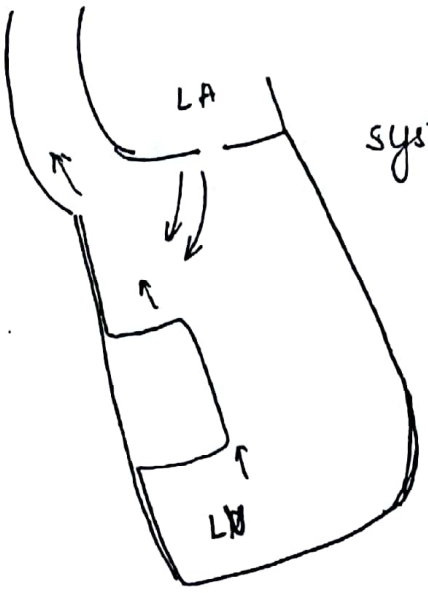
A_2 late ↑ LV ejection time ↑ (due to obstruc")

QQ

5) Most characteristic sign:-

Type → Ejection systolic

Site → (L) 3rd ICS Erb's area



(SAM)
systolic ant. movement of mitral valve towards septum
↓
further ↑ing the obstruc^{n}.

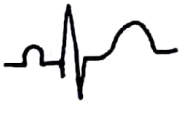
2 most imp factors affecting obstruc^{n}

① Contractility
if ↑ → SAM ↑ → obstruc^{n} ↑

② Blood in LV if ↓ → obstruc^{n} ↑
(preload)
(Blood act as physical barrier separating MV & septum)

Drug
Digoxin. C/I in HOCM.
Diuretics
Veno Dilators

Inv
1) CXR → cardiac size (N)
2) ECG →
(N)



HOCM
QRS amplitude ↑
depth > 10mm
Giant Inverted Twave

3) Echo - $\frac{\text{septum thickness}}{\text{LV free wall thickness}}$ · $\frac{3}{1}$ [reversed from (N)]

Rx

1) β blocker → Initial DOC

If CI → Non DHP CCB.

Doesn't prevent sudden cardiac death.

2) AMIODARONE

given if post H/o ventricle arrhythmia

3) Implantable defibrillator. Device (intracardiac)

↳ prevent SCD

4) Septal artery sclerosis [ethanol]

↓

causes regression of septum.

LMR

ARF

12/2/18

Cause :-

Hypersensitivity reac^{n} to Group 'A' β haemolytic Streptococci [Pharyngitis]

Type II HSN Reac^{n}.

C/F & Inv :-

Modified Jones Criteria

Major :- (5)

① **Arthritis**

Unique features

M/c major manifestation

Large joints

asymmetrical

migratory

Non-erosive (non-deformity)

Polyarthritis

Duration ≤ 4 wks

Exception - JACCOUD's arthropathy (deformities +)

② **Carditis**

M/c cause of Death = CHF

M/c layer = Endocarditis

M/c valve = Mitral

M/c Lesion = MR

L/c Valve = Pulmonary

Hypocarditis = no necrosis

[Troponin - N]

Pericarditis → Tamponade, Constrictive Pericarditis — very rare

M/c Valvular Lesion in RHD = MS

Rx

DOC - Aspirin 75mg / 1g / day

~~DOC~~ Diuretic

↓ no response

Steroid

↓ no response

Valve replacement

③ **Sydenham's Chorea**

[Ab against basal ganglia, cerebral cortex]

Motor = Tongue fibrillation
+
Ext. Rotation of hand
["scooping"]
+
"Milking action"
Disappear in sleep
♀ > ♂
Late manifestation
> 1-7 months
Neuropsychiatric disorders

Sedation
↓ no response
Valproate.
↓ no response
IVIg QQ.
(for refractory cases)

④ **Subcutaneous Nodules**

Site: extensor surface
Non-tender
Size - 0.5-2 cm

No t/t required

⑤ **Erythema Marginatum**

Site - extremities
Trunk.
(never on face)
Serpentine edge
progress fast

t/t Not required

Minor Manifestation

Clinical

1) Fever (Mlc Symptom)
2) Arthralgias

Lab

1) ↑ ESR
2) ↑ CRP
3) ↑ PR interval on ECG.
4) [due to AV node inflammation]

Essential Criteria

1) Evidence of recent streptococcal infec" (<45 days)

h/o scarlet fever is removed now.

Any one of 3 criterias -

a) Throat culture +ve

b) Ab +ve for [ASO ↑ &/or AntiDNase]

c) Rapid Streptococcal Ag test

Minimum criteria needed to make Δ of

Clinical	Major	Minor	Essential
1) 1° ARF	2 major 1	– or 2	~~1 Ab~~ + +
2) Recurrent ARF		3	+
3) Recurrent ARF on established RHD	–	2	+
4) Sydenham's ~~chorea~~ chorea	–	–	–
5) ~~CHD~~ Indolent Carditis (c/out any Kn cause)	–	–	–

Changes in Jones Criteria.

Low Prevalence	High Prevalence
ARF < 2/1 lakh school going children	> 2/1 lakh [India].
Major	
Joint Involvement = Polyarthritis	Polyarthritis or Monoarthritis or Polyarthralgia
Minor	
Fever > 38.5°C	> 38°C
Arthralgia - Polyarthralgia	Monoarthralgia.
ESR > 60 mm/hour	> 30 mm/hour

Prophylaxis :-

1) 1° Prophylaxis :- Streptococcus pharyngitis ⟶✗ ARF

- Ab of choice = Benzathine Penicillin (1.2 mU) if > 27 kg — Single Dose
  ~~if > 27~~ 0.6 mU if < 27 kg.

Should be started less than 10 days of Pharyngitis

↓ if penicillin allergy

Macrolides (erythromycin or azithromycin)

27 2° Prophylaxis ARF ⟶ Recurrent ARF

Ab of choice = Benzathine Penicillin. (1.2 or 0.6 mU) every 3-4 wkly

↓ if allergy to penicillin

Sulfadiazine Q

↓ if allergy

Macrolides

Duration of 2° prophylaxis.

1) 5 years or till pt's age 21 yrs [whichever is longer]

2) 10 yrs or till pt's age 21 yrs. [whichever is longer]

3) India - Lifelong ideally
10 years till pt's age 40 yrs (whichever longer)

Clinical A

ARF c/out carditis

ARF c/ carditis

ARF c/ RHD established

D/D of ARF :-

1) Post-Streptococcal Reactive arthritis (PSRA):-
- Small joints
- Symmetrical
- Duration > 1 month.
- Poor response to aspirin.

(2) P - paediatric
A - autoimmune
N - neuropsychiatric → NO other ARF manifestations
D - Disorder
A - associated c
S - strepto c.

Complications of ARF.

VALVULAR HEART DISEASE.

MS

Cause- M/C - RHD

M/C non-rheumatic = congenital

Pathophysiology:-

↑ LA 'P' (dyspnoea early symptom)

⇓

↑ Pulm. Vein

followed by

↑ Pulm. artery 'P'

⇓

RV pressure overload

⇓ remodelling

RV [concentric hypertrophy]

⇓ Later

RV systolic failure

⇓

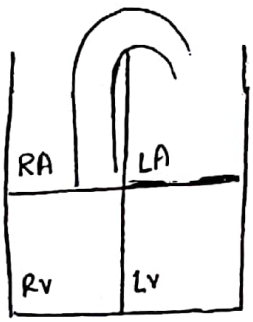
RV blood retention occur

⇓

RA 'P' ↑ ⟷ Systemic vein 'P' ↑

⇓

2nd site of stenosis → Pulmonary artery.



MR

M/C - RHD

M/C non-rheumatic = MVP

↓ CO

⇓

Gradual LA dilatation.

⇓ during diastole

↑ blood will move from LA to LV

⇓

LV volume overload.

⇓ remodelling

LV eccentric hypertrophy

COT

⇓ Later

LV systolic failure

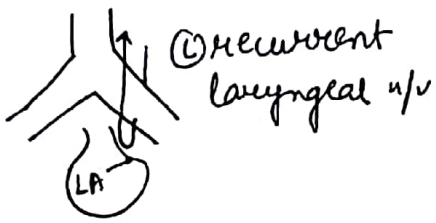
⇓

LA 'P' ↑

Symptoms	Mech
① Dyspnoea	← LA 'P' ↑
② Haemoptysis	← M/c source = Bronchial vein
③ Anasarca	← Systemic vein hydrostatic 'P' ↑

Symptoms	Mech
⊕① Fatigue	← ↓ CO
② Palpitations	← LV force of contrac" ↑
③ Dyspnoea	← LA 'P' ↑

④



Hoarseness of voice

[Ortner's syndrome]

Signs

	Due to AF	
Pulse - irregularly irregular rhythm	⊕	⊕
Pulse Deficit	⊕	⊕

due to AF

JVP →

Reverse occur

Absent	Prominent
a	v
x	y

Apex - LV (N)

Site - (N)

Nature - Tapping

LV - Dilated + vol. overload

Site - shifted laterally

Nature - Hyperdynamic

Auscultatory signs

S_1 = Loud
exception - if calcified valves

S_2 = split - wide

if RVF occur → P_2 late.

S_3 = never LVS_3

if RVF → RVS_3 +

S_4 = if RVH → RVS_4

Opening snap : +ve
becomes ⊖ if calcified valves.

Murmur

(1°)

Typ = mid-diastolic

Site - Apex

Pitch = Low pitch

if pressure gradient <40 mmHg = low pitch murmur

Radiation - Nil

Best pt's position - (L) Lateral Decubitus

Phase - expiratory

S_1 = soft

S_2 = split → wide

LV ejc° time ↓ = A_2 early

S_3 - LVS_3 ++

S_4 : LVS_4 ± [in late MR due to extreme LV dilatation making it stiff]

Opening snap = -ve

(1°)

Typ - pan-systolic

Acute MR = early systolic
MVP induced = Late systolic

Site - Apex

Pitch - High pitch

Stenotic lesions are low pitch
Regurgitant " are high pitch

Radiation - Interscapular area
Axilla

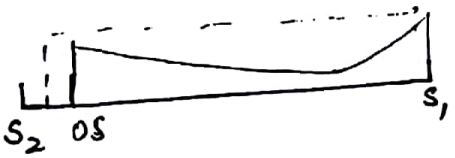
Best pt's positon - (L) Lateral decubitus

Phase - expiratory

2° murmur = ⊖

Clinical Criteria for severity

1) Opening snap
S_2-OS gap inversely related to severity



2) Length of murmur is directly related to severity

Ix

ECG- Sequence

① Ⓛ atrial enlargement

↓

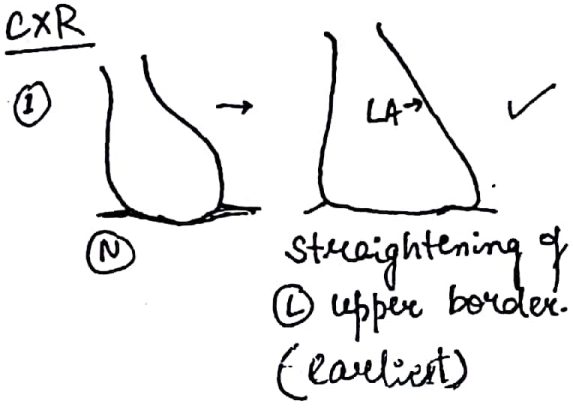
② RV H signs

↓

③ RA enlargement

Biatrial enlargement = due to Ms

CXR



2° murmur

↑ blood flow across MV 63 during diastole due to ↑ blood.

= mid-diastolic murmur

= Functional Ms → severe MR

1) Apex = shifted laterally

2) S_2 = wide split

3) S_3 = trace of LVS$_3$

4) murmur = mid-diastolic

Loudness or intensity is never a criteria for severity in Valvular Heart Disease

Ix

ECG

1) LAE

↓

2) ~~RVH signs~~ LVH signs.

CXR

✓

② Double atrial shadow

very rare.

Rx

Severe MS [area < 1.5 cm²]

(N) - 4-6 cm²

↓

NYHA symp

- ≥ II [symptomatic] → Sx
- I [asymptomatic] → AF
  - ⊕ → Consider Sx
  - ⊖ → observation

Severe MR

↓

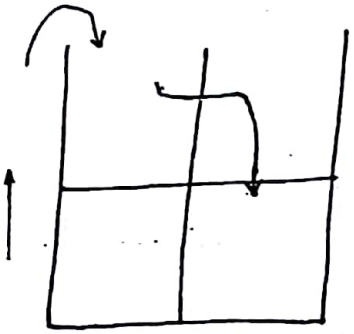
NYHA symp

- ≥ II [symptomatic] → Sx
- I [asymptomatic] → AF
  - AF ⊕ or LVEF < 60% → Sx
  - AF ⊖ or LVEF > 60% → observation

Sx

Preferred Sx / Initial Process of choice / Sx in ♀

Balloon valvotomy



Done under Lung-Heart Bypass machine.

Preferred Sx = MV Repair

↓ If not possible

MV Replacement

Criteria:

1) Isolated MS
2) no calcification
3) no LA Thrombus

↓ if not fulfilled

MV Replacement

Metallic	Bioprosthetic
Dur. 25yrs	5-10yrs
Anticoagulation = lifelong	X
Age Preference = young	elderly

Q. 26yr old, unmarried ♀. K/c/o RHD ē MS
c/o - dyspnoea on 10 steps. Echo = MVA 0.8cm².
Next Line Rx
a) observation
b) baloon valvotomy
c) Bioprosth, MV replacement
d) Metallic, MV "

Q. same history. O/E - opening snap (+ve.)
ans - (b)

Q. Same history, O/E - Pulse Deficit +20 (AF), opening snap (-nt) calcification.
ans - (d)

Q. Same history. married. OE - opening snap (-), MR (+)

ans → (d)

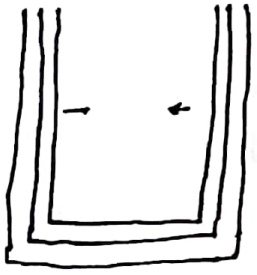
Give heparin in 1st Trimester
anticoag in 2nd Trimester - 3rd
heparin in ~~3rd~~ " delivery.
2 wks prior to.

AS

Cause - M/c age related calcification

Pathophysiology:-

LV pressure overload
↓ remodelling

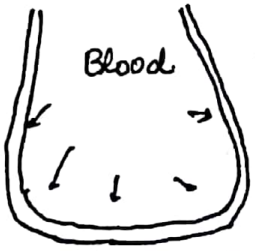


LV (concentric) Hypertrophy
↓ Later
LV systolic failure
↓
LA 'P' ↑

AR

M/c - age related degeneration

LV volume overload.
↓ remodelling



LV (eccentric) Hypertrophy
↓ Later
LV systolic failure
↓
LA 'P'

Symptoms :-

Mech.

~~1> Due to~~

1> Angina ← ↑ LV workload

1> Palpitations ← LV force of contraction ↑

2) Syncope ← Fixed CO

3) Dyspnoea ← LA 'P' ↑

[Worst Prognosis]

↓

Mortality ↑ in 1½ yr even ↑ medical Mt

Signs:-

1) Pulse - Most specific

Parvus et tardus

2) Apex - LV 'P' overload

↓

Site = (N)

Nature = Sustained

3) S_1 = Soft

S_2 = split = reverse

LV ejec° time ↑ → Late A_2

in early stages → narrow split

S_3 = + if LVF occurs

S_4 = ++

Ejection click = (+)

2) Angina [Nocturnal]

← ↓ in Diastolic BP ∴ less perfusion

↓

This occurs more during night as sympathetic activity ↓ further ↓ vascular tone.

3) Dyspnoea ← LA 'P' ↑

Most specific.

= Bisferiens

LV Dilatated + Vol. overload

Site = Shifted Laterally

Nature = Hyperdynamic

S_1 = Soft

S_2 = Single P_2.

aortic valve leaflets fail to strike.

S_3 = ++

S_4 = + Late AR.

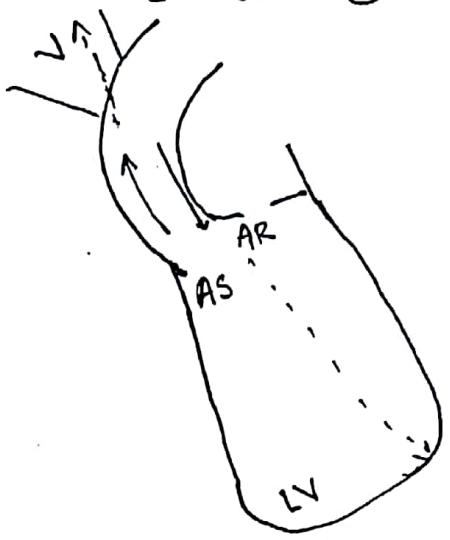
(−)

47

1° Murmur

Type: Ejection Systolic murmur

Site: Ⓡ 2nd ICS [Aortic area - 1st]



Pitch: Low

Radiation: Common carotid [or neck]

after striking arch of aorta

Radiation to apex

= GALLAVERDIN PHENOMENA

Best Pt's Position = Leaning forward. ✓ ✓

Phase - expiration ✓

Type: Early diastolic

Site: Ⓛ 3rd ICS [Erb's Area]

2nd Aortic Area

or

Neo-aortic area

Pitch = high

Radiation = towards apex

if radiation to axilla

= COLE - CECIL MURMUR

2° Murmur

Not seen in AS

1) Austin-Flint murmur
mid-Late diastolic

2) Functional AS
↑ Blood flow across aortic valve
[Ejection Systolic]

Clinical Criteria for Severity

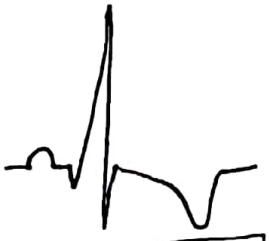
1) S_1 = Soft
2) S_2 = Reverse split
3) S_3 = (+)
4) S_4 = (+)

* **Severe Silent AS**

1? associated MS] ↓CO → Hence sound (−)
2? LVF]

I_X

ECG = Sequence
① LVH Signs
↓
② LA enlargement



ST Depression
T inversion
→ Strain pattern

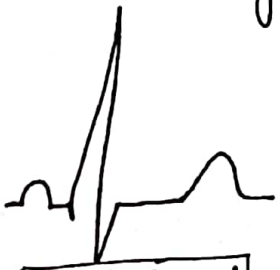
CXR
Cardiac Size = (N)

1? Any peripheral Sign of AR
2? Pulse - Bisferiance
3? Apex - Displaced Laterally
4) ~~S_1~~ - soft
5? S_3 - (+)

Q
6? 1° murmur = **Duration.**

7? Presence of 2° murmur
= Austin-Flint murmur

ECG = sequence
①. LVH
↓
② LA enlargement



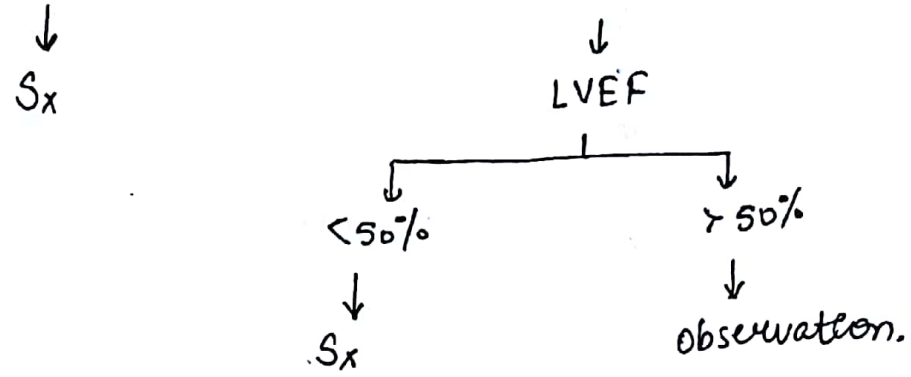
ST Normal
T upright
as inner myocytes receive blood from cavity

CXR
enlarged

R_X

Similar
Severe AS or severe AR
[Area <1cm²]
↓
NYHA symptoms

≥II (symptomatic)
I (asymptomatic)



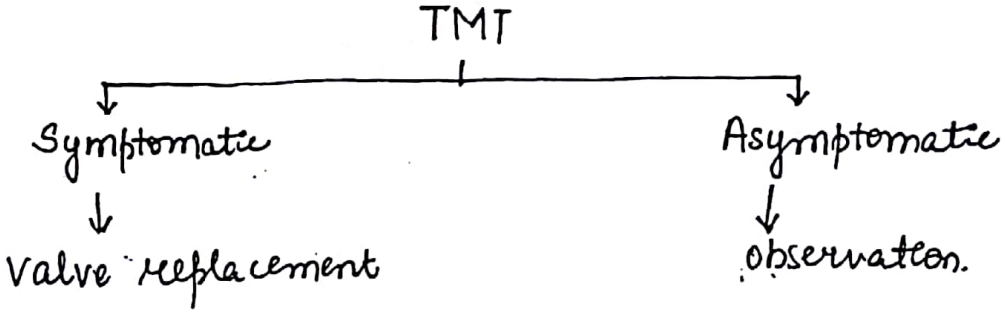
Preferred Sx = Aortic Valve Replacement

Q. 60yr old ♂, ē Aortic valve pressure gradient of 60 mmHg. K/c/o AS, c/o - equivocal dyspnoea symptoms. Next step. ?

Ans. a) observation
b) Trade mill test
c) Aortic valve Replacement
d) Diuretics.

Q. Same pt. underwent treadle mill test [Bruce Protocol] c/o Dyspnoea & Fatigue at 11 min of exercise. Next step

Ans.



Bruce Protocol

Bruce Stage	Duration
I	0 - 2:59 min
II	3 - 5:59 "
III	6 - 8:59 "
IV	9 - 11:59 "

Pt. considered symptomatic if c/o dyspnea/fatigue ≤ Stage II

Asymptomatic if c/o dyspnea/fatigue ≥ Stage III

* Severe AS + NYHA-I + underlying CABG = Aortic valve Replacement

(R) SIDED VALVULAR LESIONS

Lesion	M/c Cause	Other causes
1) TS	RHD	(X)
2) TR	RV dilatation. [eg. Pulmonary embolism] cor-pulmonale	M/c Valvular Lesion due to CARCINOID
3) PS	Congenital	Carcinoid, Rubella
4) PR	PAH	Carcinoid

Valve fibrosis → Regurgitation

Ring fibrosis → stenosis

LHR INFECTIVE ENDOCARDITIS

CAUSE :-

Predisposing Causes

1) M/c Valvular Lesion = MR > AR.

2) M/c congenital HD = VSD [® ventricle has vegetation]

3) M/c cyanotic cong. HD = TOF [Ⓛ ventricle has vegetation]
↳ systemic embolism.

4) Least common HD leading to IE = ASD

5) MC non-CV risk = " " " = IV Drug Abuse

Micro-organisms

* According to nature of valve affected.

NATIVE

- Community acquired — M/c - Strepto. Viridans
- Hospital acquired — M/c - Staph aureus

Overall M/c = Staph. aureus

PROSTHETIC

- < 12 months after Sx — M/c - Coagulase neg. Staph
- > 12 months of Sx — M/c - Strepto viridians

Overall M/c = coagulase neg.

Max incidence = 6-12 months

HIV is the only virus to cause IE.

* According to Onset of

- **Acute** [<2wks]
  - M/c = Staph aureus
  - other
    - Strepto β-haemolytic
    - Fungus
- **Subacute** [>2wks]
  - M/c = Strepto. Viridians
  - other
    - Staph coagulase neg.
    - Fungus

* Typical Bacteria of IE
  1) Strepto Viridians
  2) " Bovis [Gallolyticus] → ass/c Colonic cancer/Polyp.
  3) Staph aureus → M/c in IV Drug Abuse → (R) sided
  4) Enterococci → M/c in IV Drug Abuse → (L) sided.
  5) HACEK group

C/F + Ix

Modified DUKE's Criteria

- 2 MAJOR
- 5 MINOR
- 3 EXCLUSION

* **Major Criteria** -

(I) Evidence of micro-organisms consistent c IE.

1) ≥ 2 Blood culture (+) of Typical Bacteria
   or
2) Persistent Bacteremia of micro-organism consistent c IE.
   or
   - ≥ 2 Blood culture (+) [separated by 12 hours]
   - ≥ 3 Blood culture (+) out of ≥ 4 samples [1st & last sample separated by 1hr]

3) ≥1 Blood Culture } of Coxiella Burnetti
or
IgG↑

(II) Evidence of Endocarditis. [ECHO]

↓

① Oscillating Mass Lesion on valve or its structure
or
② Intra-cardiac abscess
or
③ New valvular regurgitant lesion ← M/c CVS complication of IE.
or
④ Partial Dehiscence of prosthetic valve

* **Minor Criteria**

1) H/o Predisposing cause = RHD, I.V. Drug Abuser.

2) Fever >38°C ← M/c symptom

3) Immune phenomena = RROG

R → **Roth's Spots** → Immune complex vasculitis in Retina
Oval
Pale centre ± haemorrhagic margin

Other causes.
a) SLE
b) CLL

O → **Osler's Nodes** → Immune complex deposits in Finger tips / Palms / Soles.
Tender
Palpable

G → GN → Immune complex deposited in
S. C_3 level ↓

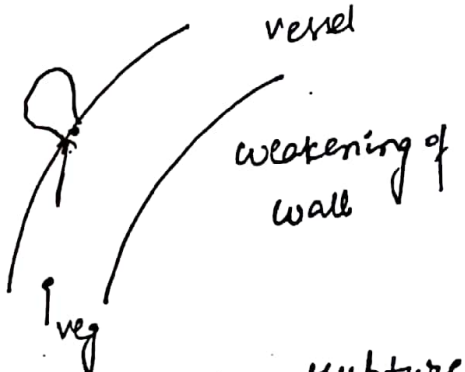
R → RA factor +ve

4Y Vascular Events

* Major Arterial Embolisation
  [L sided] M/c site → Brain [MCA territory → Parietal > Spleen
  M/c organism → Staph Aureus
  M/c valvular IE → Mitral valve

* Septic Pulmonary Infarcts
  [R sided].

* Mycotic aneurysm



* Haemorrhagic stroke [if mycotic aneurysm rupture in Brain ∃

* Conjunctiva petechae.
  M/c Peripheral Sign of IE.

* Janeway Lesion = Palms.
  Macular [non-palpable]
  Non-tender

5Y Blood Culture Positive of micro-org consistent ∴ IE
(not satisfying major criteria)
or
Serology +ve

Definitive Δ of IE = 2 Major
or
1 Major + 3 Minor
or
All 5 minor

* **Exclusion Criteria**

1) Firm alternate Δ of Fever established.
2) If fever subsided in 4 days of Antibiotic Use.
3) If there is no histopathological evidence of IE < 4 days of Antibiotic Use.

Rx + Prophylaxis of IE = given in supplement.

14/2/18

CARDIOMYOPATHY

Definition :-
Diseases of **endomyocardium**
Not due to ↑ valvular Heart disease.
2) Cong. Heart disease
3) HTN
4) Ischaemia
5) Pericardial Disease

Types :-

- Dilated CMP (M/c pattern)
- HOCM
- Restrictive CMP (Least common)

Dilated CMP
↓ Defect:
↓ contrac"
⇓
↓ in systolic func"
+
Preserved diastolic func" till late stages

HOCM
Obstruc" to LV outflow
⇓ overcome obstruc"
↑ in systolic func"
+
(↓ cavity space)
↓ diastolic func"

Restrictive CMP
Failure of relaxation
⇓
↓ in diastolic func"
⇓
systolic func" preserved.
Gross atrial Dilatation"

DILATED CMP

CAUSE - I) **Idiopathic** (M/c cause)
Rx - supportive. [chr. HF ∴ low EF]

II) Mc 2° cause - **alcohol**
Mech :- a) Direct ethanol effect
b) Becoz of Cobalt [cardiotoxic agent]
(↓ foam stabilizing agent)

Risk :- Mutation of alcohol dehydrogenase
· Mutation of ACE (?)

Dose of alcohol :- ≥120 gm/day for 5-10 years

Rx = reversible. ∵ in 3-6 months of cessation.

Other CVS manifestations of alcohol (>30g/d)

1) Dyslipidemia
   a) M/C = ↑ TG
   b) ↑ HDL Q.
   c) ↑ LDL

Ethanol
↓ ⊖
FA metabolism
↓
TG↑ ← FFA↑

2) Effect on BP
   Acute - vasodilatation = (↓ BP)
   Chronic - ⊕ sympathetic system = (↑ BP)

3) CVS events
   a) CAD → ↓ risk by ↑ HDL [French paradox]
   b) stroke → (↑ risk) due to ↑ BP
   c)

4) Arrhythmia
   alcohol binge → (AF) [Holiday Heart Syndrome]

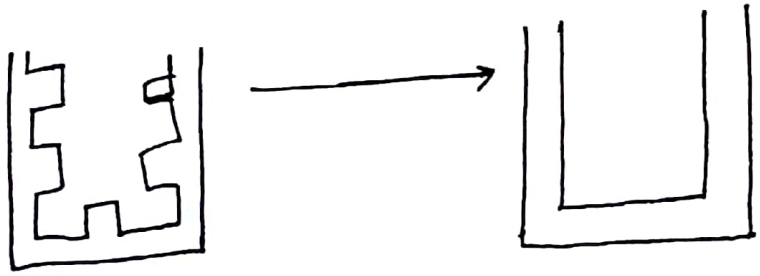
III) Genetic Causes

MOI	Q. Gene/Protein	Unique feature
1) AD	TTN / Titin → sarcomere protein. (N) helps in contrac"	M/c genetic cause of DCMP
2) AR	DSP / Desmoplakin → Desmosome protein (N) helps in synchro. contrac"	Arrhythmogenic RV Dysplasia. (ARVD) → sudden cardiac death in young population.
	NAXOS Disease	- {woolly hairs + thick palmar skin + ARVD}
3) X-R	TAZ / Tafazzin → (N) helps in compaction of ventricle cavity during embryonic development	LV non compaction. * LV thrombus since birth.

(N) V_1 =

ECG. ← epsilon wave.

V_1 -



Embryonic

IV Post Myocarditis

Causes :-

Infectious

1) MC viral - Coxsackie B
other viral infe"
- Parvovirus B19
- HIV
- Hepatitis C

2) Bacterial
M/c - Diphtheria [death is by myocarditis]
R_x - anti-toxin

3) Protozoa
M/c - Trypanosoma Cruzi
[chaga's Disease]
R_x - Benznidazole

4) Parasite
M/c - Trichinella
R_x - albendazole

Non-infectious

1) M/c - Sarcoidosis [lung involves]
M/c site → LV free wall
M/c pattern → DCMP > RCMP
R_x = steroids

2) Giant cell Myocarditis
(no lung involvement)
R_x - steroid.

3) Hypersensitivity Myocarditis
cause - Thiazide
Indomethacin
Methyldopa
R_x - cessation of drug
± steroids

Q V. Tako-Tsubo CMP / BROKEN HEART SYNDROME / APICAL BALOONING SYNDROME

C/F - ♀ + ↑ catecholamine release
⇓
vasoconstrict of LV apex
⇓
LV apex non-contractile
⇓
During systole RV apex bulge out in systole like ballon.

Ix - ECG - ST↑
Troponin = ↑ or Ⓝ
coronary angiography → no thrombus
ECHO - LV apex bulging out in systole.

→ resembles a jar used to trap octopus
⇓
hence called Tako-Tsubo.

Rx - reversible, so supportive therapy
+ α blocker followed by β blocker [like Pheochromocytoma]

VI. Peri-Partum CMP

Mech:- 1) Autoimmune damage to myocyte by foetal Ag.

2) Prolactin fragments → myocyte damage

C/F:- occur in 3rd trimester - 6 months post delivery

Risk ↑ → Twin Delivery
multipara
age > 30 yrs

Rx - 1) Diuretics

2) **Bromocriptine** [by ⊖ Prolactin].

↳ also used in Type 2 DM.

RESTRICTIVE CMP

Pathology :- Infilteration → Fibrosis

(I) Infilteration

A> In between myocytes

eg. Amyloidosis ← M/cc of RCMP

Types	Protein/cause	C/F	Rx
1> 1° amyloidosis	AL / multiple myeloma Waldenstrom macroglobulinemia NHL	Age - >50 yrs M/c organ - Renal M/cc = CVS of death unique - Black or Raccon eyes.	underlying disorder.

Factor Xa adsorb on AL protein leading to ↓ in blood → blood def. of Xa. [ecchymosis]

2> Familial	Transthyretin [liver] ↑ genetic	Age > 20 yrs M/c = CVS organ M/cc of death - CVS unique = ascending neuropathy	1) Liver Transplant only cond" where liver Transplantation is done ☐ out Liver failure

New Rx
TAFAMIDIS
↳ stabilizes ↓ transthyretin

3) Senile Cardiac Amyloidosis — Transthyretin ↳ Age. — Age > 70 yrs — Tafamidis

M/c organ } - CVS
M/c cause of death }

* 2° amyloidosis doesn't cause restrictive CMP
* ECG will show Low voltage QRS as amyloid is poor conductor
* ECHO = ↑ ventricle wall QRS

(B) Infilteration Inside Myocyte.

1) Haemochromatosis

M/c pattern of CMP → DCMP > RCMP

M/c of death in untreated pt → CVS

M/c of death in treated pt → HCC

Rx - Phlebotomy → [CMP is reversible]

2) Fabry's Disease

cause - Def" of α-~~glu~~ galactosidase
↓
Glycosphingolipid accumulate

C/F.

1) CVS → RCMP

2) Kidney → (GBM damage)

3rd H/c systemic cause of Nephrotic Syndrome

3) Abdomen - Angiokeratoma ?

Ix - Kidney Bx = GBM. ≡ Zebra Bodies
(electron microscopy)

Rx

Recombinant Galactosidase. [stop the progression of Ds]

(II) Fibrosis

1) Radiation [Ca breast/lung] } Supportive Rx.

2) Systemic sclerosis

3) Loeffler's Endocarditis

Eosinophilia

Release of ↓ Basic Protein.

Fibrosis

Rx - Steroid (by ↓ eosinophils)

CHF

ACUTE HF

↑

Acute MI
HT
Arrhythmia
IE

CHRONIC HF

Low EF [<40%]

↓ CO will reduce

Systolic failure

↑

eg. DCMP
Late AS, AR, MR

Preserved EF [>40-50%].

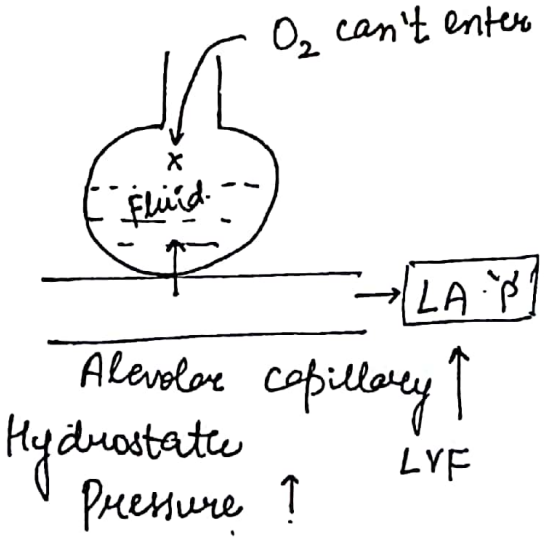
Diastolic failure

↑

eg. HOCM.
RCMP
Ageing Process

Rx of Acute HF :-

Acute HF = Acute cardiogenic Pulm. edema



AIM OF Rx - Shift alveolar fluid into capillaries

↓

by ↓ capillary hydrostatic pressure

⇓

Achieved by ↓ (R) sided Preload

1> Diuretic [Furosemide]
+
2> Morphine [venodilator]
+
3> O_2 inhalation.

← Initial Rx

↓

Systolic BP

↓ <90

Cardiogenic Shock

[cardiac index <2.2 L/min/m² + SBP <90 for >30 min]

↓

Add -

DOC - NOR-EPINEPHRINE

↓ 90-100

Add - Dobutamine

[slight vasodilator effect also]

↓ >110.

↑CO by ↓ afterload.

Add. Vasodilators

N - Nitroprusside

N - ~~Nitro~~ NTG

N - Nesiritide

Rx of Chr. Heart Failure ⊃ ↓ EF.

↓

Fluid Overload

⊕ ↓

Diuretic

⊖ ↓

Standard t/t

1> ACE Inhibitors.

By ↓ remodelling + ↓ afterload.

+

2> β blocker

By ↓ workload + ↓ sympathetic activity

a> Metoprolol
b> Carvedilol
c> Bisoprolol.

← t. vasodilatoralso

if | no response

↓

Add

↓

by ↑ contractility (or) ↓ remodelling (or) ↓ aldosterone effect

Digoxin | ~~ACE~~ ARB | ↓ Spironolactone

Chr. ↓ CO → chr ↑ aldosterone (by ⊕ RAAS)

↓

Fibrosis

↙ ↘

Heart | Blood vessels

Rx of Chr. HF ~ Preserved Ejection Fraction

↓

Rx ppt. cause

Cause - Thyrotoxicosis

♀

Anaemia

Rx underlying cause

HOCM

RCMP

Aging

↓ calorie intake

↓

↑ Sirtuin protein ♀♀

(Anti-oxidant)

PERICARDIAL DISEASES

Acute Pericarditis

→ Recovery (c out any complication)

→ (or) Pericardial effusion → if ↓ rapid → Cardiac Tamponade

→ (or) Constrictive Pericarditis

ACUTE PERICARDITIS

[ause- M/c- Idiopathic

Symp-
1) M/c- chest pain [due to rubbing c mediastinal pleura]

?

Ac. Pericarditis

Site- M/c Retrosternum

Nature- sharp pain

Radiation - Trapezius

Aggravating factors - Supine (as area of contact c pleura ↑)

Releiving factor - Leaning forward
Not relieved by nitrate

Ischaemic Pain

Retrosternum

Dull / constricting

Never sharp

(L) arm. forearm

Never Radiate to Trapezius

Exertion
Cold Temp

Rest
Sublingual nitrate

Sign - Most Specific ⇒ Pericardial Rub.

- Crackling sound due to rubbing of 2 inflammed pericardial layers
- Diastolic Phase

Ix

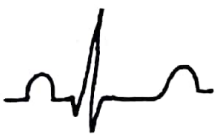
ECG :-

Stage of Ac. Pericarditis

I

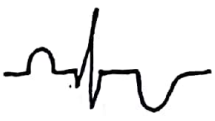
PR segment depression +
ST concave upwards ST elevation
[Smiling Phase ST elevation]

II



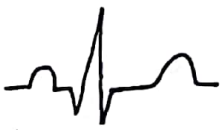
ST (N) + PR segment (N) or remain ↓

III



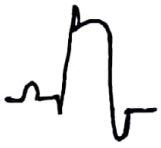
T wave inversion

IV



(N) ECG [recovery phase]

ECG

	Ac. Pericarditis	Ac. MI
① ST ↑	concave upward	convex upward.
② ST ↑ seen in	all lead. almost except - ~~aVR~~ aV_R, V_1	Specific lead
③ ST (N)	followed by T inversion	T inversion occur before T normalise 
④ trace of reciprocal ST depression in Opp. wall lead	⊖	⊕
⑤ Pathological q wave [indicate myocardial necrosis]	⊖	⊕  Deep q wave depth > 25% of R wave + Duration > 1 mm.

Rx - 1) Underlying cause

2) Idiopathic.

DOC → NSAIDS

↓ no response

Colchicine → (no response) → steroid

anti-inflammatory +

anti-fibrotic

TAMPONADE

Cause - M/c (overall) - idiopathic
M/c in India - TB

Pathophysio - Acute
"Compression" of heart + venous roots + Aortic roots
↓↓ venous return (40-50mL) ↓↓ CO

Compensatory vigorous ventricle contrac" to maintain CO.

Obstructive or shock
Compressive

Symptoms -
M/c → Dyspnoea due to ↓ in resp. M/s perfusion

* Not due to Pulmonary congestion.

Lungs - Oligemia

Signs -
Pulse - Pulsus Paradoxus
≥ 90% cases
↓
⊖ in Tamponade

CONSTRICTIVE PERICARDITIS

idiopathic

TB

Chronic
"Failure of relaxation" of heart due to stiff. Pericardium + CO is preserved
↓↓ venous return (100mL)

Compensatory vigorous ventricle contrac" to maintain CO

M/c → Swelling
due to the ↓ in venous return.
⇓
Hydrostatic 'P' ↑ in systemic veins

≤ 1/3rd cases

Absent Pulse Paradoxus in Tamponade

Tamponade

1> AR

2> CHF

JVP — Deep x

Vigorous RV constriction ⇓ Tricuspid ring pulled downward

Deep x

y = Absent

a = Prominent

y = Rapid

v = Prominent [failure of relaxation of RA]

Kussmaul sign = ⊖ as venous return doesn't ↑ significantly in Tamponade

⊕

Apex - Non-Localised

Non-Localised

S_1/S_2 — soft

soft

S_3/S_4 — ⊖

⊖

Pericardial knock ⊕ [3rd HS]

Ix

① CXR - ↑ cardiac shadow (Not true cardiomegaly)

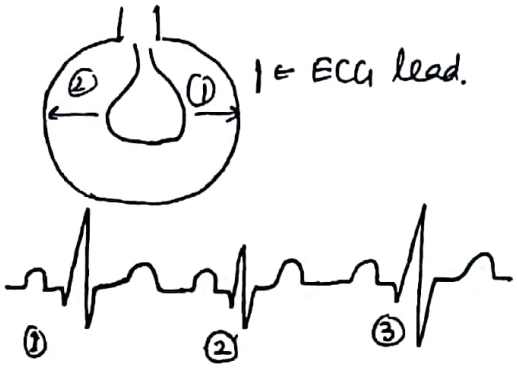
← Margins Smooth. + Lung field oligemic

CXR - cardiac size normal + calcified pericardium

2) ECG =

QRS amplitude ↓

[Electric alternans]



I = ECG lead.

ECG

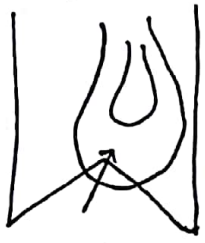
QRS amplitude ↓

[Non specific ST ↓ or T ↓]

Rx

Emergency Pericardiocentesis

Routine - Pericardiectomy



[ECHO]

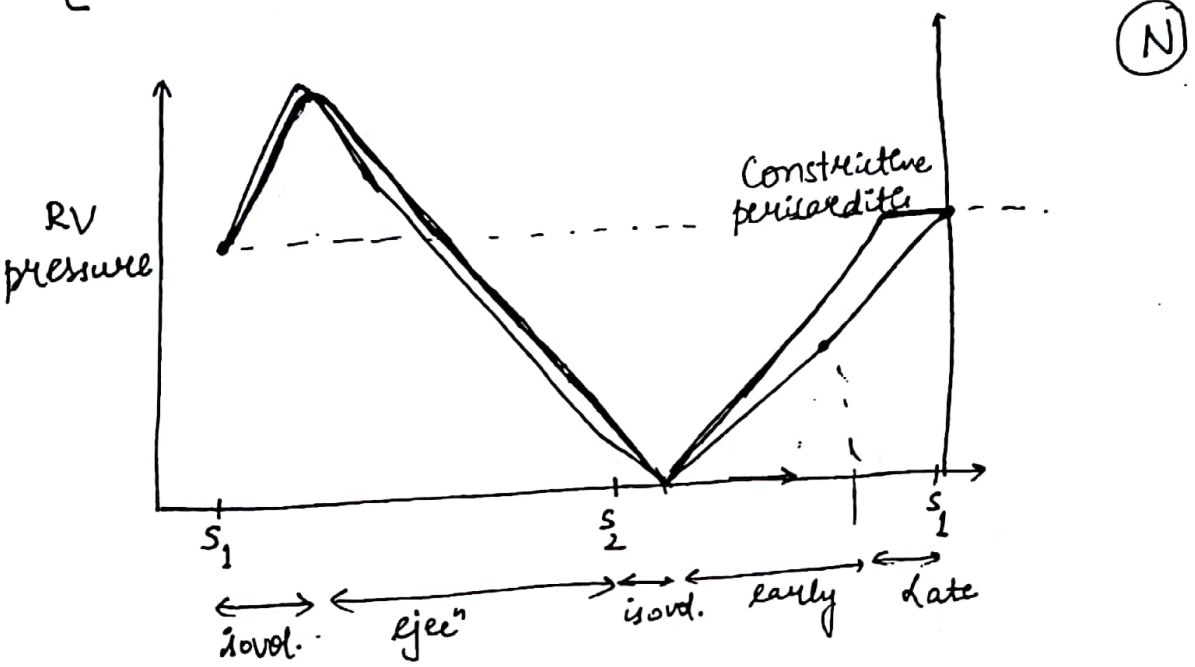
Needle [Subxiphoid area]

Signs	Description	Best Δ
1) Auenbrugger's Sign	Epigastric Bulging	Massive pericardial effusion
2) Beck's Triad	↓ BP + ↑ JVP + soft HS	Tamponade
3) Ewart's Sign.	compress (L) side airway ⇓ Collapse of distal lungs ⇓ Bronchial Breath sound (L) Infrascapular area	Massive Pericardial Effusion

4) Broadbent's sign — systolic retraction of apex due to fibrous pulling — Constrictive Pericarditis.

"Square root" sign → Constrictive Pericarditis.

[Pressure changes in RV]



LMP

SYSTEMIC HTN

Classification [AHA guideline NOV 2017]

	SBP		DBP
1) Normotensive	<120	AND	<80
2) Elevated	120-129	AND	<80
3) Stage I HTN	130-139	(OR)	80-89
4) Stage II HTN	≥140	(OR)	≥90

Causes

I. Essential / 1° HTN (no identifiable cause)
M/C cause

II. 2° HTN (identifiable cause)

↓

1) M/c 2° cause - Reno-Parenchymal
[GN, Chr KD.].
Mc Mech → vol. overload

2) 2nd M/cc of → Reno-Vascular
[Renal artery stenosis]

Mech - ⊕ RAAS

DOC - ACE-I in U/L stenosis

3) Activating Mutation of Sodium channel of tubules.

↓ DCT - Na^+ Cl- channel
Δ GORDEN'S SYNDROME

↓ CD = ℮ Na^+ channel
Δ - Liddle's Syndrome

DOC - Thiazide DOC = Amiloride.

47. Endocrine causes.

	Endocrine	Type of HT	Edema
a)	Hypothyroid	DBP ↑ (Compress bld. vessels ←	⊕ Myxoedema
b)	Conn's Syndrome Chr. ↑ aldosterone ↳ vessels fibrosis	DBP ↑	⊖ ANP released ↓ "Escape" Mechanism
c)	Hyperthyroidism	SBP ↑ (due to ↑CO)	⊖
d)	Phaeochromocytoma	SBP + DBP ↑ sustained HT > Episodic HT	⊖

5) Miscellaneous Causes

a) M/C Cong. CV cause of HTN ⇒ Coarctation of Aorta

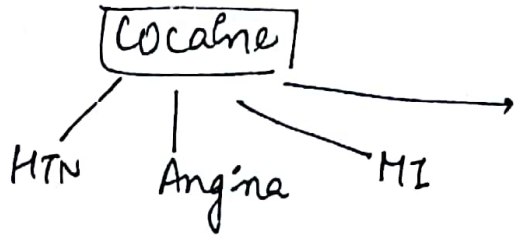
b) Systemic HTN ← sympathetic ↑ ⇒ Obstructive sleep Apnoea

+

Pulm. HTN ← hypoxia

c) PCOD = Insulin resistance
[acanthosis nigrans]

d) Drug NSAIDS by ↓ GFR
Corticosteroid
estrogen



Symptom

1) M/c - Dyspnoea [due to LHF]

M/cc of CHF = HTN

2) M/c symp due to HTN → Occipital Headache

3) Sign :) LVS_4 + (due to LVH)

I_X -

ECG Changes

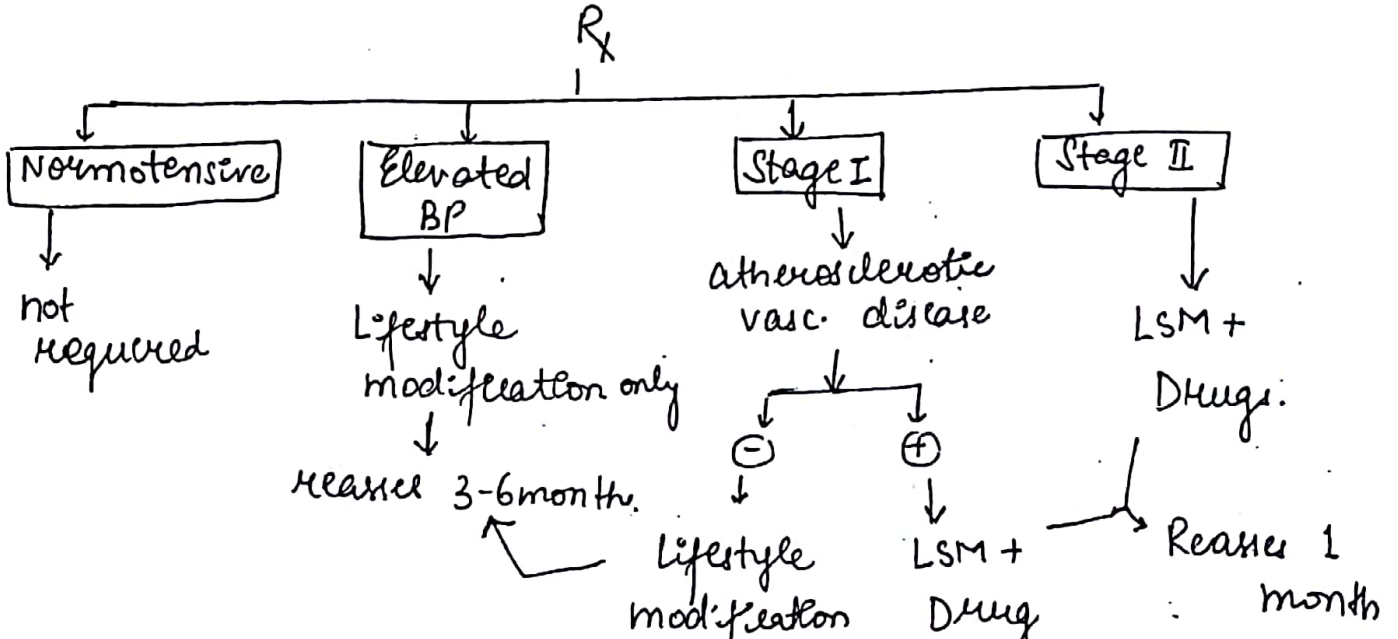
1) LVH signs

2) LA enlargement

3) LAD

R_X

Stable ≥2 reading on ≥2 occasions should be ↑ to Δ HTN



* Lifestyle Modification

1) wt. reduc"
2) ↓ Na ≤ 1.5gm/day
3) ↑ K 3.5-5gm/day cause smooth M/s relaxation
4) DASH DIET
   Dietary Action To Stop HTN
   ↓ Na^+, ↓ Fat dairy product,
   ↑ Fruits & Veg., ↓ saturated fat
5) Brisk Walk / Exercise ≥ 150 min/wk
6) Alcohol ♂ < 30g/d ♀ < 15g/d

Other Terms

1) Resistant HTN
   if BP ≥ 140/90 despite ≥ 3 drug (one of ⊆ is diabetic)
   or
   if BP < 140/90 ⊆ ≥ 4 drug
   H/cc → Non-compliance

2) White Coat HTN
   Incidence if SBP > 20 &/or DBP > 10 from non clinical readings.

3) HTN Emergency = if BP > 180/120 ⊆ Target Organ Damage

I.v. Labetalol	← 1)	Haemorrhagic Stroke
I.v. ~~Nitro~~ NTG or Nicardipine	← 2)	Ac. cardiogenic Pulm. Oedema
I.v. NTG	← 3)	Ac. MI
I.v. Esmolol	← 4)	Aortic Dissec"
Nimodipine	← 5)	SAH

* Mean BP reduction → 25% from presentation value
$\left[DBP + \frac{1}{3} PP\right]$ < 1-2 hrs.

100

* **DOC for HT Emergency = I.V. Nicardipine**

* 4) HTN Urgency = BP > $\frac{180}{120}$ + no target organ damage

R_x = combination of oral drugs.
[OPD]

5) Orthostatic Hypotension
if SBP ↓ by > 20] ☆ in 3 min of standing
DBP ↓ by > 10]

M/C cause → Hypovolemia

2° HTN associated ☆ ortho static HTN = **Phaeochromocytoma**

Chr. vol. depleted
↑
due to chr. vaso constrict°.

IHD

	Stable Angina	Unstable Angina	Non-ST ↑ MI (Subendocardial)	ST ↑ MI [Transmural]
Duration	= 2-10 min	20 min	20-30 min	> 30 min
Pain at rest	⊖	⊕	⊕	⊕
ECG at rest	Ⓝ	ST depression [except Prinzmetal Angina]	ST depression	ST elevation.
Troponins	Ⓝ	Ⓝ	↑	↑

Symptoms M/c → chest pain

Painless MI → Autonomic Dysfunc^{n} [DM, elderly]

↓

'Angina' equivalent symptoms

a> Unexplained sweating

b> " Dyspnoea

c> Sense of impending Doom

Signs M/c → LEVIN SIGN [Holding Palm or Fist against retrosternum]

Pulse - if tachycardia = Ant. wall

Bradycardia = Inf. wall

JVP - if Kussmall sign = RV MI.

S_2 = if split is wide = RVMI [late P_2]

if split is reversed = LVMI [Late A_2]

poor prognosis — S_3 - if ⊕ → indicate systolic failure [Infarct >40%]

S_4 - ⊕

[more common than S_3]

Murmurs -

- Papillary M/s Necrosis → Acute MR → Early Systolic
- Septal Rupture of ventricle → VSD → Pansystolic

Ix

(I) ECG

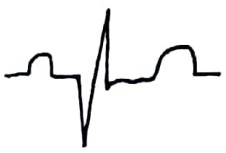
Sequence of changes — Mech

1) Tall T Wave — Leakage of K^+ [similar to hyperkalemia]

(>50% of R wave height)

2) ST ↑ (convex) Pardees Sign — Early Repolarisation of infarcted m/s

3) T↓ — Non-specific

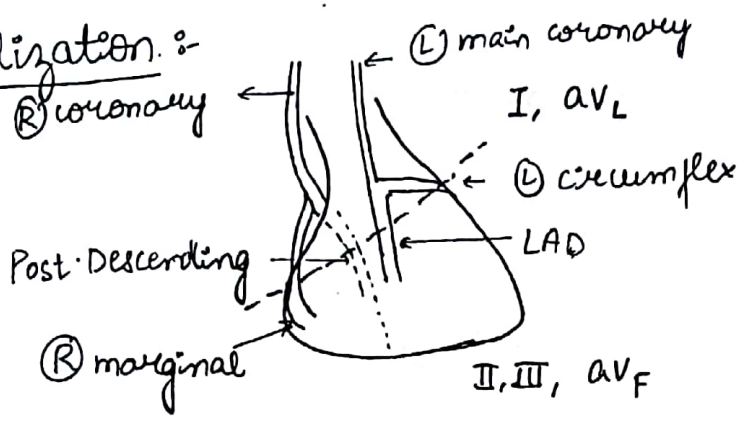
4) 

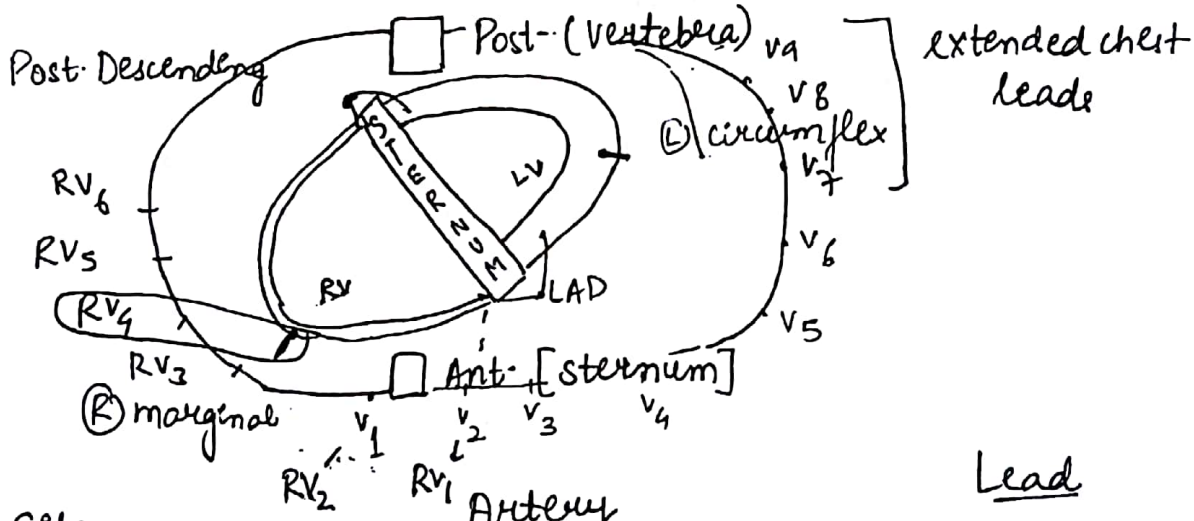
Pathological Q wave Q

Necrosis

NO use of thrombolytic therapy

Localization :-





extended chest leads

Site	Artery	Lead
① Anti septum	LAD	V_2 (V_1 or V_3)
② Ant. wall [LV]	LAD	V_3 V_4 (V_2)
③ Lateral wall	Ⓛ circumflex	V_5, V_6, I, aV_L
④ Post-wall	Post. Descending	V_7 - V_9 - ST ↑ or V_1 - V_4 → reciprocal ST ↓
⑤ RV MI	Ⓡ marginal	RV_4

⑥ Inf wall — ® coronary via post descending — II, III, aVF

⑦ Antero-Lateral MI — © main coronary — $V_1 - V_6$, I, aV_L

Rx OC = CABG (not PCI)
↓
not feasible

⑪ Cardiac Markers	Time to ↑ in blood (after symptoms)	Time to (N)
1) Heart Type FA Binding Protein	2 hrs	24 hrs
2) Myoglobin	3 hrs	24 hrs
3) Troponin I [Best] T	6 hr	10-14 days
4) CPK-MB	6 hrs	72 hrs

↳ Preferred over Troponin if re-infarc" 3-10 days

Troponin can be used in re-infarc".
if >20% ↑ from previous.

Rx ① ST ↑ MI

Initial Rx — Role

1> **Aspirin** [non-enteric coated] — Essential in all
Dose - 325mg chewable

2> **O_2 inhalation** ⟶ if O_2 saturation is ↓

3> **I.V. Morphine** ⟶ Analgesic
+
Ac. cardiogenic Pulmonary oedema
C/I in **RVMI**
[↓ Preload → further ↓ CO]

4> **Nitrate** ⟶ coronary vasodilatation.
+
If BP ↑
C/I - **RVMI**

5> **β blocker metoprolol** ⟶ ↓ workload
CI - Asthma
PR interval > 0.25 sec

6> **ACEI.** ⟶ All pts. for initial 48 hours
↓
continue if HT (+)

7> **High Dose Statins** ⟶ Anti-inflammatory +
Plaque stabilising Property.
Atorva 80mg/d.

8> **Clopidogrel** ⟶ if pt undergoing procedure
300mg loading Dose PCI.

Definitive Rx of = PCI > Thrombolysis

If ST↑ MI Presented to

after initial t/t

PCI - center
↓
do PCI
Ideal Door to Ballon Time < 90 min

Non-PCI centre
↓
If delay in shifting to PCI centre

< 120 min.
↓
Shift the pt

> 120 min
↓
do thrombolysis.
Ideal Door to Needle Time < 30 min

if symptom < 12 hours duration.
+
ST↑

If ST↑ MI + ↓BP

RVMI
(causing RVF)
Lung no crepts
Immediate Rx
I.V. fluids to ↑ preload.

Definitive Rx
PCI is done when pt is haemodynamically stable

LVMI / Ant wall MI.
(causing LVF)
Lung crepts +
↓
Intra-aortic Baloon Pulsation (IABP)
↓
PCI

Rx (II) Non-ST ↑ MI / Unstable Angina

Std. Rx

1> Anti-platelets = aspirin + clopidogrel

+

2> Anti-thrombotic agents = LMWH or Thrombin (-)

+

(3) Nitrate

+

(4) β blocker

↓ If there is no relief

Add CCB

↓ if no relief

PCI

(III) Stable Angina

1> Aspirin Life long

2> Sublingual dinitrate

3> Rx risk factors

PRINZMETAL ANGINA

Cause - Idiopathic vasospasm of epicardial coronary artery.

[non-atherosclerotic]

M/c artery affected → (R) Coronary

C/F -

* Smoker + young age
* Associated symptoms = Raynaud's phenomenon
* Pain = 12 AM to 8 AM.

I_x - ECG - ST ↑
Troponin = (N)

R_x -
1) Acute → vasodilators = Nitrate → [CCB α-Blocker]
2) Maintainance → (CCB)
3) C/I → Aspirin → (-)/Lower vasodilator PG
β blocker → ppt. vasospasm

Q. In intraoperative MI ≤ drug not used.
Best ECG Lead V_5 or V_4
(a) Heparin
(b) Atropin if AV Block
(c) CCB
(d) NTG.

LMP.

AORTIC DISSECTION

[auses -

1) M/c → HTN

M/c site → ascending aorta ® Lateral wall

2)

2) Large vessel vasculitis
Takayasu
Giant cell arteritis.

3) Atherosclerosis [M/cc of aortic aneurysm]

4) Drug - Cocaine

5) ♀

Types

A/c to Site Of Origin [Stanford classificaton]

- (A) Ascending aorta — more common, more fatal
- (B) Descending aorta

A/c to Extension [DeBakey classificaton]

- I — to descending aorta also
- II — Limited to ascending aorta
- IIIA — Above diaphragm
- IIIB — Below diaphragm.

Symptom M/c – Chest pain

Retrosternal + **Tearing** Pain + Radiation to interscapular area

Sign Asymmetrical Pulses

Acute Aortic Regurgitation [due to type A dissec"]

Ix

1) CXR → Wide mediastinum
+
Ⓛ sided Pleural effusion (20%)
⇓
D/D of Oesophageal Rupture
↓
H/o vomiting

2) Unstable pt → Trans oesophageal ECHO.

3) If pt is stable → CT

4) Gold Std. Ix → MR angio

Rx

Initial Rx → BP

- High or Ⓝ → (Target SBP 100–120 mm Hg)
  - I.V. ESMOLOL
  - Definitive Rx
- Low → I.V. fluids.

Type

A
Urgent surgical Repair.

B
Conservative
do surgery if
* Impending rupture
* Limb/visceral ischaemia

RHEUMATOLOGY

IMMUNE SYSTEM

INNATE

1) ANATOMICAL BARRIER

2) PRR's (pattern recognising Receptors)
Inflammasome Proteins (SENSORS)

3) Anti-Microbial Peptides (AMPs)
Lyzozymes - Tears/saliva

4) NK cells (BOUNCERS)
Largest WBC
Regulated by Tcells (IL-2)
Immune & Tumour surveillance
Non-immune mediated action
Only Immune cell → non-MHC restricted action.
(virus infected/mutated cells are also checked by these cells)

5) MONOCYTE - MACROPHAGE SYSTEM (Police)

6) Dendritic cells
(Most Potent APC's)

7) GRANULOCYTE SERIES (N, B, E)

8) COMPLEMENT CASCADE
regulators of immune response

9) CYTOKINE

ADAPTIVE

1) Bcells (HUMORAL)
- express $CD_{19,20}$ on surface
- when activated
↓
PLASMA CELLS
↓
Immunoglobulins (antibodies)

2) Tcells (cell mediated)
CD_4 (Helper) & CD_8 (cytotoxic)
Most Potent level of Immunity

IMMUNE EXCESS DISORDERS

INNATE (AUTOINFLAMMATORY)

FAMILIAL MEDITERRANEAN FEVER (FMF)
(Recurrent Poly-serositis)*

EPID → 10-20yrs, ♂>♀

ETIOPATH → Inherited defect of MEFV gene
↓
Overexpression of the PRR's
INNATE EXCESS ~~FEVER~~ STATE

C/F → Recurrent Febrile Illness
(each last for 6-8 weeks)
Constitutional symp:- Anorexia
wt. loss
myalgia

Mlc ↓	↓	↓	↓
Pleuritis	Peritonitis	Arthritis	Pericarditis
D/D - TB	D/D - Appendicitis	D/D Juvenile RA	D/D Rheumatic fever

Dx:- Clinical suspicion → GS (Genetic testing MEFV gene)

Rx:- COLCHICIN- Favourable response + longterm remission.

Dreaded complication :- 2° Amyloidosis - Nephrotic syndrome
High Mortality

Recurrent Febrile Illness ō Unconfirmed Infection
= Rheumatology

ADAPTIVE
(AUTOIMMUNE DISORDER)

A) Organ SPECIFIC
Myasthenia Gravis
Grave's
Pernicious Anaemia

B) SYSTEMIC
= RHEUMATOLOGY
Study of systemic autoimmune disorders.

ANTIBODY TESTING

INDEX

ANTIBODY	CLINICAL SIGNIFICANCE (Best screening)
ANA	M/c Ig found in autoimmune Disorders (>98% of case) MOST SENSITIVE Ig

ELISA ← METHODS → IF (Preferred)

Qualitative Result (+/-)
Hence it is non specific

1) Quantitative (Result in titres)
<1:160 = ⊕ in 20% Healthy population
>1:160 = SIGNIFICANT (More specific)

2) IF PATTERN (due to the Δ)

IF PATTERN	ANTIBODY	DIAGNOSIS
M/C - SPECKLED	Anti-Ro/La [SSA/SSB]	SICCA SYNDROME.
Homogenous Rim pattern	Anti-dsDNA - M/c in SLE Anti-smith - Most specific for SLE	} SLE
Centromere	Anti-centromere (specific)	→ Localised Systemic Sclerosis
Nucleolar Pattern	Anti-topoisomerase-1 (SCL-70 commercial)	→ Systemic Sclerosis

ANTIBODY	CLINICAL SIGNIFICANCE (Astie Role in SLE)
Anti-Sm (not preferred)	· MOST SPECIFIC for SLE Only in 10% (lacks sensitivity) NO correlation ~ disease activity
Anti-ds DNA (preferred)	Ⓑ Sensitive & Specific correlates ~ disease severity Associated ~ ↑ Risk - nephritis/CNS involvement.
APLA (phospholipid	Present in 60-70% cases of SLE Associated ~ vascular thrombosis [fetal Loss Most recent to be ~~incl~~ included in Δ criteria of SLE.
Anti-Histone (specific for Drug induced SLE)	CVS (HIC) ACEI, β blockers, Thiazides, Statins Methyldopa, Hydralazine, Procainamide
	Anti-microbial: INH, Dapsone, Sulfonamides
	CNS: Phenytoin, carbamazepine
	GIT: ~~Sulfono~~ Sulfasalazine, Endo: Propylthiouracil Misc: d-penicillamine New: Interferons Anti-TNFα

ANTIBODY	CLINICAL SIGNIFICANCE (Prognostic Role)	
Anti (Ro)/La ↓ Crosses placenta	↑ Risk of congenital Lupus ↓ Risk of maternal Nephritis	SSA/SSB 120 Astic Role in SICCA syndrome
Anti-Ribosomal P	↑ Neuro-psychiatric convulsion + Psychosis	↑ Risk of CNS Lupus
Anti-Neuronal Ab	↑ Neuropathy R, Painful, AXONAL	
Anti-erythrocyte	Hemolytic anaemia	↑ Risk of hematological involvement
Anti-platelet	Thrombocytopenia	

ANTIBODY	CLINICAL SIGNIFICANCE	
Anti-centromere	Localised Scleroderma (CREST syndrome)	Astic Role in SSc
Anti-SCL70	Diffuse SSc	
Anti-U_3 RNP	↑ Risk of PAH + RPGN	Prognostic Role in SSc.
Anti-U1RNP	Specific for Mixed connective Tissue Disorder	
Rheumatoid factor (RAF) IgM Ig against Fc portion of IgG	Best screening Test for RA (~~Best~~ (SENSITIVE) Correlates - Risk Bone erosions (PROGNOSIS) Non-specific for Δ	

ACPA / Anti-CCP (Most specific for R.A.)	Anti. cyclic citrullinated Protein Ab. (Acts Role in RA)	
ANCA (anti-neutrophil cytoplasmic Ag)	Vasculitis (Acts Role)	
	cANCA Anti-PR3 (proteinase-3)	pANCA Anti-MPO (myeloperoxidase)

SLE

M/c autoimmune disorder

Epid- 20,40 yrs. ♀ > ♂

cause- Idiopathic M/c

Risk factors - 1> GENETIC - TREX-1 gene defect
2> CHROMOSOMAL - Klinefelter's syn.
3> INFECTIONS - EBV
4) TOXINS - UV Rays, silicosis

Manifestation	Clinical Description.
1> Cutaneous	a> Acute :- MALAR RASH b> Chronic :- DISCOID RASH
2> Oral ulcers considered as SLE	excluding - a) nutritional b) Infective c) Behcet's disease
3> alopecia (considered as SLE)	excluding - a) Nutritional (Iron, Zn) b) Endocrine - thyroiditis (Hypo) c) Drug induced
4) Synovitis (90%) (Non erosive arthritis)	(M/c) Symmetrical polyarthritis NEVER DEFORMITY / Bone Disease

5) RENAL	Proteinuria > 3+, Granular/ RBC Cast
6) CNS	Neuropsy., Neuropathy
7) ANAEMIA →	Hemolytic - Hb ≤ 10g/dL
8) LEUCOPENIA →	WBC ≤ 4000 or Lympho ≤ 1000
9) Thrombocytopenia →	Platelet ≤ 1,00,000

Δ:- SLICC Criteria (Systemic Lupus International Collaberative Clinics)

9 clinical	6 Immunological	≥4 confirms SLE (atleast 1 of each)
ABOVE manifestations	1) ANCA ② Antesm 3) Anti Ds DNA	④ APLA ⑤ Direct Coombs Test+ve ⑥ Low serum C_3 Levels

Rx

ACUTE SLE FLARE

⇓

Life-threatening features / causes of ACUTE MORTALITY IN SLE

1) Lupus Nephritis (Type 3,4)
2) Neuropsychiatric manifestations
3) Coagulopathy / Pancytopenia

(+) → Autoimmune Crisis

(−) → MILD FLARE

Rx. IV Methyl Prednisolone PULSE ⟹ Oral Prednisolone
1 gm/day = 3-5 days 1-2 mg/kg/day

⇓

Add Steroid Sparing (Lifelong) MYCOPHENOLATE MOFETI

Approved alternatives to methylprednisolone

RITUXIMAB (MAb ⊖ CD_{20})

BELIMUMAB (MAb ⊖ BAF)

POOR ~~PROGNOSIS~~ PROGNOSIS

Affects Productive age group	unpredictable course of the disease	High cost of therapy	Long Term Adverse drug Rxn of immuno suppression	NO CURE (lifelong therapy

ACUTE ← MORTALITY IN SLE. → CHRONIC/ Longterm

1) Thrombotic events - cardiac failure
2) Opportunistic Disease

SCLERODERMA → SYSTEMIC SCLEROSIS

124

Sclerosis | Skin ⊗

>98% have systemic involvement.

Epid - 30-50 yrs, ♀ > ♂

Cause - H/c - Idiopathic

Risk factors → 1) INFECTION → CMV, Parvo B19

2) TOXIN EXPOSURE - Silicosis, "Toxic Oil Syndrome"

C/F ← H/C

1) RAYNAUD'S → can precede skin changes ≥ 10 yrs

↓

2) SKIN changes : Hands & face

	HANDS	FACE
a) OEDAMATOUS	Puffiness of fingers	& Face
b) INDURATIVE	claw hand deformity	Mask-like
c) SCLEROSIS (most specific) (HOST SPECIFIC)	Autoresorp" of terminal phalanx ⇓ shortening of Digits	"FISH-MOUTH" appearance

CLASSIFICATION - Based on Extent of Skin Involvement

ONLY SKIN (<2% cases)	Restricted to face	Proximal - elbow	only organ.
MORPHIA	Distal to elbow	Trunk ⊕	SCLERODERMA SINE SYNDROME (Least common)
En-coup-de-sabre Lesion	↓ → SSC ← ↓		
	Localised	Diffuse	

sickle

Suspected → SSC

Face + Distal to elbow LOCALISED SSc	Proximal to elbow DIFFUSE SSc
ANti-Centromere ⊕	SCL-70/Topoisomerase-1 Ab ⊕
⇓ Also called 'CREST' ✓Calcinosis ✓Raynaud's (DOC = CCB) ✓Eso. dysmotility (GERD) ✓Telangectasia s → sclerodactyly Above features are M/c E localised >> Diffuse	⇓ More risk of organ involvement Lung:- M/c type of ILD in autoimmune disorder NSIP (non-specific interstitial pneumonia) ↳ DOC = steroids ↓ Iso. Pulmonary artery HTN (DOC - Iloprost) • RPGN (Renal crisis) (DOC - captopril)
Rx = ONLY PALLIATIVE, NO CURE Unfavourable Prognosis	

SICCA SYNDROME
(Sjogren's Syndrome)

M/c manifestation — Dryness of Eyes & Mouth.
Lymphocytic infilteration of exocrine glands

CAUSES

1° SICCA (Idiopathic) (Rare)
[SICCA - is the Disease]
- High Risk → systemic (extraglandular manifestations)
- High titres → SSA/SSB Ab
- High Risk → LYMPHOMA (M/cc of death in SICCA)
- Majority → Immunosuppressants.
- POOR PROGNOSIS

2° SICCA (M/c)
[underlying disease]
- SLE, SSc, MCTD, RA, vasculitis
- 1° Biliary Cirrhosis
- chr. autoimmune Hepatitis

- only Glandular symptoms
- Low titre - SSA/SSB
- NO risk of Lymphoma
- Rx - only palliative
FAVOURABLE PROGNOSIS

C/F

GLANDULAR.

Involved	C/F	TEST	Rx
Lacrimal Gland	Dry eye	Schirmer	Artificial tears
	corneal or conjunctival erosions	Rose Bengal Test	Protective glasses
Salivary	Dry mouth	Iontophoresis	Hydration
Pancreas	Malab" Syndrome	stool FAT estimation	Enzyme replacement

SYSTEMIC

LUNGS - M/c - NSIP
Isolated PAH

Renal - (M/c)
- Distal RTA.
- Interstitial nephritis

Liver - Cirrhosis

CNS - neuropathy

LYMPHOMA - most dreaded

Rx 2° SICCA → only palliative

1° SICCA → Depends on organ involvement

GOOD PROGNOSIS (majority are 2°)

POOR PROGNOSTIC FACTORS

1> Elderly onset (>40). ♀

2> B/L parotid enlarged

3> systemic ⊕

4> High titres of SSA/SSB.

OVERLAP SYNDROMES

Epid = 10-20yrs, ♀ >> ♂

C/F = (SLE/ SSc/ SICCA) + (R.A.)

Screening = Ab → ANA +ve; RAF +ve

Specific Ab

- U1RNP +ve → MCTD
- ACPA/Anti-CCP +ve (RA + lupus) → RHUPUS
- NONE → overlap Syndrome

Rx

SLE Dominant	RA Dominant
Immunosuppression	DMARDS
Non-erosive arthritis	Erosive arthritis

PROGNOSIS – Better than individual disease

Better response to therapy

APPROACH TO JOINT DISORDERS

TRUE ARTICULAR	PAIN	PERI-ARTICULAR
✓	Active	✓
✓	Passive Movement	✗

INFLAMMATORY	Morning Stiffness DURATION	DEGENERATIVE
>30 mins		<30 mins
Resolves	AFTER ACTIVITY	Worsens → OSTEOARTHRITIS

APPROACH TO INFLAMMATORY ARTHRITIS

- MONO (1 joint)
  - → N/E Trauma
  - → Septic
  - → GOUT
- OLIGO (2-4 jts)
  - PSEUDOGOUT
  - ↑ Crystal
- POLYARTHRITIS (≥5 jts)
  - AXIAL: Ankylosing Spondylitis
  - APPENDICULAR - dominant

Symmetrical (small)

- RHEUMATOID ARTHRITIS
- PSORIATIC ARTHROPATHY (Early DIP +)

Asymmetrical (Large)

- ENTEROPATHIC ARTHROPATHY
- REACTIVE ARTHRITIS — Predominantly wt. bearing jt.

Spondyloarthropathy → (4) = AS + above 3

M/c Pattern of Joint Involvement in Diseases

↓

Most Imp parameter for Diagnosis of arthritis

RHEUMATOID ARTHRITIS

Epid- 30, 50yrs; ♀ > ♂

M/c - Idiopathic

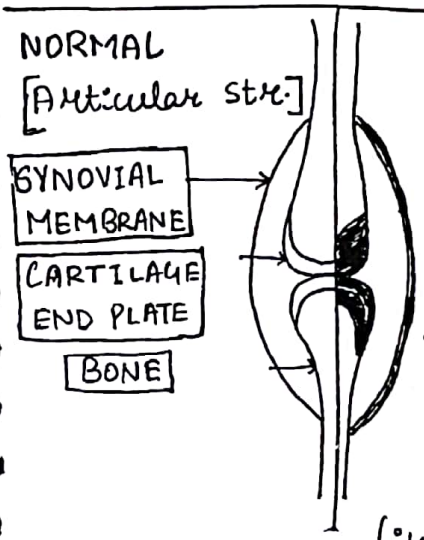
Risk Factors - 1) GENETIC - HLA-DR4 (Most cases = sporadic)

2) INFECTION = Mycoplasma, EBV.

C/F

ARTICULAR (predominant)

- → Inflammatory Poly. arthritis
- → Appendicular Dominant
- → Spine involvement - Rare
  - ↳ M/c - Atlanto-axial jt.
- → Symmetrical, small jts. of hand Wrist, MCP jt & PIP jt



EXTRA-ARTICULAR

EPISCLERITIS

LUNG: M/c Usual Interstial Pneumonia (UIP)

M/c → ♂

Pericarditis

Valvular M/c → MR

MUSCULO-SKELETAL

↓ Myopathy ↓ Osteopenia

Fast progress - OA

FELTY's (RA + Spleen)

↓

Anaemia / Neutropenia

Risk of Lymphoma

Least common

≤ 1% - advanced RA

Early DMARD Rx

Δ :- EULAR (European League against Rheumatism) Guideline - A scoring system

Ⓐ PATTERN of joint involvement (Max : 5)

- 1 jt (Predom. Large) → 0
- 2 - 10 jt → 1
- 1 - 3 jts → 2
- 4 - 10 jts (Predom. small) → 3
- > 10 jts → 5

Ⓑ SEROLOGY (Both RAF & ACPA) [Max = 3]

NEGATIVE → 0

MILD ⊕ [< 3 × upper normal limit] → 2

STRONG ⊕ [> 3 × upper limit] → 3

Ⓒ DURATION

< 6 wks - 0

> 6 wks - 1

Ⓓ ACUTE PHASE REACTANT

NEGATIVE → 0

ELEVATED → 1

Δ = ≥ 6 confirms RA.

RADIOLOGY ⊗ → Not recommended for Ass.

OLD CRITERIA :- X-Ray Hand = Bone Erosions

X-Ray - Least sensitive test

MRI - MOST SENSITIVE test

↓

Impractical

Late, irreversible stage

Earliest feature of RA

Juxta-articular osteopenia

↓

NON-SPECIFIC.

℞ Most preferred method → STAGE the severity

CDAI (Clinical Disease Activity Index)

2.8 - 10	10 - 22	>22
MILD RA	MODERATE RA	SEVERE RA
Single DMARD	COMBINATION DMARD	Early use of Biologicals

Prognosis :- Favourable → REMISSION → can be acheived in 60-85% cases

POOR PROGNOSTIC FACTORS :-

1> Elderly (>40)

2) ♀

3> >10 jts @ onset

4> High titres of RAF

5> Delay in initiation of DMARD ≥ 3 months

DMARDS	InD"	ADR	Follow-up
METHOTREXATE (MTX)	1st choice (B) single or combination.	BM ↓, Hepatotoxicity (Dose dependent S/E)	CBC, LFT - 3 monthly
	Back bone of Biologicals	MTX induced ILD unpredictable Permanent C/I to MTx use	CXR, PFT Baseline & Annually
		Teratogenicity	Counseling
HYDROXY-CHLOROQUINE	Safest in (6) ♀ 2nd choice	Bull's maculopathy (Irreversible)	Fundus, Exam, Perimetry Baseline & annually SOS
SULFASALAZINE	Safe in (6) ♀ 3rd choice	Gastritis Hepatotoxicity	LFT - Basaline & 3monthly
LEFLUNAMIDE	Approved as Mono Rx completed Family MODEST efficacy (limited use)	No synergy ⊂ other DMARDs 6X ↑ Hepatotoxicity Teratogenicity	Stop ≥2 ovulatory cycles before conception.

BIOLOGICALS = Pathophysiology of R.A.

↑↑↑ Pro-inflammatory cytokines

TNFα most potent (MOST PREFFERED) Anti-TNFα agents + **IL-1** **ANAKINRA** **IL-6** **TOCILIZUMAB**

Stimulates T cell MODULATOR = ABATERCEPT + **Stimulates B-cell** RITUXIMAB

Intracellular signalling pathways of Inflammation

eg. ~~JACK~~ JAK - Janus associated Kinases

TOFACITINIB - Tyrosine kinase ⊖ of JAK. - 1st oral Biological

ANTI - TNF α AGENTS — ADALIMUMAB, GOLIMUMAB S/C every 2-3 wks

~~ETARER~~ ETARNACEPT	INFLIXIMAB	PEGYLATED CERTOLIZUMAB → S/c every 6-8 weeks
Chimeric form Mab against TNF α receptor	Chimeric Mab against TNFα itself	Fully Humanised MAb against TNFα. itself
Limited efficacy	Excellent efficacy Anaphylaxis	Equal efficacy Safety

~~COMMON~~

Common ADR ⇒ Reactivation of TB.

Hence, Screening for active/ dormant TB is mandatory before Anti-TNF α agents.

Tuberculin (MANTOUX)	WHO → In countries (BCG vacc)
→ MOST SENSITIVE.	Best screening Test is
→ BCG vaccination. (false +ve)	Interferon γ assay (TB-GOLD/ ~~quantification~~ quantiferon)

SPONDYLOARTHROPATHY

Group of Disorders characterised by

COMMON FEATURES

1) Seronegative — RAF -ve
2) HLA B27 +ve — Strong family History
3) 1° site - "Enthesis" — Junc" Btw Bone & Tendon.
4) Axial Involvement is not Uncommon.
5) Extra articular manifestations predominate
6) Excellent response to NSAIDS → 1st Line of Rx

SpA are D/D - Inflammatory Polyarthritis

(I) ANKYLOSING SPON. / BECHETROW's / MARIE-STRUMPELL DISEASE

Epid- 10-20yrs, ♂ > ♀, 90% - HLA B27

C/F

ARTICULAR (Axial Dominant)		EXTR-ARTICULAR (Predominates)
Sacro-iliac Joint - M/C	LBP (non-specific) always B/L But asymmetrical	70% → Recurrent U/L ANT. UVEITIES
Lumbar spine	Restricted ~~movement~~ forward bending	
Thoracic spine	Restricted movement	
Cervical spine	Highest level of # in Lower part of Cx spine	

Δ

BEFORE

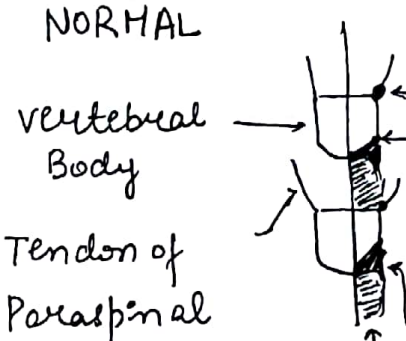
HLA-B27 → +ve → ≥2 common features of SpA (confirms A.S.)

HLA-B27 → -ve → ✗

Spine Involvement

AFTER

MRI proven sacroileitis → ≥1 common features of SpA



STAGES	R_x
ENTHESIS	NSAIDS
MARROW EDEMA	BEST TIME for Biologicals.
MARGINAL SYN DESMOPHYTES (unique feature)	DMARDS Biologicals (All TNF α agents)
FUSION (ANKYLOSIS)	

MRI is mandatory

Only Test → Detect the stage of A.S.

R_x - UNFAVOURABLE

unlike RA only 10-15% active complete Remission

(II) PSORIATIC	(III) ENTEROPATHIC	(IV) REACTIVE
M/c- "Guttate"/ Pustular type of psoriasis	M/c - U.C./Crohn's Disease	Post-infective
	Common Pathology	F./UTI — CHLAMYDIA URBAN — S.Typhi Travel Diarrhoea — Shigella
	Bowel Disease & activity — Severity of arthritis	
M/c - ONCHOLYSIS' (nail pitting) Skin Lesions 10% Uveitis ant ⇓ Symmetrical poly-arthritis (Predom - small jts) mimic RA - 5-10% pts arthritis > skin changes	M/c - Diarrhoea Most-specific = Pyoderma gangrenosum (Unique in U.C.) ⇓ Asymmetrical poly arthritis (Predom - Large jts	M/c → Febrile illness → KERATODERMA BLENORRHAGIA (Keratotic, Painless plaques - sole + Palm) ⇓ Asymmetrical - polyarth (Predom - wt. bearing jts)

Early x-Ray → DIP jt ⊕ pencil in cup deformity • MTx • Anti-~~TFα~~ TNFα agents • Tofacitinib.	Sulfasalazine Anti-TNFα	CHICKENGUNYA ARTHRITIS Hydroxychloroquine (additional anti-inflammatory action)

CRYSTAL INDUCED

	GOUT	PSEUDOGOUT
Crystal	Mon.sodium urate (M.S.U.)	Ca^{2+} pyrophos. dihydrate (C.P.P.D)
Epid	30-50 yrs ♂ > ♀	>50 yrs ♂ > ♀
Etiopath	90% - Renal Defect in Urate excretion. 10% - Diet/Drugs (Pyrazinamide/Thiazide	90% - Jt. Degeneration. 10% - Hypercalcemia = severe so, early PTH adenoma Paraneoplastic Syn
C/F	Acute - Inflammatory MONO-ARTHRITIS (M/c - 1st MTP, ankle jt)	Acute, inflammatory OLIGO (M/c - Knee, Hips, shoulder)
Screening	Serum Uric Acid	NON-SPECIFIC NORMAL VALUE DOESN'T Exclude S. Ca^{2+}
Synovial Fluid Analysis	NEEDLE SHAPED	RHOMBOID SHAPED
Polarising microscopy ↓ Demonstrate crystals ← Gold Std.	STRONG -ve Birefringence	MILD +ve Refringence

Rx	← NSAIDs	
Acute Attack	Colchicine Canakinumab (MAb IL-1β)	
Renal Failure	FEBUXOSTAT (X-O-I) Hepatic excretion. Additional anti-inflammatory	Intra-articular Steroids
Chronic Prevention	TARGET Uric acid < 6mg/dL 1st Line: X-O-Inhibitors (Allopurinol, Febuxostat) ↓ Refractory cases PEGLOTICASE Pegulated uricase debulking action on tubules	Encourage Physio therapy Avoid unnecessary Ca^{2+}/vit D_3 supplements In elderly Majority require Jt. replacement Sx.
Prog	Favourable	Unfavourable

CHARCOT'S

1st described - Tabes (Neurosyphilis)

Associations :- H/c DM, Leprosy, Amyloidosis

Pathophysio

NEUROVASCULAR	NEURO-TRAUMA
Autonomic neuropathy	Sensory neuropathy
↓	↓
Disrupts Micro-circulation	Recurrent Microtrauma

→ DEGENERATION

⇓ +

Loss of pain sensation (neuropathic jt)

M/C Forefoot Jt → Hind foot Jt → Ankle Jt

Δsis XR → 'Loose Bodies' in jt. cavity

Only Rx Strict Immobilisation → Total rest

⇓

facilitate recovery of Jt.

Only palliative → Unfavourable Prog.

VASCULITIS

(A) Based - Pathological Mechanisms

ANTIBODY (ANCA) MEDIATED	IMMUNE-complex MEDIATED	T. cell mediated
Wegener's (W.G.)	Hep. B - PAN	Giant cell arteritis
Churg strauss (C.S.S.)	Hep C - Cryoglob	Takayasu's
M.P.A.	H.S.P.	W.G.
microscopic polyangiitis	(Henoch-Schonlein Purpura)	C.S.S.

(B) Based - size of vessel affected (Preferred)

LARGE	MEDIUM	SMALL
Giant cell arteritis	Polyarteritis nodosa	
Takayasu	Kawasaki	

SMALL

ANCA +ve		ANCA -ve
Anti-PR3	Anti-MPO	H.S.P. vs Hypersensitivity
W.G.	M.P.A.	Cryoglobinemia
	C.S.S.	BECHET's Disease

G.C.A.

>50 yrs, ♀ > ♂

C/F → Artery Involved (Carotid)

Br. of EXTERAL CAROTID	Br. of INT. CAROTID	PATHOLOGY
H/c - Sup. Temporal	1st Br - Ophthalmic A.	Polymyalgia Rheumatica
Headache (worse - supine)	End artery -	Myalgia, fever, Anorexia, wt loss ≥ 3 months
± Diplopia	No collaterals	
± Jaw claudication Pain	⇓	
± Paraesthesia over Jaw	Permanent BLINDNESS	

ESR (screening) >60 (significant)

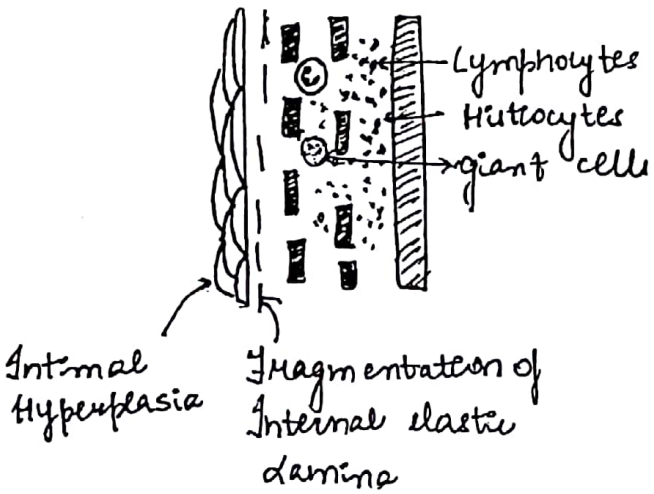
Gold Std →

↳ Temporal A. Biopsy → Minimum ≥ 2 cm Length.
→ HPE - Granulomatous vasculitis

Rx - Steroids → Relief of symptoms

↳ only Drug ∈ prevent dreaded complication = BLINDNESS

Early Rx = GOOD & PROGNOSIS



TAKAYASUS / AORTIC ARCH SYNDROME

Epid- 10-20yrs, ♀>♂

C/F- Depend on artery Involved = All direct Br. of AORTA

SUBCLAVIAN (M/C)	CAROTID VERTEBRAL	COELIAC	RENAL	CORONARY <1%
U/L claudication Unequal/ABSENT PULSELESS DISEASE	Recurrent TIA/Stroke	Chr. mesenteric Insufficiency	Refractory HTN (RAS)	Acute Coronary Syndrome

Δ - CT- AORTOGRAPHY Gold Std

Rx - Immunosuppression (Specific) + Angioplasty (Palliation)

POOR PROGNOSIS

KAWASAKI'S / Mucocutaneous L.N. Syndrome

M/c vasculitis ; <5yrs, ♂>♀

Replaced R.H.D. → M/C cause of cardiac death in children due to Acquired heart Disease

AHA Guidelines

M/c manifestation → Febrile episode

Any Fever - on/after 4th Day (min. dur 5days) DD

Dx - 4/5 of following features are ⊕

1) 90% B/L non-exudative conjunctivitis
2) Erythema over extremities
3) Peri-anal Rash
4) Strawberry Tongue
5) non-suppurative single, cervical L.N.

℞- IVIg + Long term Aspirin prophylaxis

- Relieve symptoms
- Reduces risk of coronary involvment to 4-6%
- cannot reverse coronary aneurysm

Dreaded : CORONARY ANEURYSM complication

RUPTURE (4-6% case) ⇓ Elective angioplasty prevents.

THROMBOSIS 95% of case

Prognosis - FAVOURABLE

ULINASTATIN :- Neutrophil elastase Inhibitor. (New, approved only IVIg refractory case

	PAN / SYSTEMIC NECROTISING VASCULITIS	MPA (Part of PAN prior to 1999)
Epid	30-50 yrs, ♂ > ♀	
Etiology	Classical M/C - Idiopathic 30% Chr. Hep B infection	
Pathology	Immune complex Mediated ↓ Fibrinoid necrosis Bifurcation of Medium vessel ↓ Microaneurysm formation	ANCA - mediated vasculitis ↓ Small vessel predominant ↓ 70% Anti-MPO +ve.
C/F	M/C 90% arthralgia HEMATURIA - ↓ out GN (rupture of micro aneurysm)	- always due to GN
CNS-	Mononeuritis	multiplex (Neuropathy) - asymmetrical
SKIN-	Raynaud's phenomenon	

Digital gangrene, LIVEDO		Purpuric Rash
Coronadal arteries mimic torsion	Pulmonary Spared But bronchial may be involved	Alveolar H'ge (ANCA +ve ⇒ D/D - Good Pasture's Syndrome

Δsis - Exception

Renal angio-micro aneurysm @ Bifurcation of vessels.

Biopsy - Gold std

℞ Immunosuppressants → Favourable Prognosis

WEGENER'S GRANULOMATOSIS

Or chronic Granulomatous angitis

30-50 yrs, ♂ > ♀

Closest D/D → Good Pasteur's.

C/F

Pulmonary

M/C

Lungs

- B/L abscess
- Multiple thin walled cavity
- Alveolar H'ge

URT is specific

M/C - chr. sinusitis

- Nasal bridge deformity
- Serous otitis media (GLUE)
- Subglottic stenosis (change in timbre of voice)

Renal

RPGN

Eyes

M/C - Pan-uveitis

SKIN

Purpuric Rash over L.L.

Serology (SCREENING) 70% Anti PR3 +ve (Wegener's Antigen)
30% Anti MPO +ve

~~Anti~~: Absence cannot exclude W.G.

BEST TEST → LUNG BIOPSY

Rx cyclophosphamide → favourable response
GOOD & PROGNOSIS

~~CHU~~
CHURG STRAUSS (Eosinophilia & granulomtous angitis)

30-50yrs. ♂>♀.

C/F

PULMONARY		RENAL	SKIN involvement
LUNG	URTI	RPGN	Purpuric/ urticarial rash
Late onset asthma	allergic rhenitis		

W.G. can be differentiated by ocular involvement

Dia- ~~Short course of steroid~~
Lung Biopsy /Skin Bx = Eosinophilic vasculitis

Rx- Short course of steroids
favourable Prognosis, Long term remission
GOOD & PROGNOSIS

H·S·P· (ANAPHYLACTOID PURPURA)

>90% cases - occurs <10yrs age M>F.

ADULT H·S·P. — HYPERSENSITIVITY VASCULITIS

EPID - 20-40yrs, ♂ > ♀

Etiopath Post Infective H/C - preceded by URTI

C/F	PALPABLE PURPURA	
LL + Buttocks	Distribution	Generalised
Common Abd. pain, Malaena	Mucus memb. involvement	Uncommon
3-5% - IgA deposits on GBM - Gross Hematuria	Renal involvement	NEVER OCCURS
Capillaries	Site - Biopsy (Gold std)	Post capillary venule

Rx - Reassurance/ Self Limiting Disease.

ESSENTIAL MIXED CRYOGLOBULINEMIA (EMC)

↓
Usually indicate Idiopathic cause

Majority = 90% = 2° cause
- Multiple myeloma
- Chr. Hep. C., Hep B
- Lymphoproliferative states

Pathophy:- Exposure to cold ($T < 37°C$) → Cryoglobulins ppt (Ig ± ppt.)

↓	↓
H/C - Skin capillaries	Renal tubulus
98% - multiple areas of skin necrosis	A.T.N. (Direct toxicity)

Δ sis - Incubate plasma in cold bath → ppt. ⊕

Rx + Prog - underlying cause (unfavourable)

BEHCHET'S DISEASE → HLA B5 $^{1}_{148}$

Epid- 30-50 yrs, ♀ > ♂ (worser in ♂)

MAJOR	MINOR
Recurrent, painful, oral aphthous ulcers	1> Recurrent superficial thrombophlebites 2> B/L Hypopyon 3> Erythema nodosum 4> Painful genital ulcers 5> Pathergy Test +ve Skin Prick > 5mm deep ↓ Induration (+)

Δ Sx - MAJOR + 2 MINOR — confirms.

Rx - Steroids - excellent response

Favourable Prognosis

FIBROMYALGIA (Pain Sensitivity Syndrome)

Epid - 30-50yrs, ♀ > ♂

Risk - Stress

Pathophy - ↓↓ Blood flow to Thalamus

(MINOR) ↓↓ Cortisol response to stress

C/F - • Multiple aches & pains (somatic complaint)
≥ 3 months

• Associated c Defect of NREM sleep

Asi - Clinical - 18 point pain testing (screening)
(>11/18 +ve tenderness → significant)

MR spectroscopy - gold std.

Rx - Pregabalin.
Gabapentin
TCA
SSRI.

Unfavourable Prognosis → Prone to analgesic abuse
Poor Q.L.I.

CHRONIC FATIGUE SYNDROME

20-40yrs, ♂ > ♀

C/F - FATIGUE ≥ 6 weeks

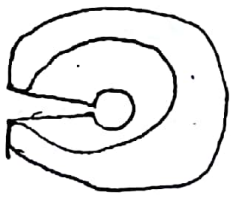
Asx - of exclusion

1> OBesity

2> Substance abuse

3> All medical causes
- 1) Nutritional
- 2) Endocrine — Hypothy, DM.
- 3) Chr. Infection
- 4) autoimmune
- 5) neoplasm

Rx = Lifestyle Modification



RESPIRATORY

LUNG DEVELOPMENT

5 stages

1) Embryonic stage → Lung buds
2) Pseudoglandular stage - upto terminal Bronchole
3) Canalicular - Alveolar ducts
4) Saccular - Primitive alveoli
5) Alveolar - Mature alveoli

BRONCHOPULMONARY SEQUESTRATION

Def^{n}. Separation of part of lung during development from tracheobronchial tree & separate blood supply.

TYPES

EXTRA LOBAR	INTRALOBAR (M/c)
Separated & having separate covering	separated part in adjacent lung & covered by lung's pleura

M/c site → (L) lower lobe post basal segment

M/c Blood supply → Thoracic aorta

IOC :- CT Angiography or MR angiography

Rx - Resection if pt. is symptomatic

SURFACTANT

1) Dipalmitoye Phosphatidyl choline / Lecithen.
2) Produced by Type II pneumocytes
3) also by clara cell.
4) Removed by Alveolar macrophage
5) Functions :-
   a) surface Tension ↓
   b) maintain alveolar stability / FRC
   c) Compliance
6) Surfactant induc" starts at **20wk**
   Peak at **35wk**

So, if < 35 wk ⇒ Respiratory distress syndrome
or
Hyaline membrane Disease.

Pathophysiology of RDS

surfactant deficiency → ↓ collapsed alveoli → To open collapsed alveoli → ↑ work of Breathing → Respiratory Distress

Respiratory Distress → ↓ energy resources → Hypoxemia + Met. acidosis → caused Damage to Alveolar cell → Form Hyaline Layer → HYALINE MEMBRANE DISEASE

Hypoxemia + Met. acidosis → Pul. vasoconstric" → ↑ (R) sided Pr. → Patent foramen ovale → R-L Shunt → CYANOSIS

X-Ray findings :-

1) Reticulo ~~granular~~ granular pattern
2) Ground glassing
3) White out Lungs
4) ↓ lung volume (↓↓FRC)

Inv :-

Lecithin / Sphingomyelin > 2 ⇒ MATURE LUNG

Rx :- mild to moderate ⇒ O_2 + CPAP

Severe ⇒ Invasive Mech. ventilation + Surfactant ~~Deficien~~ Replacement

~~Surfacto~~ [Hyaline appears Pink on Biopsy]

PULMONARY ALVEOLAR PROTEINOSIS

Surfactant clearance is impaired

Etiology :- 1° form (M/C) → Auto Ab against GM CSF

2° form → ✓ Acute Silicosis
✓ Haematopoietic malignancy
✓ Immunodeficiency

Silica particles are toxic to alveolar macrophage
Chr. Silicosis pt are prone to TB.

In malignancy, macrophages are not matured enough to carry out func".

In immunodeficiency, macrophages ↓

Pathophysiology-

↓ Diffusion for O_2 → Hypoxemia.

Δ :-

1) Broncho alveolar Lavage → milky white

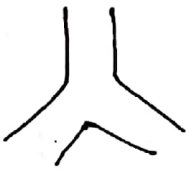
2) BAL → PAS +ve

3) CT Chest → CRAZY PAVING PATTERN

Rx- Whole Lung Lavage

WIEBELS LUNG MODEL

Trachea —23 Generation→ Alveoli



Trachea
↓
Principal Bronchus
↓
Lobar Bronchus
↓
Segmental Bronchus
↓
Terminal Bronchiole
↓
Respiratory Bronchiole
↓
Alveolar duct & Sac

Functional / ventilatory unit /
Acinus = Distal to terminal Bronchiole

Radiological unit / 2° Pulmonary Lobule
= Group of acinus (5-7)
↑
involved in EMPHYSEMA

upto terminal Bronchiole = Conducting Pathway

Ⓡ Main Bronchus	Ⓛ Main Bronchus
Aspiration is more common this side as it is short, stout, straight	**Bronchiectasis** more common in Ⓛ lower part → narrow angulated & drainage

BP Segments + ASPIRATION PNEUMONIA.

M/c segment involved in Asp. Pneumonia :
- ® Lower Lobe superior seg or ® upper Lobe Post

M/c segment involved in Asp. Pneumonia in supine

" " " Asp. Pneumonia in sitting/standing = ® Lower Lobe posterior Basal

" " " Asp. Pneumonia in Bending forward ® middle Lobe

Best Inv :- **Bronchoscopy**

HEMOPTYSIS

Lung
- High Pr. Systemic circulation ⇒ Bronchial artery
- Low Pr. Pulmonary " ⇒ Pulmonary artery

M/c source of hemoptysis → Bronchial artery

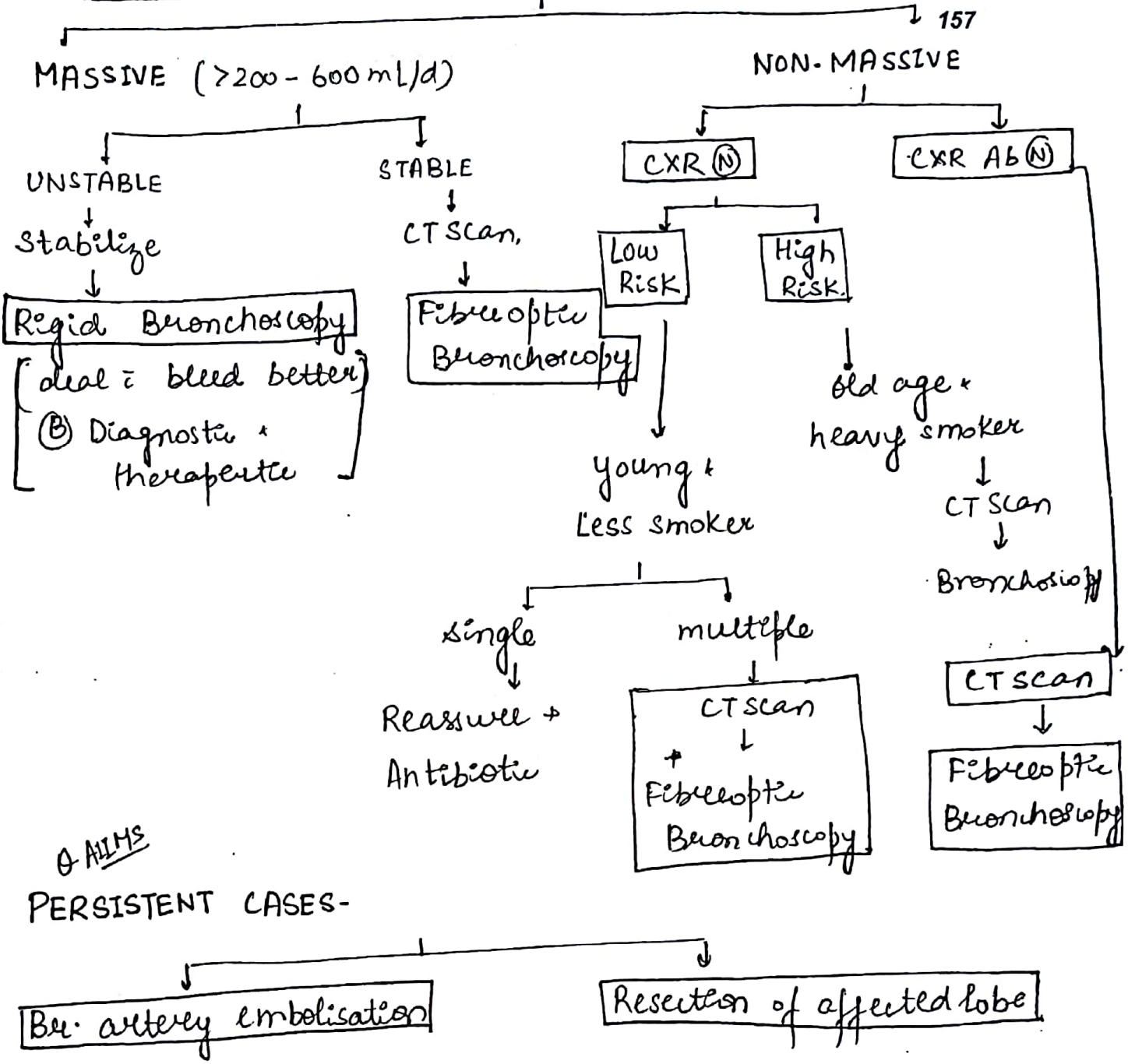
M/c source of massive hemoptysis ↑

M/cc of hemoptysis in India → TB

M/cc of " worldwide → TB

M/cc of Death in ↓ hemoptysis (massive) → Asphyxiation. ∵ Blood clot.

APPROACH TO HEMOPTYSIS



AIIMS

PERSISTENT CASES-

- Br. artery embolisation
- Resection of affected lobe

Source of hemoptysis in Mitral Stenosis = [Rupture of Pulmonary Bronchial venous connection → Br. veins]

Source of hemoptysis in Pulmonary embolism → Pulmonary artery

M/C Source of hemoptysis in TB → Br. artery

~~Rasmosen's~~ aneurysm → Pulmonary artery
Rasmussen's

organism that causes pseudohemoptysis
: Serratia ~~marcha~~ marcescens

INTRA PLEURAL PR.

Lung always tries to collapse to centre ⟶

Chest wall always tries to move outward ⟵

↓

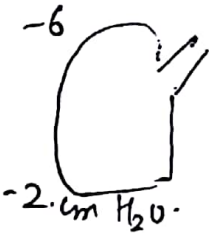
There is a Balancing Force Between the 2

↓

-ve Intrapleural Pressure (IPP)

[Usually -ve during (N) respiration
Maintains equilibrium Lung volume ⇒ FRC / Relaxing volume]

(N) Value = -2 to -6 cm H_2O.



More -ve IPP
Deep Inspiration
Pulley
Collapse
Fibrosis

Less -ve IPP / +ve IPP
1) Forced Expiration
* cough, valsalva manoeuvre
2) Pushing Lesions
3) * Tension Pneumothorax
* Mass " "

COMPLIANCE

→ Stretchibility of Lung.

→ Change in unit volume per unit change in pressure

$$C = \frac{\Delta V}{\Delta P}$$

Static compliance = air flow & resistance not considered

Dynamic ,, → air flow & resistance considered

EMPHYSEMA PATHOPHYSIOLOGY

Insp: Exp. = 2s : 3s

elastic febres.

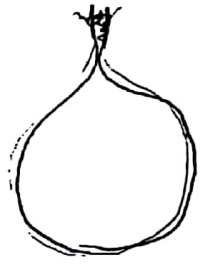
(N)

end expiration

If elastic febres Damaged. → Emphysema at end expiration.

early closure

Air Trapping →



Dynamic Hyperinflation

↓ diameter of airway

↑ Airway resistance

↓ Dynamic compliance in emphysema

Loss of elastic febres → ↑ static compliance

CXR

1) B/L Hypertranslucency
2) Flat Diaphragm
3) Tubular Heart
4) Barrel shaped chest wall

Emphysema –
- RV ↑
- FRC ↑
- TLC ↑

↓ compliance

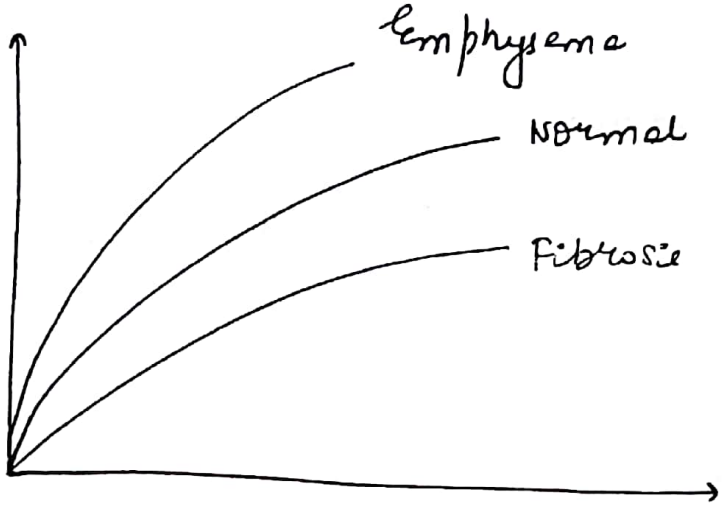
1) Surfactant Deficiency
2) ARDS
3) Pulmonary oedema
4) Fibrosis [ILD
5) 100% O_2 damage

↑ Compliance

1) old age
2) emphysema

Static comp ↑

Dynamic comp ↓ (↑ airway resistance)



HOOVER'S SIGN → Paradoxical inward movement of lower ribcage during inspiration

severe COPD ↓

since diaphragm is not there, thats why.

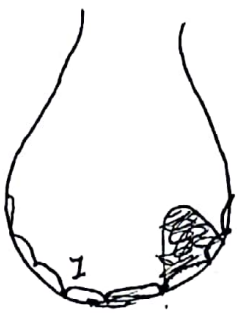
HISTOLOGY OF ALVEOLI

TYPE I

Pavement epithelium

Vulnerable to damage

More surface area



TYP II

Secretes surfactant

Can divide & reconstitute Type I cells

More No.

ZONES OF LUNG

Vertical regions based on hydrostatic Pressure

P_A = alveolar pressure

P_a = arterial "

P_v = venous "

Zone 1 = $P_A > P_a > P_v$

2 = $P_a > P_A > P_v$

3 = $P_a > P_v > P_A$

$P_A > P_a > P_v$

$P_a > P_A > P_v$

$P_a > P_v$ P_A

(N) Lung = combination of Zone II & III.

DEAD SPACE =

Area ventilated but no sufficient gas exchange (blood flow)

Anatomical D.S.

Ext. nares upto Terminal Bronchiole.

Measured by Fowler's method

N_2 used

Physiologic D.S.

PDS = Anat DS + Alveolar D.S.

In (N) Alveolar D.S. = 0

(N) P.D.S. = Anat D.S.

* Bohrs equation

↑ Anat D.S.

1> Neck extension
2> Bronchodilation
3> old age

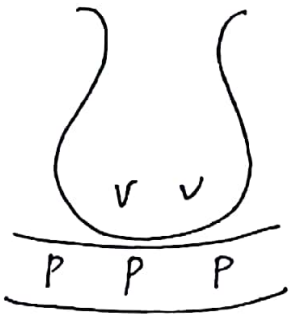
↓ Anat D.S.

1> Neck Flexion
2> Bronchoconstriction
3> Orotracheal intubation / Tracheostomy

Bypass nasal airway

Bypass oral, nasal airway.

↑↑ Alv. D.S–



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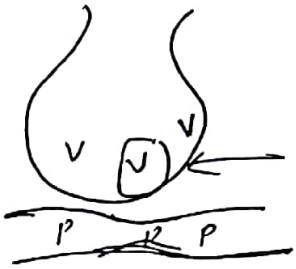
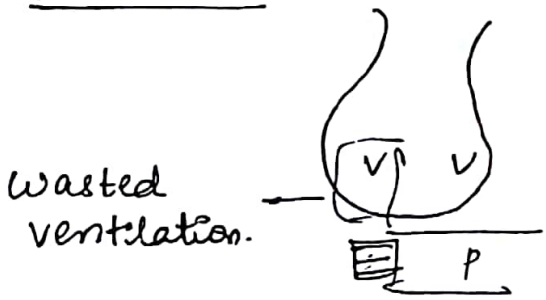


wasted ventilation =

P. Embolism



In P. Embolism, predominant Defect is in Perfusion

MECHANISMS OF HYPOXEMIA

(I) V/P mismatch (H/C)

(II) Shunt

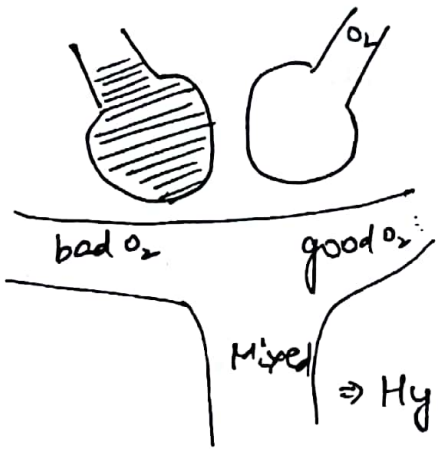
(III) Diffusion Defect

(IV) Hypoventilation

(II) SHUNT-

Bypass of (Diversion) blood ↓out oxygenation.

- INTRACARDIAC
  - (R) → (L) shunt
- INTRAPULMONARY
  1. Sev. Pneumonia
  2. ARDS



⇒ Hypoxemia

Less responsive to supplemental O_2.

R_x = Mechanical Ventilation.

R_x infection.

Cure pathology.

$\frac{V}{P}$ Ratio

BASE
- Max. Ventilation
- Max. Perfusion
- Min. V/P ratio

APEX
- Min. ventilation
- Min. Perfusion
- Max. V/P ratio

	V	P	V/P	PAO_2	$PACO_2$
APEX	2L	0.5L	4.	130	28
MIDZONE	4L	5L	0.8	104	35
BASE	6L	10L	0.6	92	42

1° TB ⇒ Mid & Lower Lobe

2° TB ⇒ Apex.

↳ active disease due to proliferation of Bacilli

Reason

↑ O_2 tension ↑ V/P ratio.

DIFFUSION CAPACITY OF LUNG (T_{CO}) (DLCO)

↓ DLCO

1) Fibrosis o/ ILD
2) Severe emphysema
3) Pneumonia
4) ARDS
5) Sarcoidosis

No blood for exchange

6) P. Embolism
7) Anaemia
8) Pul. HTN

↑ DLCO

1) Polycythemia.
2) Exercise (↑ Blood flow)
3) Alveolar H'ge
   ↳ good pasteur's
   Wegenere
4) B Acute Asthma
   ↑ sed eosinophil inflammation
   ↓
   No produc"
   ↓
   P. vasodilatation
   ↓
   ↑ DLCO

New FeNO = Test for Acute Asthma

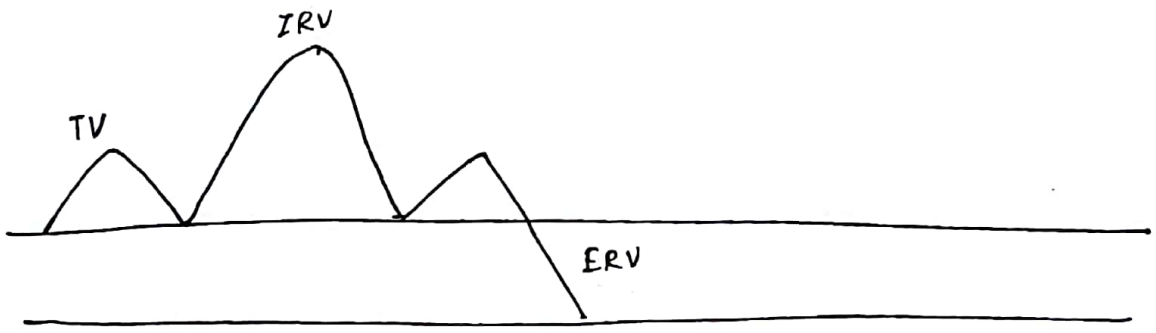
SPIROMETRY

Tidal Volume = Normally in/out = 500 mL

IRV = air accomodated ⊼ effort after ↑ Tidal inhalation = 3000 mL

ERV = air expelled ⊼ effort after Tidal expiration = 1100 mL

RV = Air that remains after ~~flex~~ forcible expiration = 1200 mL



VC = Volume expelled forcibly after max. inhalation.

TV + ERV + IRV

IC = TV + IRV

FRC = ~~E~~RV + RV

TLC = TV + IRV + ERV + RV

VC

IC

FRC

Conventional spirometer = can't measure
- → RV
- → FRC
- → TLC

Methods for RV, FRC, TLC:
- He Dilution Method
- N_2 washout
- Body Plethysmography. (Best)

DYNAMIC LUNG VOL

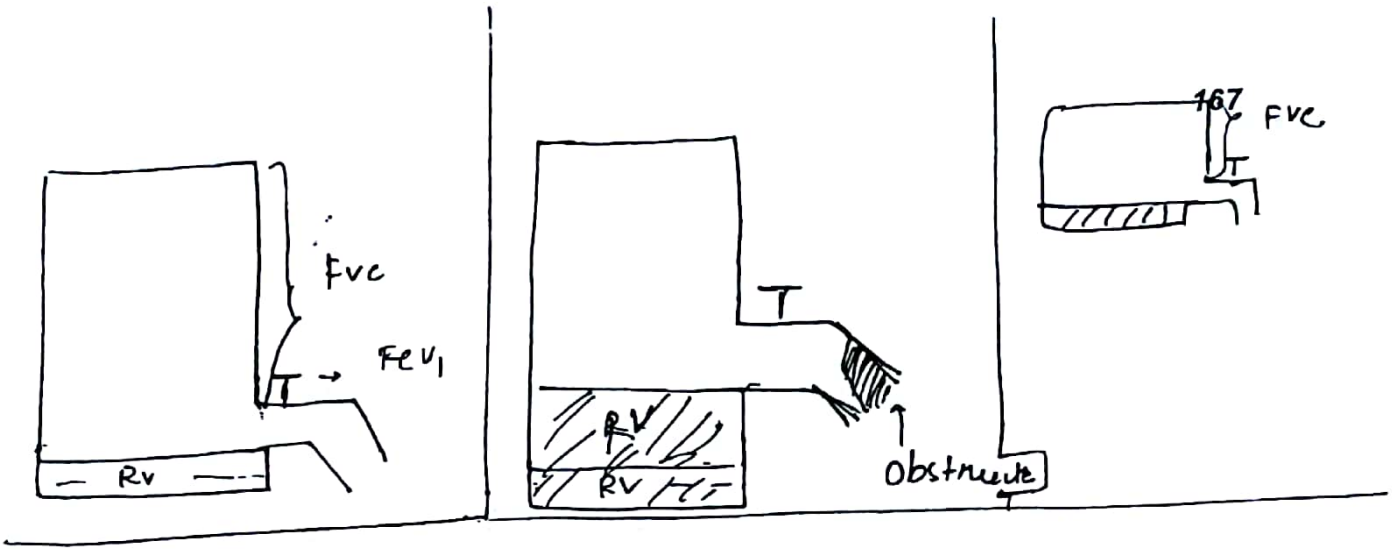
1) Forced Vital Capacity = Rapid + forcible VC

2) Timed Vital Capacity:
- → FEV_1 = FVC @ end of 1st sec = 80%
- → FEV_2 FVC @ end of 2nd sec = 90%
- → FEV_3 FVC @ end of 3rd sec = 98%

3) PEFR = Peak expiratory Flow Rate
- → Peak of FVC
- → Indicates **Large** airflow flow
- → 400-500 mL/min

4) MEFR → Avg. velocity during mid portion of exhalation.
- → sensitive indication of **small** airway function
- → 300mL/min

(N)	OBSTRUCTIVE	RESTRICTIVE
FVC (N)	FEV_1 ↓↓	FEV_1 (N)/↓
FEV_1 (N)	FVC (N)	FVC ↓↓↓
$\frac{FEV_1}{FVC}$ = (N)	$\frac{FEV_1}{FVC}$ = ↓↓	$\frac{FEV_1}{FVC}$ = ↑/(N)



OBSTRICTIVE

1) Asthma
2) Bronchiectasis
3) COPD → Chr. Bronchitis
   → Emphysema

RESTRICTIVE

Intrensic RLD
Pul. parenchyma involved

1) Fibrosis
2) Pneumonia
3) Sarcoidosis
4) Occupational lung disease
5)

Extrensic RLD
Pul. parenchyma uninvolved.

1) Kyphoscoliosis
2) Neuromuscular Disease
   a) GBS
   b) Polio myelitis
   c) Myasthenia Gravis
   d) Amy. Lat Sclerosis
3) Diaphragmatic Dysfunction

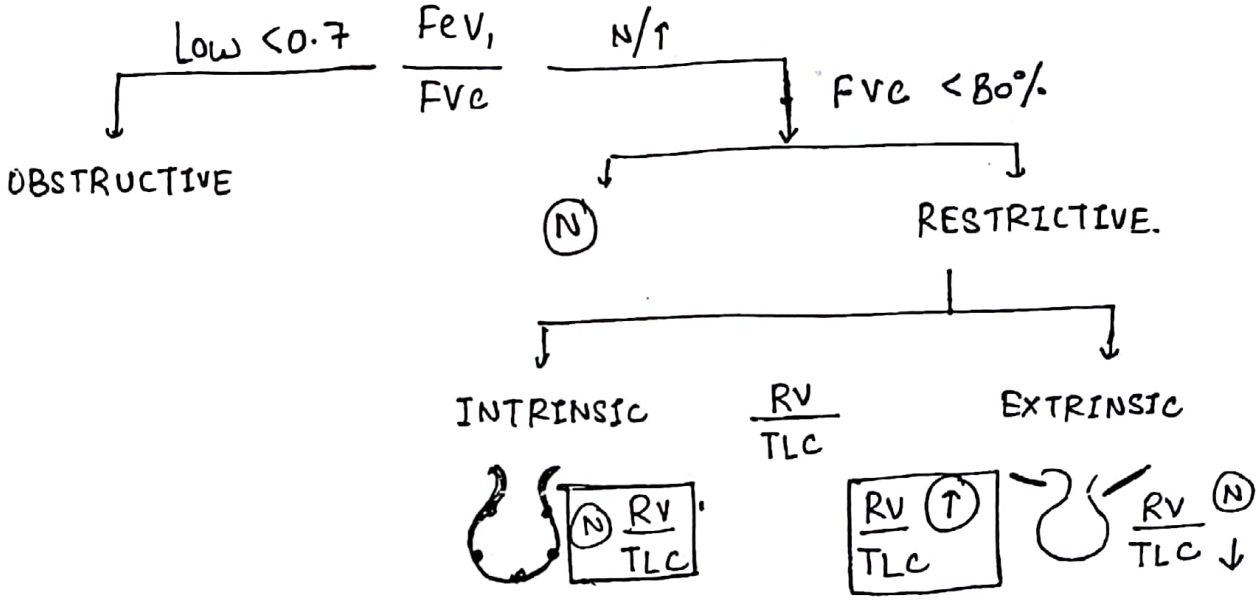
EMPHYSEMA

1) Obstructive
2) $\frac{FeV_1}{FVC}$ ↓↓
3) RV ↑, FRC ↑, TLC ↑
4) Compliance
   - Static (↑) — DLCO ↓
   - Dynamic (↓)

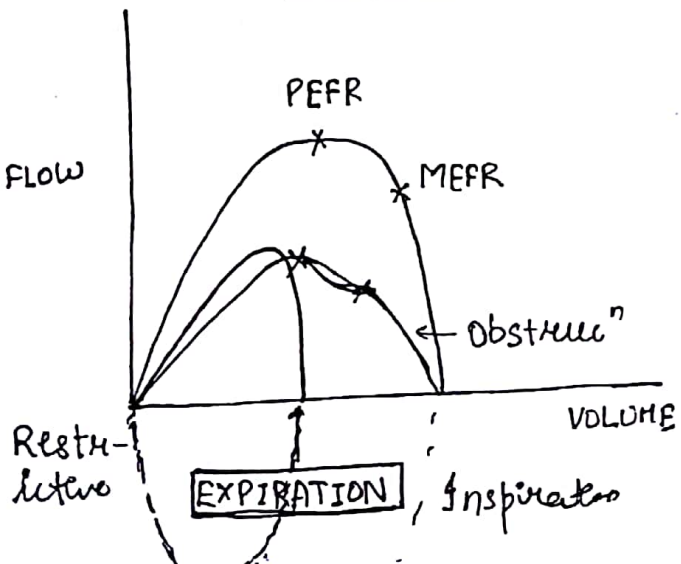
FIBROSIS / ILD

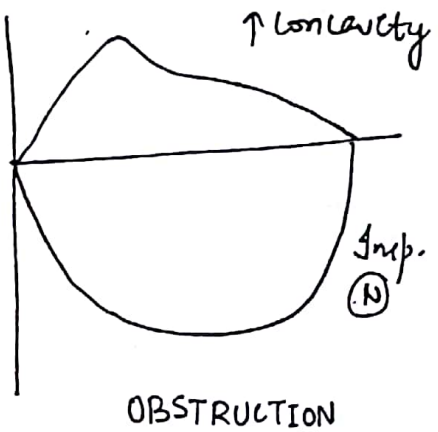
1) Restrictive
2) $\frac{FeV_1}{FVC}$ ↑/(N)
3) RV ↓, FRC ↓, TLC ↓
4) Compliance ↓
5) DLCO ↓

INTERPRETATION OF SPIROMETRY

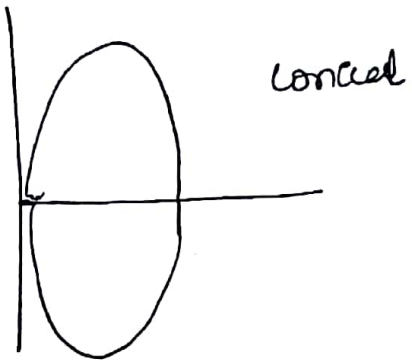


FLOW VOLUME LOOPS

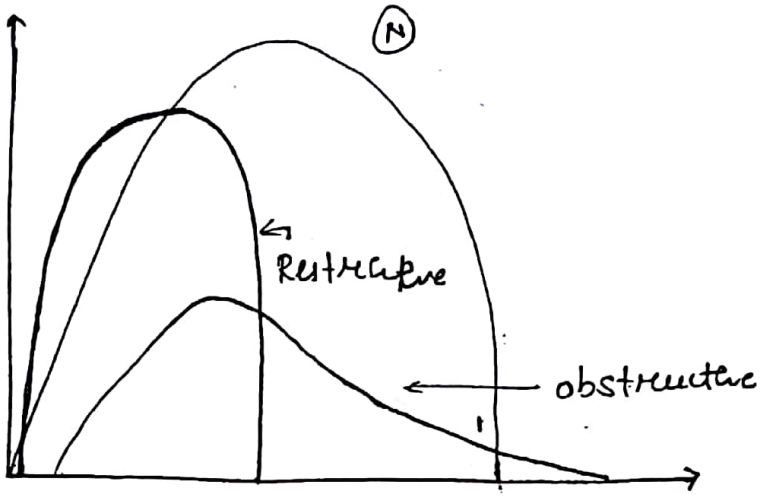




OBSTRUCTION



RESTRICTIVE



♀ FeV_1 (N) . ~~FEV~~ FVC (N). $\frac{FeV_1}{FVC}$ (N) ⇒ ~~N~~

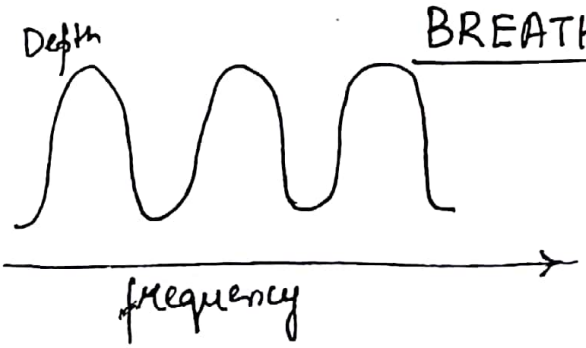
↓ spO_2 on ~~exam~~ exertion

↓ DLCO (young ♀)

⇓

1° Pulmonary HTN

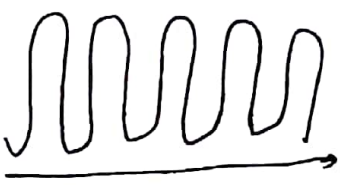
BREATHING PATTERNS



(N)

1) KUSSMAUL'S BREATHING :-

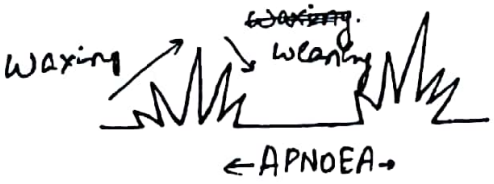
Rapid & Deep Breathing



eg. sev. Metabolic acidosis → DKA, Uraemia

2) CHEYNE STOKES BREATHING.

→ Periodic Breathing ~ cyclical Pattern.



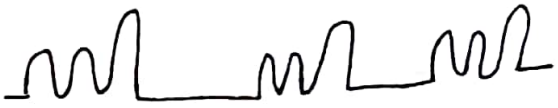
→ altered response to CO_2.

eg of CHF, narcotic overdose, Head injury

3) BIOTS BREATHING

- Irregular respiration ~ Apnoea

eg. Meningitis
↑ ICP



4) ATAXIC BREATHING

Irregularly irregular resp^n ~ ↑ Apnoea

till pt. goes into resp. arrest

eg. Brainstem injury.

BREATH SOUNDS

(N)

→ Vesicular Breathing

→ Similar to sounds of rustling of leaves

→ Low pitch, soft

I:E = 3:1

No pause.

Ab (N)

Bronchial Breathing

Similar to tracheal sound

High pitch, Harsh

I:E = 1:1

pause

1) Tubular Breathing → Consolidation

2) Cavernous " → Cavity

3) Amphoric " → Metallic quality

eg. Bronchopleural fistula

ADVENTITIOUS BREATH SOUNDS :-

WHEEZE (musical)

Produced when airflow past an obstruction due to vibration of airways

- **Monophonic**
  - Local involvement
  - eg. Bronchial Tumour
- **Polyphonic**
  - Diffuse involvement
  - eg. Asthma, COPD

Rhonchi :- Low pitch wheeze

CREPTS / CRACKLES / RALES

Non-musical sounds

1) When air flows into secretions

⇒ Bubbling noise

↓

cause crepts

Bronchiectasis

2) When alveoli suddenly pop open during inspiration

ILD

Velcro crepts

Fine crepts

(B) Fine & Course Crepts

1) P. Oedema (fine >> course)
2) Pneumonia
3) TB

STRIDOR:- Loud, audible, inspiratory & expiratory wheeze due to Laryngospasm
F.B.
Laryngeal oedema
Subglottic stenosis

~~LES~~ -

PULLING	NO PULL/PUSH	PUSHING LESION
Collapse Fibrosis	Consolidation	Pleural effusion Pneumothorax
Percussion = Dull in collapse Impaired in fibrosis	Dull note	Stony dull in P. Eff. Hyper-resonant/Tympanic in pneumothorax
Auscultation		
BS ⊖ in collapse BS ↓↓ in fibrosis	Bronchial Breathing ⊕	BS ↓ to ⊖
CXR		
collapse – Homogenous white	Air Broncho gram	Pl. eff = White meniscoid fluid level.
Fibrosis - Heterogeneously white		Pneumothorax = Black ± compressed lung margin

	PLEURAL EFFUSION	HYDROPNEUMO THORAX
Straight line of Dullness	⊖	⊕
Shifting Dullness	⊖	⊕
Succusion splash	⊖	⊕
Sound of coin.	⊖	⊕

RESPIRATORY FAILURE

Low pO_2 < 60 mm Hg , High $Paco_2$ > 45 mm Hg.
(HYPOXIA) (HYPERCAPNIA)

Type I RF - Hypoxemic RF

Type II RF - Hypercapnic RF

Type III RF - Perioperative RF due to lung atelectasis associated ⊼ general anaesthesia

Type IV RF - due to hypoperfusion of respiratory m/s due to shock.

TYPE I

Diffusion Defect
↓ Transfer of O_2.

$P_{A-a}O_2$ = 10 mm Hg

P_AO_2 = (N)

$Pa\,o_2$ = ↓

$P_{(A-a)}O_2$ = ↑↑

$Paco_2$ = (N)/↓

TYPE II

Hypoventilation
↓ Resp. Effort

P_AO_2 = ↓

PaO_2 = ↓

$P_{(A-a)}O_2$ = (N)

$Paco_2$ = ↑

pH ↓↓ (Resp. Acidosis)

CAUSES

Pneumonia
ARDS
ILD
Pulmonary oedema
P. thromboembolism [Highest $P_{A-a}O_2$]

R_x O_2 + R_x of underlying disease

If pt. not improving
Pneumonia
ARDS

Invasive +ve pressure ventilation preferred

CENTRAL CAUSE

Narcotic use
Head injury

OBSTRUCTION

. F.B.
Severe COPD

PERIPHERAL

Neuromuscular Disorder

DIAPHRAGM CAUSE

Palsy

⇒ **COPD** - pneumonia

O_2 + R_x underlying cause

If pt not improving
[COPD / NMD]

Non-invasive +ve pressure ventilation is 1st choice

NIPPV [BiPAP (NIV commonly used)
CPAP]

If no response ⇒ IPPV

C/I of non-Invasive ventilation

1) altered sensorium
2) ↑ chances of aspiration
3) cardiac arrest
4) Hemodynamically unstable
5) Un co-operative pts.

6) Claustrophobic

7) Active GI Bleed

8) Recent Facial Trauma or Sx

ARDS

Defn :- Acute shortness of Breath + Hypoxemia + Diffuse Pulmonary infiltrate

Causes:-

DIRECT

1) Pneumonia
2) Aspirating gastric content
3) Lung contusion
4) Near drowning
5) Toxin inhalation

INDIRECT

1) Sepsis (M/c).
2) Severe trauma
3) ~~Blood~~ multiple Blood Transfusion.
4) Severe Burns.
5) Pancreatitis

OTHER NAMES :-

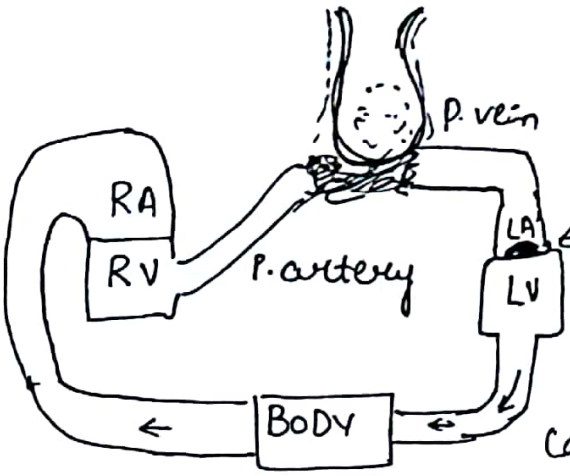
1> Noncardiogenic Pul. oedema
2> ↑ permeability Pul. "
3> Low pressure Pul "
4> Diffuse Alveolar Damage (most characteristic)
5> Shock Lung
6> Wet Lung

Pathogenesis

Cardiogenic P. oedema

Non-cardiogen P.Edema

CARDIOGENIC P. Edema



↓

↑ Pul. Capillary Pr.

↓

Pul. oedema

↓

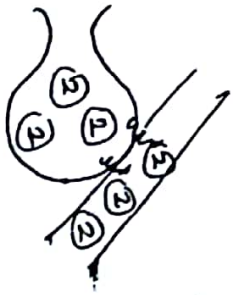
↑ PA. HTN

↓

RHF

PCWP = ↑ in CPE.

NON-CARDIOGENIC



Damage to capillary endothelium & alveolar epithelium.

↑ Neutrophil entry = inflammation.

& damage = ↑ inflammatory exudate.

SHOCK LUNG.

PCWP / Pul. Arterial Occlusion Pressure

→ Swanzganz catheter used

→ Indirect measure of LAP

→ In CPE PCWP > 18 mm Hg

In NCPE PCWP < 18 mm Hg

Dx:- Berlin 2012 Definition

1) Acute Onset < 7 day

2) Origin of oedema ⇒ non-cardiogenic & PCWP < 18 mm Hg

3) B/L diffuse infiltrate in CXR - PA

4) $\frac{PaO_2}{FiO_2}$ < 60 mm Hg / 0.2 = < 300.

$\frac{PaO_2}{FiO_2}$ 200 - 300 = Mild ARDs

$\frac{PaO_2}{FiO_2}$ 100 - 200 = Mod. ARDs

$\frac{PaO_2}{FiO_2}$ < 100 = Severe ARDs

℞ Most Recommended Strategy / Beneficial :-

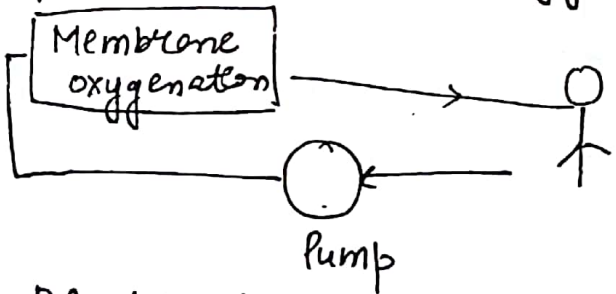
1) Low Tidal Volume Mechanical Ventilation (4-6 mL/kg Body wt.)
- Assist control mode to avoid ventilation associated Lung Injury

2) Adequate +ve End Expiratory Pressure

3) Gluco-corticoid may be helpful.

*Newer Ventilation Mode :-

1) Extra corporeal Membrane Oxygenation.



Mech :- Blood is pumped into membrane oxygenator ⇒ oxygenated blood sent back into body.
Beneficial in severe ARDS.

2) Prone Ventilation.

MECH:: In prone ventilation. diaphragmatic Pressure on lower alveoli ↓ ⇒ ↑sed alveoli for oxygenation

~~at wt. of abdomen ↓~~

For Benefit ⇒ Done for 16 consecutive hours.

→ Helpful in improving oxygenation in pts c severe Hypoxemia.

→ Not helpful in pt. c pre-existing chest wall deformity/ severe fibrosis.

3) High Frequency Oscillator Ventilation

→ Low tidal volume are given c more frequency

→ Beneficial in few studies

TRALI

(Transfusion Related Acute Lung Injury)

→ Occurs in or during 6hr of transfusion.

→ Donor Plasma antibodies Vs Recipient leukocyte

→ Mediator release

→ Feature of ARDS

Rx: supportive

H/o of Transfusion related fatality

P. THROMBOEMBOLISM (M/c of Cor. Pulmonale)

Migration of thrombus ∫ into Pulmonary artery

M/c source: Pelvic veins.

CAUSES

1°

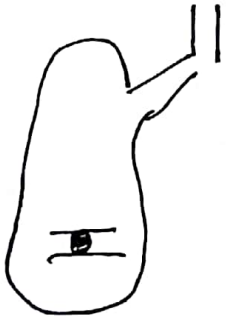
1) Protein C, S deficiency
2) Factor V Leiden mutation.
3) Lupus anticoagulant
4) Antiphospholipid antibody syndrome
5) Hyper homocysteinuria

2°

1) Prolonged immobilisation
2) Recent Trauma. Sx
3) High estrogen state
   eg. ♀,
   estrogen containing pills
4) malignancy
5) Nephrotic syndrome

PATHOPHYSIOLOGY

LUNG

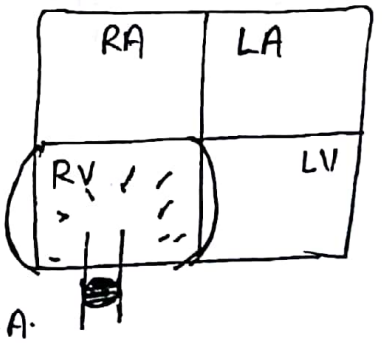


1) ↑ Pul. arterial Pressure
   ↳ rupture of vessel
   ↓
   Hemoptysis

2) ↑ Alv. Dead space = Hypoxemia
   ⇓
   Shortness of Breath.

3) ↑ Serotonin by platelets
   ↳ Bronchospasm → airway ↑ Resistance

HEART



↑ R.V. Pressure
RV Dilatation
RV Hypokinesia
Movement of septum into LV ⇒ Ventricular Interdependence
⇓
SHOCK

[COR Pulmonale]

4) Lung ischaemia → ↑ infl. mediators

5) Pleuritis → chest pain

6) Pleural effusion → Exudate >> Transudate

TRIAD

1) Chest pain
2) SOB (M/C symptom)
3) Hemoptysis.

COR PULMONALE :- alteration in str. & function of (R) ventricle due to 1° disorder of Resp. System excluding disease of (L) heart

M/C of chr. cor pulmonale → COPD

M/C of Acute " " → Massive PTE ⇓ present c shock

DIAGNOSIS

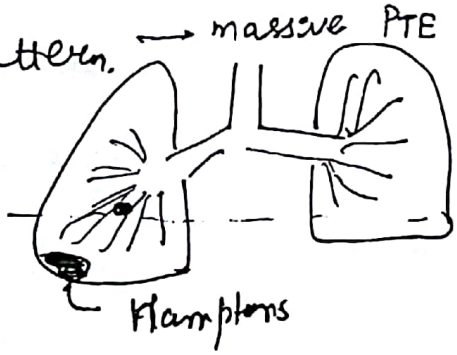
1) ABG → Type I Resp. Failure

2) ECG → M/C → Tachycardia, T wave inversion $V_1 - V_4$

3) Most specific → $S_1 Q_3 T_3$ pattern. → massive PTE

4) CXR → (N) M/C

FOCAL OLIGEMIA (Westermark Sign)



2) Wedge shaped deformity above diaphragm
Hampton's hump

3) Palla's sign - Dilatation of (R) Descending Pul. artery

4) D-Dimer :-
Fibrin Degradation product
Elevated in PTE
Sensitive not specific
poor predictive value but good neg. predictive value

5) Ioc ⇒ CT Pulm. Angio

6) Gold Std ⇒ Invasive Pul angiography

7) V/p scan. - outdated → ♀
used in Contrast intolerance.

Rx

MASSIVE PE
↓
Shock + RV Dysfunc"
↓
Thrombolysis >
Surgical Embolectomy

SUBMASSIVE PE.
↓
(N) BP + RV dysfunc"
↓
Individual Rx
Thrombolysis /
Anticoagulation

MINIMAL PE
↓
(N) BP + (N) RV function.
↓
Anti-coagulation.

PULMONARY HTN

MPAP > 25mmHg @ rest

MPAP > 30mm Hg ↑ exercise

MECH. ↓ WHO CLASSIFICATION

Group I - Direct involvement of Pul. artery

a) Heritable cause/ 1° Pul HTN - mutation in $BMPR_2$

↓

↑ smooth m/l proliferation

↓

young ♀.

Biopsy → Plexiform lesion.

b) Connective Tissue Disorder.

M/C cause ⇒ scleroderma, SLE.

c) Drugs / Toxin - Fenfluramine.

Toxic rapseed oil

Group 2 - Due to (L) Heart Disease

Group 3 - Due to Resp. diseases.

COPD/ ILD / Bronchiectasis/ OSA

Hypoxemia → Pulm. vasoconstriction → P. HTN → Cor Pulmonale

Group 4 - Due to chronic thromboembolic events in Pulm. circulation.

Group 5 - Miscellaneous / unclear cause

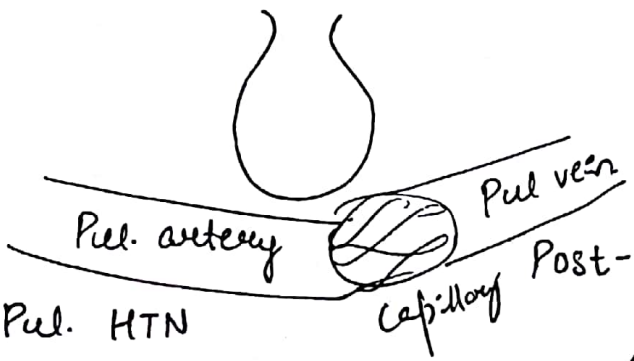
Sarcoidosis

Sickle cell Disease

Langerhans cell histiocytosis / Eosinophilic Granuloma (misnomer)

~~Lymphangiomatosis~~

Lymphangioleiomyomatosis



Pre-cap Pul. HTN

↓

Group ①, ③, ④

MPAP > 25mmHg

PCWP < 15mm Hg

Post-capillary Pul. HTN

↓

GROUP ②

MPAP > 25 mm Hg

PCWP > 15mm Hg

℞

GROUP ① + Refractory cases from other groups

1) CCB - Nifedipine (now not used frequently)

2) PDE 5 Inhibitor

Sildinafil

Tadafil

3) Endothelin Receptor antagonist

Bosentan

Ambrisentan.

Other Groups

℞ underlying disease

4) Prostacyclin -
Epoprostenol (IV)
Iloprost (Inhaled)

5) Guanyl cyclase activator
Riociguat

DOC for Low Risk Cases :- Initial monotherapy of either PDS Inhibitor or ETRA ↓ followed by combination Rx.

DOC for High Risk / Emergency :- Prostacyclins (Symptoms at Rest)

PNEUMONIA

Acute resp illness characterised by Radiological Pulmonary shadowing.

CLASSIFICATION -

COMMUNITY-ACQUIRED P.	HOSPITAL ACQUIRED P.	VENTILATOR ASSOCIATED P.
→ Occurs in ambulatory individuals.	Occurs after 48 hrs of hospital stay.	Occurs 48-72 hrs after endotracheal intubation + Mech ventilation
→ <48 hrs of hospitalisation	Mcc HAP Gram-ve Bacilli > Staph. aureus	
M/cc CAP → Strept. pneumonia		
Mcc CAP - Hospitalisation ↓ ICU Admin		

VAP

<5d | >5day

Early

↓

M/C Strept. pneumonia

H. influenza

Drug sensitive org.

So, good response

Late

↓

Drug resistant org

M/c :

Pseudomonal

Staph. aureus

Acinetobactor

↓

Poore response

CLINICAL CLASSIFICATION

TYPICAL

Fever + Productive cough

Predominant neutrophilic leucytosis

Gram staining → reveal organisms

CXR → Alveolar exudates

M/c - Strept. Pneumoniae

Staph. aureus

Klebsella

Pseudomonal

ATYPICAL

Interstitial Inflammation

Fever + cough ⇒ scanty sputum

Mild Leucocytes

Gram staining → no organism

CXR - NO alveolar oxidation

- Interstial pattern

M/c - Mycoplasma

Legionella

Coxiella

Chlamydia

Viral Pneumonia

TYPICAL PNEUMONIA

(I) STREPT

Risk Factors — M/c
- Smoker
- alcoholic
- DM

c/F Red rusty Sputum

CXR  Localised involvement of lobe/segment

(M/c) pattern in CAP

Rx - β lactams

(II) STAPH

IV drug users pneumonia

Fatal pneumonia post viral illness

mucopurulent sputum

CXR 

Bronchopneumonia

B/L, patchy involvement

(M/c) pattern in nosocomial Pneumonia

Pneumatocele + cavety + Lung abscess may be seen

Rx MRSA = Vancomycin

VRSA = Linezolid

(III) KLEIBSELLA

Alcoholics
DM
malnourished

Red currant Jelly Sputum

CXR 

Bulging fissure sign

- cavities
- Dense consolidation
- Lower lobe involvement seen if hematogenous spread

Rx -
Blactam + Aminoglyoside

(IV) PSEUDOMONAS

→ Frequently occurs as VAP

→ occur as Recurrent pneumonia in → Structural Lung disease, cystic fibrosis, Bronchiectasis

→ Fever, mucopurulent secretion, Leucocytosis.

- B/L infiltration of CXR

Rx - Two Anti pseudomonal ABs of 2 different class.

Antipseudomonal ~~ABs~~ β lactam + FQ (or) Aminoglycoside

ATYPICAL PNEUMONIA

MYCOPLASMA / Walking P.

M/c atypical pneumonia

Eaton agent pneumonia

Man → Man transmission.

Extrapulmonary features

1) CNS - GBS
peripheral neuropathy

2) Ear - Bullous myringitis

3) Blood - ↑ cold agglutinins
Heamolytic anaemia

4) CVS - Myocarditis
Pericarditis

5) Skin - Erythema Nodosum

No cell wall (+)

Rx - Macrolide / FQ / Tetracycline

LEGIONELLA

M/c mode of Transmission -
micro aspiration > Aerosolization

Spreads through contaminated water

Limited man to man transmission

Special Features :-

1) Associated GI features : diarrhoea

2) " CNS features :-
confusion, headache,
high grade fever

3) Altered LFTs

4) S. Na^+ < 130 meq

Gram staining → no organism

Poor response to β lactams

Old age, Immunocompromised

occurs in 10 days discharge from hospital

Rx - FQs / Macrolide / Tetracycline

↓

Resp FQs - Levo / Moxi

PNEUMOCYSTIS PNEUMONIA (PCP)

M/c opportunistic infection in HIV = TB

M/c pneumonia in HIV = TB

M/cc pleural effusion in HIV = TB

M/cc fungal pneumonia in HIV = PCP

R/F:-

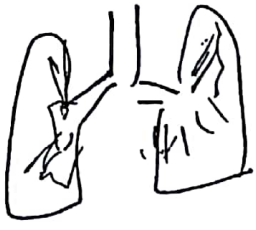
1) $CD_4 < 200$ /µL in HIV
2) Long Term Immunosuppressive Rx
3) Organ Transplant
4) 1° Immunocompromised

C/F:-

Subacute onset
Fever
Shortness of Breath
Hypoxemia

CXR:-

Perihilar infiltrates
Diffuse interstitial infiltrate
In few - pneumatocele
Complicate a Pneumothorax



Δ:- Visualize the cyst → Wright - Giemsa
→ Gomori - methamine stain.
Broncho-alveolar lavage (Best sample)

Rx - COTRIMOXAZOLE (Septran)

If sulpha allergy → 1) Clendamycin + Primaquine
2) Trimethoprim + Dapsone
3) Pentamidine
4) Atovequone

DOC for Prophylaxis → COTRIMOXAZOLE
↓
DOC for NOCARDIOSIS.

VIRAL PNEUMONIA

BIRD FLU (H_5N_1)

- Avian Influenza
- Less M → M transmission
  Epidemic not pandemic

DOC - Oseltamivir

SWINE FLU (H_1N_1)

- ↑↑ M → M transmission
- Epidemic + Pandemic

DOC - Oseltamivir
75mg BD for 5 days
(neuraminidase Inhibitor)

Doc prophylaxis - Oseltamivir
75mg OD for 10 day

other drugs - Zanamivir
Peramivir

ASSESMENT of SEVERITY_

C onfusion

Urea > 7 mmol/L or > 20 mg

RR > 30/min

B - SBP. < 90 mm Hg DBP < 60 mm Hg

65 Age age > 65

0-1 ⇒ Home Rx ē antibiotic

2 ⇒ Hospitalisation . Rx

3-5 ⇒ Consider as severe pneumonia , may require ICU admincon.

EMPIRICAL REGIMEN FOR HOSPITALISED Pt OF PNEUMONIA

⇒ TYPICAL + ATYPICAL

β lactam + Macrolide

LUNG ABSCESS

1° ~~ABS~~ form

M/c type

Due to aspiration

M/c organism - oral anaerobes

↓

Rx - IV - Clindamycin.

2° form

Occurs due to pre-existing disease process in lung

Bronchial obstruction

Immuno deficiency

Staph, Klebsiella

Rx - Broad spectrum ABs

Strategies to Prevent VAP :-

1) Elevation of Head of Bed 30°-45°

2) Oral Decontamination ⊂ Chlorhexidine

3) Sedation vacation (↓ sedation)

4) Assesment of readiness to extubate daily

5) Use of NIV wherever feasible

X Frequent change of Tubex

ORAL ANAEROBES-

→ Peptostreptococci

→ Fusobacterium

→ Bacteroide

PLEURAL EFFUSION

LIGHT's CRITERIA (H/c)

TRANSUDATE

$\frac{\text{Ple. fluid. Protein}}{\text{S. protein}} < 0.5$

$\frac{\text{Pl. fluid LDH}}{\text{S. LDH}} < 0.6$

Cause-
1> CHF (H/cc overall)
2> Hepatic Hydrothorax
3> Nephrotic Sx

EXUDATE

> 0.5, 0.6.

Cytology = ? malignant cells
cell count
Gram staining ? infection
TB marker = ADA, Interferon γ

Special Features

1> Low glucose ple. fluid (< 60mg%)
a> Empyema
b> Malignancy
c> RA
d) TB (Rare)

2> High Amylase
a) Pancreatitis
b) Oesophageal rupture
c) malignancy

3> High Lipid Ple. Eff / white coloured

Chylothorax
Accumulation of Chyle due to disrup' of thoracic duct
Pl. TGA > 110mg%
H/c - Surgical Trauma, Malignancy

Pseudochylothorax
Accumulation of cholesterol crystals in long standing eff.
TB, RA, Ch. empyema, myxoedema
cholesterol > 200 mg%.

Milky white BAL
193
Alveolar Proteinosis

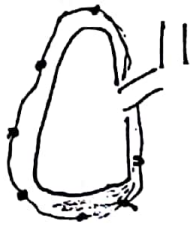
* Parapneumonic Eff
  M/c of exudative Pleural Eff
  Eff associated c Pneumonia
  Bronchiectasis
  Lung abscess

Indications of ICD insertion in parapneumonic Eff :-

1) Pus in pleural cavity
2) pH < 7.2 (pleural fluid)
3) Ple f. glucose < 60mg%
4) Loculated pleural effusion
5) Gram staining reveals organisms

TB Effusion

- M/c exudative effusion in India
- Occurs due to hypersensitivity response to TB Bacilli in Pleural Tissue



- Exudative — Lymphocyte predominant
  ADA >40 IU
  IFN γ > 140 pg/mL
  ↓ mesothelial cells
- Pleural Fluid for AFB only positive in 20-30% cases.
  Gold Std — Thoracoscopic pleural Biopsy + Culture for M. tb.

PNEUMOTHORAX & PNEUMOMEDIASTINUM

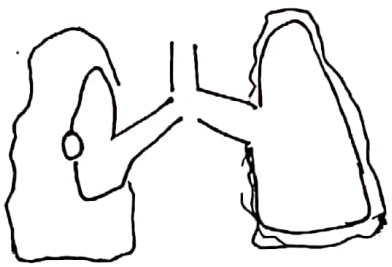
Classification of Pneumothorax :-

- SPONTANEOUS
  - 1°
    - No underlying Lung disease
  - 2°
    - Pre-existing lung disease
      - COPD (Mcc of 2° spon. pneumothorax)
      - Bronchiectasis
      - ILD, TB
- TRAUMATIC
  - Iatrogenic
    - 1) Transthoracic needle aspiration (Mlc)
    - 2) Mech. ventilation
    - 3) Insertion of subclavian catheter
  - Chest wall injuries
    - RTA.

TENSION PNEUMOTHORAX

1> Large air leak

2> Air Leak serves as Ball valve (or) one way valve mechanism



3> ↑↑ Positive intrapleural Pressure

4> Compressing adj lung + medastenal vessels

↓

↓ VR

↓

Shock (medical emergency)

5> Rx- Next step / Best step- Insertion of wide bore needle @ 2nd I.C.S. anteriorly mid clavicular line on affected side followed by ICD insertion.

High Inspiratory Pressure alarm on ventilator can suggest ~~Pneu~~ Tension Pneumothorax.

Pneumo Mediastinum

Air in mediastinum

C/F - Shortness of Breath
Chest pain
HAMMAN'S Crunch → Crunching sound synchronous c heart Beat

CXR - Continuous Diaphragm Sign.
Subcutaneous Emphysema

ASTHMA

Characterised By recurrent symptoms due to variable & reversible bronchoconstric" caused due to airway hyper-responsiveness to variety of stimuli

COPD - characterised by persistent symptoms & airflow limitation due to airway & alveolar abN caused by significant exposure to noxious stimuli.

ASTHMA	COPD
Allergan related	Smoking related
Reversible airflow limitation	Persistent airflow limitation
Early Presentation	Delayed presentation
Relief c Bronchodilators	only partial response

TYPES & PATHOGENESIS

EXTRINSIC / ATOPIC / ALLERGIC	INTRINSIC / ~~NONALLERGIC~~ NONATOPIC / IDIOSYNCRATIC
Allergen related	Viral infection ⇒ Trigger
S. IgE ↑	S. IgE (N)
Skin test +ve for allergen	Skin test -ve
Mild form	Severe forms
Young onset	Late onset

M/C allergen world
↳ HOUSE DUST MITE / Dermatophagoides

Pollen → cause Thunderstorm Asthma

Δ :-

1) SPIROMETRY

obstructive

Bronchodilator reversibility = ↑ FeV_1 > 12% (or) 200cc after SABA.

FeV_1 65% $\xrightarrow[15\,min]{SABA}$ FeV_1 80%

2) PEFR variability

>20% diurnal variation.

3) METH. CHOLINE challenge Test / Broncho provocation Testing

fall in FEV_1 > 20% after meth. choline.

for airway hyper-responsiveness

4) FeNO > 50 PPb ≈ Eosinophilic inflammation.

ACUTE SEVERE ASTHMA.

C/F-

1) Pt. speaks in words
2) can't recline
3) RR > 30/min
4) HR > 120/min
5) B/L Wheeze
6) Accessory muscle use
7) Pulsus Paradoxus → [Raped change in intrapleural pr. causes this.]

Functional Parameters :-

1) PEFR < 50% predictive value.
2) SpO_2 < 90%
3) PaO_2 < 60mmHg

→ Type I Resp. Failure

~~First~~ Type 2RF can occure in severe cases
↳ due to fatigue of resp. muscles.

* Life Threatening Asthma :-

1) Patient - altered sensation
2) Silent chest
3) ↓ Respiratory effort
4) PaO_2 < 60mmHg
5) $PaCO_2$ ↑↑

Rx - 1) O_2 +
2) SABA + (salbutamol) + Inhaled corticosteroid
· SAMA (Ipratropium)
2) I.V. Steroid ← ↓Inflammation
↑ sensitivity of β_2 receptor to bronchodilator

3) Theophylline now not used routenely

4) In few cases **IV $MgSO_4$** given

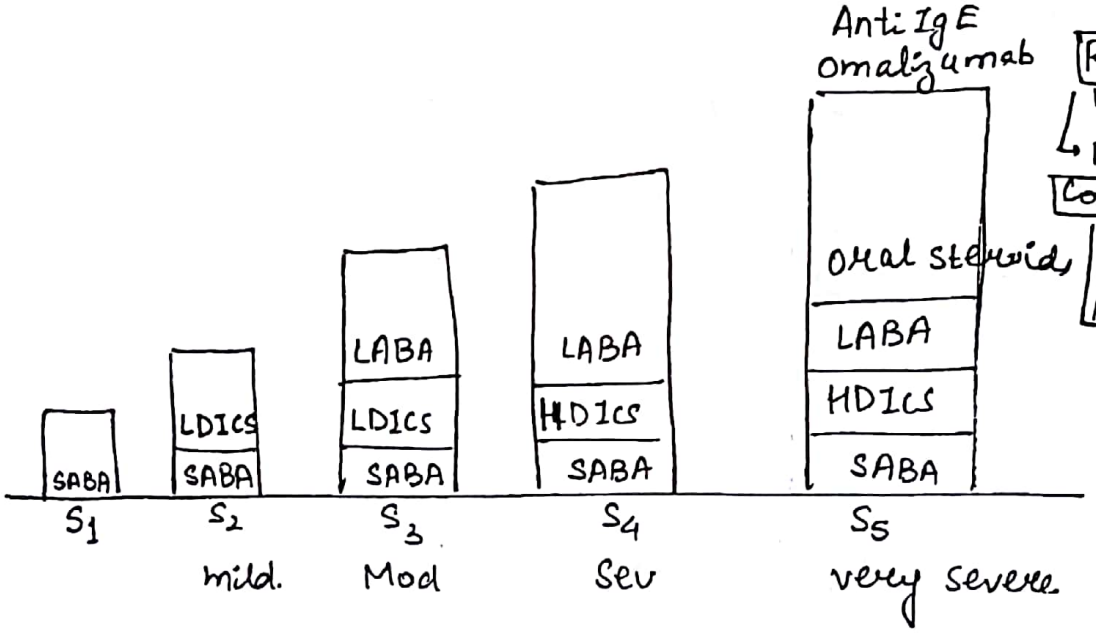
5) In deteriorating /life threatening case ⇒ **Invasive** Mech. ventilation.

↙ High inspiratory flow

↘ ↑ Expiration Time I:E = 1:3 or 1:7.

Step Wise Therapy & Classification

	Intermittent	Persistent		
		Mild	Mod	Sev
Day Time S_x	< 2/week	> 2/week	daily	through-out day
Night time awakening	< 2/month	> 2/month	> 2/week	daily



LDICs → low dose ICs.

HDICs → High dose ICs.

Most Imp. in Asthma management is pt. ~~self~~ education & active self Mx. 199

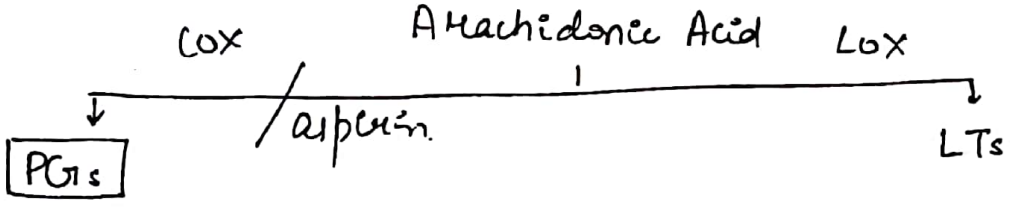
EXERCISE INDUCED ASTHMA

In susceptible individuals, exercise can induce asthma more frequent during cold & dry climate > hot humid condition.

DOC for short term prophylaxis = SABA > Anti-leukotriens / Mast cell stabilizer.

DOC for Long term prophylaxis & overall control of disease } Corticosteroids

ASPIRIN INDUCED ASTHMA



Samter's TRIAD–

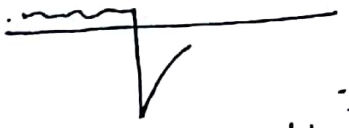
Nasal polyposis + Aspirin sensitivity + Asthma

In susceptible individuals. aspirin blocks COX pathway & shifts balance towards LOX pathway ⇒ ↑ LTs ⇓ Bronchospasm.

Rx = ICS + ~~Aspirin~~ SABA + Anti-leukotrienes + Aspirin desensitization.

BRITTLE ASTHMA

Unstable Disease ≈ frequent exacerbations

(N)	Type 1 Brittle	Type 2 Brittle
Lung function	Persistent fluctuation in lung functions 	Near normal Lung function → Rapid fall . death. 
	Difficult to Rx asthma * Oral corticosteroids + continuous infusion = β_2 agonist	Localised anaphylaxis ↓ Laryngospasm DOC :- Subcutaneous epinephrine + Adrenaline

CORTICOSTEROID RESISTANT ASTHMA

Poor response to Rx after 2 weeks of oral corticosteroids (40mg/day) Rx

steroid sparing drugs can be used.

Anti IgE = **Omalizumab.**

Anti IL5 = **Mepolizumab**

COPD

CHR. BRONCHITIS :-

Cough ± sputum for >3 months in 2 consecutive years

EMPHYSEMA :-

Destruc" distal to terminal bronchiole.

R/F :-

1) Smoking
2) α_1 AT Deficiency
3) Indoor + outdoor pollution.
4) ~~Cold~~ exposure coal.

→ young age
→ Less smoking H/o
→ Family H/o - Chr. 14, AR.
→ B/L Lower predominant
→ Bronchiectasis
→ Unexplained Liver Disease.

2)

TYPES OF EMPHYSEMA

CENTRIACINAR	PANACINAR	DISTAL ACINAR
<u>occurence</u> Smokers M/c overall. Upper lobes	α_1AT Def. More severe in LL	Adjacent to fibrotic foci. Upper 2/3rd of Lung
<u>Pathology</u> 		
RB involved alveolar duct + Sac spared	Resp. Bronchiole + Alv. Duct + Sac involved	Resp. Bronchiole spared Alv. duct + sac involved

Δ:- 1) SPIROMETRY

$\frac{FeV_1}{FVC} < 0.7 \approx$ Obstructive

No significant Bronchodilator reversability

GOLD Staging (Global Iniative for obstructive Lung Disease)

I Mild $FeV_1/FVC < 0.7$ FeV $\geq 80\%$ Pred FeV_1

II Mold. " " " FeV_1 50-79 % " "

III Severe " " " FeV_1 30-49% " "

IV very severe " " " $FeV_1 < 30\%$ pred. value

Prognosis Index

BMI

Obstruction (FeV_1)

Dyspnoea (MRC scale)

Exercise Capacity ⇒ Distance covered in 6 minute walk test

Low score ⇒ Good Prog.

High score ⇒ Poor Prog, ↑ mortality

CHARACTER	BLUE BLOATER	PINK PUFFERS
PATHOLOGY	Chr. Bronchitis.	Emphysema.
SYMPTOM	Cough ± expectoration	Shortnes of Breath
APPEARANCE + POSTURE	obese + comfortable at rest	lean + tachypnoeic at rest
Breath sounds	Rhonchi - Noisy	Less noisy
CXR	↑ Interstitial Marking obstructive	Hyperinflated Lung obstructive

Rx :-

1> Smoking cessation. → most imp. intervention.

2> BRONCHODILATORS

A> LABA

Ultra LABA → O.D. Dose

- ✓Indacetrol
- ✓Vilanterol
- ✓Oladetrol

B) LAMA

Tiotropium

Umiclinidium

Glycopyronium.

3> STEROID :-

a) Inhaled

↓ freq. of exacerbation

b) Systemic

During exacerbation.

4> SELECTIVE PDE_4 INHIBITOR :-

Roflumilast

5> ANTIBIOTICS :-

During exacerbation (H. influenza)

6) MUCOLYTICS -

N Acetyl cysteine

7) If Hypoxemia → Long Term O_2 therapy (15 hours a day)
low flow O_2

8) Lung volume Reduction surgery

9> LUNG TRANSPLANTATION (M/c Indication for lung transplantation in COPD)

10> During exacerbation, 1st choice - non-invasive ventilation.
> Invasive ,,

BRONCHIECTASIS

Ab Ⓝ Permanent Dilatation of bronchi due to loss of muscle & elastic tissue.

Initiating event
↓
Altered mucociliary clearance
↙
obstruction.

Vicious Cycle Theory

↓
Recurrent infection → Inflammation → Destruction & dilatation → Altered mucociliary clearance

C/F :-
copious sputum
coarse crepts

ETIOLOGY & MECH :-

I) BRONCHIAL OBSTRUCTION

a) Intramural

Tumours - Carcinoid
Sq. cell carcinoma
Small cell carcinoma

b) Extrinsic Compression.

Enlarged TB hilar LN can compress Ⓡ middle Lobe Bronchus → Ⓡ middle Lobe collapse & bronchiectasis
⇓
BROCK'S SYNDROME.

II> BRONCHIAL INJURY

A) Infection

TB, adenovirus

B) Altered Immune response

→ Connective Tissue Disorders

→ Allergic Bronchopulmonary Aspergillosis (ABPA)

III> TRACTION BRONCHIECTASIS in ILDs

IV> GENETIC CAUSES

A> 1° ciliary dyskinesia

B> Cystic fibrosis

C> Cartilage Defect

- William campbell s.
- Mounier Kuhn syndrome

D) Yellow Nail Syndrome

Cong. Lymphoedema + Yellow nail + Pleural Effusion + Bronchiectasis

CYSTRIC FIBROSIS

Inheritence - AR

Chromosome 7q

Gene - CFTR

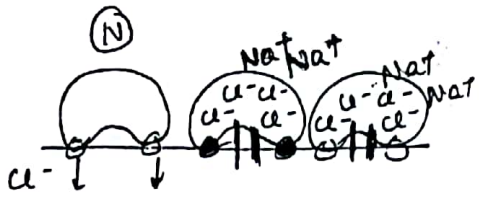
Channel - Cl^-

Mutations - Class I - VI

M/c class II, ΔF508

" Thick secretions "

(I)



Resp. Tract

GIT

Reproductive Tract

watery secretions

Thick viscid secretions dehydrated

(II)

Sweat Gland

ENaC → responsible for pathophysiologic process

SCREENING Test

↑ Sweat Cl^- > 60 mEq.

Other Inv:-

1) DNA analysis for mutations

2) ↑ Nasal Pot^n Difference

3) CFTR Gene sequencing :- Gold Std.

SYSTEMIC MANIFESTATIONS:-

1) Respiratory Tract -

URT
↓
Recurrent infections
Sinusitis

LRT
↓
Recurrent pneumonia
(M/c pseudomonas), steph.
Bronchiectasis, Lung abscess
Empyema, P. thrombosis,
Resp. failure, Hypoxemia,
P. HTN, Cor Pulmonale

2) GIT
neonate Meconium ileus.

Liver → Biliary cirrhosis,

GB - Gall stone

Pancreas

- Exocrine insufficiency - early manifestations
- DM, → occurs later.

3) Reproductive Tract -

♂ In utero occlusion of vas Deferens by thick secretions → AZOOSPERMIA. → infertile

♀ Thick cervical secretions

℞

1) CFTR Modulators :-

Ivacaftor - G551D mutation class III

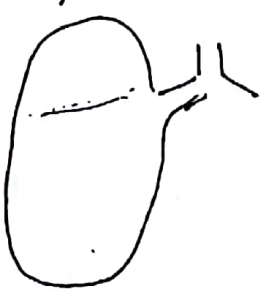
Lumecaftor + Ivacaftor - tried in class II

TYPES OF BRONCHIECTASIS -

H/c - Cylindrical Varicose Saccular

SITES of B'XIs -

1) Upper Lobe



1) Cystic fibrosis
2) TB
3) Post radiation BXIs

2) Lower Lobe

1) Interstial Lung Disease
2) Chr. recurrent aspiration
3) Immunodeficiency state

3) Middle Lobe - non-tubercular mycobacterium.

Mycobacterium avium complex (MAC)

Rx of B'XIS-

1) Airway clearance.

Mucolytics ← → Chest Physiotherapy.

2) Antibiotics

During exacerbation

Prophylaxis

- Long term: Azithromycin (6 months)
- Inhaled: Tobramycin (1 month on-off)

3) Bronchodilator + ICS beneficial in some

4) If Hypoxemia ⇒ O_2.

5) Localised Disease → Sx

6) Diffused " → Lung Transplantation.

High flow O_2 not recommended. Y ?

1> Abolition of Hypoxemic resp. drive

2> High O_2 given can cause release of CO_2 from RBC
↳ HALDANE EFFECT.

IOC :- HRCT Chest

EOSINOPHILIC LUNG DISEASES

[Peripheral eosinophilia + Lung infilterates]

CLASSIFICATION

Unknown cause	Known cause
1) Acute eosinophilic pneumonia	1> PARASITIC INFESTATIONS (Nematods)
2) Chronic " "	Loeffler's pneumonia
3) Hypereosinophilic syndrome	2) ABPA
4> Churg strauss Sx	3) Drugs :- Nitrofurantoin, sulfonamides, Isoniazid, Pencillamine

Hypereosinophilic Syndrome -
Persistent (6 months) eosinophilia > 1500/mm^3.
& end organ infilteration.

CHARACTER	Ac. EP	Chr. E. P.
Smoking H/o	+++, new onset smokers	±
Asthma H/o	--	++
CF - Radiology	Acute shortness of Breath + Hypoxemia + B/L diffuse infilterates.	Cough + wheeze. Peripheral opacities
Peripheral eosinophilia	Initially not seen but seen during later course of disease	Usually seen

	AEP	CEP
BAL eosinophilia	BAL > 25% eosinophil	BAL > 40% eosinophil
Rx	steroid	steroid

ASPERGILLUS & LUNG

I> HYPERSENSITIVITY RXN. → DOC :- steroid

Type I ↓ Asthma

Type I', III, IV ↓ ABPA

II> PNEUMONIA IN IMMUNOCOMPROMISED → DOC :- VORICONAZOLE.

= Invasive Aspergillosis

Transbronchial angioinvasion. → may develop hemoptysis
· Fever + SOB.

DOC for (I) & (IV) ⇒ STEROID.

DOC for (II) ⇒ VORICONAZOLE

III> COLONISATION IN PREXISTING LUNG CAVITY

Aspergilloma / Fungall BALL

CXR → 1) Air crescent Sign.
2) Ball changing its position :- decubitus.

Rx - Resection if pt. is symptomatic

CRITERIA FOR ABPA

1) Predisposing cond^{n} - ✓Asthma
✓Cystic Fibrosis

2) Peripheral **Eosinophilia**

3) S. IgE → **> 1000 IU**

4) Aspergillus specific IgE & IgG will be +nt

5) Skin test +ve **aspergillus fumigatus.**

6) CxR - **fleeting opacities** → upper zone

7) Central (or) Proximal **B' XIs**.

Doc:- Systemic steroids.

CT chest -
- ✓Finger in glove
- ✓Toothpaste

HYPERSENSITIVITY PNEUMONITIS
or Extrinsic Allergic Alveolitis

Type III + IV HSN

S. IgE → (N)

No. peripheral eosinophilia

BIOPSY → non caseating granuloma + cellular bronchiolitis + Interstitial inflammation.

Eg:

DISEASE	EXPOSURE	ANTIGEN
1) Farmar's Lung	Moldy hay	Micropolyspora fen: (Thermoactenomyces Sacchari: Thermo actino myeter)
2) Bagassosis	Sugarcane dust	
3) Bird fancier Lung	Pigeon excreta	Avian protein
4) Malt warker Lung	Mouldy Barley	Asp. clavatus
5) Hot tab lung	Contaminated water	Non-Tuberculer mycobacterium

Astic CRITERIA :-

1) Exposure to known antigens
2) Presence of serum precipitins against offending Ag.
3) Occurence of symptoms in 4-6 hrs of exposure
4) Reoccurence of symptoms on exposure
5) Inspiratory crepitation.
6) wt. loss

TYPES

	CT Chest
ACUTE - hours to days	Ground glass opacities
SUBACUTE - week.	Centrilobular nodules
CHRONIC - Month	Fibrosis (upper zone)

Rx - Most Important → Avoidance of allergen
Systemic steroids

ILD

Def":- Group of Disorders characterised by predominant involvement of interstitium progressing to fibrosis & vary in mechanism & magnitude.

ETIOLOGY:-

I> Inhalational ILD

- Organic Dust → Hypersensitivity Pneumonitis
- Inorganic Dust → Silica, Asbestosis

II> Drugs / Radiotherapy
- Amiodarone
- Methotrexate
- Busulfan

III> Connective Tissue Disorder
- Scleroderma
- RA
- SLE

IV> IBDs

V> Infections - TB

VI> Malignancy

VII> Sarcoidosis

VIII> Idiopathic

PATHOLOGICAL PATTERNS:-

1> Usual Interstitial Pneumonia (UIP)

2> Non-specific " " (NSIP)

3> Acute Interstitial Pneumonia (AIP)

4) Cryptogenic Organising pneumonia (COP)

5) Respiratory Bronchiolitis (RBILD)

6) Desquamative Interstitial Pneumonia (DIP)

7) Lymphocytic " " (LIP)

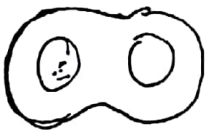
IOC :. ~~CT~~ HRCT chest

Confirmatory Test :. Surgical Lung Biopsy

RADIOLOGIC PATTERNS

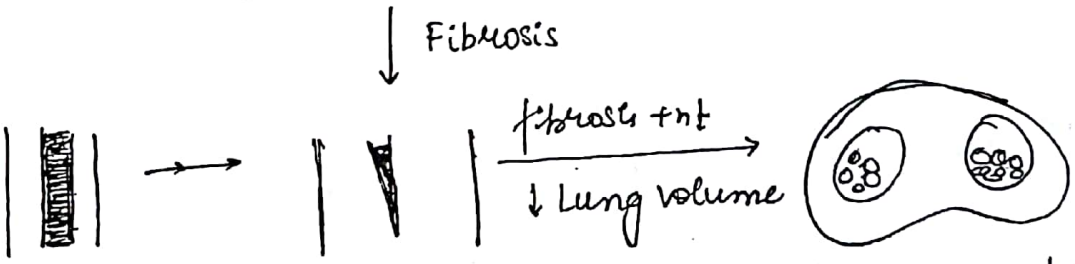
Reticular Pattern.

CT Chest



Mild opacity = Ground Glass opacity

Used density = consolidation.



	Usual Interstitial Pneumonia	NSIP. (H/c form of connective tissue disorder associated ILD)
M/C form	or Idiopathic Pul. Fibrosis	
C/F.	50-60yrs ♂ > ♀, Smoker. insidious, Auscultation - Inspiratory crepts. Exam - clubbing	40-50yrs ♀ > ♂ Non-smoker, subacute onset.
Biopsy	Heterogeneous involvement Fibroblastic foci	No fibroblastic foci Lymphocytic inflammation
Radiology	- B/L Lower zone & - subpleural involvement - Minimal Ground glass opacity - Significant Traction B'XIS - Honeycombing	B/L ground glass opacities Minimal Traction Bronchiectasis Rare honeycombing
Rx + Prognosis	Poor response oo Pirfenidone Nintedanib	Good response. ī oo steroid

ACUTE INTERSTITIAL PNEUMONIA / HAMMAR RICH SYNDROME

Pt- present ī acute SOB + Hypoxemia + Diffuse infiltrate

Idiopathic ARDS

Rx- supportive. High mortality

CRYPTOGENIC ORGANISING PNEUMONIA / BRONCHIOLITIS OBLITERANS ORGANISING PNEUMONIA (BOOP)

1) Pneumonia like illness
2) Proliferation of granulation tissue in airway ⇒ MAISON BODIES

3) Presence of Interstial infilterate.

CXR :- B/L Peripheral Consolidation.

Rx :- STEROID.

SMOKING AND ILD:

Resp. Bronchiolitis associated ILD

Desquamative Interstitial Pneumonia

Adult Pulmonary Langerhans cell histocytosis

Acute eosinophilic pneumonia

Pulmonary heamorrhage syndromes

Idiopathic pulmonary fibrosis

ILD: Less Prevalent In Smokers :-

1) Sarcoidosis

2) Hypersensitivity pneumonitis

SARCOIDOSIS

Multisystem Disorder characterised by non-caseating Granuloma.

Etiology :- 1) Autoimmune

2) Propionibacterium

3) Mycobacterium

4) unknown.

5) Genetic susptibilty - HLA DRB, 1101

M/C → Pul. Involvement.

Scadding Staging I- Hilar adenopathy 

II- " LN↑ + Lung infilterates 

III- Lung infilterates alone 

IV- Fibrosis 

Upper zone predominant Disease

PHENOTYPES

1> LUPUS PERINIO-

Cutaneous involvement → Bridge of nose
area beneath eyes + cheeks

2> LOFGREN SYNDROME-

Erythema nodosum, Hilar LN↑
Uveitis (MC - Anterior), Arthritis

3> UVEO-PAROTID FEVER

Uveitis + Parotiditis + Fever + CN 7th Palsy

Δ:-

1> (IG) → release ACE. + $1,25(OH)_2$ Vit D

Non-caseating granuloma → ↑S.ACE >2times (N)

$1,25(OH)_2$ Vit D → Hypercalcemia

2> Blood :- Peripheral Lymphopenia - sequestration of lymphocytes into lung

3> Bronchoscopy :-

BAL - Lymphocytes $\frac{CD4}{CD8}$ ↑

4> Biopsy - Non-caseating granuloma

IOC → Incompatible clinical scenario → Biopsy of involved organ showing non-caseating granuloma is s/o Sarcoidosis

5) CT chest → Lung infiltrates
LN ↑

In TB LN → Caseating ⇒ Central hypodensity ± peripheral rim enhancement

Sarcoidosis → uniform density

6) Gallium scan

a) ↑ uptake by Parotid + Lacrimal gland - b) ↑ uptake by mediastinal LN

"PANDA SIGN"

"LAMBA SIGN"

℞ Steroid + Immunosuppressor.

↑ LEVELS OF ACE

1) Sarcoidosis
2) Leprosy
3) Gaucher's Disease
4) Hyperthyroidism
5) Disseminated granulomatous infec such as
6) miliary TB

Pneumonic: [Sar Le Ga DM ~~Hyper wo~~ thyro wale]

CONNECTIVE TISSUE DISORDER & LUNG

RA

M/c pulmonary manifestation → pleuritis

Low Glucose Pleural Effusion

ILD → NSIP, B'xis

Rheumatoid ~~Arthritis~~ nodule

CAPLAN's Syndrome. [RA + Pneumoconiosis] [silica expo, coal expo]

SLE

M/c pul. manifestation = Pleuritis

Acute lupus pneumonitis.
⇒ Pulmonary capillaritis + Deffuse alveolar H'ge

ILD → NSIP.

Shrinking Lung Syndrome

Diaphragmatic involvement in SLE.

SCLERODERMA

HIDE BOUND CHEST.

ILD NSIP ⟶ UIP, Pul. HTN

MCC of death in scleroderma → Pulmonary cause

POLYMYOSITIS

↑ Anti JO1 ABS (

→ Anti Synthetase Sx.

→ C/F – 1) Fever
2) Myositis
3) ILD
4) Arthritis
5) Mechanic Hands

DIFFUSE ALVEOLAR Hge / Pul HEMOSIDEROSIS

IDIOPATHIC Pul. hemosiderosis

1) Intra alveolar bleed
2) Fe accumulation as hemosiderin in alveolar macrophages
3) Fe deficiency anaemia

Pul. RENAL SYNDROME

1) SLE.
2) Good Pasture Syndrome
3) Small vessel vasculetis
   - Wegener's granulomatosis.
     1) Necrotising granulomatous vasculitis
     2) RPGN
     3) necrotising involvement of
        - URT → Epistaxie, sinusitis
        - LRT → Cavities, Diff. Alv. Hge

OCCUPATIONAL LUNG DISEASES

SILICOSIS

H/C occupational Lung Disease worldwide

< 2.5 μ = Dangerous particles

ASBESTOSIS

occupation Ship building, Construc° worker

Particle ~~ curvy serpentine
>> straight amphibole (carcinogenic)

FEATURES

1) Pleural Plaques
   - Most specific for asbestosis
2) Fibrosis
   - ∝ duration & exposure

SILICOSIS

Sand blasting, quarying

crystalline silica
Amorphous silica
1) Silicotic nodules

2) Merging of nodules → progressive massive fibrosis

COAL-WORKERS PNEUMOCONIOSIS

Coal miners

~~Anthracite~~ ~~Bituminous~~

1) ~~Anthracosis~~
   1) Anthracite
   2) Bituminous
2) Anthracosis
3) Coal macules
3) complicated CWP
4) ↑ COPD

3) Benign pleural effusion.

4) M/c malignancy associated c it
⇓
LUNG CANCER
Smoking + asbestosis.
⇒ synergistic

Most specific
↳ MESOTHELIOMA

Lower zone Disease

Round Atelectasis

Organised Pleff. around segment
↓
Localised atelectasis
⇓
COMET TAIL appearance

3) Silico-TB:- Chronic exposure

4) Alveolar proteinosis
↳ acute exposure

5) Malignancy.
CXR - Hilar LN + egg shell calcification

Upper zone Disease

5) Malignancy

SLEEP APNOEA

Apnoea - Cessation of airflow for atleast 10 sec.

Hypopnoea - >30% reduction in airflow associated c
>3% fall in SpO_2.

SLEEP APNOEA

CENTRAL

Resp. effort ⊖

Apnoea ⊕

Resp. drive ⊖

eg CHF

Narcotic Abuse

OBSTRUCTIVE

Apnoea ⊕

Persisting Resp. effort

↑ collapsibility of airway at Neck.

R/F for obstructive Sleep Apnoea :-

1) obesity
2) ♂
3) Craniofacial Ab Ⓝ
4) Hypothyroidism
5) Alcoholism

PATHOPHYSIOLOGY-

H/C Symptom → Snoring.

APNOEA → HYPOXEMIA → Pul. HTN, & Cor Pulmonale

↓

Arousal

↓

↑ Catecholamine Surg

↑ daytime sleepiness, Loss of interest, Depression, Personality changes, RTA ← Loss of quality of sleep

Uncontrolled HTN & Poor glycemic control

CAD, MI, arrhythmia, Sudden cardiac death, CVA.

Gold Std Δ :- Polysomnography

1) EEG
2) EOG
3) ECG
4) EMG
5) SpO_2.
6) Oronasal flow
7) Snoremic
8) Thorax & Abd. movement sensor
9) Body position / Limb movement

Other scales for assesment :-

1) Epworth sleepiness scale
2) STOP BANG Questionaire.

SEVERITY of OSA ⇒ APNOEA HYPOPNEA INDEX (AHI)

$$\frac{\text{No. of Apnoea + Hypopnoea}}{\text{Hour.}}$$

< 5/hr ⇒ (N)

5-14/hr ⇒ Mild OSA → Behavioural Rx

15-29/hr ⇒ Mod. OSA
≥ 30/hr ⇒ Severe OSA
→ Medical Rx of choice
CPAP – mild OSA + Commorbidities

In few case → Uvulo palatopharyngo plasty.

MALIGNANCY

1° LUNG MALIGNANCY :-

- Non-Small Cell Lung Cancer (NSCLC)
  1) Adeno Ca M/C worldwide
  2) Sq. cell Carcinoma MC in India
  3) Large cell "
- Small cell Lung Cancer (SCLCC)
  1) Small cell Ca / Oat cell tumour.

LOCATION & ASSOCIATION OF TUMOURS :-

1) Central Location & Cigerette smoking

⇒ Sq. cell & small cell (strongest association)
Endobronchial Location.

2) Peripheral location & Less ~~me~~ smoking

Adeno Ca (♀, young ♂, Less smoker) & Large cell

3) Cavitation

Squamous & Large.

	ADENO	SQUAMOUS	SMALL CELL
Oncogene	KRAS / EGFR / ALK	FGFR, PI3K	myc, Bcl225
Biopsy	Glandular differentiation	Keratinisation + intercellular keratin bridges	Small round cell ī hyperchromatic nuclei
Features	→ Lepidic pattern	Central	(B) chemo & radio sensitive
	Lung → Lung metastasis	Cigarette	Rapid recurrence
	Scar Ca → Adeno ca (M/c ca in abbestosis)	Cavity	↑ metastasis
		Calcemia	↑ SVC obstruc"
	↑ Clubbing → Hypertrophic osteoarthropathy	~~Hypo~~ Life threatening	POOR PROGNOSIS
	Paraneoplastic ↳ Hematologic	↑ parathormone related peptid	↑ Paraneoplastic Syndromes

PARANEOPLASTIC associated ī S'CLC

M/cc of ectopic ACTH ↓ SCLC.

1) Hyponatremia – SIADH
2) Hypokalemia – ectopic ACTH
3) Hypocalcemia – Calcitonin
4) Lambert Eaton Syndrome

CLINICAL MANIFESTATIONS of SCLC

1) Irritation → Cough (M/c symptom)
2) Hemoptysis – tumour infilterates vessel
3) ↑ size & causes → Bronchial obstruc" (Fever, SOB)
4) Pleural involvement ⇒ Pleuritis
Chest pain, Pleural eff → SOB

5) Skin & Intercostal n/vs. → Chest pain.

6) Pericarditis / Pericardial effusion.

7) Esophagus → dysphagia

8) Recurrent Laryngeal n/v → Hoarseness of voice

9) SVC obstruction.

10) Stellate Ganglion → HORNER's Syndrome
(sympathetic ganglion)

↓

- Anhydrosis
- Miosis
- Ptosis
- Loss of ciliospinal reflex
- Enophthalmos

Migratory thrombophlebitis
= Trousseau's Syndrome
+ clubbing = Adeno Ca

11) Distant Metastasis :· Brain / Bone / Liver.

H/C site → Brain

Most specific → Adrenals.

INVESTIGATIONS :-

1) CYTOLOGY → Sputum, Pleural fluid } malignant cells

2) CXR - PA - Solitary Pulm. nodule
Collapse
LN ↑
Pleural Eff

3) CT - Chest - Precise anatomical Location.

4) Gold Std → BIOPSY < CT guided
Bronchoscopy

5> PET SCAN - staging

6> Bone Scan

Rx

- NSCLC
  - Resectable
    - Stage I, II, IIIA
      - ↓
      - Surgery
  - Unresectable
    - IIIB, IV
      - ↓
      - Medical Rx
        - Squamous
          - ↓
          - Cisplatin + Gemcitabine/Paclitaxel
        - Adeno
          - ↓
          - Cisplatin + Pembrexed.
          - Targeted Rx
            - ↓
            - EGFR Antagonist - Erlotinib, gefotinib
            - ALK Antagonist Crizofinib.
- SCLC
  - ↓
  - Medical Rx
    - Chemo Rx + Radio Rx.
      - ↓
      - Cisplatin + Etoposide

Adeno Ca/ ♀/ non-smoker/ Asian ⇒ EGFR mutation.

Pancoast Tx - usually occurs ε Sq cell
Located at apex.
May involve stellate ganglion.

PANCOAST SYNDROME = 1> Tumour in Lung APex
2> Involve → 1st 2 ribs
→ Stellate Ganglion.
→ $C_8 T_1 T_2$ → Pain, weakness in Ulnar distribution

TUBERCULOSIS

Tabes

NOMENCLATURE

Tabes Pulmonale - Pul. TB (M/C)

Tabes mesentrica - Abd. TB

Carries sicca - Shoulder TB

Potts Disease - Spinal TB

Spina ventosa - TB Dactylitis

Scrofula - LN TB (M/c extrapulmonary)

Lupus vulgaris - Skin TB

Poncet Disease - TB Rheumatism

ORGANISM & LAB DIAGNOSIS

1> Direct Microscopy → ZN staining / Led FM

Under ZN staining to visualize each mL of sputum should contain 10,000 bacilli

2> Solid Culture → LJ media 6-8 week

3> Liquid ,, → BACTEC
MGIT
Septi check
} ~~6-8 week~~ 7-10 day +ve result

4> Rapid Molecular Method

a> CBNAAT → / Gene expert → TB Bacilli + Rif. sensitivity 2 hours.

b> Line probe assay / LPA → TB Bacilli + Drug sensitivity (1st Line & 2nd Line drug) = 48-72 hour

Most Rapid method to identify of TB → Direct microscopy

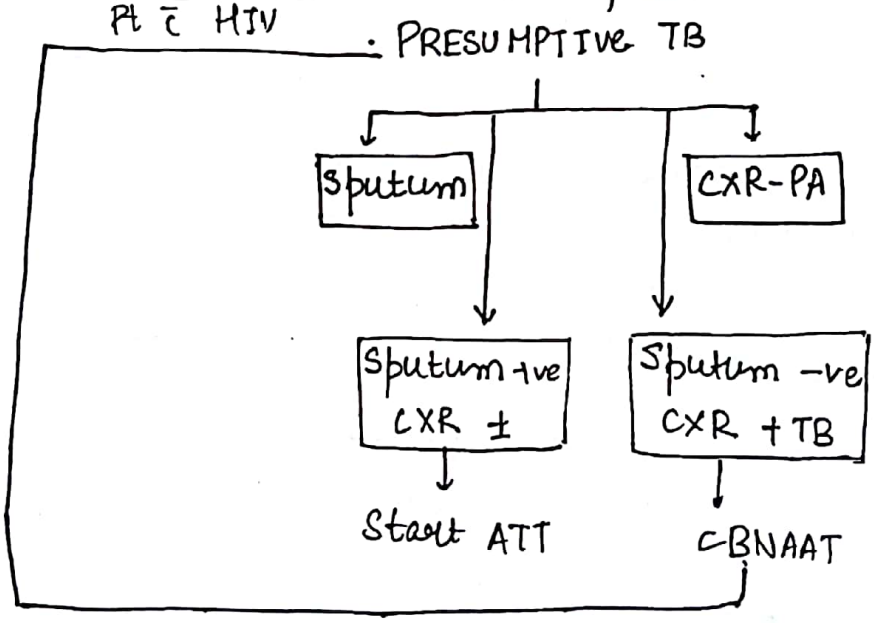
Most Rapid method for Rifampicin sensitivity = Gene expert

PRESUMPTIVE TB

Any one of the following

- Cough > 2 wks
- Fever > 2 weeks
- Hemoptysis
- wt. loss
- Abnormalities on CXR - PA view

ALGORITHM FOR Δ of TB



IGRA / Quantiferon Gold

Advantages :-

1> TB specific Ag → CFP & ESAT used

2> Less cross-reactivity c BCG & Non Tubercular mycobacterium

3> Blood Test

4> Serial Testing can be done c out boosting phenomena

5> Single visit to hospital.

Disadvantage

Can't differentiate Infection vs Active disease

PATHOLOGY

1° TB → unsensitised individual

2° TB → Post 1° TB → sensitised individual → Reinfection / Reactivation

1° TB

→ TB bacilli → mid + lower zone

→ Area of 1st contact

1° focus / Ghon's focus

→ Alveolar macrophage engulf TB bacilli

↓

⊖ Phagolysosome fusion

↓

↑ survival of M.tb.

→ For immunity macrophages reach hilar LN ⇒ LN ↑

Ghon's complex → Ghon's focus + LN ↑.

In LN →

↑ TH_1 response

* ↑ IFN-γ , TNFα

⇓

↑ Killing capacity of macrophage

↓

Limit TB

Memory cells are formed

2° TB

→ TB bacilli reach apex & actively grow.

→ Bodys immune response will try to wall off infection.

→ After few weeks, Delayed Type HSN response produced & destroys TB bacilli & Lung Parenchyma

2° TB is more infectious & it is active disease.

Calcified Ghon's Complex ⇒ Reinke's complex.

TB/HIV

* If ART is started 1st → ↑ Risk of immune Reconstitution Inflammatory syndrome (IRIS)

Start ATT 1st & merge ART in 2 weeks. to 2 months

ATT = Always The Treatment

* If pt. is on TLE regimen. → Rifampicin can be given

If pt. is on Neviparine / Protease Inhibitor

↓

Rifampicin can't be given

Rifabutin is given.

~~DISSEI~~

DISSEMINATED TB

CLASSICAL MILIARY TB	CRYPTIC MILIARY TB
1°/2° form Hematogenous / Lymphogenous spread. Pathognomic ⇒ Choroidal Tubercles Sputum → -ve CXR - 1-2mm, Bil Symmetric Homogeneous, millet shaped shadowing	Elderly, chr. symptom Fever, wt. loss, anaemia CXR - (N) Sputum → -ve Pt. collapses ⇒ death ∴ autopsy reveals meningeal tubercles This is also miliary TB. but hidden one CXR.

NON-REACTIVE (or) AREACTIVE TB

Rare form

Acute Septicaemic form.

Underlying hematological abnormality

Fatal form

Autopsy shows areas of necrosis ± out granuloma formation

Rx

New Case = 2HRZE + 4HRE = 6 months = DAILY

Previously Rx: 2HRZES + 1HRZE + 5HRE = 8 month = DAILY

HDR TB = Resistance to both H & R = DAILY

6-9 mnth → E + Z + Kanamycin + Levoflox + Cycloserine + Ethionamide

18 mnth → E + Levoflox + Cycloserine + Ethionamide

XDR-TB :- MDR-TB + Resistance to 1 2nd Line aminoglycosid + Resistance to 1 FQ

6-12 mnth - Capreomycin + Moxi + PAS + Clofazamine + High dose INH + Amoxyclav + Linezolid

18 months - Moxi + PAS + Clofazimine + High Dose INH + Amoxyclav + Linezolid

(24 - 30 months)

NEWER Anti-TB Drugs

BEDAQUILINE / Sirturo

2012

Diaryl quinolone

MOA:- ATP synthase inhibition

S/E - QT Prolongation

DR TB.

Conditional acces in India

DELAMANID

2014

Nitroimidazole

MOA:- Mycolic acid synthase inhibitor

S/E - QT Prolongation

DRTB

Soon available in India

Dose - 400mg

duration - 24 weeks.

ACID, BASE, BALANCE & ABG

I) NORMAL VALUES

pH	7.35 - 7.45
$PaCO_2$	35 - 40 mmHg
HCO_3^-	22 - 26 meq
PaO_2	70 - 100 mmHg

$pH \leq 7.35 \Rightarrow$ Acidosis

$pH \geq 7.45 \Rightarrow$ Alkalosis

(N) $PaCO_2 = 40$

$HCO_3^- = 26$.

II) Relation Between pH, $PaCO_2$ & HCO_3^-

↳ Henderson Hasselbach Equation

$$pH = 6.1 + \log \frac{[HCO_3^-]}{PaCO_2 \times 0.03} \Rightarrow pH \propto \frac{HCO_3^-}{PaCO_2}$$

$$\downarrow pH \uparrow \propto \frac{HCO_3 \uparrow}{PaCO_2 \uparrow} \Rightarrow \frac{BASE}{ACID}.$$

III) REGULATION OF PH $PaCO_2$ & HCO_3^-

Lungs ↑↓ CO_2 ⇒ Resp. process

Kidneys ↑↓ HCO_3^- ⇒ Met. process

SIMPLE ACID BASE DISORDER

1° process + Adequate compensatory response

Respiratory Acidosis

pH↓ $PaCO_2$↑ HCO_3^-↑

Metabolic Acidosis

pH↓ $PaCO_2$↓ HCO_3↓

Resp. Alkalosis

pH↑ $PaCO_2$↓ HCO_3^-↓

Metabolic alkalosis

pH↑ $PaCO_2$↑ HCO_3^-↑

In simple acid base disorder, always 1° change & compensation move together

In 1° resp. process → change in pH w.r.t. $PaCO_2$ & HCO_3^- in opposite direc"

In 1° met. process – change in pH w.r.t $PaCO_3$ & HCO_3^- in same direction

ROME

resp. opp, met. same direction.

Q. pH = 7.33, $PaCO_2$ 60, HCO_3^- 34
↓ ↑ ↑ ⇒ Resp. Acidosis
acidosis

Q pH = 7.48, $PaCO_2$ 26 HCO_3 16
↑ ↓ ↓ ⇒ Resp. Alkalosis
alkalosis

Q. pH = 7.27, $PaCO_2$ 25 HCO_3^- 10
↕ ↓ ↓ ⇒ Met. Acidosis

Q pH = 7.55 $PaCO_2$ 50 HCO_3^- 40
↑ ↑ ↑ ⇒ Met. Alkalosis

COMPENSATION

Resp. Acidosis

Acute For every 10mmHg ↑ $PaCO_2$, HCO_3^- ↑ by 1 meq.

Chronic For every 10mmHg ↑ $PaCO_2$, HCO_3^- ↑ by 4meq

Resp. Alkalosis

Acute For every 10mmHg ↓ $PaCO_2$, HCO_3^- ↓ by 2 meq

Chronic " " 10mmHg ↓ $PaCO_2$ HCO_3^- ↓ by 4meq

Q Acute F.B. ingestion, pH = 7.32, $PaCO_3$ = 70, HCO_3^- - 29.

↓ ↓ ↑ ↑

Acidosis Acidosis.

$40 \xrightarrow{30} 70$ $26 \xrightarrow{3} 29$.

Resp. acidosis ~~complemen~~ compensatory met. alkalosis

Q Chr. neuromuscular disorder

pH = 7.34 $PaCO_2$ = 60 HCO_3^- 34

↓ ↑ ↑

chr resp. acidosis

$40 \xrightarrow{20} 60$ $26 \xrightarrow{8} 34$

ans:- Chr. resp. acidosis ~ compensatory met. alkalosis.

Chr. compensated Resp. Acidosis.

Metabolic Acidosis

Acute expected $PaCO_2 = (1.5 \times HCO_3^-) + 8 \pm 2$. [Winter's formula]

Q. pH = 7.27, HCO_3^- = 10, $PaCO_2$ = ?

$(1.5 \times 10) + 8 \pm 2$

$15 + 8 \pm 2$

21 - 25 ⇒ compensated

Q. pH = 7.26, $PaCO_2$ = 18, HCO_3^- = 6?

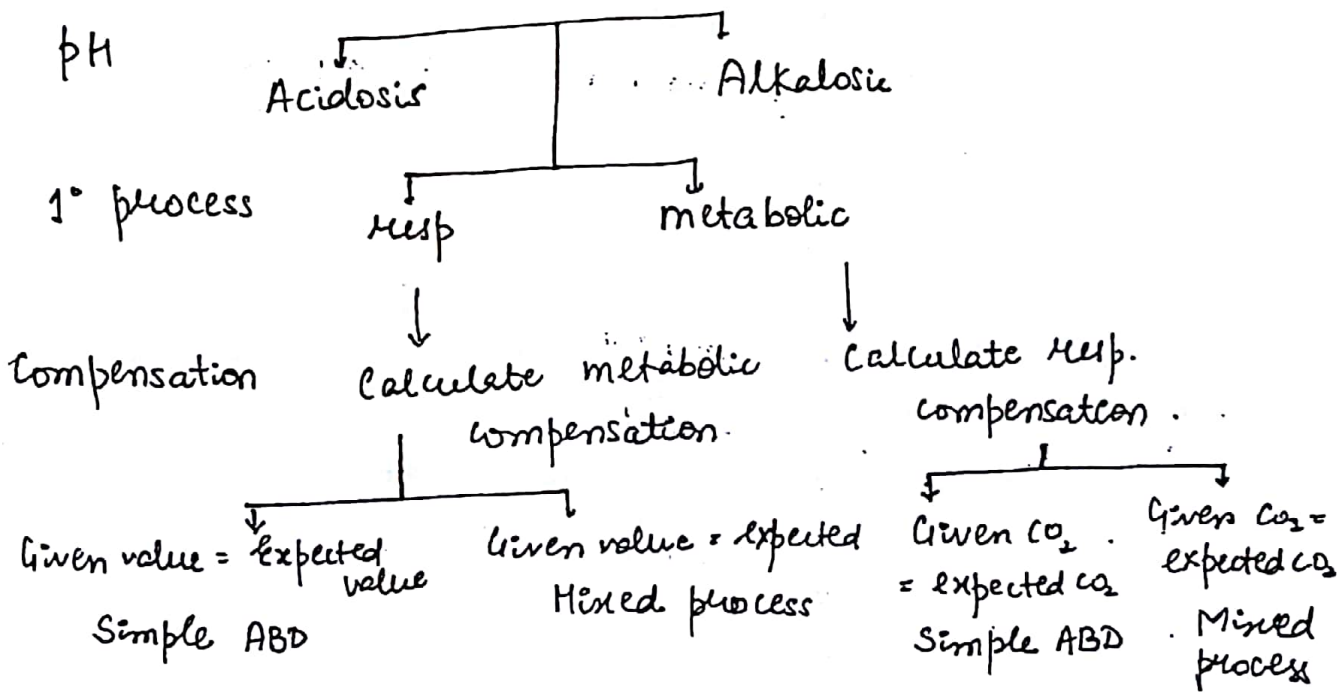
$(1.5 \times 6) + 8 \pm 2$ = ~~9 ± 2~~ ~~26~~ ~~7 - 11~~.

$9 + 8 \pm 2$ = 17 ± 2 = 15 - 19.

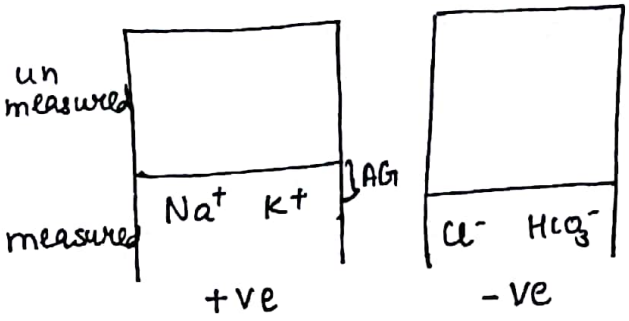
Met. acidosis + compensatory alkalosis

Metabolic Alkalosis

Expected $PaCO_2 = [HCO_3^- + 15]$



METABOLIC ACIDOSIS & CONCEPT OF ANION GAP



$(Na^+ + K^+) - (Cl^- + HCO_3^-)$ = Anion Gap.

$(Na^+ + K^+)$ + unmeased cations = $(Cl^- + HCO_3^-)$ + unmeasured anions

$(Na^+ + K^+) - (Cl^- + HCO_3^-)$ = unmeasured anions − unmeasured cations

[Anion Gap] = unmeasured anions − unmeasured cations

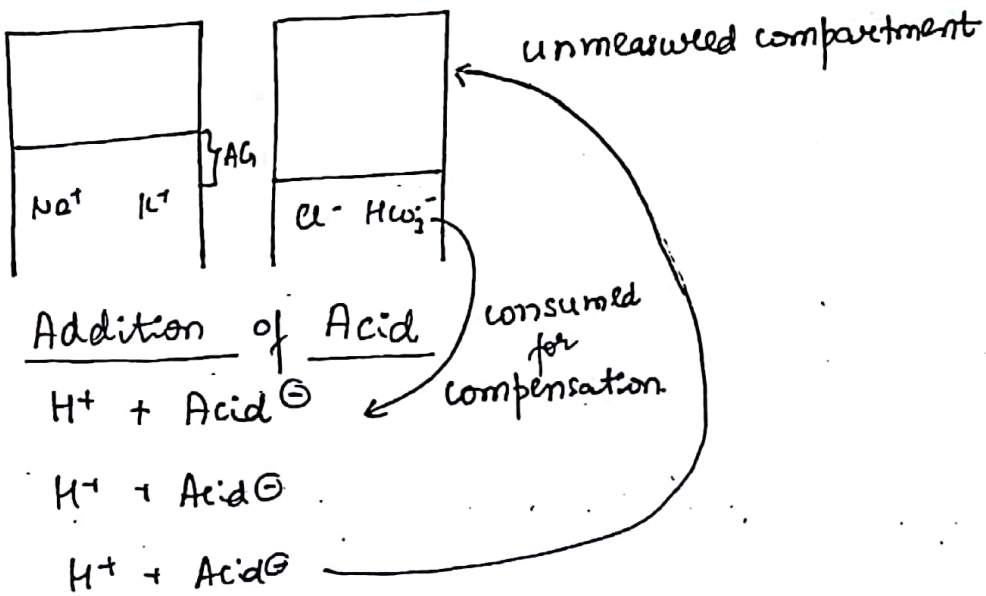
Common cause of ↑ in Anion Gap = ↑ in unmeasured anions

New Formula for Anion Gap

$(Na^+) - (Cl^- + HCO_3^-)$ = AG

8-12 mEq.

HIGH AG METABOLIC ACIDOSIS



In pure High AG Metabolic Acidosis

Rise in AG = fall in HCO_3^-

AG - 10 = 25 - Given carbonate.

$\Delta AG = \Delta HCO_3^-$

CAUSES :-

I) TOXINS / DRUGS - 1) Methanol

2) Paraldehyde

3) Ethylene glycol. / antifreeze
↳ oxalic acid.
Oxaluria

4) Salicylates.

II) Keto acidosis - 1) DKA

2) Alcoholic keto acidosis

3) Starvatation

III) Renal Failure

IV) Lactic Acidosis

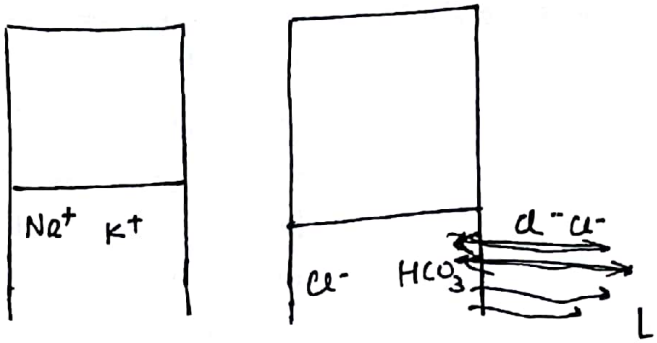
a) Type A Lactic Acidosis ⇒ [Hypoxemia / ↓ perfusion]

eg. shock
Anaemia
CO poisoning

b) Type B Lactic Acidosis = [Perfusion ⓝ]

eg. Renal failure
Hepatic failure
Drugs - metformin
Zidovudine

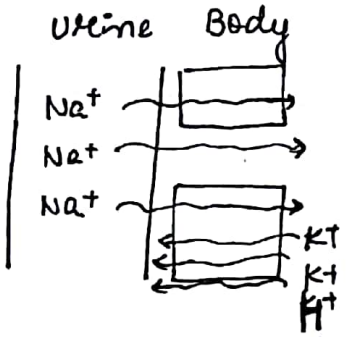
(N) AG METABOLIC ACIDOSIS



Loss of HCO_3^-

Hyperchloremic Metabolic Acidosis

RENIN - Angiotensin - Aldosterone System in Acid. Base



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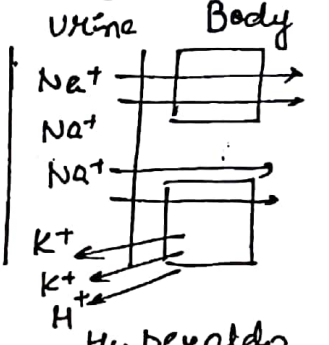
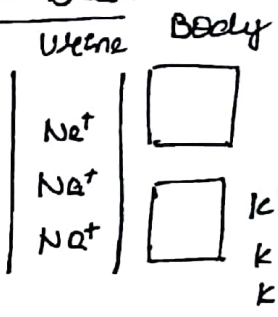


↑ RAAS

Hyperaldosteronism

Hypokalemia + Met. alkalosis



⊖ RAAS

Hypoaldosterone

Hyperkalemia + Met. acidosis

CAUSES

I) GIT CAUSE

1) Diarrhoea
2) Pancreatic fistula
3) Ureterosigmoidostomy
4) Enterocutaneous fistula

II) RENAL CAUSE

1) RTA
2) Drugs
   - (a) Carbonic anhydrase inhibitor
   - (b) ACEI
   - (c) ARB
   - (d) Aldosterone antagonist

RTA

Type I RTA Type II RTA Type IV RTA

Met. acidosis + hypokalemia

met. acidosis + Hyperkalemia (H/c type)

Causes

Hyporenemic state

Aldosterone resistance

" deficiency

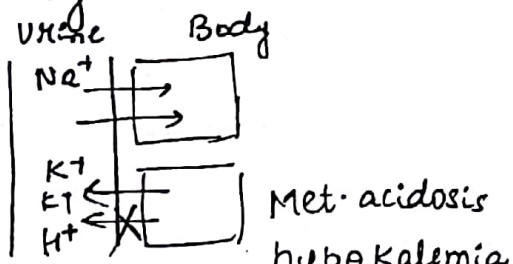
Hyporenemic state

↳ Diabetic nephropathy

Chr. tubulo interstitial

Type I RTA

- Distal RTA
- H^+ excretion Lost at collecting Duct

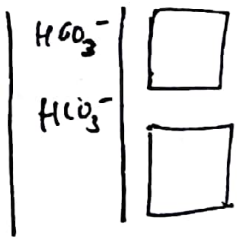


Met. acidosis
hypokalemia

Type II RTA

Proximal RTA

HCO_3^- reabsorption lost in PCT



Bicarbonaturia can induce Kalliuresis

Met. acidosis + Hypokalemia

Urine anion Gap :-

To differentiate (N) anion gap Met acidosis of diarrhoea v/s RTA

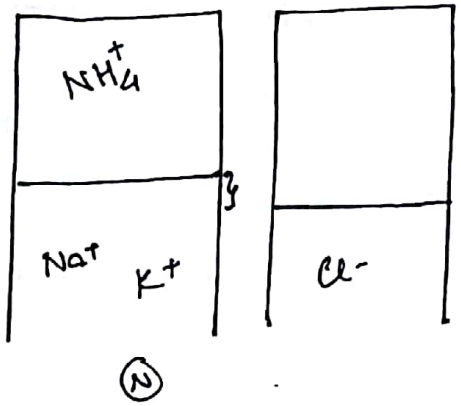
$$UAG = [Na^+ + K^+] - Cl^-$$

(N) value = 0-5.

---- | +++

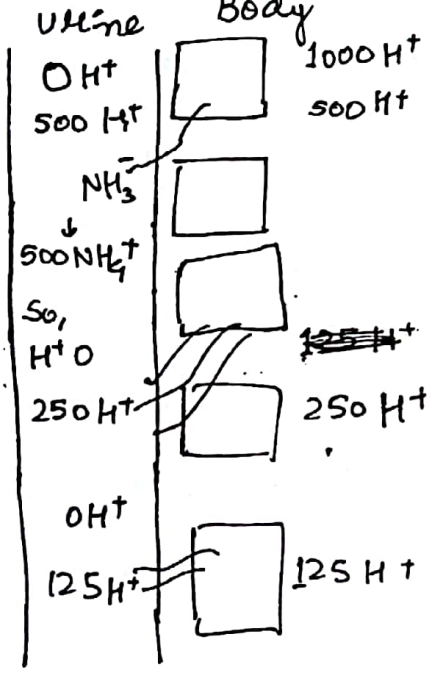
↓ | ↑

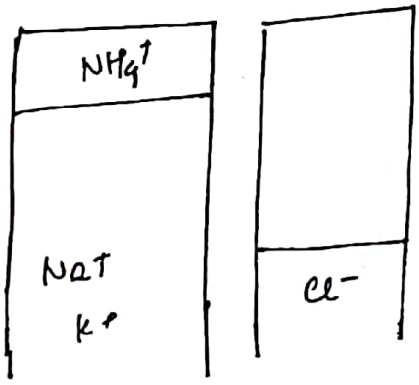
taking 0 as reference level



(N)

Renal Handling of Acid



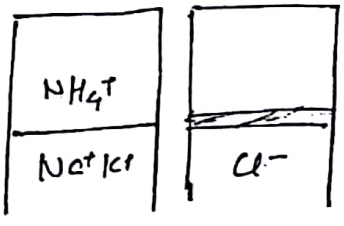


RTA = UAG +ve.

Diarrhoea :- Met. acidosis.

10,000 H+

Urinary NH_4^+ is increased.



UAG --ve

RTA :-

UAG is indirect measure of urinary NH_4^+ excretion.

UAG is negitive in GIT cause diarrhoea

GIT

METABOLIC ALKALOSIS

Initiating event	Persisting event
1) ECFV contraction, hypotension	2° Hyperaldosteronism
2) ↑ 1° mineralocorticoid excess	⟶ ECFV expansion & HTN
(B) initiating + persisting event)	

SALINE RESPONSIVE / Cl^- response	SALINE UNRESPONSIVE / Cl^- unresponsive
U_{Cl^-} < 20 meq	UCl^- > 20 mEq
1) vomiting	1) 1° Hyperaldosteronism — HTN
2) Ryle's Tube aspiration	2) Cushing's Syndrome — HTN
3) Diuretic use	3) Renin secreting Tumour — HTN
4) Post hypercapnic Met. alkalosis	4) Renal artery stenosis — HTN
	5) Liddle's Syndrome — HTN
	6) Bartter Syndrome — hypo to (N) tension
	7) Gitelman Syndrome — hypo to (N) tension

RESPIRATORY ACIDOSIS

Type 2 Resp. Failure

RESPIRATORY ALKALOSIS

CHRONIC Resp. Alkalosis :

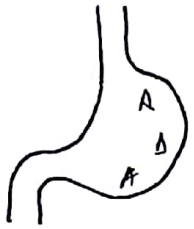
M/c acid Base Ab(N) in critically ill pt

1) Pain, Panic, Psychogenic, Progesterone
⇒ Hyperventilation

2) Aspirin
a) vomiting → met. ~~acidosis~~ alkalosis

2) High AG metabolic acidosis. → Resp. alkalosis.

→ When aspirin goes to blood



3) Theophylline

4) Fever, sepsis (change in sensitivity of Resp. centre)

5) CHF → Pul. oedema → stimulate of chemoreceptors

6) Cirrhosis of Liver → ↑ Glutamate

7) Severe ~~Hypotension~~ Hypoxemia ⇒ hyperventilation.

8) ↑ ICP

ICU pts are also prone to Resp. alkalosis due to pain, panic, psychogenic

Q. pH = 7.32, $PaCO_2$ = 60, HCO_3^- : 34.
↓ ↑ ↑ = Chr. compensated Resp. Acidosis.
40 → 60 (20) 24 → 34 (10)

Q. pH. 7.35 $PaCO_2$ = 60 HCO_3^- 40.
↓ ↑ ↑ = Given value > Expected HCO_3^-
Chr. Resp. acidosis + Add. metabolic alkalosis

Q. pH 7.28 $PaCO_2$ = 60 HCO_3^- 26
↓ ↑ (N) Given value < Expected HCO_3^-
Chr. Resp. acidosis + Add. metabolic acidosis

AG High AG or Normal AG.

In pure High AGMA $\Delta AG = \Delta HCO_3^-$

Rise in AG = fall in HCO_3^-

[Given AG - 10] = [25 - Given HCO_3^-]

Q. Pt. is having DKA.

pts AG = 20 $HCO_3^- = 15$

$\Delta AG = 20 - 10$ $\Delta HCO_3^- = 25 - 15$

10 10

⇒ Pure HAG Met. Acidosis.

Q. Pt is DKA.

Pt. AG = 20 $HCO_3^- = 20$

$\Delta AG = 10$ $\Delta HCO_3 = 25 - 20 = 5$

$\Delta AG > \Delta HCO_3^-$ → Additional metabolic ~~acidosis~~ alkalosis

*High
~~Additional~~ AGMA + addition Met Alk

Q. DKA AG = 20 $HCO_3^- = 10$

ΔAG 20 - 10 $\Delta HCO_3^- = 25 - 10$

= 10 = 15

$\Delta AG < \Delta HCO_3^-$

High AGMA + (N) AG metabolic acidosis

Compare ΔAG & ΔHCO_3^- relation.

$\Delta AG = \Delta HCO_3^- \Rightarrow$ Pure HAGMA

If $\Delta AG > \Delta HCO_3^- \Rightarrow$ HAGMA + additional met. alkalosis

If $\Delta AG < \Delta HCO3^- \Rightarrow$ HAGMA + additional met acidosis

Q pH - 7.2 ↓ $PaCO_2$ - 60 ↑ HCO_2^- 19 ↓

~~Acidosis~~ Acidosis (mixed disturbance)

~~Q pH~~ 20.

NEPHROLOGY

PHYSIOLOGY

Kidney performs Diverse func" :-

1) Excretory :- urine formation

2) Homeostasis :- water & acid base balance

3) Hormonal :- erythropoietin synthesis & Vit D activation.

4) RENAL BLOOD FLOW

Kidneys are highly vascular.

Receives 25% of c.output

Even in presence of adverse cond" to the renal blood flow -

1) Dehydration

2) Hypotension

3) Renal artery stenosis

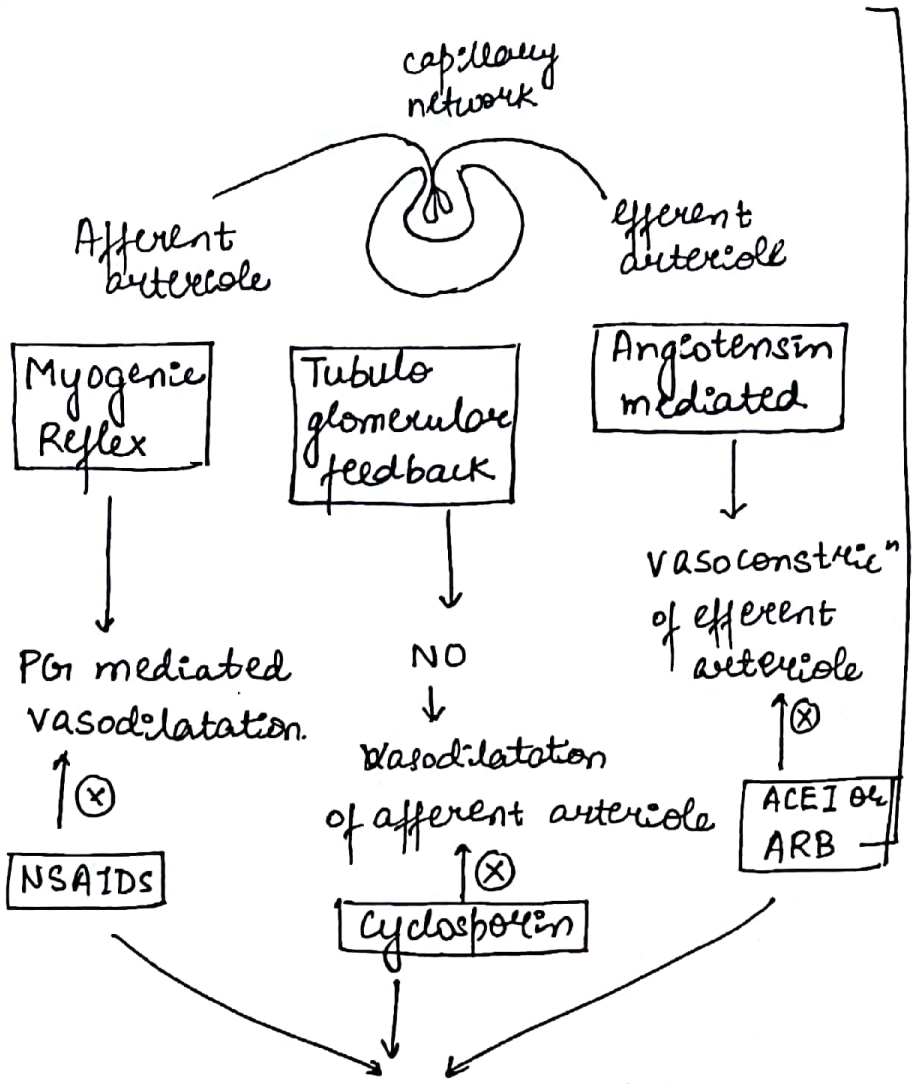
↓

Autoregulatory mechanisms activated

↓

Maintain adequate GFR.

1) ↑ Glomerular capillary Pressure



Can Disrupt autoregulation

If used in the presence of adverse ~~cond~~ conditions, these can precipitate hypoperfusion

⇓

Pre-Renal AKI

RENAL ARTERY STENOSIS

Cause → 1) 90% → atheros/arteriosclerosis

2) 10% → FMD (fibromuscular Dysplasia)

Pathophysiology →

Activates ~~the~~ RAAs

Vasoconstriction | Na^+/H_2O retension.

M/C C/F → Sy. HTN

[M/C cause - 2° HTN - Renovascular]

ESG GUIDELINES - evaluation & Management

When to suspect/ screen for R.A.S.?

1) young HTN (onset <30 yrs of age)
2) Severe HTN <55 yrs of age (>160/110 mm of Hg)
3) HTN emergencies (sudden ↑ BP ± target organ damage)
4) Refractory HTN (uncontrolled ≥3, 1 is a diuretic)
5) Decline in GFR ≥30% after ACEI therapy (Disrupts autoregulation)
6) Asymmetrical kidneys on USG (Diff. ≥ 1.5cm)
7) Unexplained Renal failure

Screening Tests	Specific
1) Duplex Doppler (Best) >98% sensitivity - Non-invasive, easy available	1) Conventional Renal angiography GRADING
2) CT-Renal Angiography ↓ C/I → GFR ≤60 mL/min	% of Stenosis: Severity & Rx <50% (Mild): No further testing 50-70% (Moderate): Follow-up >70% (severe): Always haemodynamically significant ↓ Elective Rx
3) MR-Renal angiography C/I → GFR ≤30 mL/min	
4) DTPA Scan (radio-isotope) (Functional assesment of Kidney)	

R_x 1st line → Medical

U/L	B/L
ACEI (only drug ≤ protects (N) Kidney)	ACEI - C/I CCB β blocker Diuretics

MOA of ACEI in U/L RAS.

↓ glomerular capillary pr. → (N) capillary pressure

↓

Renin - angiotensin - Eff. arteriolar vasoconstriction

ACEI (+) → (x) → ↓ Capillary HTN

comes towards NORMAL

↓

Predispose:- glomerulosclerosis

(B) - Endothelial injury / GBM injury

Prognosis -
Favourable

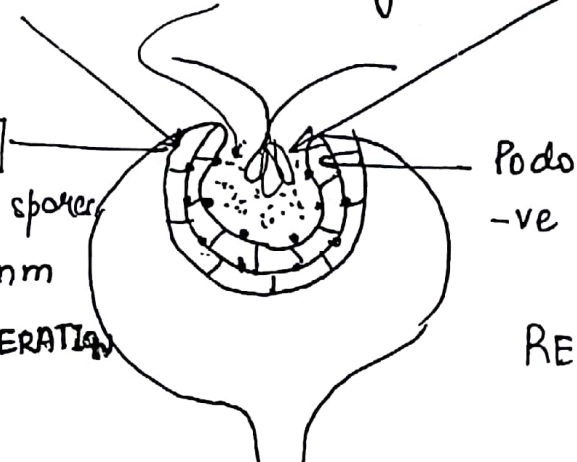
Angioplasty

1) All - severe RAS
2) cause in FMD (focal stenosis → so, easily R_x ⊂ angioplasty)
3) Refractory Heart failure (Flash Pulmonary Oedema)

URINE FORMATION

1st step → Ultrafilteration → Glomerulus

Intra-GBM ← Mesangium → outside GBM. (extra-GBM)



microscopic spaces
Avg = 9-11nm
MECH. FILTERATION

Podocytes (foot processes of GBM)
-ve electrostatic charge

REPEL ANIONS

a) All Blood Components RBCs, WBCs, platelets	① Albumin ② Lipoproteins
b) All plasma proteins (except albumin ≃ 4.6 nm)	③ AT-III, Protein S, C

GLOMERULONEPHRITIS

Predominantly affect GBM except Minimal Change Disease (only podocytes affected)

1) Dysmorphic Heamaturia (MPe)	1) NO HEMATURIA.
2) RBC cast - Most specific	2) Selective Proteinuria (albuminaria)
3) Non-selective proteinuria	3) Dyslipidaemia
4) Glomerular range proteinuria [≥2 g/day / 1.73 m^2]	4) Hypercoagulable state

TUBULES

Reabsorption & secretion. (concentrating Ability)

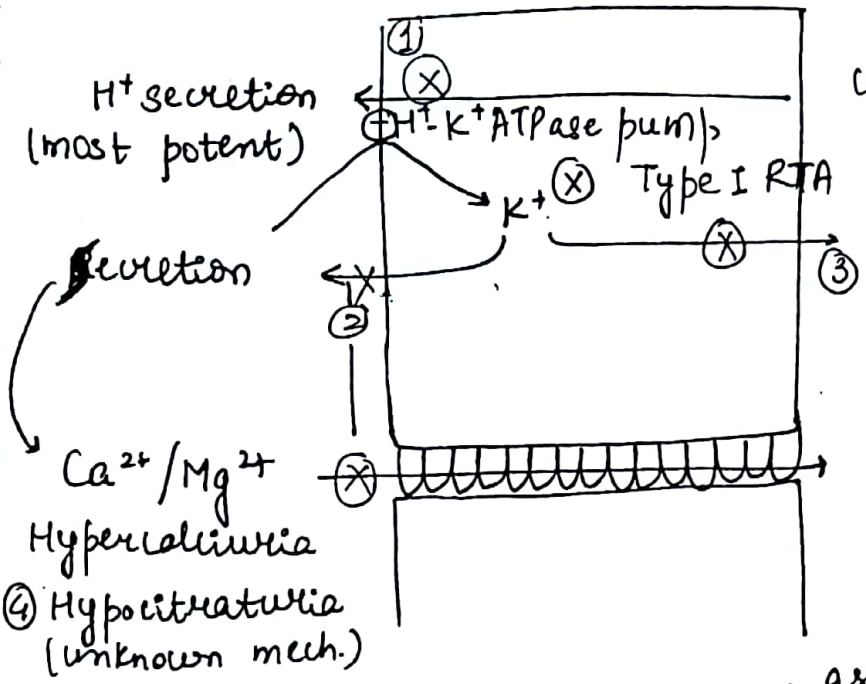
Mechanisms:- Tubular transport

A) Cellular transport (across the cell)	B) Paracellular (in bet' cells of tubule)	
	PCT	DCT
1) ACTIVE → ATPase pumps.	Leaky epithelia ⇓ Allows BULK Transport	Tight Junctions ⇓ Highly regulated
2) PASSIVE → exchange/ co-transporters.		

DCT

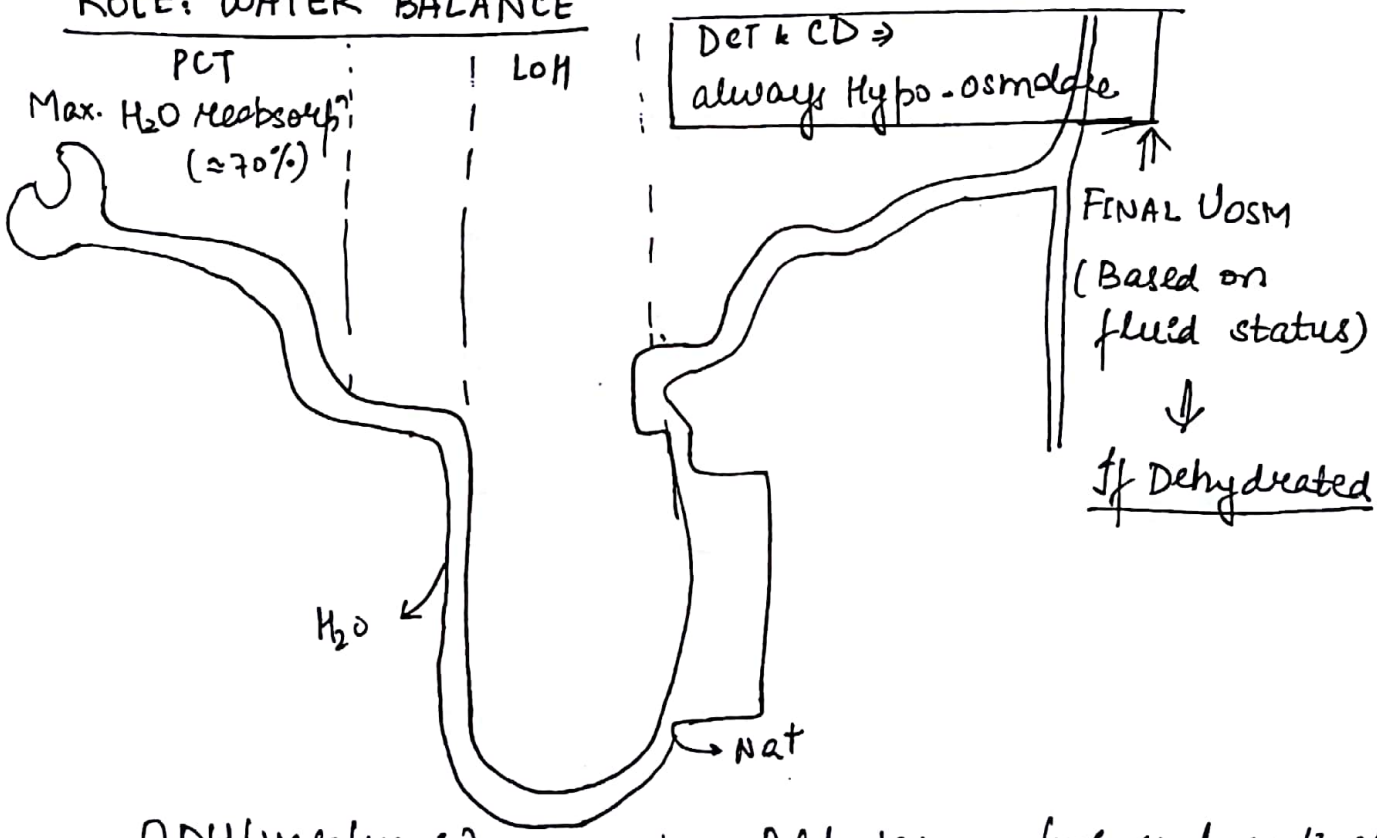
URINE

BODY



ROLE: WATER BALANCE

→ association : Endocrine



ADH (Vasopressin)

V_2 receptors

AQUAPORIN channels

⇓

facilitates H_2O reabsorptn

⇓

Restores plasma volume

Aldosterone (mineralocorticoid)

⇓

upregulates eNa+ channels.

⇓

Na+ reabsorptn ⇓ Secretes

H_2O " H^+ & K^+ in exchange

Def^{n}:- Hypotonic Polyuria (D. Insipidus)	Excess:- oliguria (SIADH)	Def^{n}:- Addisons (GC + MC Def^{n})	Excess:- CONN's ~~syn~~ CUSHING's Syn. ↓ Hypokalemic Alkalosis

HYPOKALEMIC ALKALOSIS

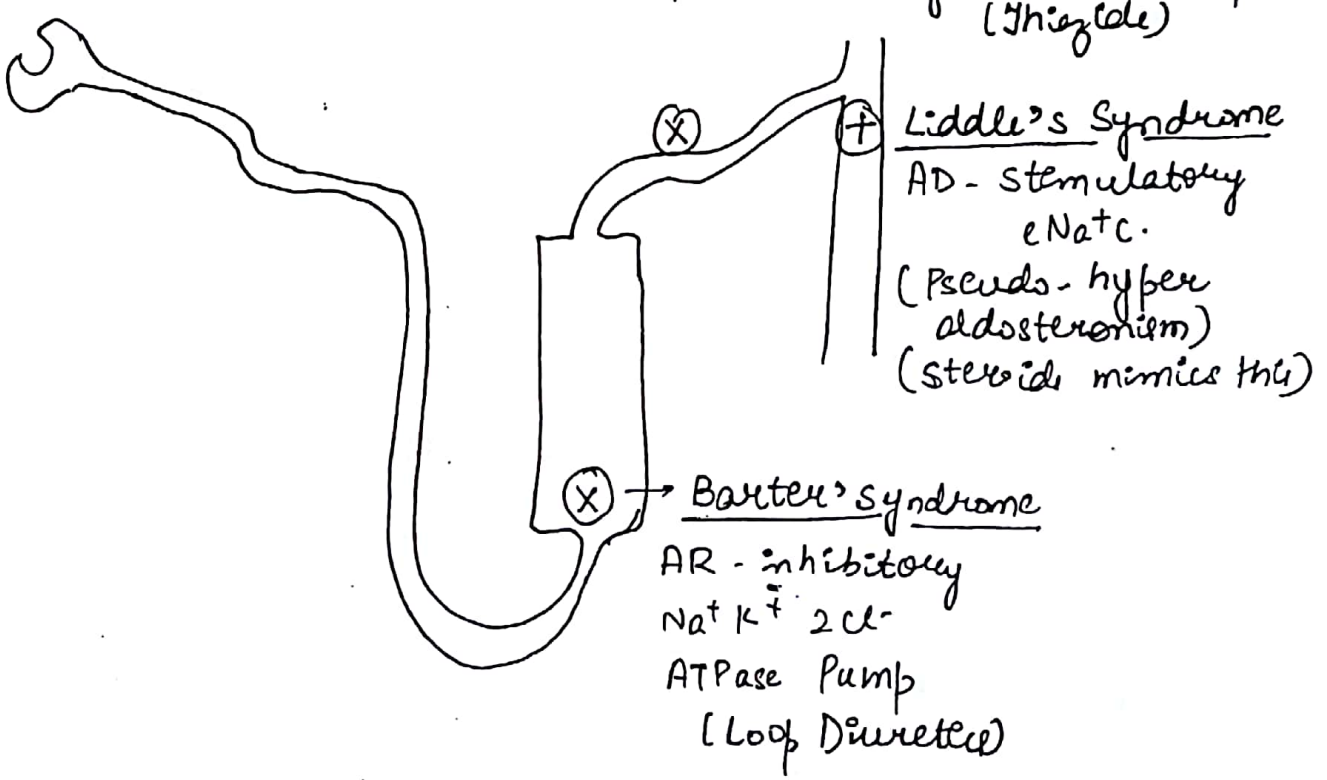
Due to aldosterone excess state

Cause :- 1> Endocrine (MC)

2> Chronic Drug use
- Loop Diuretics
- Thiazides
- Steroids

3) Inherited Channelopathies

INHERITED CHANNELOPATHIES



	Bartter's Syndrome (6 genetic mut^{n})	Gitelman's Syndrome	LIDDLE's Syndrome
1) Epid	→ I.U.L ⟶ adolescence.	20-30 yrs	20-30 yrs.
2) Patho	$Na^+ - K^+ - 2Cl^-$ pump Ⓧ Ⓧ Ⓧ - severe ⇓ 1) Ⓧ Ⓧ Ⓧ H_2O reabsorp^{n}	$Na^+ - Cl^-$ cotransport Ⓧ Mild ⇓ Ⓧ H_2O reabsorp^{n}	eNa$^+$ c ⊕ Mild ⇓ ⊕ H_2O reabsorp^{n}
3) Plasma volume	↓ ↓ ↓	↓	↑
4) B.P.	↓ ↓ ↓	~~↓~~ Ⓝ	↑
5) Renin Angiotensin Aldosterone	↑↑↑ ↑↑↑	↑ ↑	↓↓↓ ↓↓↓
6) Associated Defects (unknown) mech	30% - ↯SNHL. (Deaf) ↯ Paracellular (Ca) transport defect (Hypercalciuria)	Paracellular (Mg^{2+}) transport Defect	Pseudo-hyperaldosteronism.
7) C/F	1) Polyhydramnios 2) Failure to thrive 3) Hypotension. (syncope) 4) Renal calculi	Muscle cramps Paralytic ileus Cardiac arrhythmias	Asymptomatic Detection - HTN in young
8) ABG analysis	⟵ Metabolic alkalosis. ⟶		
9) S. K^+	⟵ Low ⟶		

	Loop Diuretics	Thiazide	Steroids258
10) Exclude chr. use			
11) Best Test S. Renin	↑↑↑	↑	↓↓↓
12) Rx	← HYDRATION →		✕
	← K+ supplements →		
	Trial of NSAIDS as majority → ↑ PG. hence palliative (slows prognosis)	Mg2+ supplements ↓ minimises symptoms	AMILORIDE DOC ENac antagonist ~Safe in ⓟ + ~Long term use offers cure ~BEST Prog
13) Prognosis	WORST (no cure)	Favourable	

ROLE OF KIDNEY IN ACID BASE BALANCE

Human Body → "Pro-~~acidic~~ acidic state"

Every living cell requires Energy (ATP)

During ATP Produce" → Acid is ~~dig~~ generated.

Ⓝ pH = 7.35 - 7.45 (slightly Basic)

MECHANISMS → ABB → Regulate pH efficiently

1) **Buffering**

At tissue level

HCO_3^- (extra cellular)

$\Downarrow$

$[H^+] + [HCO_3^-] \rightarrow CO_2 + H_2O$

BACKUP

PO_4^{--} (Intra cellular) (Bones)

Resp mechanism

excretes acid in form of CO_2

Renal Mechanism

Most Potent

↓

Acidification of Urine

Most Imp. form of H^+ Secretion in urine → NH_4^+ ion.

Combines Cl^- → NH_4Cl

U_{H^+} ∝ U_{Ca^-} levels.

HCO_3^- exhausted ← ACIDEMIA ⓝ U_{pH} = 6.5-7.0 (Blood pH - ⓝ)

PO_4^- required

Bone resorption

Rickets	Osteo malacia

⇓

Expected U_{pH} < 5.5 } (Highly acidic)
U_{Ca^-} ↑↑ } ⇒ if kidneys are ⓝ

RTA

↳ Defect in acidification of urine
(U_{pH} > 5.5, U_{Ca^-} - Low in disease)

RTA

② HCO_3^- reabsorption
(Iso-nutrient reabsorption)

Ⓧ Type 2 RTA
(proximal RTA)

③ HCO_3^- regeneration
(Action - carbonic anhydrase)

Ⓧ Type 3 RTA
(Marble Brain Disease)

- < 100 cases (worldwide)
- Majority :- cerebral calcification.
  also - marble bone disease
  (osteopetrosis)

Not included in routine classification.

① H^+ secretion

H^+-K^+ ATPase

Ⓐ

Type I
(Distal RTA)

④ Minor role
Aldosterone
H^+/K^+ secretion.
in exchange of
$Na^+ + H_2O$.

Type 4 RTA
(Hyperacidosis)

RTA	Type I	Type II	Type IV (M/c RTA)
Epidemio-	<10yr, M>F (Most severe)	20-30yr M=F (mild)	>50yr, M=F (Mildest)
	M/c inherited RTA		M/c RTA
Cause	Inherited	Inherited	Mildest (Acquired)
Association	30% autoimune M/c - Sicca syndrome SLE ↳ Mixed connective tissue Disorder	FANCONI'S syndrome - glycosuria - aminoaciduria Syndactyly	Early CKI. ACEI/ARB K+ sparing diuretic Trimethoprim.
C/F	① short stature, Rickets ② Hypercalciuria → ↑ Renal calculi (st-one) Nephrocalcinosis ③ Hypomagnesemia → M/s cramps	① mild acidemia Asymptomatic ② Vit D_3/PO_4 def. (2° to loss in urine) → Osteomalacia	① mildest acidemia Asymptomatic ② Rarely Hyper K+ complications
ABG analysis	← Metabolic Acidosis →		
Anion gap	← (N) anion gap →		
U_{AG}	$(U_{Na^+} + U_{K^+}) - U_{Cl^-}$ [High/Positive]		
U_{pH}	always >5.5	maybe < 5.5	always <5.5

S. K^+ Low (N) High

Rx ← Oral HCO_3^- supp. →

← Oral K^+ →

Citrate. supp. ↓ Renal calculi (No Cure)

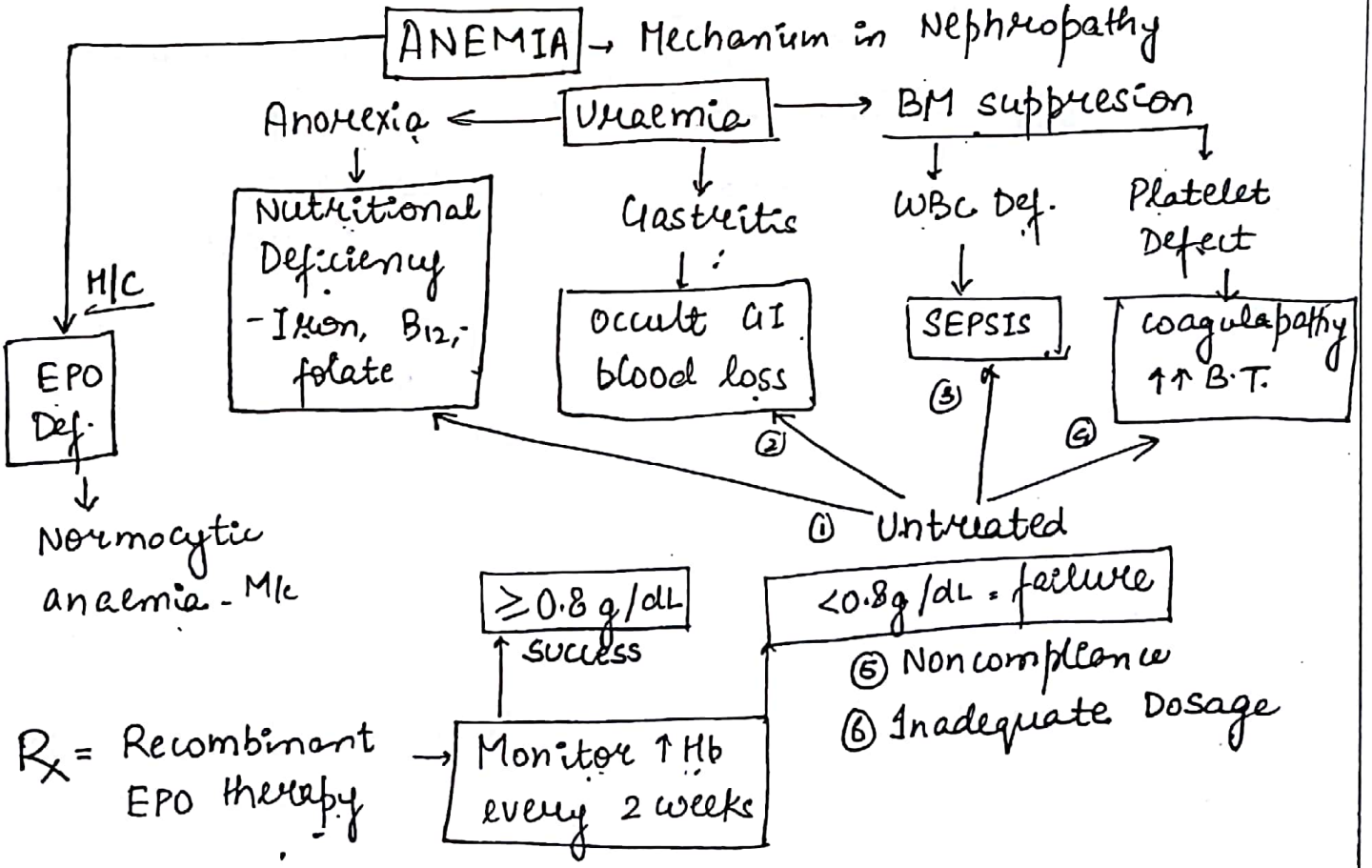
Vit D_3 / PO_4 supplements ↓ Bone Disease

Stop offending drug ↳ offers cure.

Prog. WORST Favourable BEST.

ANEMIA

Defect in Erythropoiten Synthesis



Vit D → final step of activation into [Vit D_3]
& its reabsorption occurs in [PCT]

↓ if Defective

BONE DISORDERS - in nephropathy
only C.K.I - Minimum (≥ 6 months) disease

RENAL OSTEODYSTROPHY

MIC
OSTEOMALACIA
- Vit D_3 def.
  - Oral vit D_3
- Chronic acidemia
  - Oral HCO_3^-

OSTEITIS CYSTICA FIBROSA
- 2° Hyper = PTH.
- Hypocalcemia
  - Most Imp. Hyper PO_4^-
    - SEVELEMER (Binding Resin)
  - Nutritional Def
    - Oral Ca^{2+}

ADYNAMIC BONE DISEASE
- Remodelling Defect of Bone
- Poor wt. Bearing
  - Encourage mobility

ASSESSMENT METHODS IN NEPHROLOGY

S. CREATININE LEVELS (Best) screening Test)

C. PRODUCED	EXCRETED
endogeneously @ constant Rate By Protein Breakdown.	Freely filtered at glomerulus Barely secreted/ reabsorbed @ tubules

S creatinine α GFR

↓ GFR → ↑ S. creatinine level

Renal Dysfunc" — Early • sensitive marker

Limitations of Test

- nonspecific for Δ of nephropathy.
- may not co-relate immediate outcome of the disease (Limited Prognostic value)

FALSE +ve ↑ S. creatinine

↑ Produc"

a) High Protein Diet
b) strenous exercise. (athletes)

c) Infection (sepsis)
d) Inflammation (A.I.D.)
e) Neoplasms (some)

Alternative Test To S. creat

S. CYSTATIN - C LEVELS

Produced endogeneously By all nucleated cells @ constant Rate	Freely filtered @ glomerulus Excretion α GFR.

Adv - not related to Diet or Exercise

NOVEL MARKERS OF AKI. = Specific for Δ si of Nephropathy

NGAL (neutrophil gelatinase associated Lipocalcen)

KIM-1 (kidney Injury molecule)

IL-18

Tested in spot urine sample

Are secreted by tubules in response to injury.

Hence detectable only in Renal causes of AKI. (nephropathy)

TESTS - Detect :- SITE/ CAUSE/ SEVERITY

URINALYSIS | USG-KUB (structure) | GFR ESTIMATION. (functional status)

Proteinuria | Albuminuria | Hematuria | Pyuria | Cast/Sediment

PROTEINURIA

Defⁿ - >150 mg / 24 hours.

Detected using Dipstick Method (very sensitive)

- Non-specific for Δ si of Nephropathy
- Valuable in K/C/O - Nephropathy = identify SITE. (Based on quantity)

<2g/day (Tubular Range → Tubulointerstial Disorders	≥2g/d/1.73m² (Glomerular Range Proteinuria)	
	<3.5g/d	≥3.5g/d.
	Nephritic range	Nephrotic Range

ALBUMINURIA

>30mg/24hrs (More specific marker)

QUANTITATIVE TESTS	Micro-alb	Gross-alb
24hr urinary alb. estimation (most reliable / gold std)	30-300 mg of Alb/24hrs	>300mg
(Most Preferred) Spot urinary ACR (alb/creat. ratio)	30-300 mg of Alb/gm of creat	>300 mg
USE:- PROGNOSTIC ↓ Staging of CKI	- Early marker - Reversible stages DOC = ACEI	Late/Irreversible stages

Approach → HEMATURIA (RBC in urine)

Step 1 - Establish

"SIGNIFICANT" (any1)	"INSIGNIFICANT"
• >3-100 RBC/hpf ≥ 3 occassions • >100 RBC/hpf single occasion. • GROSS HEMATURIA	only observation. Repeat after 48hrs

↓

Step2 – Urine microscopy : RBC morphology in Urine

EUMORPHIC	DYSMORPHIC (SOURCE → Renal, Disease → GN)		
Source - Below the Renal Pelvis	GROSS H.	Microscopic Hematuria	
Renal calculi Cystitis Carcinoma bladder ⇓ **Radiological Testing** X-Ray, USG, CT } KUB ⇓ Inconclusive ⇓ **Cystoscopy ± Biopsy**	IgA nephropathy	Post-infective causes Post-streptococcal GN (PSGN) Hep B- Polyarteritis Nodosa Hep C - Cryoglobulenemia SABE	Lupus Nephritis (SLE)
	NORMAL	C_3 = initially Low Returns to (N) - 6-8wks	Persistently Low complement Levels

Approach - PYURIA. (Pus/WBC in urine)

Step1 : "SIGNIFICANT" >5 WBC/hpf in centrifuged sample → Observe/Repeat if not significant

Step 2 :- URINE CULTURE.

M/c cause of significant pyuria = UTI.

↓ ⊖

STERILE PYURIA

CAUSES

Infective

M/c - Partially Rx UTI.
(>72 hrs antibiotics)

FASTIDIOUS organisms
(special growth requirement)
- Chlamydia → Mcc of STD ♀
- Renal T.B.

Inflammatory

1) Renal Calculi
2) **Papillary Necrosis**
(severe tubular necrosis)
vascular insufficiency - Mech.
↓
DM - analgesic abuse
Sickle - Kawasaki Disease
3) Post - Radiatherapy
4) Post - Transplant Rejection.

Approach :- CASTS / SEDIMENTS

Common CASTS But non-specific for Diagnosis

M/c cast in urine
HYALINE CAST
Most Benign cast
NO further Rx / test
↑
M/c found in AKI.

M/c cast in nephropathy
GRANULAR / CELLULAR
Present in Ⓑ
Tubulo-interstitia GN

RARE CASTS (10-15% cases)	DIAGNOSTIC
RBC cast	GN * (Acute GN)
WBC cast	Pyelonephritis
Muddy Brown Cast	Acute Tubular Necrosis
Eosinophilic Cast	Acute Interstitial Nephritis
Broad / waxy Cast ↑ WORST CAST	C.K.I.* Indicates total break down of tubules.

USG-KUB

(N)	Ab (N) & Its Interpretation
1> SITE :- Anatomical	ECTOPIC → NO relation to function
2> SIZE :- 7-11 cms < 7cm (Shrunken) CKI (exception) →	> 11 cms – Enlarged / Bulky AKI. → classical in acute Interstitial Nephritis Early DM nephropathy Adult PKD. (APKD) HIV associated Nephropathy Renal amyloidosis
3> SYMMETRY < 1.5cms	> 1.5cms - assymmetrical Kidneys. Pathology ⇒ always in smaller Kidneys
4> ECHOTEXTURE = (N)	Increased Echogenecity ↓ Active Disease in the Kidney
5> Cortico-Medullary Differentation (CMD)	Most Imp. parameter AKI (Vs) CKI Preserved | Loss
6> COLLECTING SYSTEM - (N)	Obstructive uropathy

GFR ESTIMATION (Functional Status)

Most preferred = Creat. clearance
(Indirect/ surrogate marker)
Easy, cheap, no radiation expo
Cockcroft Gault formulae (Estimated)

$$eGFR = \frac{[140 - Age] \times wt.(kg)}{72 \times S.creat} \quad (\sigma')$$

$- [\ ] \times 0.85 \quad \varphi$

Most Reliable/ Gold std :-
Radio-isotope scan.
(DTPA, MAG-3)
Direct method.
Accurate
Single Kidney GFR
Segmental GFR.
Total Kidney GFR.

Disad
1) Inaccurate (esp in AKI)
2) only - total Kidney GFR

Disad
Invasive
Expensive
Radiation exposure

Uses - MEDICAL
1) Staging of CKI
2) Follow-up - chronic medical Renal Disease
eg. DM, HTN, HIV associated Nephropathy
3) Dose adjustment of Nephrotoxic drug

Uses
- Pre-Transplant assesment of DONOR
- Pre-op assesment of uro Sx
- Mediolegal
- Decision making
  ↳ to operate on better kidney
  never done B/L → risk of infection ↑

INDEX : RENAL DISORDERS

AKI	Parameters	CKI
Preserved	USG = CMD	Lost
(N) or ↑	USG - size	(N) or ↓
Fluctuates - P_{osm}	$U_{osmolarity}$	Isothenuria
Hyaline Cast	CASTS	Broad waxy Cast
(−) uncommon	Anaemia	(+) common.
uncommon.	Renal Osteodystrophy	(+)

AKI

- pre-renal
- Renal
  - T.I.
    - ATN
    - Acute Interstitial Nephritis
  - GN
- Post-Renal

CKI

- Acq.
  - H/c - DM
- Inherited
  - Alports
  - APKD

R.R.T (Renal Replacement Therapy)

AKI

Def^{n}:- Abrupt decline in GFR over short period of time [271]

KDIGO Guidelines (Kidney disease improving Global outcome - part of National Kidney Found^{n}

Any 1

- ↓ U.O. ≤ 0.5mL/kg/hr ≥ 6hrs. [oliguria].
- ↑ S.Cr. ≥ 0.3 mg/dL from Baseline ≤ 48hrs
- ↑ S.Cr ≥ 1.5x Baseline (50% increase) ≤ 7 days.

Causes of AKI

MC

Pre-renal	Renal		Post-Renal
60-85% - HYPOPERFUSION	INTRINSIC		1-5% - OBSTRUCTIVE UROPATHY
1) Dehydration Diarrhoea Hypoalbuminemia Massive H'ge Burns (Insensitive loses through skin)	95% Tubulo Interstitial Disorders.	5% GN	
2) Hypotension Cardiogenic Septic shock.			
3) Drugs - disrupt autoregulation.			

C/F	PR	Renal	Post-R
	Classical 3 stages	1) Non-oliguric AKI	Loin pain
	Oliguria <400mL/d	eg. SEPSIS	Dysuria
	anuria <100mL/d	(In Tubulo-Interstitial)	Urgency
	Diuretic phase (recovery)	2> Hematuria - GN	

Rarely - Serious UREMIC MANIFESTATIONS

(Cause - mortality in A.K.I.)

1> Encephalopathy / convulsion

2> Pericarditis / shock

3> Coagulopathy

Asis → KDIGO Guidelines.

Approach - AKI

USG - Collecting System → (+) → Post - Renal AKI

↓ (-) → Excludes Post-Renal AKI.

PARAMETER	PRE-RENAL	RENAL
MECHANISMS	RAAS ⊕ ↓ Na^+/H_2O reabsorption ↑↑ urate reabsorption.	Loss of concentrating ability Na+ lost in urine Dilute urine
BUN : Creat	>20:1	<12:1.
U_{Na}	<20mEq	>40mEq
F_{Na^+}	<1%	>2%

U_{osm}	> 500 mosm/L	< 350 mosm/L
CASTS	Hyaline casts	Granular/cellular
USG- Echotexture	(N)	↑ / Bright kidney
Single Best Novel markers of AKI	UNDETECTABLE	DETECTABLE

Rx PALLIATIVE

Indications of Dialysis

1) UREA > 100
2) CREAT > 7
3) SERIOUS UREMIC MANIFESTATIONS
4) Refractory Pulmonary oedema
5) Hyperkalemia > 6.5 mEq
6) Refractory pH < 7.20

Single most Imp. Indication for emergency Dialysis

7) Ingested Dialysable Toxin

(commonly used. Accidental/suicidal)

a) Salicylates
b) Methanol
c) Lithium
d) Polyethylene glycol (solvent)

SPECIFIC

Depends on cause

(A) Post-Renal AKI
Early Sx relief
Excellent recovery

(B) Pre-Renal AKI
Fluid challenge (1st Line)
Inotrophs
Antibiotics
Stop offending drug
Excellent recovery
Delay in Rx → Progress to ATN

(C) RENAL AKI.
↓
Further evaluation.

Approach - RENAL AKI.

95% | 5%

Tubulo. Interstial	Parameters	GN
<2g/day	PROTEINURIA	>2g/day
(-)	HEMATURIA	Common.
Granular	CASTs	RBc.

T.I. ✓

ATN	Parameters	Acute Interstial Nephritis
>4%	$FeNa^+$	2-4%
(N)	USG - Size	enlarged / Bulky
Muddy Brown	CASTs	Eosinophiluria

ATN (Tubule - M/c site)

Anatomy
Prone to vascular Insufficiency

Physiology
Site of conc"

Direct → Luminal Contents

1) Untreated Pre-Renal
2) Sepsis
3) Contrast Induced Nephropathy
4) Drugs - aminoglycosides
5) Toxins - Heavy metal poison.
6) Cryoglobulinemia
7) Myoglobinuria
8) Hemoglobinuria

AIN

1) Allergic Response to Drug (M/c - 95% of case)
   - NSAIDs
   - Sulfonamides
   - Penicillin.
   - cephalosporin
   - Rifampicin
   - FQs
   - Dapsone
   - Nitrofurantoin
   - Contrast agents.
2) Viral Infec"
3) autoimmune
4) Lymphoproliferative

Supportive therapy - Underlying cause	Rx
4-6 wks	Avg. recovery
1-5%	Risk of ESKD
Favourable	Prognosis

Stop offending Drug. Supportive Rx
1-2 wks
<1%
Good

GLOMERULONEPHRITIS

Causes :-

Ⓐ PATHOLOGICAL :- Mesangial Involvement on Biopsy

⊕ Proliferative GN

- Mesangio-proliferative GN (IgA, PSGN)
- Crescentric GN (worst prog) (RPGN)
- Membrano-~~capy~~ proliferative GN
  MPGN - mesangio-capillary

⊖ Non-Proliferative GN

- Minimal Change Disease
- FSGN
- Membranous nephropathy

Ⓑ CLINICAL PRESENTATION of GN (More Preferred)

Asymptomatic proteinuria/ microscopic hematuria	Nephritic	Nephrotic	Reno-vascular HTN	C.K.I
MIC	→ Hematuria → HTN → Rapid ↓ GFR. (Risk - RPGN) → Proteinuria <3.5g/day	→ Anasarca (serous cavity) → Hypercoagulable State → Preserved GFR >3.5g/day		eg. Alport's Syndrome

Nephritic	Nephrotic
• PSGN • Lupus nephritis • RPGN	Children → MCD Adults → FSGS Elderly (>50 yrs) → membranous nephropathy
⇓	
Proliferative GN	Non-Proliferative
More likely nephritic	More likely nephrotic

MESANGIO-PROLIFERATIVE

	IgA nephropathy		PSGN
M/c cause	Worldwide		India
Epidemio	20-30 yr, ♂=♀		5-15 yrs. ♂=♀
Etiopath	← Post-infective	M/c	preceded by URTI →
Latent Period	< 1st week Syn-pharyngitic		1-3 weeks ← SKIN 4-6 weeks ←
C/F	Recurrent Gross Hematuria 10-15% - Persistent microscopic	HEMATURIA HTN IUFR → Common	Microscopic hematuria [classical nephritic syndrome].
	Uncommon Benign nature of the disease		
Screening (Serology)	S. IgA-I level ↑↑↑		Anti DNAase (70% cases +) ASO, anti-hyaluronidase
Serum complement	(N)		Initially Low Returns to (N) in 6-8 wks

Biopsy ←	Mesangio-Proliferative changes →	
Immuno flowrescence ←	Granular Pattern of Ig deposits →	
	Anti IgA staining	Anti IgG Staining
Rx	Reassurance Majority - self Limiting Risk of RPGN ≤ 1% Plamapheresis	→ Penicillin - no role in nephropathy To eradicate residual Infec. → Long Term prophylaxis. ⊗ Low relapse rates
Prognosis	BEST among GN	2nd Best (Risk of RPGN-1-5%

POOR PROGNOSTIC FACTORS

1) Elderly onset (> 40yrs)
2) Nephrotic
3) Progression to RPGN — any GN requires RRT ≤ 1 month of onset

LUPUS NEPHRITIS

Kidney involvement - most dreaded.

organ involvement in SLE → H/c/c of acute mortality

Deposition of Anti-ds DNA on GBM. (100% specific)

Type	PATHOLOGY	C/F	Rx
I	Minimal Mesangial proliferation.	Asympt - Proteinuria microscopic Hematuria Preserved GFR	No active Rx
II	Diffuse mesangial proliferation.		

III	Focal nephritis	Classical nephritic syndrome	I.V. methyl prednisolone therapy
IV	Diffuse nephritis	High risk - RPGN (15-20%)	
V	MPGN/membranous	Nephrotic Synd.	oral steroids
VI	Glomerulo-Sclerosis	CKI	Consider RRT

RPGN ⟺ Crescenteric GN

(Clinical Dx) (Biopsy finding)

APPROACH – RPGN

Anti GBM Ab

GOODPASTURE's Syndrome (GPS)

Autoimmune

20-40yrs ♂ > ♀

α_3 subunit - Type 4 collagen

↓

Goodpasture's Ag

Alveolar BM | GBM

(Pulmonary + Renal Syndrome)

Alveolar H'ge | RPGN

⇓

MC among smokers.

I.F. :- Linear pattern of Ig deposits

Rx ← PLASMAPHERESIS →

Prognosis ← POOR > 70% acute mortality →

ANCA

Vasculitis

mimics GPS

So, D/D. for Pulmonary-Renal Syndrome

- Wegener's
- Churge-strauss
- microscopic polyangeitis (MPA)

Sparse Ig deposits (pauci-immune)

Serum. Complement levels

Low C_3

↓

Anti dsDNA

Lupus (SLE)

↓⊖

Anti-DNA ase

PSGN

↓⊖

HbsAg

PAN

HCV-Ab

cryoglobinemia

↓

ECHO :- SABE

Plasmapheresis

Poor Prog.

(N) C_3

IgA

Henoch-Schloenlein Purpura

MPGN

Biopsy Based Δ sis

70% cases → Low C_3 Level

30-50 yrs.

♂ > ♀

90% causes → 2° causes

Causes

1> Infections – Leprosy
Malaria
Syphilis
Hep. B
Hep. C

2> Autoimmune – Type V ~~MPGN~~ Lupus nephritis

3> Solid organ Tumours – [H/c Renal manifestation = MPGN]

4> Lymphoproliferative states

C/F

Majority → "NEPHROTIC SYNDROME"

Δsis

Renal Biopsy – Double BM /
Tram track appearance of GBM.

[Only INTRA-GBM MESANGIAL involvement]
↳ causes splitting of GBM.

10% Idiopathic → R_x - Immunosuppressants

FSGS (Mlc - adults)

- 1° (idio) Mlc Biopsy finding = sclerosing type of FSGS
- 2° Causes (85%) end point of DM, HTN, Reflux induced
  - Most severe collapsing type of FSGS
  - HIV associated nephropathy

C/F - HTN
Early & severe features

Rx underlying disease + strict HTN control

Risk of ESRD: common - slow 15-20 yrs

Acute mortality: No — Favourable Prognosis

MEMBRANOUS NEPHROPATHY (Mc > 50 yrs)

- 1° (idio)
  - EM finding (Gold std) Spike & Dome appearance of GBM
  - NEPHROTIC
  - WORST Hypercoagulable State
  - Hence, max. risk → RV thrombosis
  - Anti-coagulation (all cases) + Immunosuppressants
  - Risk of ESRD: Common - 5-10 yrs
  - Acute mortality: Present (vascular) — WORST PROG.
- 2° Causes: same as in MPGN

C.K.I.

Gradual ↓ GFR ≥ 3 months duration.

Kidneys → Large functional Reserve.

Clinical Disease ≥ 70% Loss of nephrons ≈ 25-40 mL/min eGFR

C/F -

1) UREMIC symptoms (M/c) → M/c neurological feature (90%)

→ Encephalopathy / convulsions
→ Pericarditis / shock
→ Gastritis / Anorexia
→ Infertility / Loss of Libido
→ Proximal myopathy
→ Peripheral neuropathy
→ Restless Leg syndrome
→ Generalised pruritus

Peripheral neuropathy
- (axonal variant)
- Poor recovery inspite dialysis

2) FLUID OVERLOAD symptoms
peri-orbital oedema
peripheral "
CHF

3) Metabolic acidosis

4) ANAEMIA - CKI

5) Renal osteodystrophy

Asu - Done

Rx STAGE of CKI	2 Parameters: Albuminuria	eGFR	Rx
I	Micro albuminuria (Reversible stage)	90 - 120 mL/min	ACEI + strict control of Risk factors (DM, HTN)
II		60 - 89 mL/min	
III	Gross (irreversible stage)	30 - 59 mL/min	Counsel + Prepare for RRT
IV		15 - 29 mL/min	
V ESRD	Gross	< 15 mL/min (> 90% nephron Loss)	RRT is mandatory

Specific Rx - Depends on Cause. → DM, alport, APKD

DIABETIC NEPHROPATHY

Microvascular complication of DM.

Pathophysio → Hyperglycemia (1)

- (2) ↑ Glycated end products → oxidative injury vascular endothelial → HYPOPERFUSION → Microalbuminuria
- GLYCOSURIA = ↑ urine osm → RAAS activation ⊕ (absence of dehydration) → (3) Efferent arteriolar vasoconstrict" → ↑ Glomerular capillary Pressure (already (N)) → Capillary HTN → GLOMERULOSCLEROSIS (F.S.G.S.)
  - (1) ↑ GFR → supra-(N)
  - Gradual nephron Loss
    - (2) Returns to (N)
    - (5) ESKD (> 90% Loss)

Stage	Duration of DM	Alb.	eGFR.	Rx
① Hyper functioning	1-5yrs	⊖	supra-Ⓝ > 120 mL/min. ⇓	Strict DM control ①
② Silent stage	5-8yrs	⊖	Returns to Ⓝ	Adequate Hydration. + ②
③ Incipient (subclinical)	8-12 yrs	Micro albuminuria +ve	CKI stage I/II	ACEI / ARB ③
Early - EM → Thickening of GBM non-specific to Dis				
④ OVERT (symptomatic)	12-18 yrs	Gross	CKI Stage 3/4	Consider RRT
⑤ ESRD	18-25 yrs	Gross	Stage ⑤	RRT is mandatory

LATE/ Advanced/EM → Nodular glomerulosclerosis
irreversible (K-W - Kimmelstiel - Wilson nodules)

ALPORT'S SYNDROME

M/c- XL -Ⓡ defect
20-40 yrs.
♂ > ♀

α_5 subunit - Type IV collagen = ABSENT

H/C ↓ GBM	↓ Cochlear B.M.	↓ Lens		↓ Skin
		H/C ≈ 75%	Most specific	
G.N ↓ Recurrent Hematuria	SNHL	Dot & fleck retinopathy (Not specific)	Ant. Lenticonus (≈ 25% cases)	Asymptomatic

Dx Sig - Renal Biopsy ⇒ "BASKET-WEAVE" appearence of GBM.

only Rx - Renal Transplant
↳ Never recurs in graft
Excellent survival

Post-Transplant Complication - Mimic Recurrence (Hematuria)
↓ ↓
(RARE) → [already on Immunosuppression] Anti-GBM disease (Ab against α_5 subunit).

POLYCYSTIC KIDNEY DISEASE

Group of inherited Disorders characterised by

A) multiple cysts in multiple organs
- Kidney
- Liver
- Pancreas
- Spleen

B) Berry Aneurysm
↑ risk of SAH

C) Colonic Diverticuloses
↓
Recurrent Colitis
↓
↑ oxalate reabsorp" from gut
↓
Hyperoxaluria
↓
Oxalate Renal calculi

Mode of Inheritance

AD-PKD (H/C)
⇓
Survive till adulthood
Called - adult - Polycystic KD

AR-PKD (Rare)
⇓
Never survive >10yrs of age

APKD-1	APKD-2	PKHD (Hepatic)
POLYCYSTIN-1	POLYCYSTIN-2	Fibrocystin
Chr. 16	Chr. 4	Chr 6
moderate form	mildest form	most severe
20-30yrs.	30-50yr of age	I.U. Life / Infancy

C/F	AD	AR
	M/C Recurrent Loin Pain + Hematuria / fever (Infection in Renal cyst) M/C - Extra-renal (Hepatic cysts) - mechanical compression - Bil. radicles - cholestasis / cholangitis	- oligohydramnios (30% fetal Loss) - Uremic symptoms in infancy - ESKD ≃ 10 yrs of age - Cirrhosis ≤ 10 yrs of age (CAROLI's Disease = Defect of Intra-Hepatic Biliary Radicals Present ≃ 3% cases
Dx is USG	<30 yrs: ⊕ ≥ 2 renal cysts, each kidney ≥ 1 30-59 yrs: ≥ 4 renal cyst, ≥ 2 in each	
Rx - Renal Transplant No recurrence Good Prognosis		No cure Grave Prognosis

RENAL REPLACEMENT THERAPY

BEST FORM → TRANSPLANT

- Potential cure
- Better survival
- Better quality of life

DIALYSIS

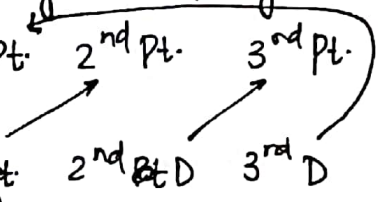
only filteration.
Palliative Rx only

⇓

Limited Donor Availability

DOMINO Tx

Kidney swapping



HLA Registry

All Sx must be done on same calender

(Limits - chain size)

HAPLO-Identical

(MHC/HLA matching) — 6 Ag matching

Class I	A	B	C
Class II	DP	DQ	DR.

> 3 = good match.

≤ 3 = Poor match.
(Less than half match)

- Most imp. HLA match is HLA-DR
  ↓
  Best success

DIALYSIS

HEMODIALYSIS (H.D.)

- vascular access
  (Cannula, AV fistula)
  High Complications Rates
  (Bleeding, sepsis, Thrombosis)
- H.D. centers
  (Limited availability)
- Biocompatible - methyl cellulose polymer (filter)

PERITONEAL (P.D.)

- Intraperitoneal catheter placement → done ↓ LA
  Low complication rates
  (≤ 1% risk → Peritonitis)
- no problem
  only C/I → Para H/O recurrent GI Sx

Lower cost - omentum acts as filter

• Risk → Infection transmission (HIV, Hep B, Hep C, CMV)	• No Risk → Installing sterile peritoneal Dialysate fluid
• Huge Hemodynamic/osmotic shift → poorly tolerated (M/C) acute comp^{n} → HYPOTENSION – Muscle cramps / Fatigue • Sudden cardiac death In cardiomyopathy EF < 15% ↳ C/I	• LOW SHIFTS → Better Tolerated Safe in cardiomyopathy & Post cardiac Sx
• Risk → HYPOGLYCEMIA Preferred Form. Excellent filteration Rate 800 - 1200 mL/min	Risk → HYPERGLYCEMIA/ Wt. Gain Poor Filteration 15-25 mL/min. only Back-up

DIALYSIS ASSOCIATED AMYLOIDOSIS

- Accumulation of β_2 microglobulin (β_2-MG)
- In the musculoskeletal system
- M/C → entrapment neuropathy
- On dialysis ≈ 3-7yrs
- Neither form (HD/PD) can filter β_2-MG.
- X-Ray Hand - Deposits in metacarpals.
- only R_x = Renal Transplant

PRE-TRANSPLANT - Indications

1) APKD
2) Horse-shoe kid
3) Obstructive uropathy

} ↑ Risk of infections in the native kidneys

⇓

Post Transplant Immunosuppresion

↙

Septicaemia → stop Immunosuppresants

⇓

Rejection of Graft

CNS

achin_mehra@yahoo.com

Priyachin mehra

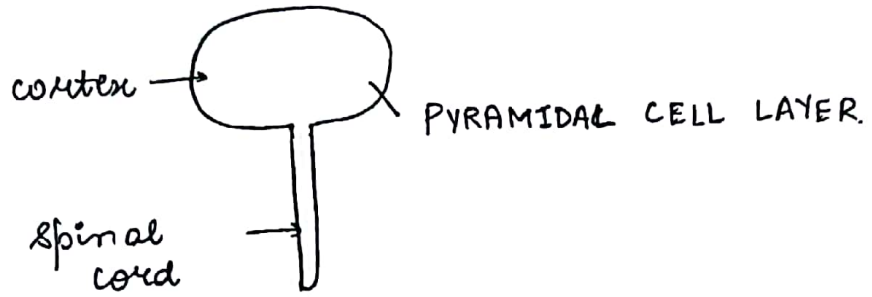
SEIZURE DISORDER & EPILEPSY

SAECIRE

= to take possesion of

SEIZURE

Paroxysmal event due to hypersynchronous CNS discharges



EPILEPSY

≥2 unprovoked seizure

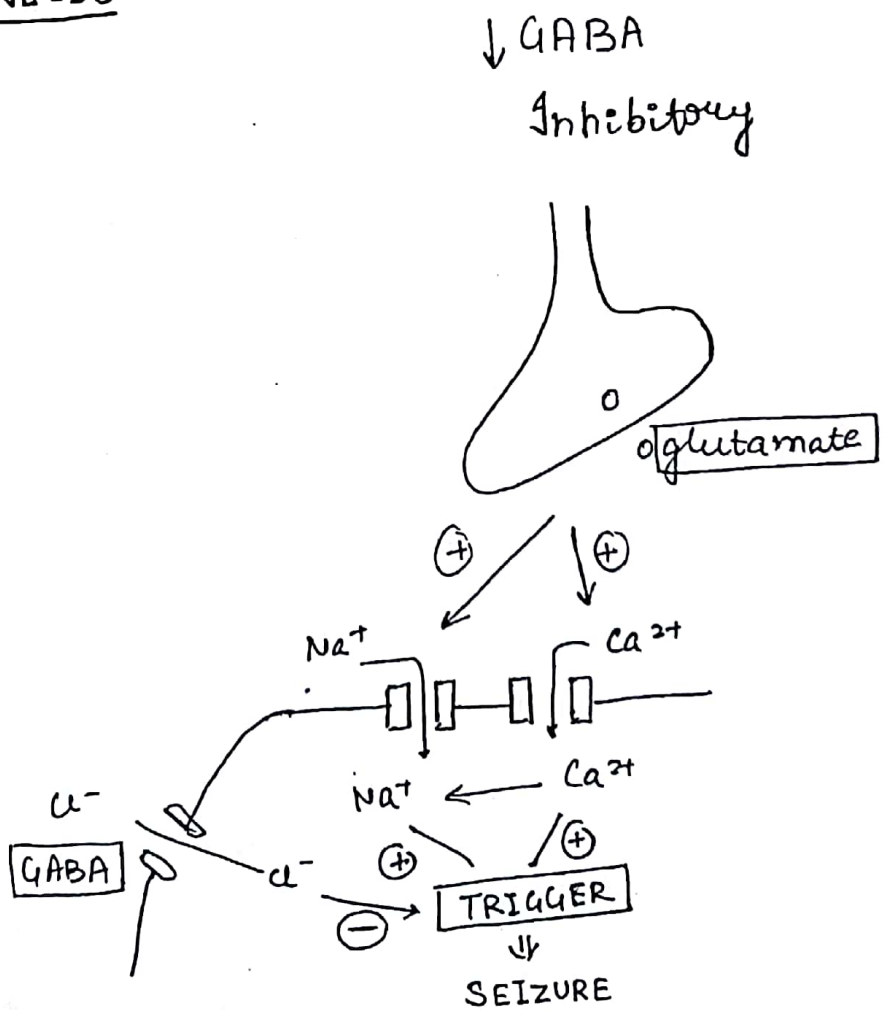
EPILEPTOGENESIS

↑ GLUTAMATE

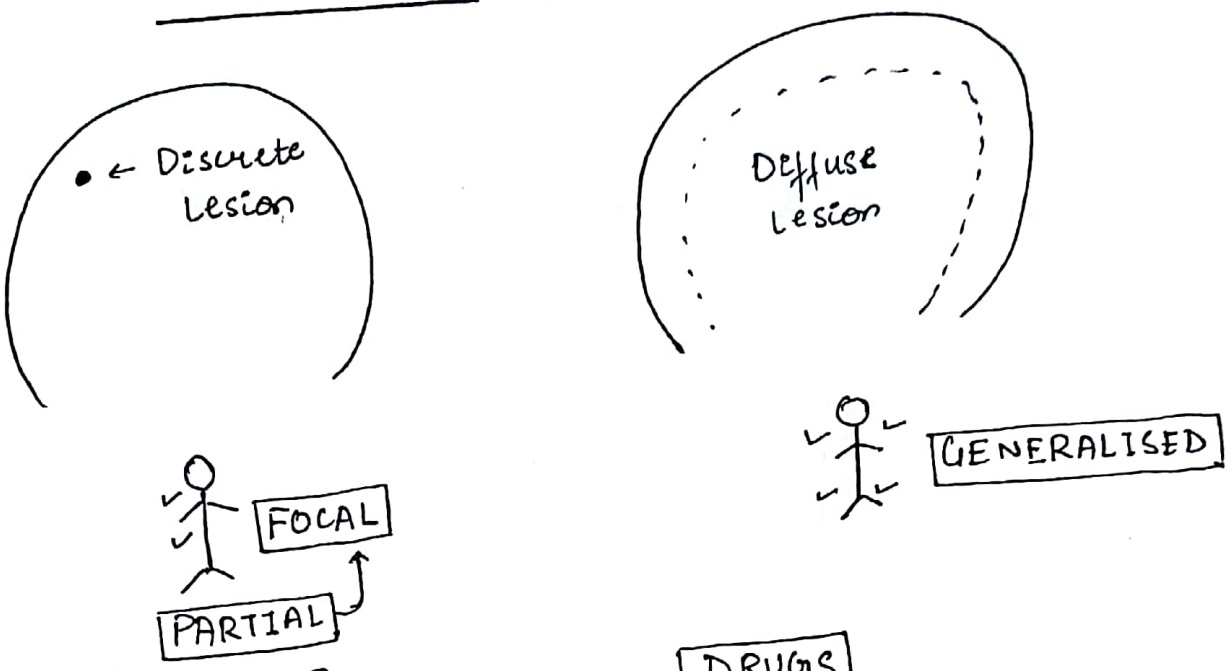
excitatory

↓ GABA

Inhibitory



CLASSIFICATION OF SEIZURES



Structural Ab(N)

DRUGS

Antibiotics - Quinolone

Antivirals - Acyclovir

Antimalarials → mefloquine
→ chloroquine

Analgesics - Tramadol

TOXINS

ABUSE
Cocaine
Amphetamine

WITHDRAWAL
Alcohol

METABOLIC

1) ↓Na+ (M/c Biochemical Ab(N) ppt. seizure)
↓
due to cerebral oedema
(<100 ↑)

2) ↑K+, ↓K+ ⇒ doesn't cause

FOCAL SEIZURES

↓

LOSS OF CONSCIOUSNESS

‖

Contact

‖

Cognition

→ ⊕ = Dys cognitive (complex) ↖

→ ⊖ = Non Dys cognitive (simple) ↙ PARTIAL

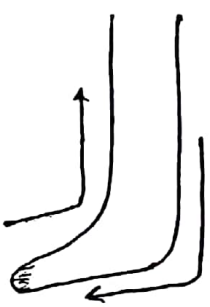
TODD'S PALSY

→ Post Ictal Paralysis

→ Self recoverable

↳ starts in **1st 24 hours** of onset

FOCAL SEZZURE



Distal → Proximal

JACKSONIAN MARCH

→ focal seizure arising ~~from~~ in a Limb.

GENERALISED

ABSCENCE SEIZURE / PETIT MAL EPILEPSY / PYKNOLEPSY

→ Loss of contact ⊂ environment

→ Tone of Body (N)

→ ABrupt onset

→ ≤30 sec

→ Subtle Motor Signs ⊕ (minor)

→ AURA ⊖

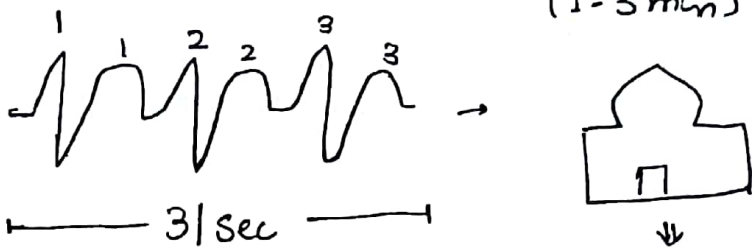
→ NO post Ictal confusion

Starts - 4–8 yrs of age

Spontaneous Remission
in 60–70% by 16 years of Age

EEG :- B/L 2–4 Hz spike & wave

Precipitated by Hyperventilation.
(1–3 min)



3 spikes & 3 waves

SPIKE & DOME pattern
or
Spike & wave "

ATYPICAL ABSCENCE SEIZURE

→ Loss of consciousness – Less abrupt
↑ Duration.

→ mental Retardation

→ Structural Ab (N)

→ EEG – ≤ 2.5 Hz spike & wave
(slow)

→ Resistant to Anti epileptic Drug

MYOCLONIC SEIZURE

↓
Jerky movement

CAUSE - 1) Hypoxia
2) Degenerative

H/o Hanging → compressed Carotid
↓
Cause hypoxia.

JUVENILE MYOCLONIC EPILEPSY

- Early Adolescence
- Family H/o
- Chromosome No. 6
- unknown cause. ⇒ ✗ hypoxia
  ✗ Degeneration.

- B/L Myoclonic jerks
  - on awakening
  - ppt by → Fatigue, Alcohol

- IQ (N)
- Loss of consciousness (−)
- subtle motor signs (−) [AUTOMATISM] → Eye Blinking, Lip smaking

MAJORITY may turn into GTCS. pt

GENERALISED TONIC CLONIC SEIZURE

GRAND MALL EPILEPSY

PREMONITARY SYMPTOMS-
Nausea
vomiting
Abdominal Pain

AURA → (+) Focal
(−) Generalised

↓

Hallucinations

- Olfactory, gustatory → MEDIAL TEMPORAL
- Auditory → LATERAL TEMPORAL
- Visual → OCCIPITAL

[NOTE: Aura seen in Focal Lesions.]

↑ Tone
- flexors of UL, Extensors of LL → DECORTICATE POSTURING
- NECK VERSIVE HEAD TURNING
- Intercoastal, Adductor (Larynx) → ICTAL CRY, Cyanosis +

↓

Clonic (Jerky)

↓

Post Ictal Confusion (Urinary Incontinence)

JUVENILE MYOCLONIC EPILEPSY

- Myoclonus
- Majority → GTCS
- 1/3rd → Absence Seizure

M/C presentation of JME is MYOCLONUS (AIIMS)

MESIAL TEMPORAL LOBE EPILEPSY

- Focal seizure ± Loss of consciousness [DYSGOGNITIVE]
- DEJA VU
- Febrile seizure.
- Enlarged Temporal Horn
  Small Temporal Lobe
  Hippocampal Scleroses
  → Rx → Temporal Lobectomy
  → Rx OC = Sx antero-medial part removed
  → Amygdalo Hippocampectomy
- Resistant to anti-epileptics

S. PROLACTIN
↑ 30 mins after True seizure

ANTI-EPILEPTIC DRUG

A.E.D. X 2 years —TAPER→ 3rd year
↓
Stop.

Sudden withdrawal of DRUG ⇒ ppt. seizure.

Seizure ppt. while withdrawal in 1st 3 months. more commonly.

1st episode of seizure

✗ DRUG	✓ DRUG
Provoked	Unprovoked
→ Febrile seizure	→ Status epilepticus
→ Alcohol withdrawal	→ Family H/o ⊕
⇓	→ Ab⊕ neurological exam"
BZD - Injectable	

Chlordiazepoxide
Oral
for gen. alcohol withdrawal
not for seizures

Ab(N) - EEG
↘ CT/MRI.

IOC
⇓
seizure ⇒ EEG

DOC =

↑ EFFECT

↓ SIDE EFFECT

FOCAL

L - Lamotrigine → STEVENS JOHNSON SYNDROME (1%)

O - Oxcarbamazepine → ↓ Na^+ (SIADH)

C - Carbamazepine → ↓ Na^+ (SIADH)
→ Aplastic anaemia

P - Phenytoin →
- ypersensitivity
- yper glycemia
- yperplasia of gums
- ydantoin syndrone
- irsutism
- epatitis

[6H]

+

megaloblastic anaemia
[↑ excretion of folate]

+

osteomalacia

L - Levertiracetam
- irritability
- mood disorder

FETAL HYDANTOIN ⇒
- Microcephaly
- Hypoxia of Limbs
- Cleft
  - Lip
  - Palate

→ Valproate
→ Phenytoin
→ Carbamazepine

GTCS

Valproate
Lamotrigine
Topiramate

ABSCENCE

ETHOSUXIMIDE - DOC

ATYPICAL ABSENCE SEIZURE

Valproate ←
Lamotrigine

SAFEST A.E.D

Lamotrigine > Carbamazepine > Pheno barbitone
↓ teratogenic
↑ sedative even for fetus

DOC → as per seizure type
monotherapy
Lowest effective Dose

GTCS → Valproate → Neural Tube Defect → (N) Preg. 1-2%
↘ c A.E.D. = 10-20%

A.E.D is not 100% Teratogenic
Do not change Rx During ♀ becoz changing Rx can ppt. seizure [Break Through].

Seizure frequency during ♀
50% - Unchanged
20% - ↓
30% - ↑ → emesis,

Y ↑ in 30%

1) Emesis → ↓ absorptn of drug

2) Hormones

Progesterone	Estrogen [Epileptogenic]
↑ Seizure threshold	↓ seizure threshold

A.E.D. Excreted In Breast Milk

MAXIMUM	MINIMUM
Levetiracetam	valproate

Breast feeding is recommended
AED is also continued

JME

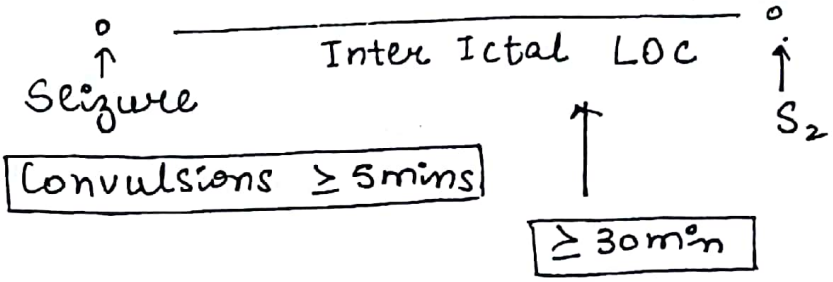
A.E.D. x Lifelong
DOC = Valproate
Levetiracetam

⇒ **DRUGS NOT USED IN JME**

→ Carbamazepine
→ Phenytoin
→ Lamotrigine
→ ↑ myoclonus

⇒ PRE ♀ on valproate
↓ change to
Levetiracetam

STATUS EPILEPTICUS



EPILEPSIA PARTIALIS CONTINUA

⇒ continuous partial seizure

⇒ Status epilepticus in focal seizure

1st Drug LORAZEPAM (0.1 mg/kg) DOC or MIDAZOLAM (0.2 mg/kg)

↓

I.V. A.E.D.

PHENYTOIN

20 mg/kg @ 50 mg/min

- 0 order kinetics
- cardiotoxic

× Dextrose ⇒ Phenytoin ppts
Normal Saline

FOS PHENYTOIN
@ 150 mg/min
↓ Hypersensitive
mixed ± Dextrose
I/M

OR

VALPROATE
(25 mg/kg)

OR

LEVETRIACETAM
(20-30 mg/kg)

[POST - TRAUMATIC EPILEPSY → LEVETRIACETAM.]

+ seizure

↓

I.V. MIDAZOLAM
0.2 mg/kg → 0.2 - 0.6 mg/kg/hr

OR

I.V. PROPOFOL

↓ +Seizure

↓

THIOPENTONE

CARBAZEPINE → not recommended in status as found in oral form

MOVEMENT DISORDERS

ATHETOSIS / CRAWLING

→ Slow
→ Sinuous
→ writhing
→ Seen in Lesions of GLOBUS PALLIDUS → G A P

CHOREA / DANCE like movement

Semi purposeful movement

Lesion - CAUDATE NUCLEUS

↑

CORPUS STRIATUM

CAUSES -

C - Chorea Gravidarum
H - Huntington's Chorea
O - OCP
R - Rheumatic / Sydenham's Chorea
E - Endocrine / Thyrotoxicosis
A - Atherosclerotic / Senile

M/C/C ⇒ SLE

HEMIBALLISMUS ⇒ Exclusively on ONE SIDE

- ✓ Large Amplitude
- ✓ Flinging
- ✓ Proximal
- ✓ Limb
- ✓ Lesion ⇒ SUBTHALAMIC NUCLEUS (STN)

⇓

C/L

PARKINSONISM

Degeneration / Atrophy ⇒ SUBSTANTIA NIGRA PARS COMPACTA (SNPC)

⇑

LEWY BODY

- → Intra-neuronal
- → Intra-cytoplasmic
- → Eosinophilic inclusion Body
- → Contains α synuclein

↓ DA

Level (N) 100% → 70%

↓ 30%

RIGIDITY

↑ ACh

TREMORS

ETIOLOGY :-

1) DRUGS ⇒ DA ⊖ (MC/C of 2° Parkinsonism)

- TYPICAL ANTIPSYCHOTICS
  - Haloperidol
  - CPZ
  - METOCLOPRAMIDE

DA Depletors ⇒ Methyldopa, Reserpine

2> TOXINS → CO
→ Mangnese
→ MPTP - Heroin Addicts.

3> TRAUMA
Boxers

4> FAMILIAL / GENETIC
↓
MUTATIONS
↓
GENES → α synuclein gene — Chr. 4
PARKIN gene — Chr. 6
LRRK-2 gene — Chr. 12
<40 yrs
>40 yrs
Age OF onset
⇓
EARLY ONSET

5> IDIOPATHIC -
85-90% pts.
⇓
PARKINSON DISEASE. (M/c type)
=
PARALYSIS AGITANS

C/F :-
UL > LL
Spares neck
- TREMORS → 1st M/c symptom
  → Resting - Pill rolling movement
  4-6 Hz.
- RIGIDITY
- AKINESIA
- POSTURAL INSTABILITY — Last symptom or advanced.

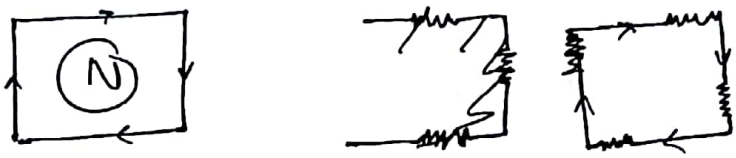
asymmetrical

TITUBATION → ⊖ Pancuronium
↓ ⊕
cerebellum

TREMOR

RESTING TREMOR ⇒ PARKINSONISM

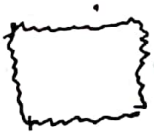
INTESIONAL TREMOR ⇒ CEREBELLAR LESIONS



FLAPPING TREMOR = HEPATIC ENCEPHALOPATHY
"ASTERIXIS" UREMIC "
CO_2 narcosis

FINE TREMORS = THYROTOXICOSIS

BENIGN ESSENTIAL TREMORS



→ 5 - 11 Hz
→ AD inheritance
→ UL > LL
→ ORIGIN = cerebellum
→ ↑ anxiety
↓ on alcohol consumption
= R_x → Propranolol

RIGIDITY – BEST Jt to show Rigidity = WRIST
Resistance to passive movement

LEAD PIPE → EXTRA PYRAMIDAL SYNDROME

COG WHEEL → PARKINSONISM → UL = COG WHEEL
LL = LED PIPE

Superimposed tremors on leg lead pipe

CLASP KNIFE – UMNL

RIGIDITY	SPASTICITY
Tone ↑ Flexors = Extensors	Flexors > Extensors
Bidirectional	unidirectional
	velocity Dependent

GAIT

FESTINATING GAIT → Parkinsonism
(ready to run)
Kinesia Paradox
↳ ↑ acceleration on running

+ spasticity
~~LL~~ ↑
Wk. Distal > Proximal
↑

CIRCUMDUCTION GAIT – Hemiparesis → corticospinal tract

WADDLING GAIT → Myopathy (Proximal)

Lurching GAIT → Polio Lesion → Ant. Horn cells.

BROAD BASED → Cerebellum → Drunken Gait

HIGH STEPPAGE → Foot Drop] neuropathy Deep Peroneal N/V

STAMPING → TABES DORCALIS

↳ Lesion – post column
↓
Loss of Vibration

POSTURAL INSTABILITY

Loss of Postural Reflexes → FALL

MICROGRAPHIA
Small handwriting
(N) I am a doctor
(PD) I am a doct-

MONOTONOUS SPEECH

Hypophonia

MASK LIKE $ FACE

Depression

Dementia

SYMMETRICAL
↳ unresponsive to Levodopa

PARKINSONISM + ATYPICAL PK

1> Progressive Supranuclear Palsy / STEEL RICHARDSON SYNDROME

→ Extended Posture
→ Defective Downward Gaze
→ H/o fall ⟷ early in this type
→ Dementia
⊖ Tremors

2> LEWY BODY DEMENTIA. (LBD)

Parkinsonism + Visual Hallucination

3> MULTIPLE SYSTEM ATROPHY (MSA)

Parkinsonism + cerebellum + Autonomic symptom Instability

4> CORTICO BASILAR DEGENERATION (CBD)

Parkinsonism + myoclonus + Dystonia
sustained Poisturing

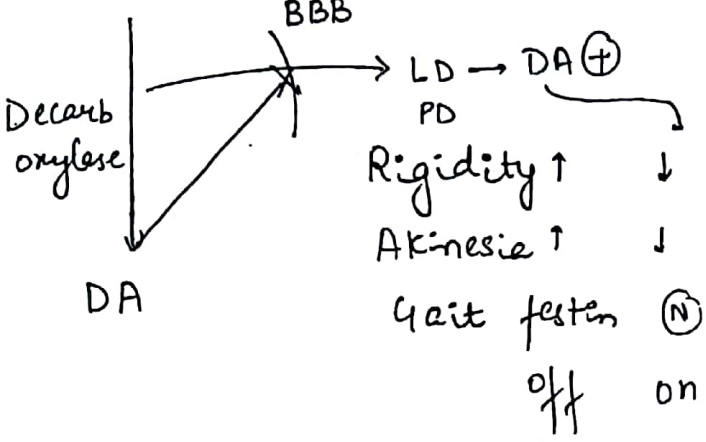
Rx

PD

↓ DA
(rigidity)

↑ ACh
(Tremor)

1> LEVODOPA → DOC



2> PERIPHERAL DECARBOXYLASE INHIBITORS

→ CARBIDOPA
→ BENSERAZIDE

3> MAO B ⊖

→ SELEGELINE
→ RESAGILINE
(neuroprotective)

3> COMT ⊖

→ ENTACAPONE
→ TOLCAPONE

5) AMANTADINE
↑ DA Level

6) DA + D_2
→ PRAMIPRAZOLE
→ Ropinirole
→ Rotigotin

8> ANTICHOLINERGICS
TRIHEXYPHENYDYL

J) APO MORPHINE

↓ sedative — DA ⊕ (Injectable) — off ↓ on — RESCUE THERAPY

CEREBRVOVASCULAR ACCIDENT (CVA)

STROKE

→ Focal neurological Deficit due to vascular cause > 24 hrs

→ TIA (Transient Ischaemic Attack) -

< 24hrs

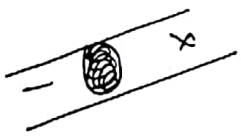
most → for 1 hour

20 mL/100gm brain tissue/min = Ischaemia + Infarction ⊖

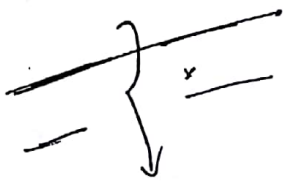
16 mL/min × 1hour = Infarction ⊕

0 mL/min × 4-10 min = DEATH

CLASSIFICATION



ISCHEMIC (85%)



HAEMORRHAGIC (15%)

EMBOLIC (75%) — M/c/c AF. → non-rheumatic AF

THROMBOTIC (25%)

Most epileptogenic stroke

Embolic > H'ge > Thrombotic

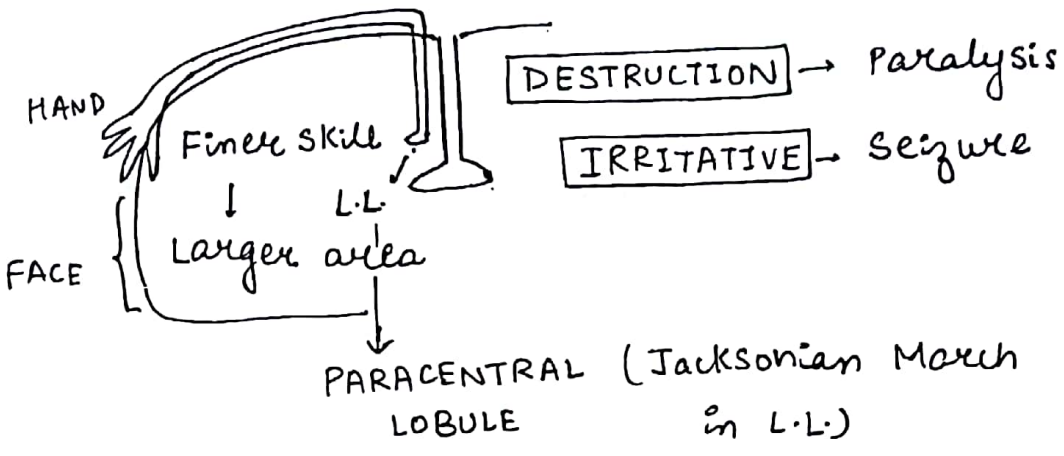
↓

cerebral oedema

Lacunar Infarcts - subcortical
So no seizures

FRONTAL LOBE

1> 1° MOTOR AREA



2> MICTURITION AREA → LESION
⊖ → ? where Social Inhibition
↓
Incontinence [Infant Bladder]

3> SUPPLEMENTARY MOTOR AREA → LESION
⊖ Primitive Reflexes
- sucking ⊕
- grasping ⊕

⇓
[Resurgence of Primitive Reflexes]

4> BROCA'S AREA
- Word area
- Located in Inf. Temporal Gyrus

5> PRE FRONTAL AREA → LESION → [ANTI SOCIAL BEHAVIOUR]

↑ CONTROL

↑ EMOTIONS

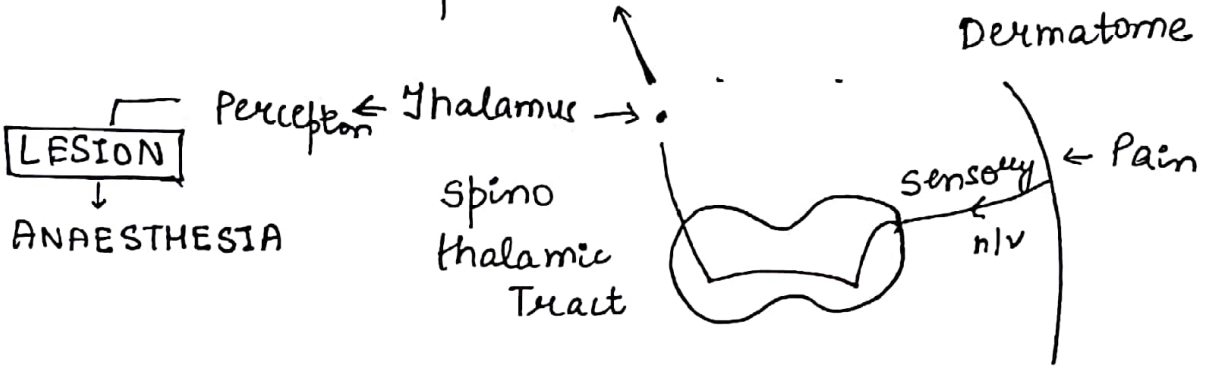
↓ FORMED → Limbic system

CIVIC LOBE = FRONTAL LOBE

PARIETAL LOBE

1> 1° SENSORY AREA

Localisation of stimulus



2> STEREOGNOSIS

Ability to identify on touch.

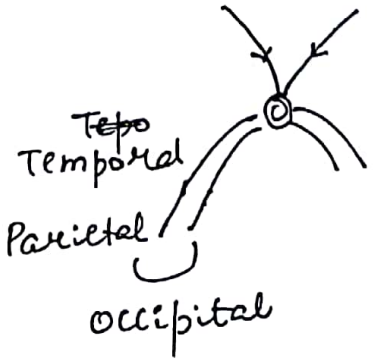
3> TASTE

LESION → DYSGUSIA

4> OPTIC RADIATION

⇓

SCOTOMA



5) ANGULAR GYRUS

Stores images a/c
→ Reading
→ Calculation
→ Naming Fingers

LESION

DEVELOPMENTAL

a> (R) to (L) confusion
b> DYSGRAPHIA (Reading)
c> DYSLEXIA (Learning)
d> ACALCULIA
e> Finger AGNOSIA
Cannot Identify

GERSTMAN SYNDROME

↓

Lesion = (L) Hemisphere

(N) BOMBAY

BOMBAY

(R) to (L) confusion

TEMPORAL LOBE

1> 1° AUDITARY AREA

Hearing ↓

LESION → CORTICAL DEAFNESS

2> WERNICKE's AREA

Sup. Temporal Gyrus
Comprehension

3> OLFACTION → ANOSMIA

4> OPTIC RADIATION → SCOTOMA

5> DEEP/MEDIAL TEMPORAL LOBE

Memory

MEMORY

Immediate → Short term → MEDIAL TEMOPARAL

Short term → converted to Long Term → Stored

- converted to Long Term – Hippocampus
- Stored – Neocortex

AMNESIA

NEO CORTEX → Retrograde

TEMPORAL → Anterograde

AMNESIA → AUDITORY

+ WR, BR+

LEFT / DOMINANT / CATEGORICAL ← AUDITORY

RIGHT / NON-DOMINANT / REPRESENTATIVE ← VISUAL

- WR, BR -

WR - Wernicke

BR - Broca's

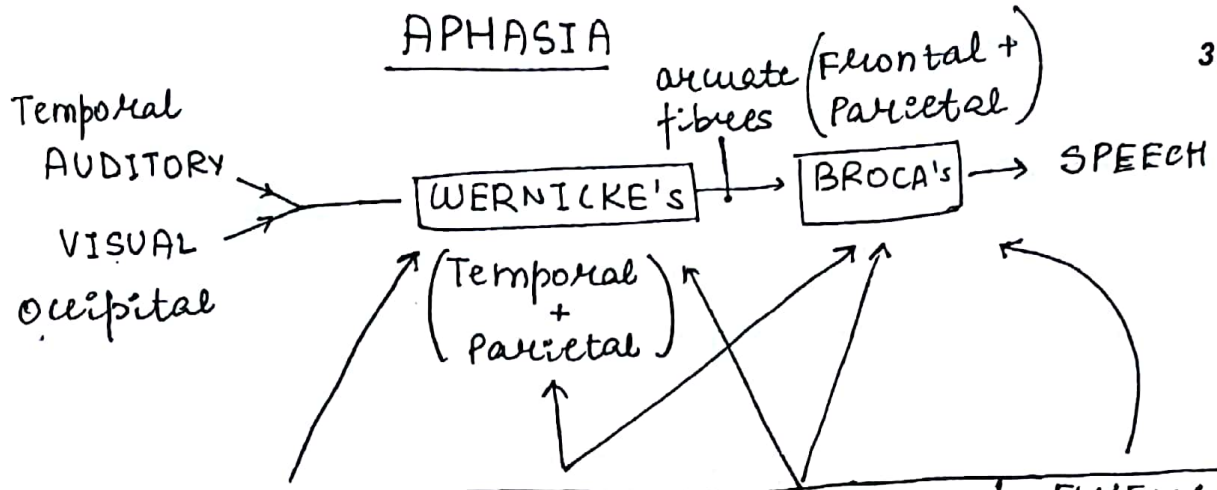
Inability to Recognise Faces (Prosopagnosia)

Handedness → Right → 90%

Handedness → Left → 60%

Left hemisphere → Dominant

APHASIA



APHASIA	COMPR.	NAMING	REPETITION	FLUENCY
WR.	⊖	⊖ · Neologism	⊖	Ⓝ/↑ EXPLOSIVE JARGON speech
BROCA	Ⓝ	⊖ Telegraphic speech Melodic Circumlution speech	⊖	↓ Insight ⊕ Depression
CONDUCTION ↓ arcuate fibres damaged	Ⓝ	⊖	⊖	Ⓝ
TRANS CORTICAL Sensory (Post)	⊖	⊖	Ⓝ	Ⓝ/↑
Trans Cortical ~~Sensory~~ Motor (Antecor)	Ⓝ	⊖	Ⓝ	↓

Mixed Trans cortical (Isolation Aphasia)	(-)	(-)	(N) Echolalia	(-)
Pure Word Deafness Auditory Damage	(-)	(N)	(-)	(N)
Pure Word Blindness (Alexia)	↓ Reading	(N)	(N)	(N)
Anomic Aphasia	(N)	(-)	(N)	(N)

- M/c type
- angular gyrus

seen in ↓

- Alzeihmer
- Head Trauma
- Metabolic Encephalopathy

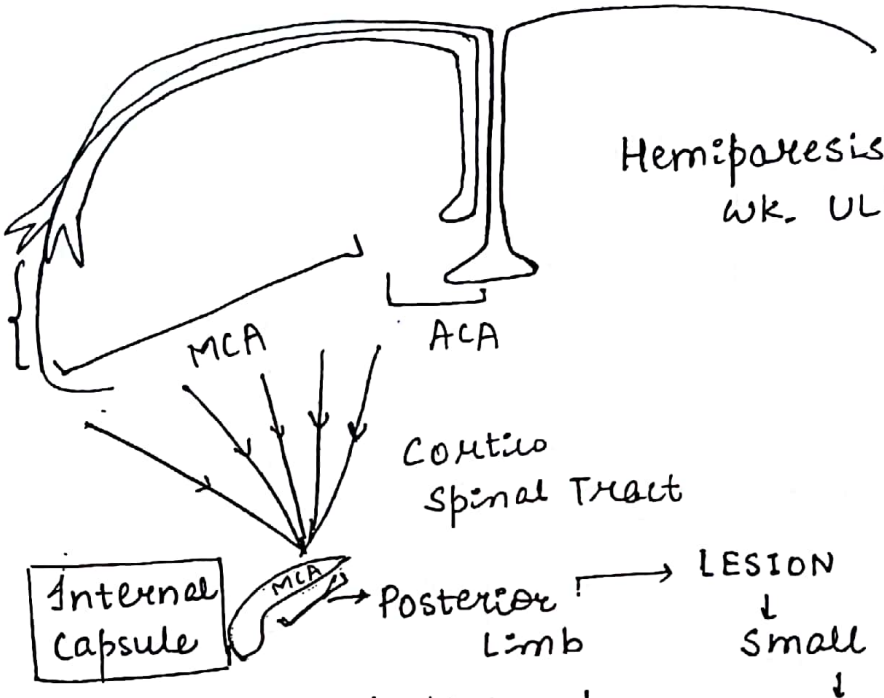
SCANNING Speech — I AM A DOCTOR

↳ CEREBELLAR Lesion.

⇒ Broca's Lesion ⇒ Couldn't write a Dictation

Ant Cerebral Artery

- FRONTAL
  - Paracentral Lobule ↔ L.L. weakness, Incontinence
  - Supplementary motor → Primitive Reflexes (+)
  - Prefrontal → Antisocial Behaviour



Hemiparesis
Wk. UL > LL ⇒ MCA involved

LESION → Small Lesion → Large Deficit → Dense hemi paresis → [Pure motor]

APHASIA → MCA (L) → Broca's, Wernicke's

AMNESIA → Post. cerebral artery → medial Temporal → Hippocampus

GAIT APRAXIA → Ant. cerebral artery → ⊖ movement

Rx [ISCHEMIC]

1> THROMBOLYSIS

Recombinant tissue Plasminogen activator (rtPA)

(I.V.) = 0.9 mg/kg → 10% → Loading Dose
→ 90% → Infusion × 1 hour.

MAX DOSE = 90 mg

WINDOW PERIOD = 4.5 hours from onset

2> ANTIPLATELETS

ASPIRIN

NO clopidogrel

3> ANTI COAGULANTS → AF
→ Prosthetic valve

HEPARIN

↓

WARFARIN

B POWER

GRADING (MRC scale)

0 → no movement

1 → flickering

2 → with gravity eliminated

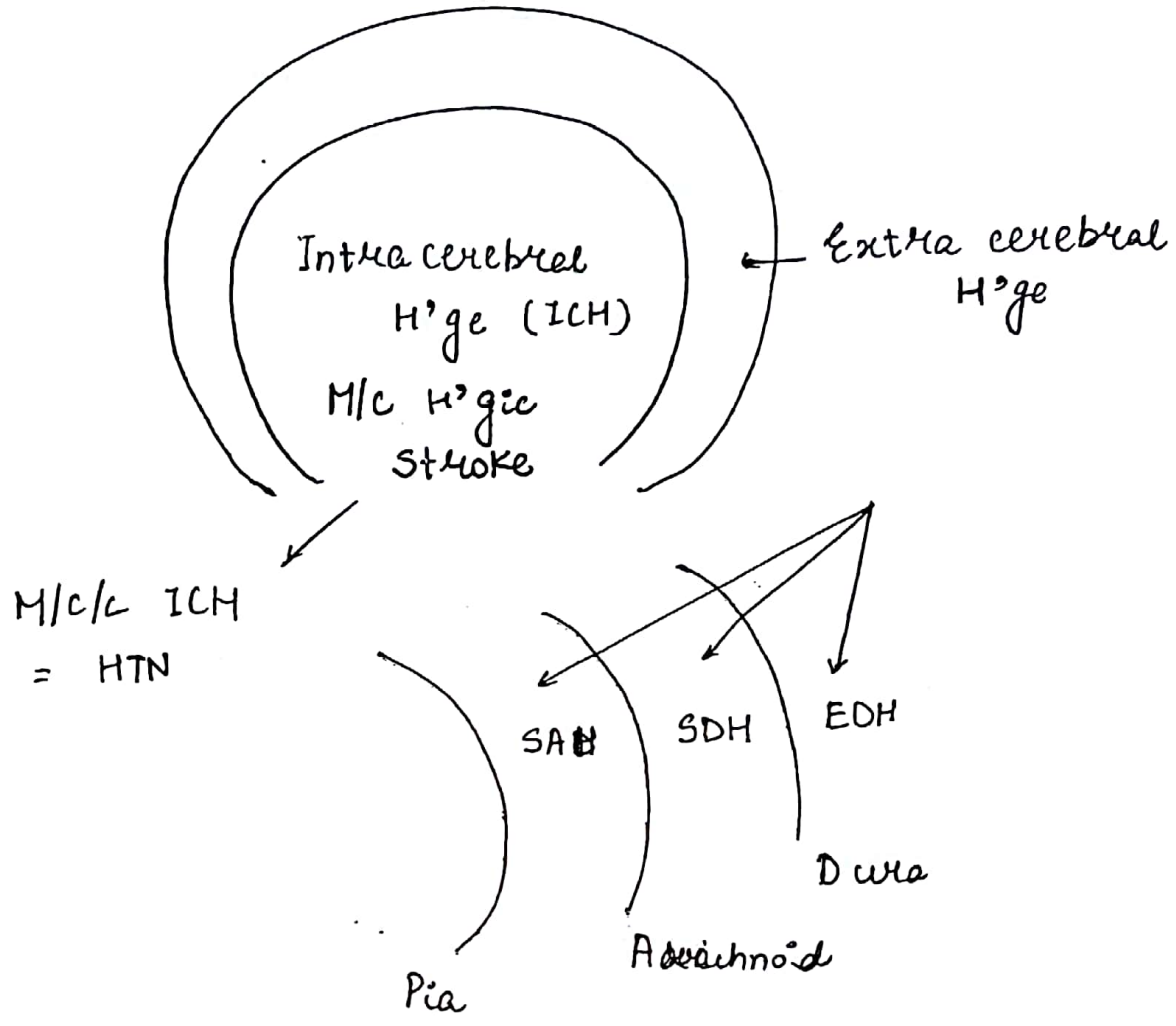
3 → against gravity

4 → against Resistance

5 → NORMAL

Power
↑ (1/5 → 4/5) ⇒ EMBOLIC
↓ (4/5 → 1/5) ⇒ THROMBOTIC

HAEMORRHAGIC STROKE



HTN ICH

SITES

1) Basal Ganglia (Putamen)] HEMI PARESIS — M/c site

2) Thalamus ← HEMI ANAESTHESIA

3) Cerebellum ← ATAXIA, ↖ VERTIGO] Rx Decompression diameter >3cm

Worst Prog 4) Pontine ↑ HR, RR, Temp, Sweating

B/L extensor plantar

PIN POINT → OP Poisoning

PUPIL → morphine

* also seen in-

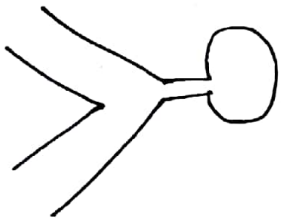
000 SAH H'ge

S.A. Space

↳ CSF → Formed CHOROID PLEXUS

Absorbed ARACHNOID VILLI.

CIRCLE OF WILLIS



SACCULAR / BERRY ANEURYSM

ETIOLOGY

1> Trauma (M/C/C)

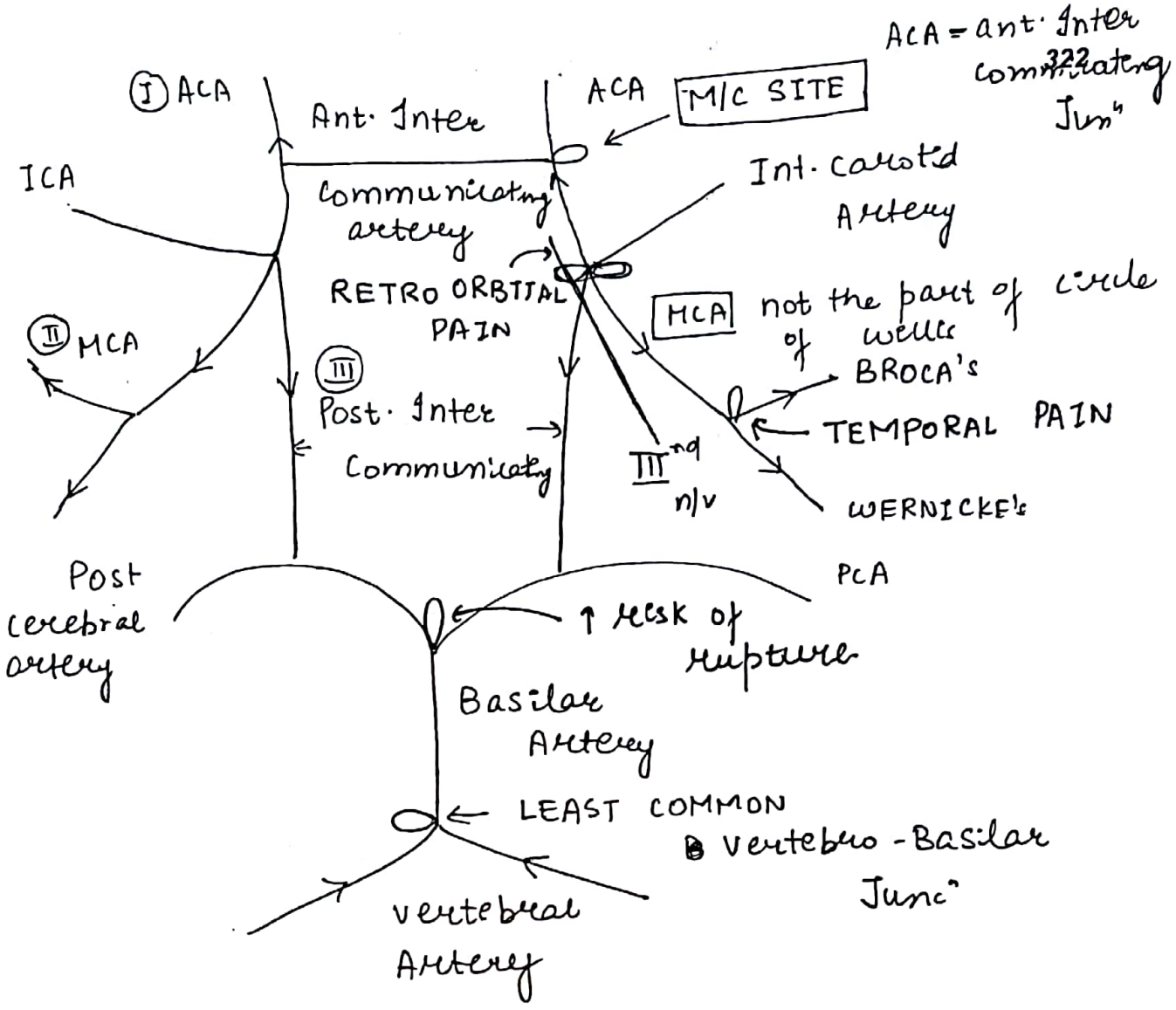
2> Rupture of Berry Aneurysm (M/CC spontaneous (non-traumatic) SAH)

3> A-V malformations

4> Extension from ICH

5> Idiopathic

- LOCATION = Perimesencephalic cistern
- Angiography ⇒ (N)
- Source = venous



85% of aneurysm ⇒ ANT. CIRCULATION

15% " ⇒ POST. CIRCULATION

↓

Less common

↑ risk of Rupture

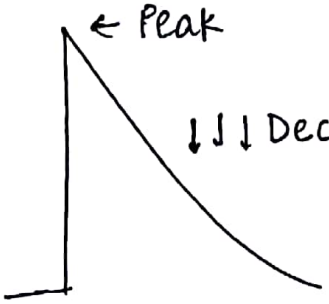
M/c cranial n/v

- Berry Aneurysm ⇒ III rd
- ↑ ICT ⇒ VI th
- GBS ⇒ VII th
- DM ⇒ III rd th
- HIV ⇒ VII th
- Sarcoidosis ⇒ VII th

Paralysed = VII th

C/F-

Onset / Immediate



[THUNDER CLAP HEADACHE]

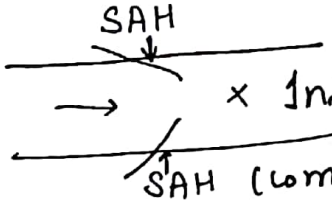
Neck Rigidity

Loss of consciousness (transient)

No focal neurological Deficit

DELAYED

1> Vasospasm



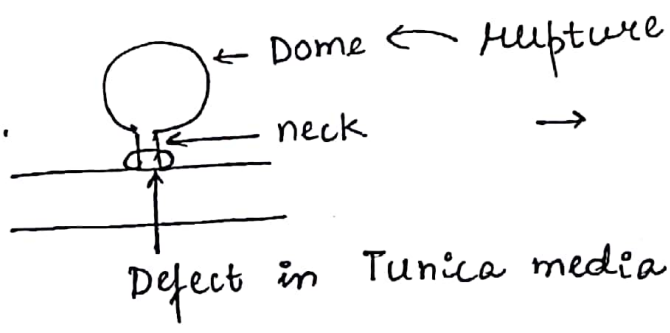
4-14 days after SAH

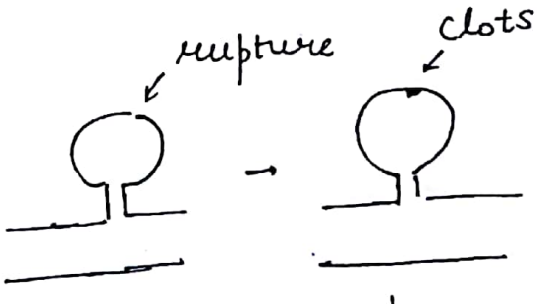
↓

Peaks in 1st 7 days of onset

M.C.C → mortality
→ morbidity

2> Re ruptured





↓

may rebleed if undetected

30% Re-rupture in 1st month

Peaks in 1st 7 days.

3> Hydrocephalus

SAH → BLOOD

BLOOD → Blocks Arachnoid villi → ↓ CSF Absorption → ↑ ICT

4> ↓ Na^+ Hypovolemia

↑ ICT → BNP

CEREBRAL SALT WASTING DISEASE

H_2O ↓ → ↓ Na^+

INVESTIGATIONS

NEUROIMAGING

CT
Acute H'ge (clot)
Calcified

MRI
Inflammation
Infarction
Ischaemic

CVA → CVA → NCCT (Brain) [To exclude acute H'ge]

IOC

Infarct. → MRI (Brain) [To exclude acute Infarct]

IOC

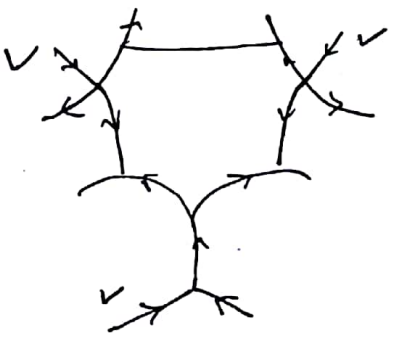
Acute SAH = NCCT (Brain)

Aneurysm = ANGIOGRAPHY

↳ DYE
- ⊖ → MR angio
- ⊕ → 4 vessel angio
  - ↳ 2 ICA
  - ↳ 2 VA

↓

Injected
- ↳ 2 ICA + 1 VA
- ↓
- via femoral vein



Digital Substraction Angiography (DSA)

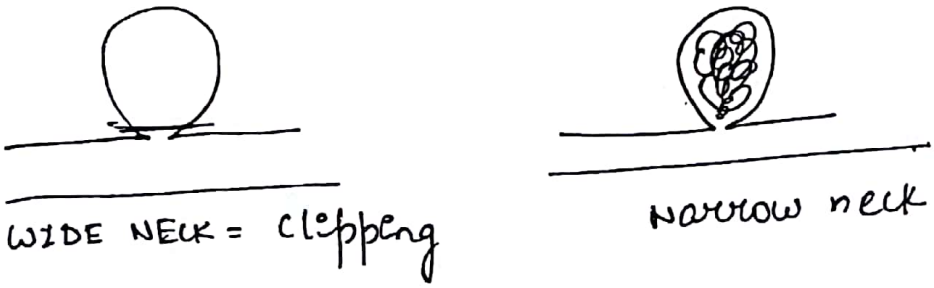
Subtract Bone

Rx

SURGICAL

TITANIUM ↑ clipping

PLATINUM ↑ coiling (BETTER)



WIDE NECK = Clipping

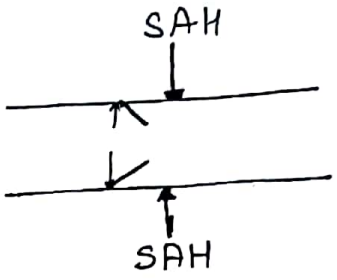
Narrow neck = coiling

⇒ NIMODIPINE ⊖ vasospasm

↓

Intracerebral

⇒ 3H → HTN [160/90]
→ Hypervolemic
→ Hemodiluten (I.V. fluid)



SDH

occurs due to rupture of cortical Bridging veins

EDH

Rupture of middle meningeal artery (MMA)

HEAD INJURY (closed)

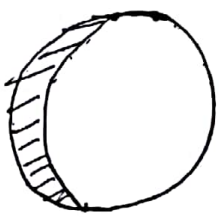
↓

Headache + neurological Deficit

↓

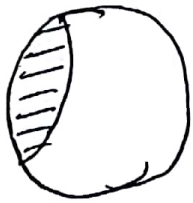
Progresses

Days - weeks - months
slowly



SEMILUNAR

Hours - minutes
Rapidly



LENTICULAR

SDH — CT > MRI

- Acute = HYPER-DENSE
- Subacute = ISODENSE
- Chronic = HYPO DENSE

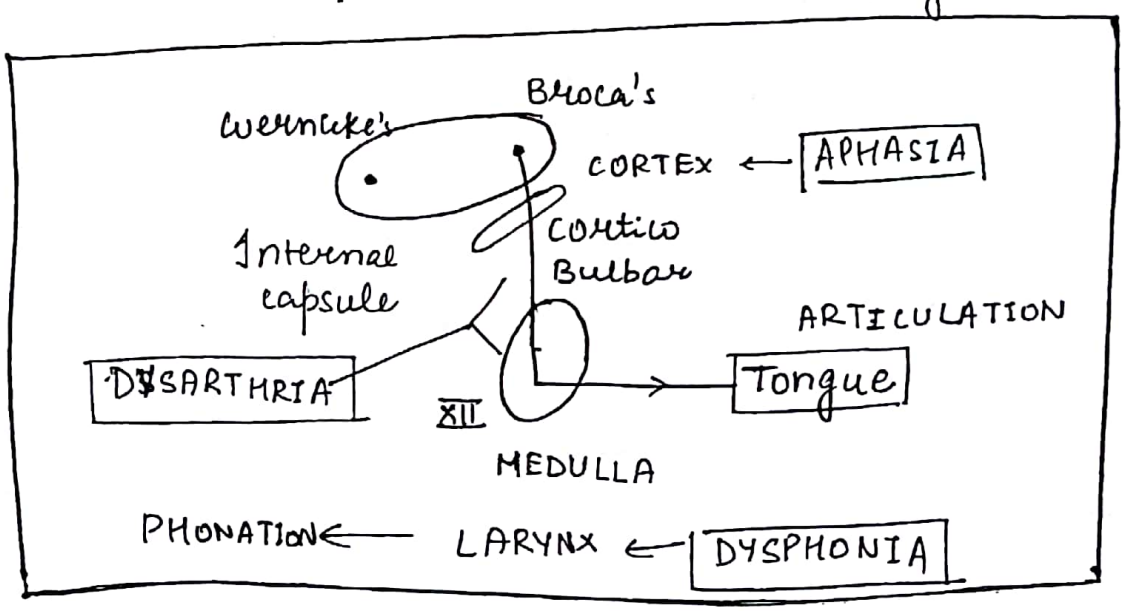
MRI > CT

LUCID INTERVAL = EDH

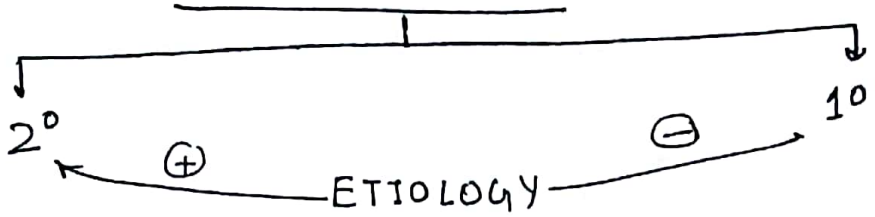
H'gic CVA

- ICH >
  - HTN
    - Putamen
    - Thalamus → SUB CORTICAL
    - Cerebellum → SUB CORTICAL
    - Pons → SUB CORTICAL
  - A-V malformation → CORTICAL / LOBAR H'ge
- ECH
  - SAH ← H/C
  - SDH ← BOXERS
  - EDH

Post-Traumatic



HEADACHE



TEMPORAL ARTERITIS

Elderly

♀ > ♂

Headache ⇒ Throbbing
Stabbing

Scalp Tenderness → touching inflammed artery

Jaw claudication [SPECIFIC]
↳ Difficulty in chewing food

Blindness ← irreversible
↳ due to involvement of post cerebral artery

Inv-
↑ ESR
, Biopsy → Temporal Artery Biopsy
↓
Giant cells

Rx- DOC = STEROIDS

PSEUDO TUMOUR CEREBRI / BENIGN IDIOPATHIC INTRACRANIAL HTN

M/c- young obese, ♀

Headache

Projectile vomiting (nausea ⊖)

Papilloedema

ventricle size (N)

No focal neurological Deficit

↓ CSF Absorption

ETIOLOGY

1) Hypervitaminosis A
2) Expired Tetracycline
3) OCP
4) steroid withdrawal (Abrupt)

M/C/C ⇓ Idiopathic

Rx = ACETAZOLAMIDE
↓ CSF formation.

TENSION HEADACHE

♀ > ♂

M/c 1° Headache = Tension Headache

Associated ⊽ DEPRESSION

Tension is not an etiology

Dull Aching Pain
Band like

Rx
- EPISODIC → <15 day/mnth = ANALGESICS
- CHRONIC → >15 day/mnth = T.C.A. (Amytryptiline)

Rx of choice

MIGRAINE

♀ > ♂

4-72 hours

≥ 2
- P → Pulsatile
- U → U/L
- M → Moderate to severe in Intensity
- A → aggravation

+ any 1
- nausea (M.C.)
- Vomiting

or any 1
- Photophobia
- Phonophobia

AURA = visual > sensory

- (+) CLASSICAL (20%)
- (−) COMMON (80%)

ACCEPTED THEORY

(I) Cortical Spreading Dissociation

Main Trigger → vaso constrict" ⇒ [SCOTOMA]

↑

Intracranial (occipital)

↓

vasodilatation ⇒ FLASHES OF LIGHT ← FORTIFICATION SPECTRA

vasodilation

Headache ↓ ⊕

Meningeal irritation → Pain → Brain

Calcitonin gene related Peptide

CGRP

(II) SEROTONINERGIC

[5HT ⊖] ⇒ Throbbing

R_x = 5HT ⊖

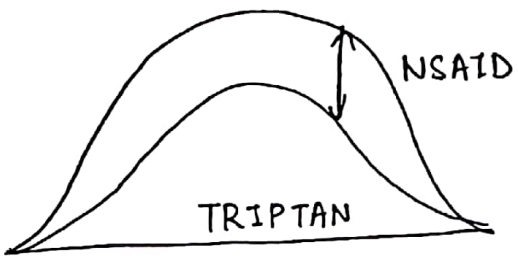
NON SELECTIVE → ergotamine

SELECTIVE → 1B/1D

[Triptans]

DOC for acute attack

RIZA triptan > SUMA triptan



(III) DOPAMINERGIC → DA ⊖

Metoclopramide

DA ⊕ - nausea

PROPHYLAXIS × 5 - 6 months

① β ⊖ ⇒ Propranolol (widely used)

② TCA ⇒ Amitryptaline

③ CCB → Flunarizine

④ A.E.D. → Valproate
Topiramate
Gabapentine
Ethosuximide
↓
Not Recommended.

CLUSTER HEADACHE

♂ > ♀

Peri / Retro Orbital Pain
- U/L
- 30 min - 2 hours
- ppt. by consumption of alcohol
- awakens from sleep.

Autonomic (+) hyperactivity → Lacrimation
→ Rhinorrhoea

Rx = O_2 inhalation (RxOC)
@ 10 - 12 L/min × 10 - 15 min

Prophylaxis = Verapamil (DOC)
(lifelong)

PAIN

SENSITIVE

- → Circle of willis
- → Meningeal arteries
- → Dural sinuses / veins

INSENSITIVE

- → Duramater
- → Arachnoid Mater
- → Choroid Plexus
- → Ventricular Ependyma

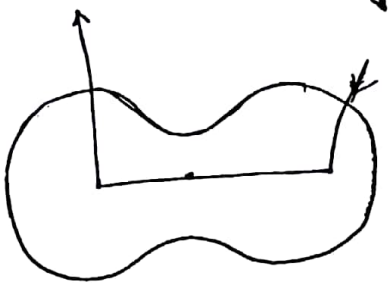
D/D of MIGRAINE

1) Glaucoma

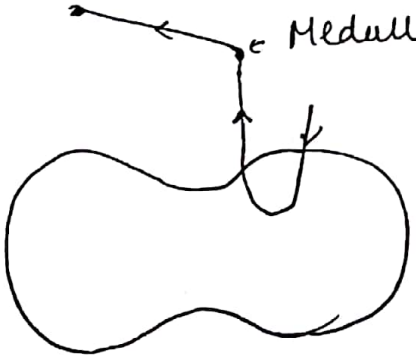
(S) ↑ SPINAL CORD ↓ (M)

ASCENDING / SENSORY

SPINOTHALAMIC → Pain, Temp, Crude Touch



POST. / DORSAL COLUMN ← vibration
← ~~It~~ proprioception (Jt. position)
← Fine touch.



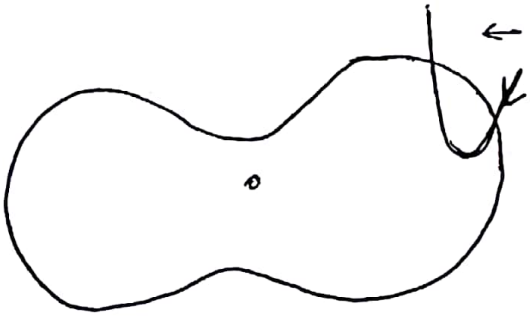
LESION

↳ Stamping Gait

ROMBERG's TEST (+) → sways ⊂ eyes closed

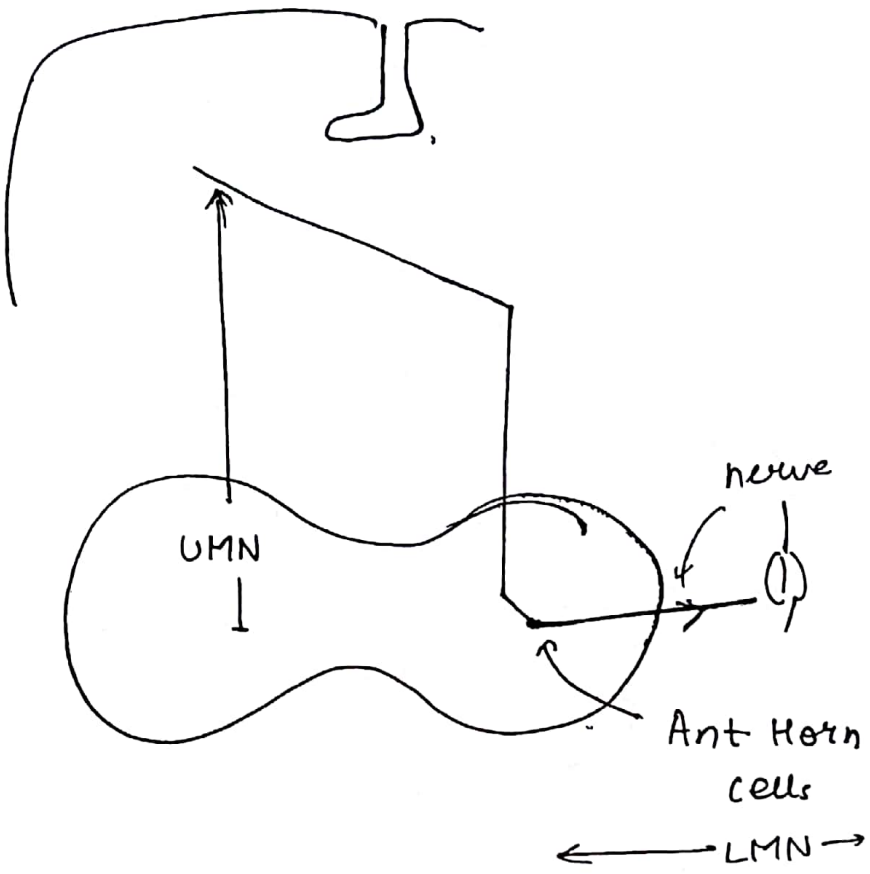
SPINOCEREBELLAR TRACT

↳ Subconscious proprioception



DESCENDING TRACT

CORTICOSPINAL TRACT



PARALYSIS

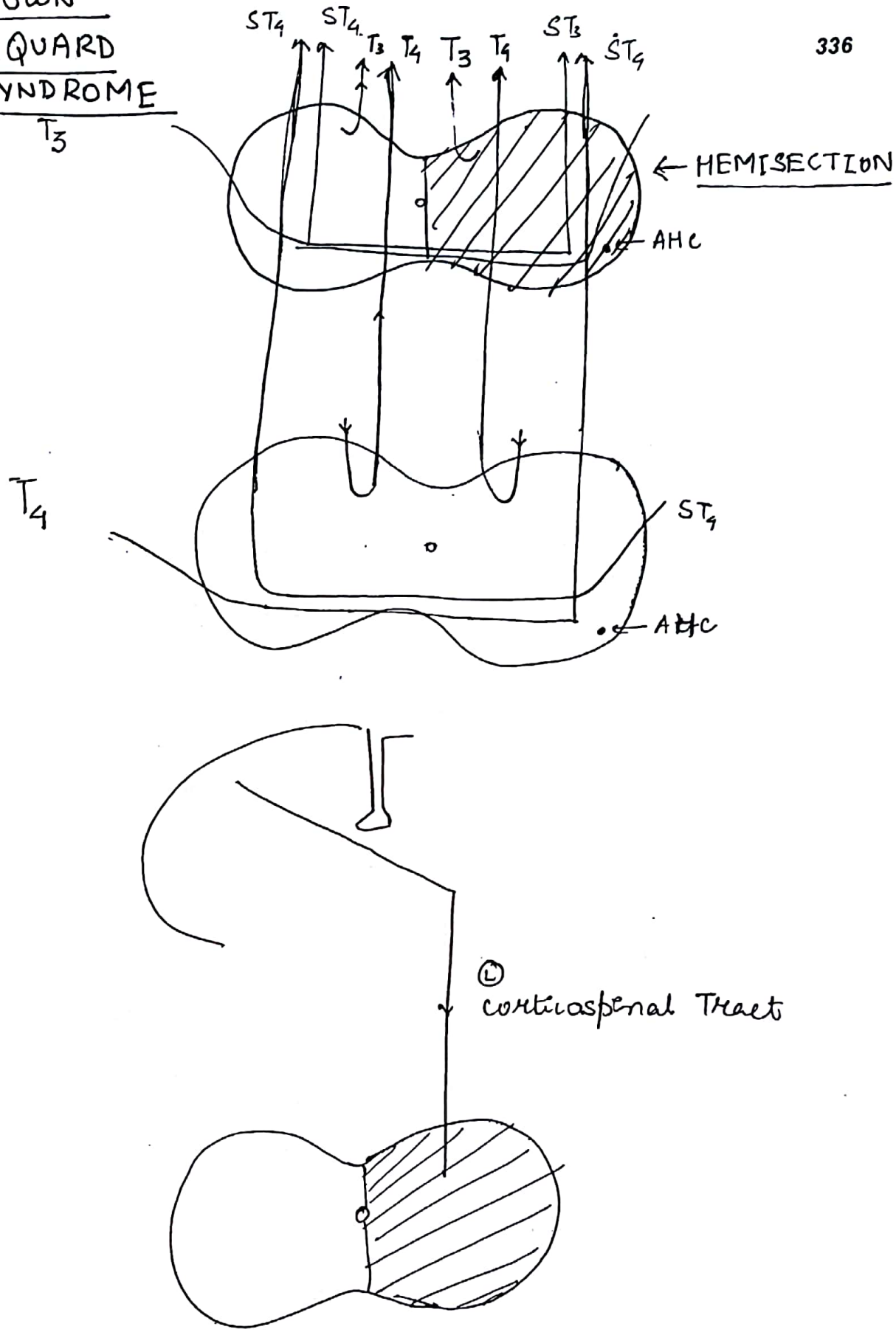
UMN

- **Tone** ↑ (spasticity)
- **DTR** Brisk
- **Plantar** Extensor [Babinski +]

LMN

- ↓ (flaccidity)
- Dull / absent
- Wasting / atrophy ⊕
- **Fasciculation**
  - Twitch → visible / Palpable
  - LESION
  - ↳ Ant. Horn cell.

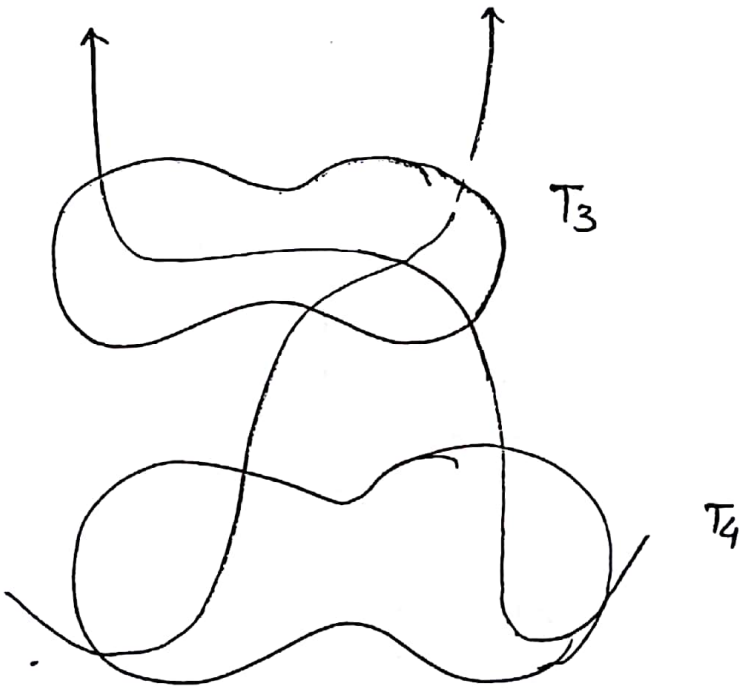
BROWN SEQUARD SYNDROME



HEMISECTION of T_3

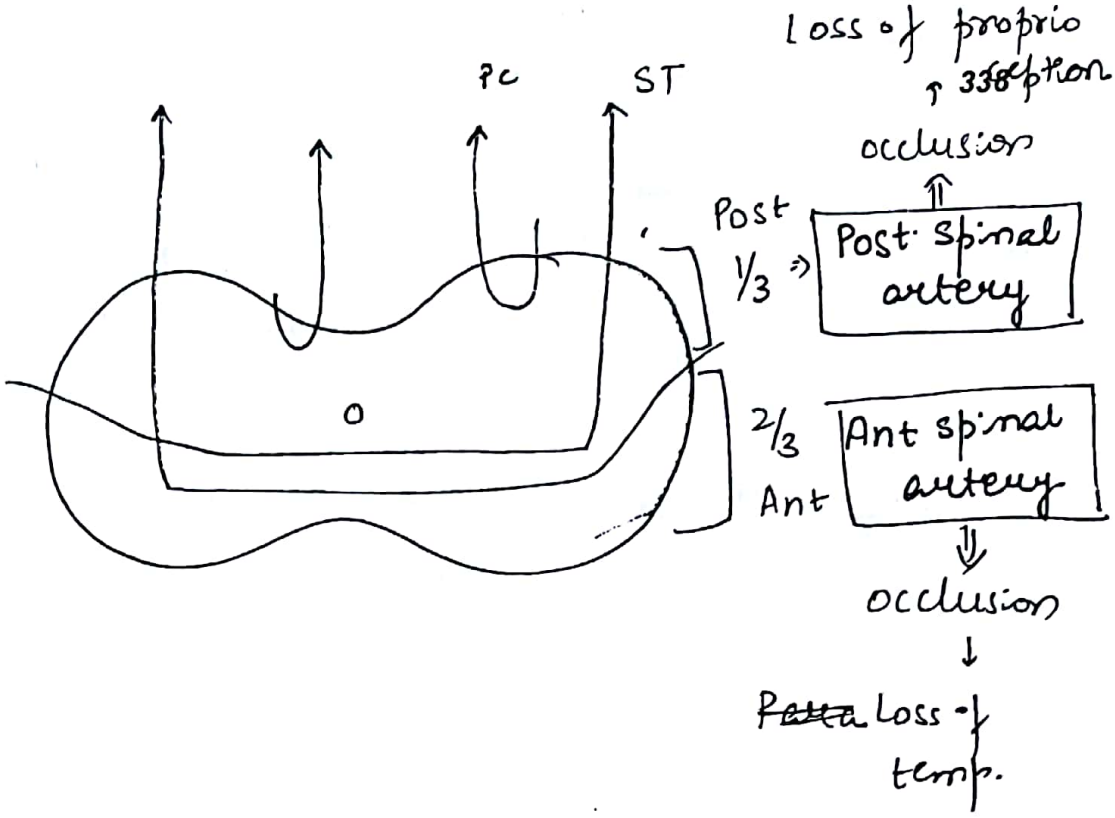
At T_4 → Loss of Spinothalamic → C/L
Post. column → I/L
weakness → UMN I/L.

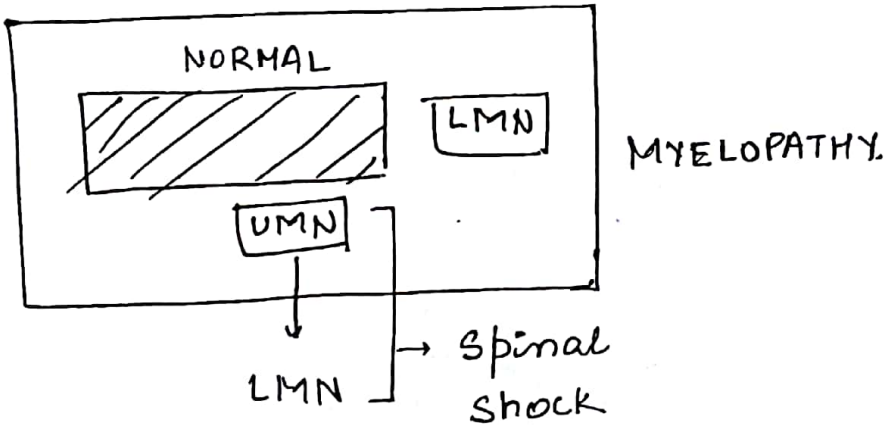
At T_{43} = Loss of Post column - I/L
weakness - LMN, I/L
** Spinothalamic - I/L,



AT THE LEVEL ⇒ Spinothalamic, Post. column, LMN → SAME SIDE

BELOW The LEVEL ⇒
Spinothalamic ↓ opposite side.
P.C., UMN → same side





QQ SPINAL SHOCK

"Transient" LMN weakness below the level of lesion

↓

most occurs @ 48-72 hrs

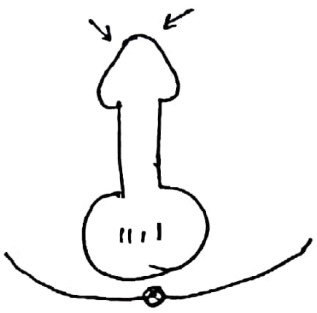
→ Flaccidity
→ Areflexia
→ Urinary retention.

→ Sensory Loss

→ Wasting ⊖ ⟹ → Transient process
internal nutrition is intact

Spinal Shock = LMN - Wasting

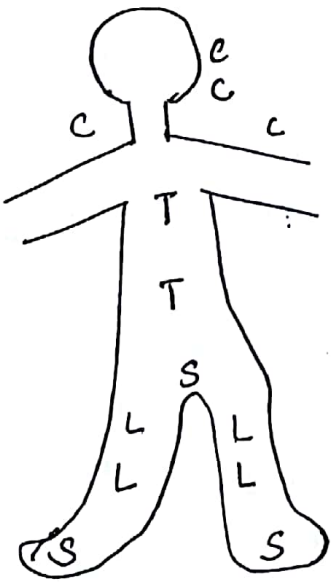
1st Reflex Recover-
BULBOCAVERNOUS. ⇒ EXTERNAL ANAL SPHINCTER.

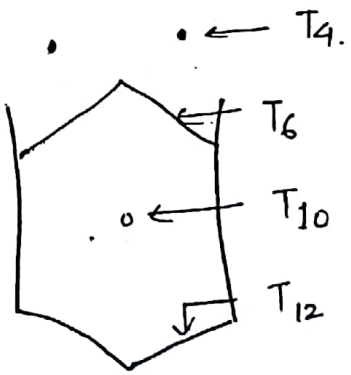


CREMASTERIC

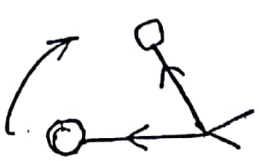
↓

FLEXOR WITHDRAWAL.





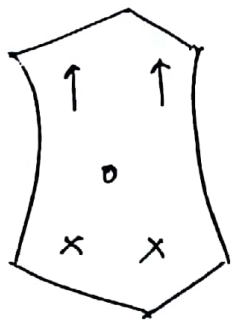
BEEVOR SIGN



BEVOR SIGN

Supine ⟶ Sitting positon

↓ umbilicus moves upward ⇒ Lesion @/below T_{10}

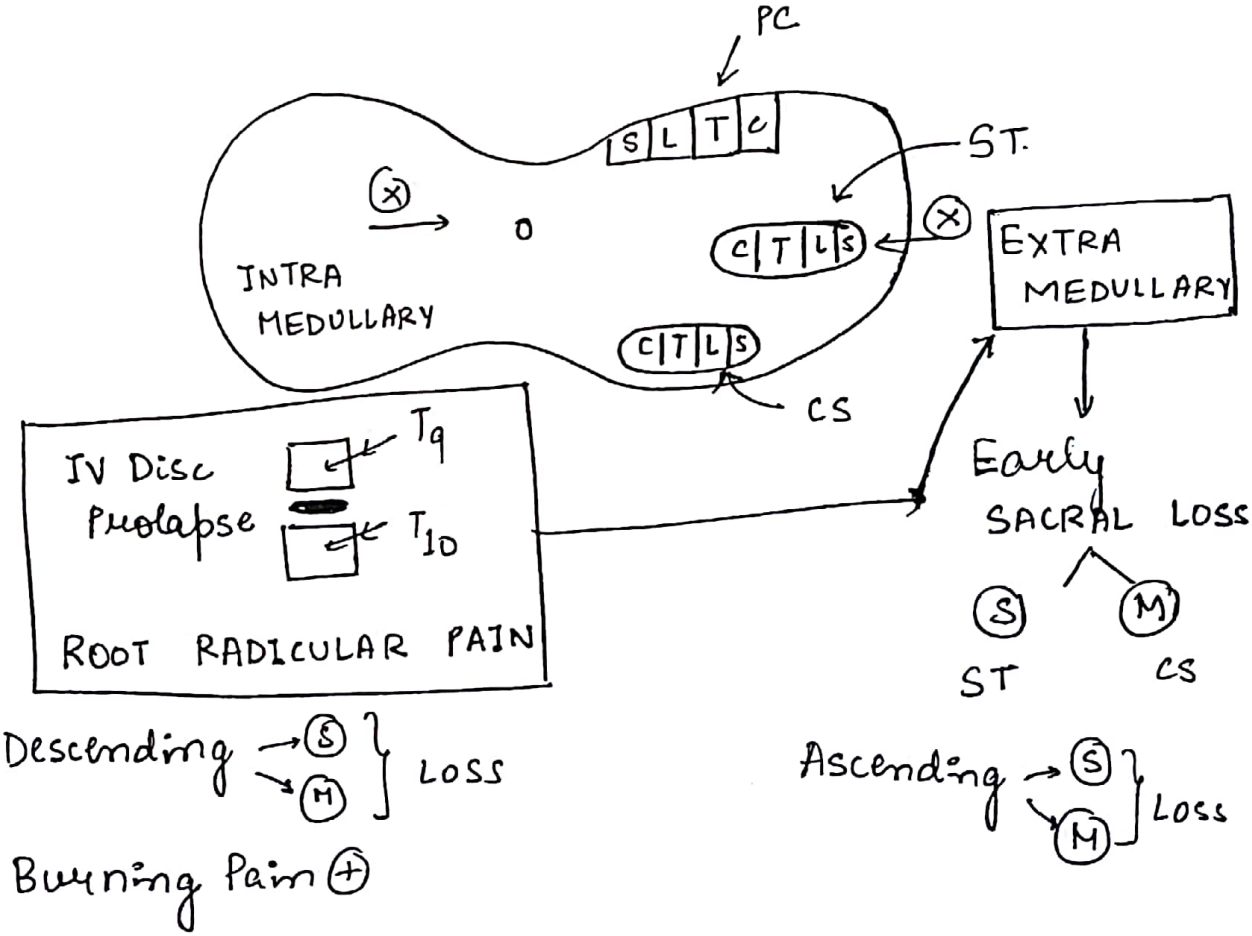


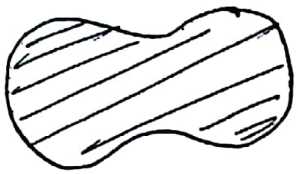
PRONATOR DRIFT SIGN

Weak Side

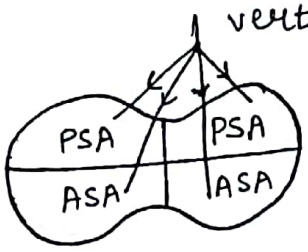
PRONATION + ↓ DRIFT

} Injury CS Tract
CVA in Evolution.



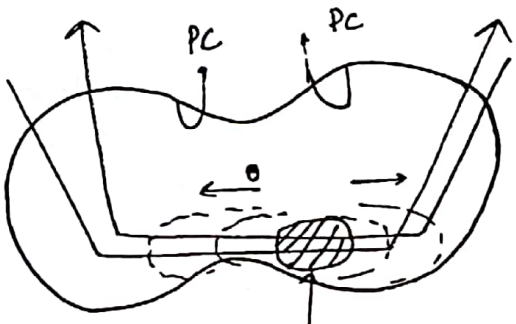


⇒ TRANSVERSE MYELITIS → extramedullary lead to transverse myelitis.



Occulcion of 1 side ASA + PSA
↑
due to vasculitis
⇒ BROWN SEQUARD

QQ SYRINGOMYELIA



Selective Loss of
- Pain
- Temp

DISSOCIATED ANAESTHESIA

SYRINX = cavity
Assymetrical

M/C site = Lower cervical upper Thoracic

CAUSE :-

1) congenital
2) 3T
   - Trauma
   - Tumour
   - TB

AT THE LEVEL ⇒ LMN weakness
BELOW THE LEVEL ⇒ UMN weakness

[CAPE LIKE DISTRIBUTION OF SENSORY LOSS]

q/c

CHIARI MALFORMATION > 50%
(Type 1)

⇓

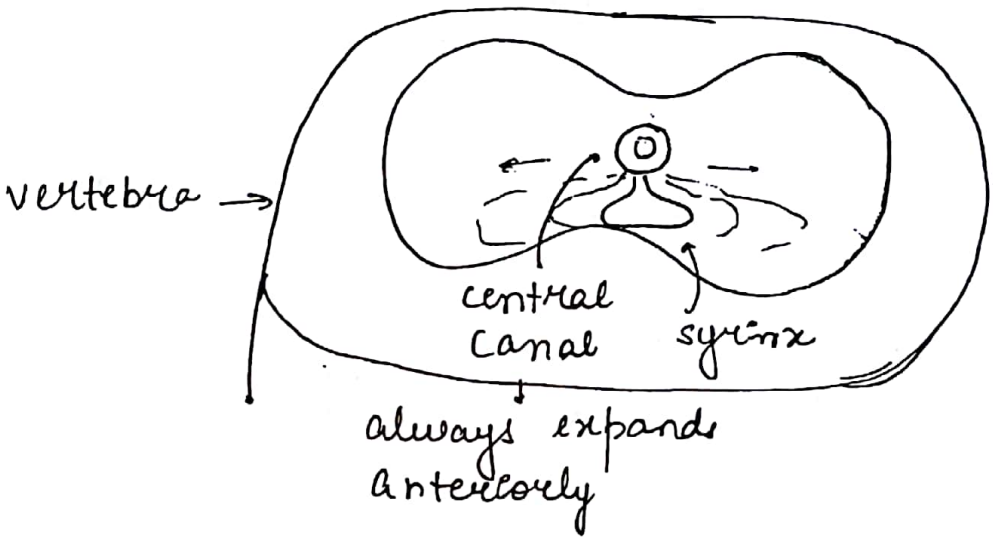
Cerebellar tonsillar herniation into foramen Magnum

↓

compresses central canal containing CSF

↓

it starts enlarging due to compression



Rx = DECOMPRESSION LAMINECTOMY

| to relieve pressure on ~~be~~ expanding spinal cord from vertebra

DISAD

↳ doesn't relieve symptoms.

NOTES (C/F of syringomyelia)

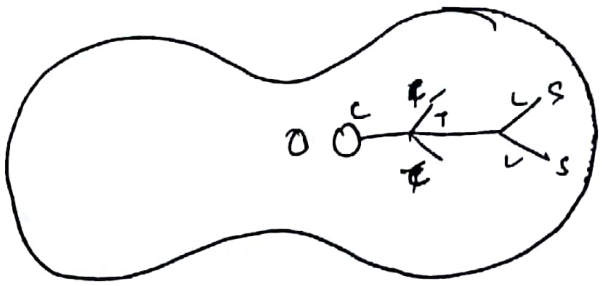
→ Painless burning of hands occur easily

↓

Trophic ulcers

→ absent biceps Jerk (C5, C6)

→ extensor plantars [L5, S1]



URINARY BLADDER

FRONTAL (Paracentral Lobule) where ⇒ ACA

↓

PONS CENTRE

- ⊕ < contraction, micturition] PARA $[S_2\ S_3\ S_4]$
- ⊖ < Relaxation, storage] SYMPATHETIC $[T_{11} - L_2]$

↑ Sensory S_2, S_3, S_4

[A] $S_2\ S_3\ S_4$ ⊖ [AUTONOMOUS BLADDER]

$S_2\ S_3\ S_4$

⊖ → sensory
⊖ → Para

$T_{11} - L_2$

++ L Sympathetic

HYPOTONIC
FLACCID
LARGE CAPACITY
OVERFLOW
INCONTINENCE

[B] $T_{11} - L_2$ ⊖ [AUTOMATIC BLADDER]

$T_{11} - L_2$ — ⊖ Symp

S_2, S_3, S_4 — ++ < sensory, parasymp

- HYPER TONIC
- SPASTIC
- LOW CAPACITY
- URGE INCONTINENCE

CONUS MEDULLARIS

S.C. ends opp. to L_1 L_2.

$S_1 - S_5$ segments

KNEE JERK

$L_3 - L_4$ ++ [N]

ANKLE-JERK

$S_1 - S_2$ ⊖

BLADDER

AUTONOMOUS (early) → Intra /

CAUDA EQUINA

nerve Roots

$L_1 - L_5$

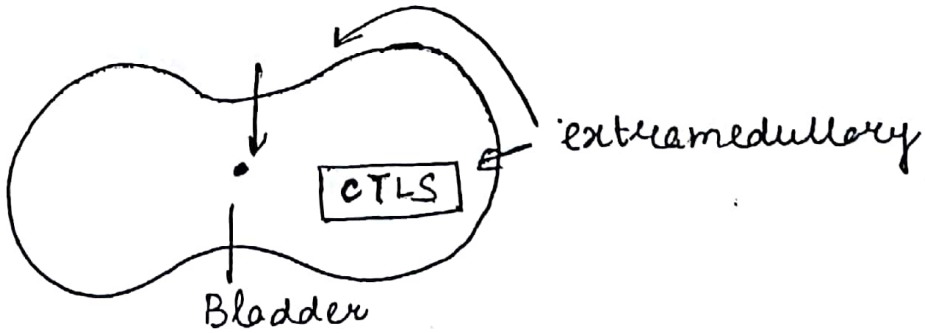
$S_1 - S_5$

⊖

⊖

MIXED (NEUROGENIC)

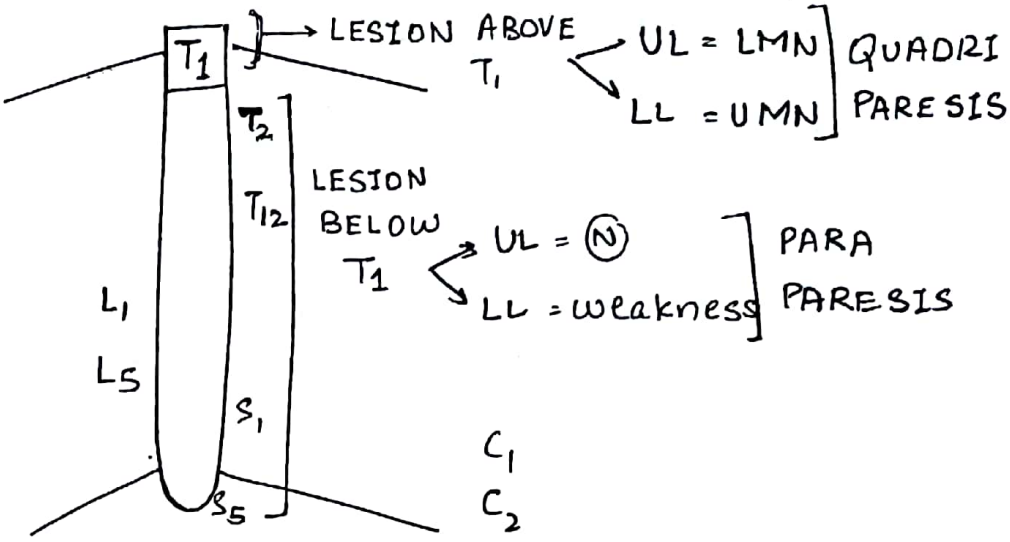
(Late) ↑ Extra

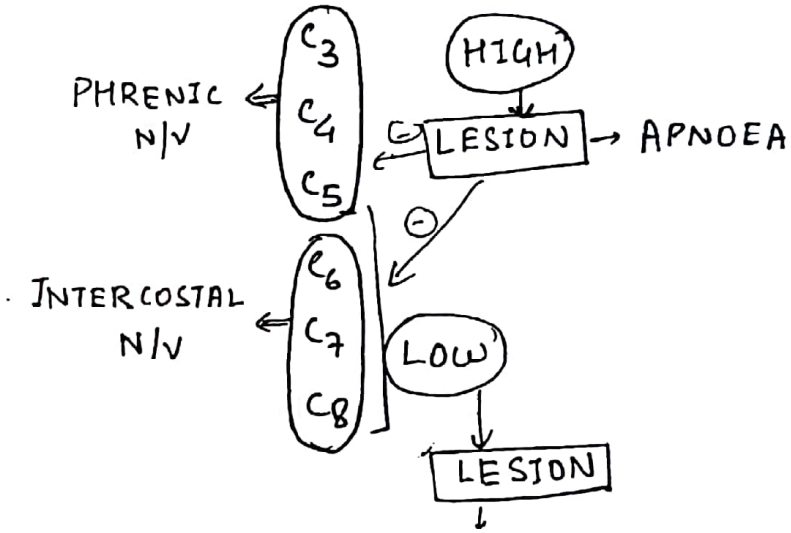


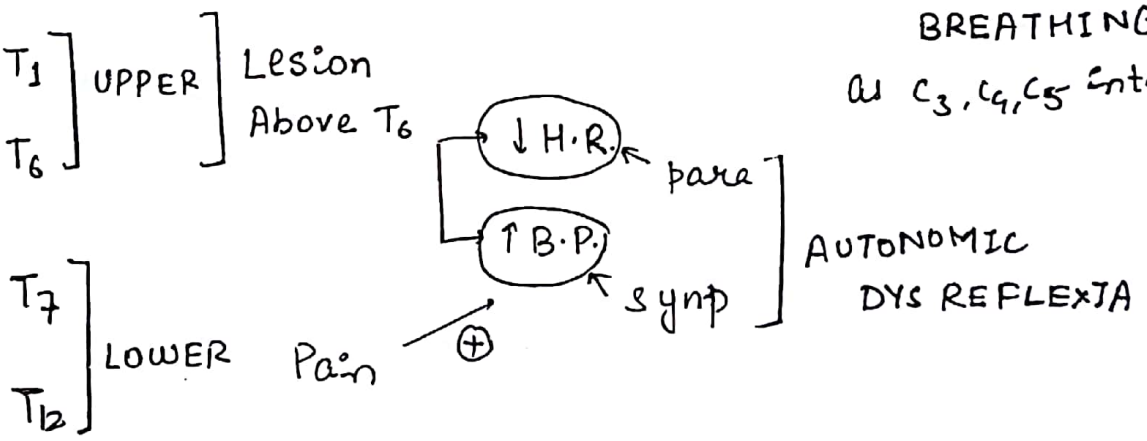
Asymmetrical

Areflexic

LMN Paralysis

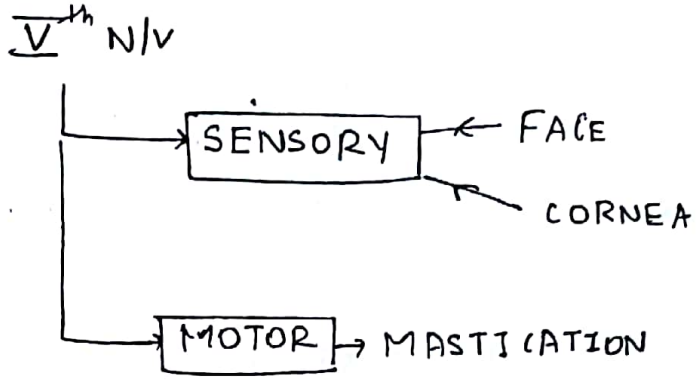






R_x = NIFEDINE
CLONIDINE

TRIGEMINAL N/V



NUCLEUS

SUPRANUCLEAR → UMN

PONS

NUCLEAR → LMN

INFRANUCLEAR

C_1 ×
C_2 ×
C_3 ×
C_4 ×

SPINAL
||
SENSORY

MYELOPATHY

⊖

⇓

Loss of sensations over Face

Jaw Jerk → BRISK → UMN

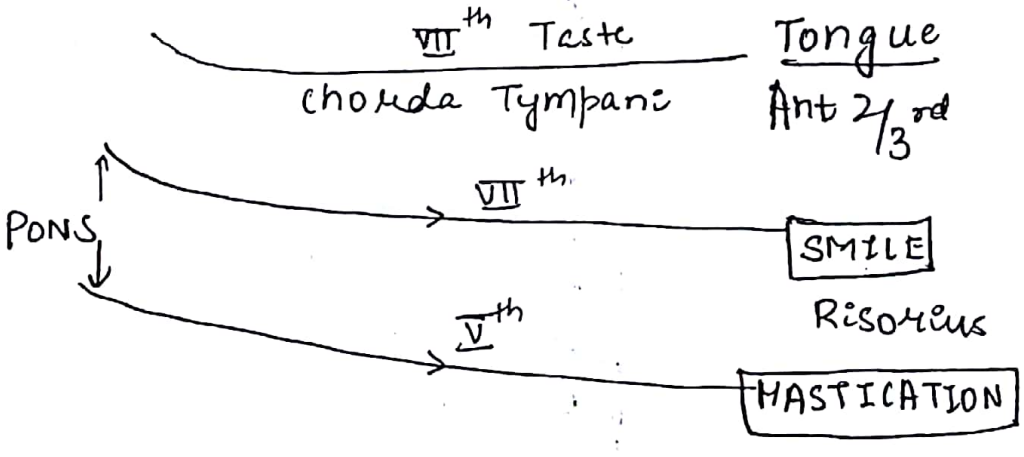
V th
V th

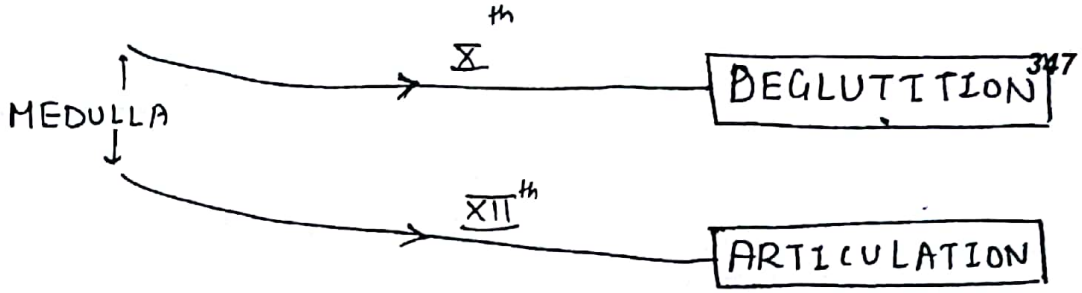
↓

Supranuclear

↓

[Lesion above PONS]





~~FACIAL N/v~~

TRIGEMINAL NEURALGIA

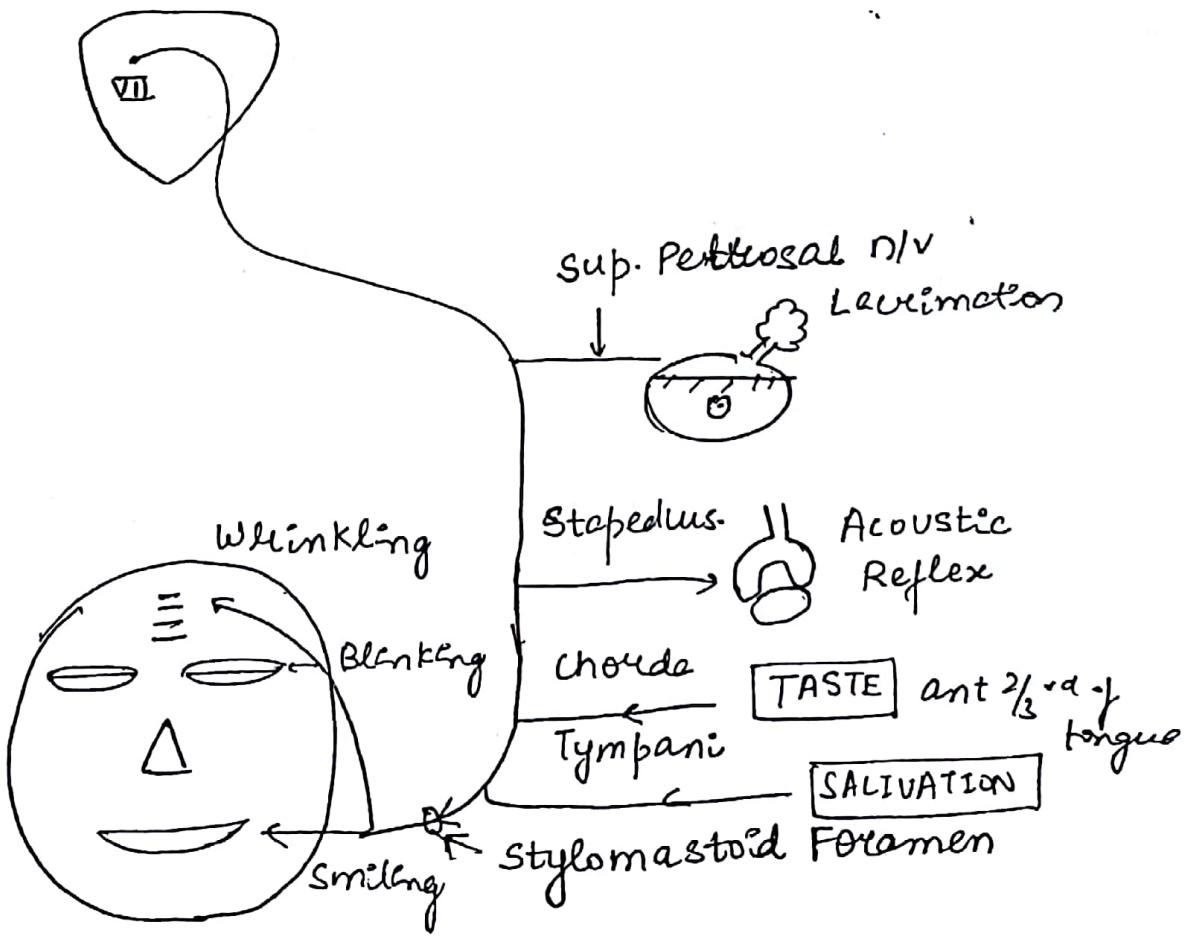
Electric shock on Face / TIc DOLOREAUX

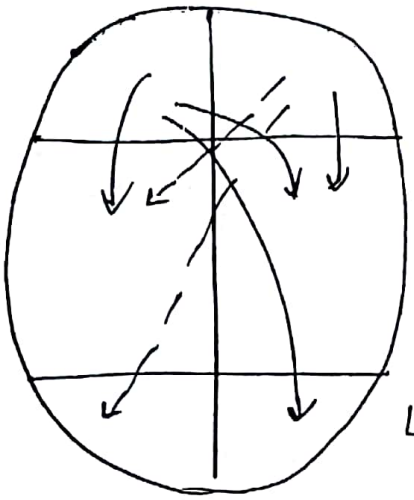
Rx → Injec" of C_2H_5OH / glycerol in gasserion ganglion

RHIZOTOMY - Radio Frequency Ablation

FACIAL N/V (VII th)

PONS

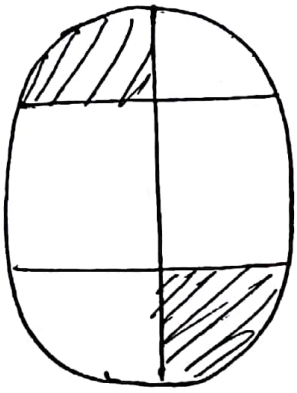




Upper $2/3^{rd}$ Face is having B/L cortical innervation

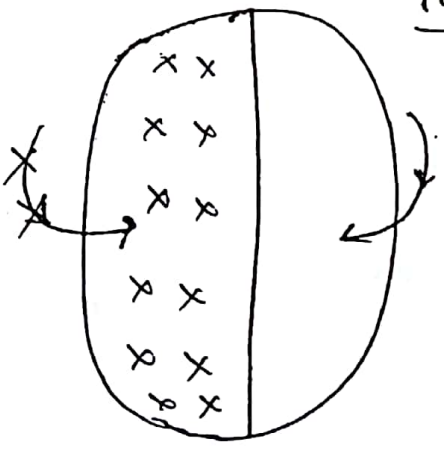
Lower $1/3^{rd}$ of Face supplied by opposite cortex

A)



Cortical lesion ⇒ UMN PARALYSIS
(Supranuclear)

B)



PONS LESION ⇒ LMN PARALYSIS

U/L →

CAUSE

1) Trauma
2) Herpes zoster virus [RAMSAY HUNT SYNDROME]
3) Idiopathic [BELLS PALSY]

B/L

CAUSE

1) UBs
2) HIV
3) Sarcoidosis

RECOVERY

Aberrant Reinnervation

1> CROCODILE TEAR SYNDROME

2> SYNKINESIA (smiling Blinking together)

H/O ⇒ S/O CERVICAL CORD INJURY

1) Fall from height
2) Road Traffic accident
3) Hanging

LHERMITTE SYMPTOM

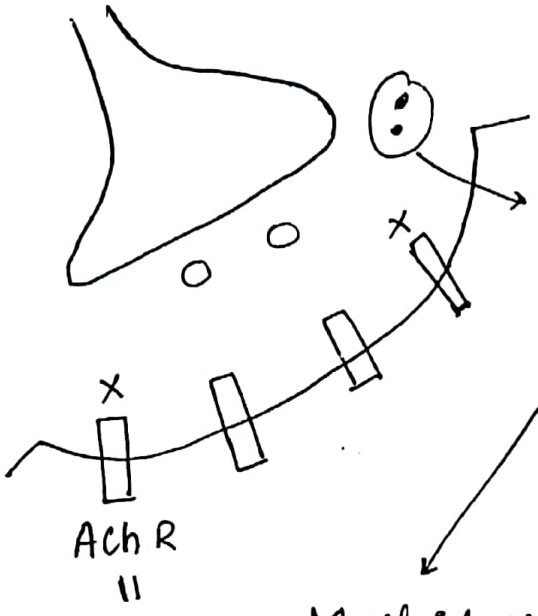
↓

MULTIPLE SCLEROSIS on flexion of neck ↓ Pain / electric shock across spine

MYASTHENIA GRAVIS

ACh (R) ANTIBODIES

Destroy > Block



ACh E → ↓ ACh Levels

THYMIC AB(N)

↳ 75% Myasthenia Gravis

↳ 65% Hyperplasia

↳ 10% Thymoma

↳ LOCAL → Compressive

↳ PARANEOPLASTIC

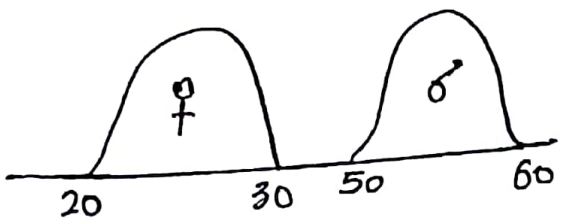
Myeloid cells
↓
antigenically mimic ACh(R)

So, Antibodies cross react

MRI (chest)

- Pure red cell Aplasia
- Pernicious Anaemia
- Hypo γ globinemia
- Dermatomyositis

♀ : ♂ = 3:2



3-7% MG
↓
suffer from Hypothyroidism } So, Inv = TSH. 351

C/F :-

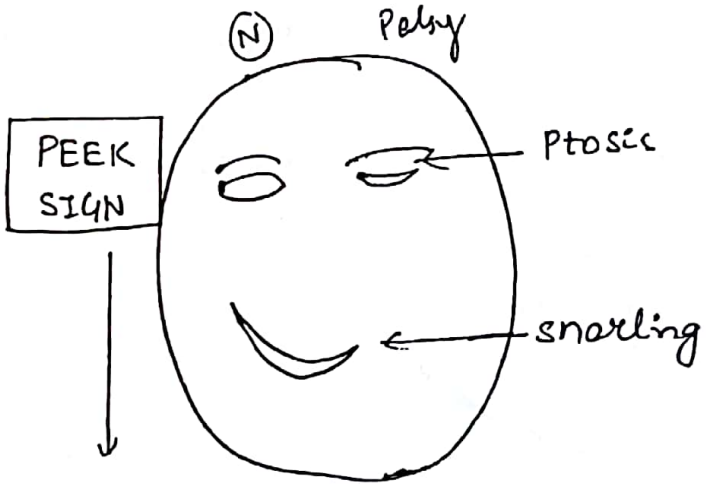
1> Easy fatiguability
- Proximal
- Asymmetrical

a> OCULAR [1st m/s to involve; M/C m/s to involve]

Ptosis — opthalmoplegia

2) FACIAL

Snarling
↓
can't maintain smile for long



close eyes for some time then opens as if seeing through small aperture

3> SKELETAL

N → DTR
- Sensory intact
- Bladder
- Cognition

INV:-

1> EDROPHONIUM / TENSILON TEST

↓

shorter acting

Peripheral action

[BEST SCREENING TEST]

2> ACh (R) Antibodies

MOST SPECIFIC TEST

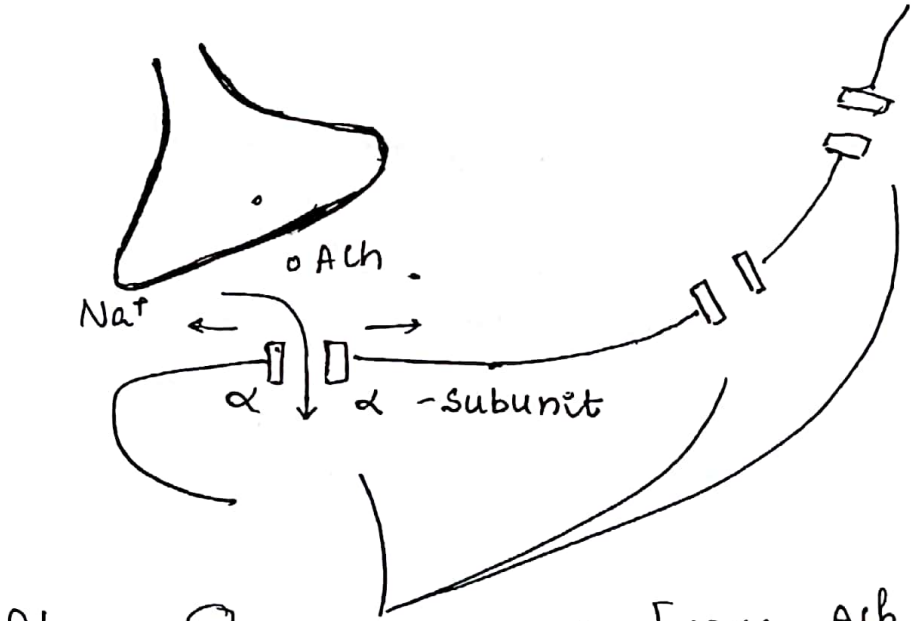
+ in [85% of pts. ε gen. MG.

↳ 50% **Ocular MG.** → [Eye symptoms x 3yrs]

-ve doesn't rule out MG.

3> MUSCLE SPECIFIC TYROSINE KINASE (MUSK)

MUSK Antibodies



Ab ⊖ → CLUSTERING ⊕ ↑

↓

Lipoprotein Related Protein

[ADV:- Ach can act on all (R) at same time

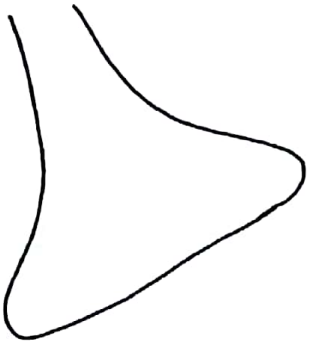
⊕ ↑

⊖ ↑ MUSK

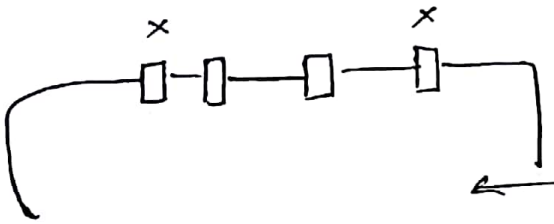
Ab against musk → +ve in 40% AChR Ab ⊖

→ +ve in BULBAR MG

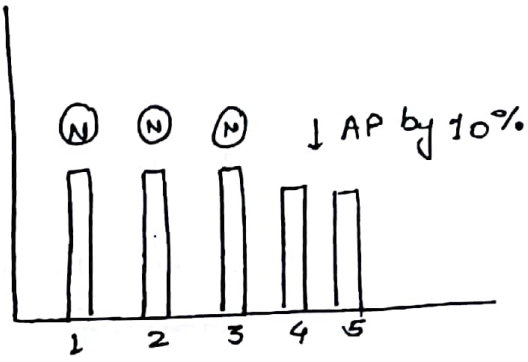
47 RAPID/REPEATED NERVE STIMULATION (RNS) 353



• ACh



Action Potential (A.P.)



DECREMENTAL RESPONSE

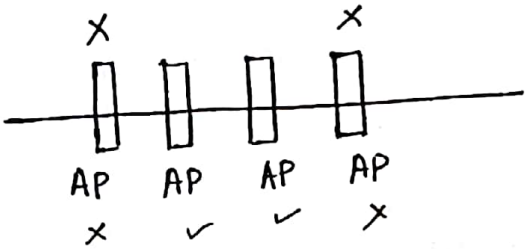
⇓

S/o MG.

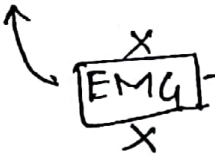
5> SINGLE FIBRE EMG (SFEMG)

↑

MOST SENSITIVE TEST
CONFIRMATORY
GOLD STD. TEST.



Difference in AP. ⇒ JITTER ↑↑.



→ shows myopathic pattern

doesn't record Jitter well.

BEST

SFEMG > EDROPHONIUM > RNS

Rx

1> AChE ⊖

DOC → PYRIDOSTIGMINE
AchT
Oral

NEOSTIGMINE
Ach ↑↑↑
Cholinergic crisis
Injectable

2> IMMUNOSUPPRESANTS
MYCOPHENOLATE MOFETIL (MMF) — Best

3> IvIg
4> Plasmapheresis
→ Refractory MG
Myasthenic crisis
↳ resp m/s weakness
↑ ?
Infection.

5> THYMECTOMY
35% MG → Drug Free
85% MG → Symptom Remission
It is Recommended Inspite of medical control. [15-55yrs] [MUSK Ab ⊖]
MOST USEFUL → In Thymoma pts.
↳ local effect
↳ Paraneoplastic synd.

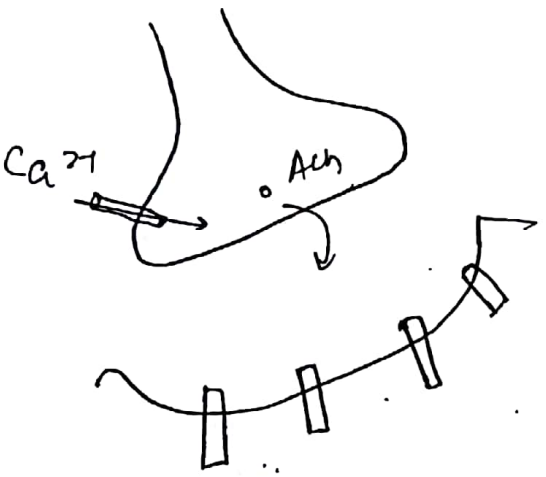
NOT USEFUL IN
<15 yrs ⇓ Immuno Def.
>55yrs ⇓ Vestigial

→ Ocular MG

- Risk surgery >> Disease
- MUSK Ab ⊕ [↓ Benefit]

LAMBERTEN EATON MYASTHENIC SYNDROME

[LEMS] [PARANEOPLASTIC SYNDROME]



P/Q Ca^{2+} CHANNELS

Voltage Gated

Ab

// antigen similarity

Small cell Ca Lung (SCC)

↓ Ach Release

[PRE SYNAPTIC DEFECT]

C/F:-

Weakness skeletal > Facial > ocular [NOTE - MG opp. seq.].

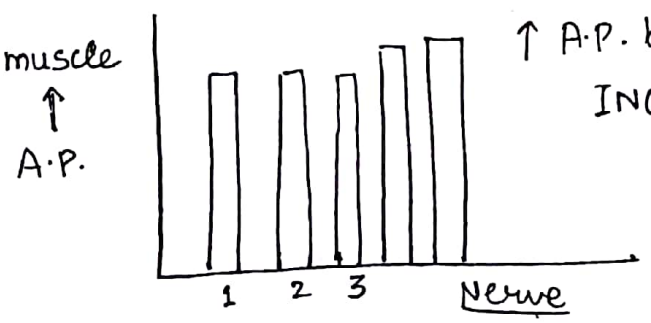
DTR ↓ / ⊖ [MG, DTR ⓝ]

Bladder Involved [MG, Bladder ⓝ]

INV:-

1) Edrophonium +ve. (weakly +ve compared to MG)

2) Rapid N/V Stimulation Test



↑ A.P. by 10%

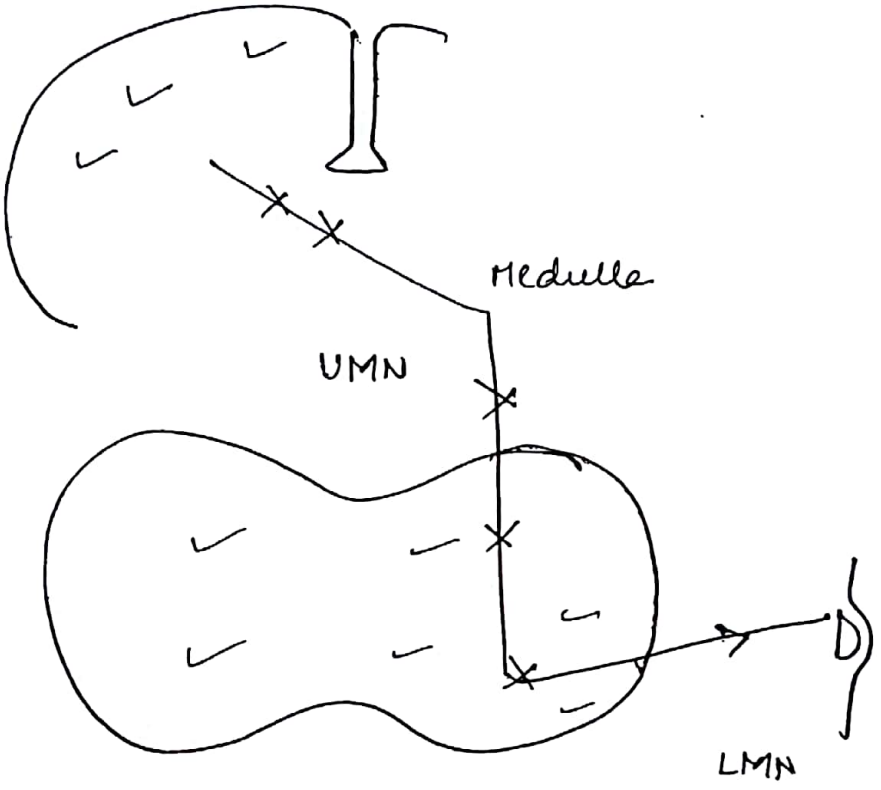
INCREMENTAL RESPONSE

Rx -

↳ 3, Diaminopyridine ← DOC

3DAP [TAch Release]

MOTOR NEURON DISEASE



① AMYOTROPHIC LATERAL SCLEROSIS (M/C)

Cortico spinal Tract ← UMN ± LMN ← due to AHC

weakness is starts distally.

Amyotrophic ⇒ no trophic factors

weakness occurs.

(II) 1° LATERAL SCLEROSIS (PLS)

Degeneration of CS Tract ⇒ UMN

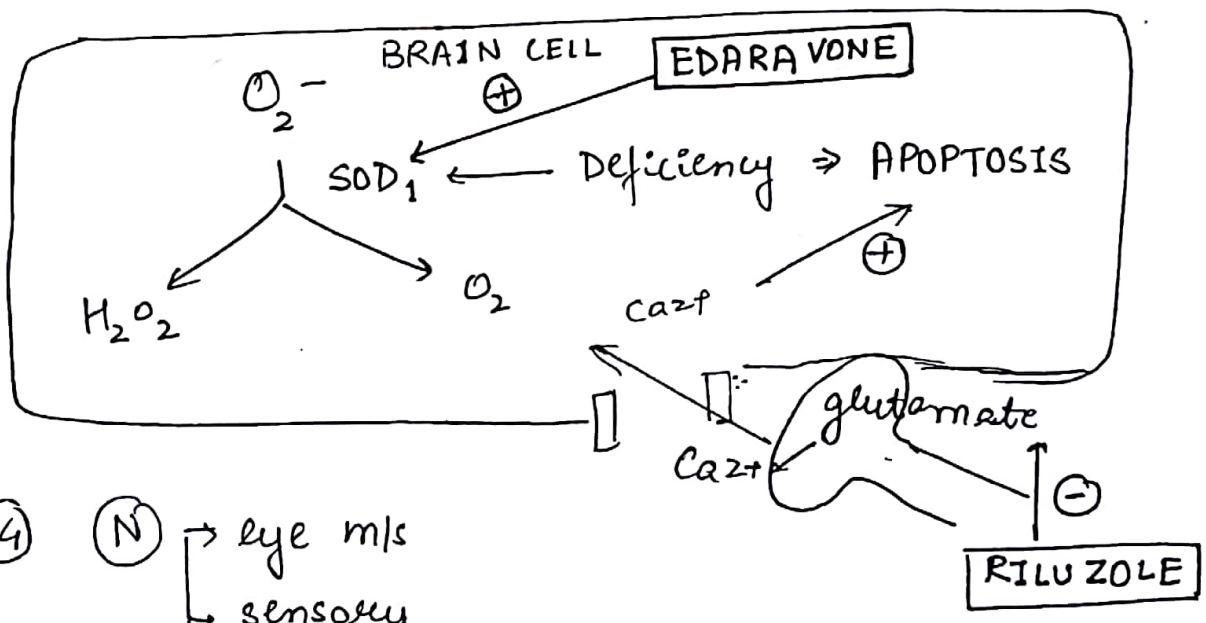
(III) SPINAL MUSCULAR ATROPHY

only LMN

ALS

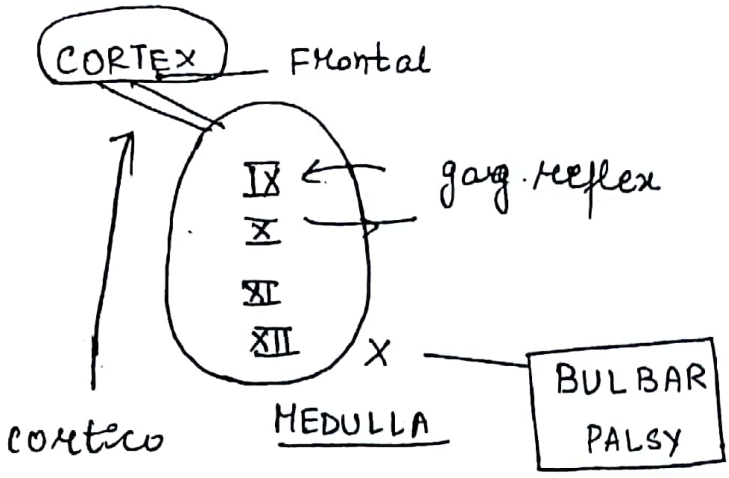
C/F -

1) Elderly
2) Fasciculations ← [PATHOGNOMIC]
3) SUPEDXIDE DISMUTASE (SOD1) Deficiency



(4) (N) → Eye m/s
- sensory
- Bladder
- Cognition.

(5)



PSEUDO BULBAR PALSY		BULBAR PALSY	
Dysarthria	+	++	→ ALS → Polio → M.G. [Bulbar MG]
Dysphagia	+	++	
Labile Effect	+	⊖	
Gag Reflex	+++	⊖	

ATAXIA

DRG = Dorsal Root ganglia

	FREIDRICH ATAXIA	TABES DORSALIS	SUBACUTE COMBINED DEGERATION
TRACTS	POST. Pyr./C.S. Spino cerebellar	POST.	POST. Pyr./C.S. Peripheral n/vs
VIBRATION	⊖	⊖	⊖
PROPIO-CEPTION			
PAIN, TEMP	⊕	⊕	⊕
DTR.	⊖ Early DRG involved	⊕	⊕ → ⊖ neuropathy
Babinski	+ve	⊖	+ve
ASSOCIATE D T	cardiomyopathy Optic Atrophy DM.	Syphilis ARP ⊕ Bladder disturbance	↓ vit B_{12} Megaloblastic anaemia

FREIDRICH's

Trinucleotide Repeat sequence = GAA

AR

Chr. 9

TABES DORSALIS

Syphilis.

Argyll Robertson Pupil.

Bladder Disturbance

SACD

↓ vit B_{12}.

↓

Megaloblastic Anaemia

CEREBELLAR LESIONS

Dysmetria – Past Pointing

Titubation → persistent head knodding

Intentional Tremor

Dysdiadokinesia

Pendular knee Jerk

Romberg's Test ⊕ → Lesion in Post. column

Broad Based Gait

Tendency to fall towards Lesion.

ALZHEIMER DISEASE

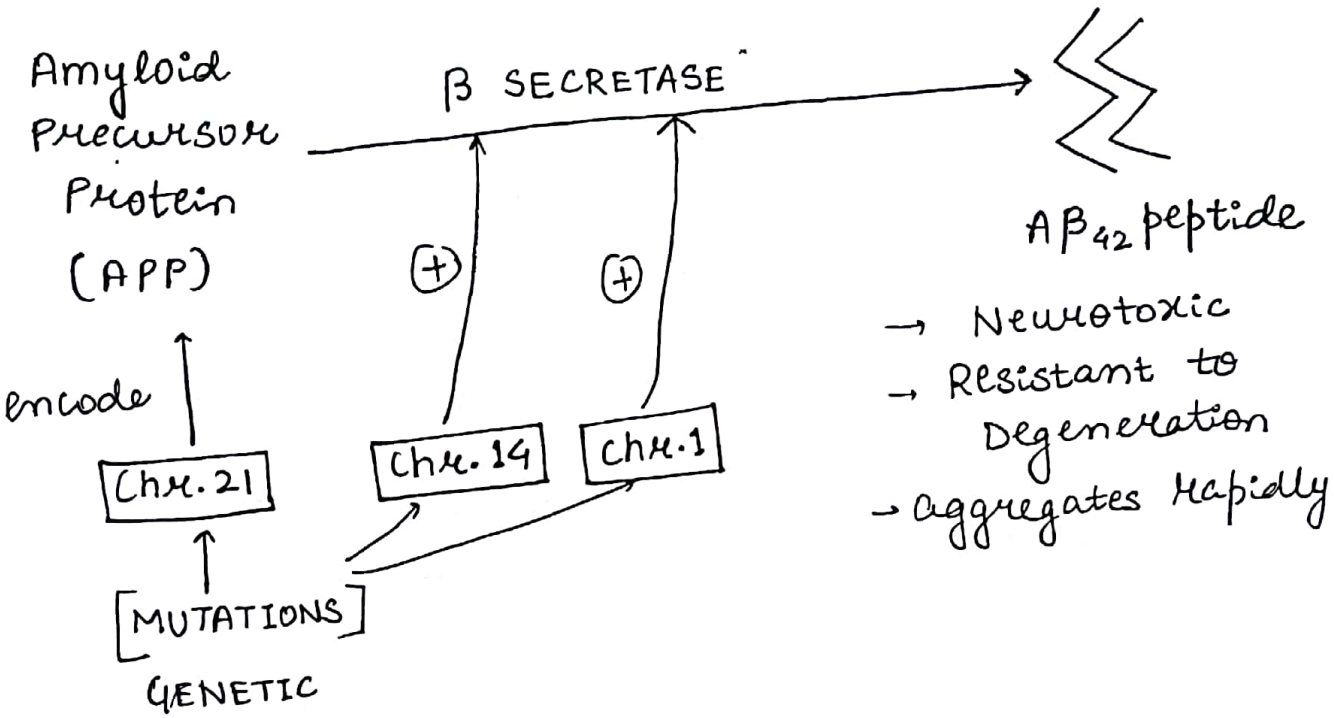
AMYLOIDOSIS

↓

ATROPHY

↓

AMNESIA



RISK

↑

Elderly

♀

Chr. 19 - Apo E_4 gene

Aluminium

Mercury

Family H/O

Low Education (poor maths)

↓

Post Menopausal Estrogen

NSAID Use

Apo E_2 gene.

Smoking

↓ Risk → Parkinsonism

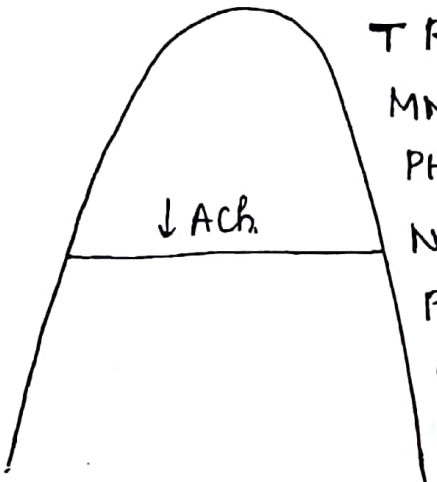
→ Ulcerative colitis

ATROPHY

Temporal
Parietal
+
Hippocampus

→ Earliest

C/F



TROPHY
MNNESIA (anterograde)
PHASIA (Anomie)
NOSOGNOSIA (unaware)
PRAXIA
GNOSIA (can't identify)
NOSMIA
SPIRATION PNEUMONIA (cause of death)

→ ACALCULIA is not seen. [DSM CRITERIA]

→ AGNOSIA not seen in early onset Alzeihmer's (age < 65yrs) [ICD CRITERIA]

→ DELUSION (false belief) = OF DOUBLES → Doctor replaced by Enemy | CAPGRAS syndrome (in 10% pts)

BIOPSY

APP ⟶ ≷≷ → ≷≷ NFT

1> NEUROFIBRILLARY TRIANGLES

Intracellular
Correlate ⊂ severity

TAU - Hyper PO_4^- microtubular proteins
s/o neurodegeneration

Also seen in TAUPathies

1> Fronto Temporal Dementia

- Behavioural Ab(N) due to frontal lobe involvement → early, → severe
- memory loss → Late → mild
- Age of onset <65yrs
- Insight ⊖

2> Progressive Supranuclear Palsy (PSP)

- extended posture
- downward gaze ⊖ - fall
- dementia

3> Corticobasilar Degeneration [PD + myoclonus + Dystonia]

27 SENILE NEURITIC PLAQUES (SNP)

→ extracellular

→ Correlate ↑ Age

CEREBRAL AMYLOID ANGIOPATHY (CAA)

- Large Vessel cortical → Alzeihmer's Disease
- Small vessel subcortical → Progressive Supranuclear Palsy

→ DEMENTIA

3) GRANULOVASCULAR DEGENERATION

Best seen in HIPPOCAMPUS

HUNTINGTON's CHOREA

→ Huntington gene [Chr 4 - short arm]] Trinucleotide Repeat sequence defect
CAG > 40 repeats.

→ AD inheritance

→ 2 successive generations are affected

→ 1 Parent affected
[Chance 50%) 1:2

→ If Both parents affected.
[chance 75%] (3:4)

ANTICIPATION

(11-50yr)
- ♂ (Father) = Early onset 2nd Decade
- Mother = Late Onset 4th Decade.

LENGTHENING

Larger Defect → ↑ severe
Larger Defect → Early onset (from father)

Father Repeats	Mother Repeats
400	400
↓	↓
40,000	400

anticipation
↳ occurs due to lengthening.

C/F -

AD inheritance
Seizure → if inherited from father
Chorea
Athetosis
Dementia
Personality changes

ATROPHY – in CAUDATE NUCLEUS.

↓ACh ↓GABA Intra striatal
↑ DA

Rx → DA ⊖ → Haloperidol
DA Depletor → Tetrabenzine ← DOC

NORMAL PRESSURE HYDROCEPHALUS (NPH)

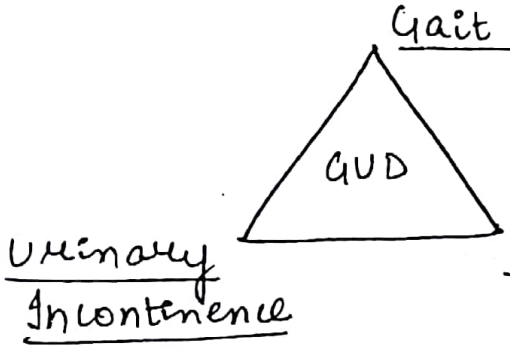
CSF PRESSURE → (N) = 50 - 150

↳ NPH = 150-180

↓ CSF Absorption. ← SAH

↑ ↳ Meningitis

C/F



MAGNETIC GAIT

→ external hip rotation

→ shorter strides

→ Low gradend clearance..

SCISSORING GAIT → spastic CP

CHARLIE CHAPLIN GAIT → Tibial Torsion

Rx V-P shunt

↓

1st / Most responsive symptom to improve on VP shunt

ATAXIA

QQ WERNICKE'S ENCEPHALOPATHY

PREDISPOSED –

1) Hyperemesis
2) Alcohol Intake

→ B_1 Deficiency

↓

CO-FACTOR for.

α-keto glutarate dehydrogenate
Pyruvate Dehydrogenase

↓

GLUCOSE ACCUMULATION

↓

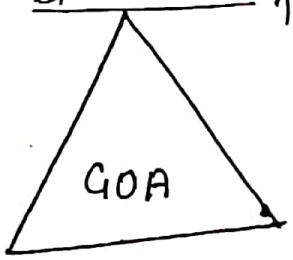
Mitochondrial Damage

↓

NEUROTOXIC

C/F

GLOBAL confusion.



Ophthalmoplegia

Ataxia

Rx THIAMINE REPLACEMENT x 14 Days.
(100 mg/day)

1st Improve = ophthalmoplegia

[Glucose Infusion can Precipitate it]

KORSAKOFF'S PSYCHOSIS / ALCOHOL DEMENTIA

DEMENTIA ⟶ CONFABULATION
False story to hide memory loss

SITES

Periaqueductal Grey Matter
Mamillary Bodies
Thalamus → [AMNESTIC DEFECT]

CONFUSIONAL STATE

1) seizure
2) T.I.A.
3) Metabolic → ↓ glucose
↳ alcohol

TRASIENT GLOBAL AMNESIA

Both anterograde + Retrograde amnesia

CNS INFECTIONS

BACTERIAL / PYOGENIC MENINGITIES

M/C/C

Adolescent / Adult = N. MENINGITIDIS (Epidemic)

Elderly = STEPTO. PNEUMONIA (Community acquired)

CSF

	(N)	PYOGENIC
Appearance	Transparent	Turbid
cell count	≤5	Pleocytosis (N>7L)
Protein	15-45 mg/dL	↑↑
Glucose	40-70 mg/dL	↓↓↓
Cl⁻	116-126 meq/L	↓/(N)

Hypoglycorrhizia = ↓ CSF Glucose

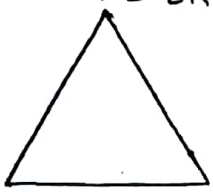
Rx

N-MENINGITIDES → ceftriaxone x 7 Days

S. PNEUMONIAE → ceftriaxone + vancomycin] x 14 Days

>60 yrs pt → LISTERIA → Ampicillin

C/F



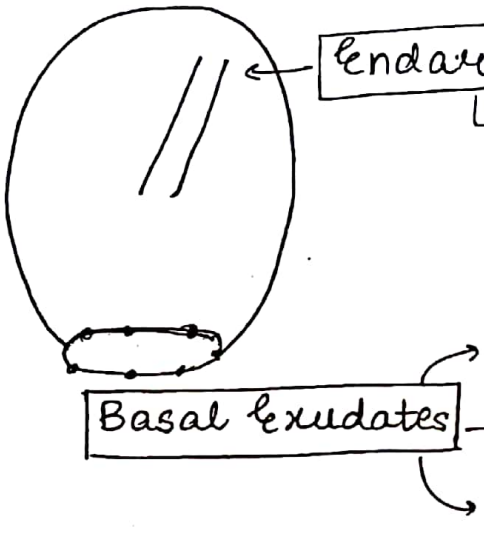
± HEADACHE.

Dexamethasone
10 mg IV Stat
↓
1st Dose of antibiotic

TBM

M/c Meningitis in India

TBM ATT × 1 month
↓ sensorium
① ATT induced hepatitis
↳ hepatic encephalopathy
② ↑ ICT → cerebral salt wasting
③ Infarct
④ Tuberculoma
⑤ Hydrocephalus



CSF

→ COB-WEB
→ Pleocytosis [L >> N]
→ Protein ↑↑↑
→ Glucose ↓ Cl^- ↓↓↓

GOLD STD TEST = Culture of CSF

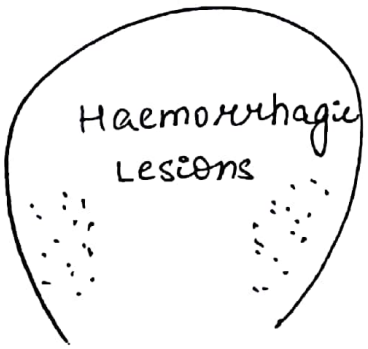
℞
ATT × 12-18 months (↓ Reactivation)
Steroids × 2 mnths [⊖ Endarteritis]

VIRAL ENCEPHALITIES

M/C C → ENTEROVIRUS

- epidemic = ARBOVIRUS
- sporadic = HSV type 1

HSV ENCEPHALITIS



CSF

→ xanthochromia

- SAH — CT Scan. → (N) CSF xanthochromia
- Traumatic LP

→ Pleocytosis
→ ↑ Protein
→ (N) Glucose
→ Cl^- ↓

MOST SENSITIVE TEST = PCR for HSV in CSF

MRI — Bitemporal Hyperintensities.

	T_1	T_2
Brain	↑	↓
CSF	↓	↑

↑ = itis

℞ Acyclovir- 10 mg/kg IV 8 hrly × 14 days

↓

↓
CSF
PCR for HSV
↙
Prognosis ↳ ⊕ = continue same Rx for 7 days.
↳ ⊖ = Stop Rx.

PROGRESSIVE MULTIFOCAL LEUCOENCEPHALOPATHY (PMLE)

Jc virus → oligodendrocyte
Inclusion bodies

A/C -
Immunocompromised host
↳ HIV + (80%, M/C host)
Transplant Recipient

C/F - Visual field Defects. (M/C)

Inv
MRI → Hyperintensities
↘ Demyelination
↓
CSF (PCR for Jc virus)
↓
Brain Biopsy

Rx
not available

Prognosis Death 3-6 months of onset

PRION DISEASE

CREUTZFELD JACKOB DISEASE (CJD)

DNA/RNA ⊖

Transmittable → Dural Grafts
→ corneal Grafts

C/F-
Dementia + myoclonus (M/C)

Inv
EEG- Biphasic waves
Brain Biopsy - spongeform degeneration

Rx- not available

NCC [Neurocysticercosis]

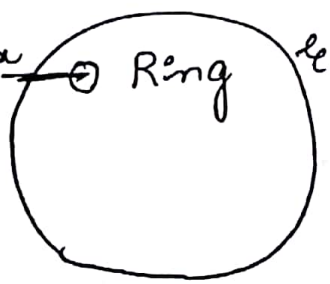
Agent = Taenia Solium

HOST = DEFINITIVE = Human — accidental intermediate Host
INTERMEDIATE = PIG

Via → consumption of undercooked Pork
→ consumption of undercooked raw vegetables

C/F- seizure (M/C)

Inv-
CE → CT
→ MRI



STAGES

VESICULAR (Viable)	Oedema +
COLLOIDAL (Dying)	+++
CALCIFIED (Dead)	-

℞

ANTI-PARASITIC

DOC → ALBENDAZOLE

↓

15 mg/kg/Day × 8-28 days

+ Steroids + A.E.D. × 6 months

↓

CT scan

↓

calcified

Taper 2-3 months

↓

STOP.

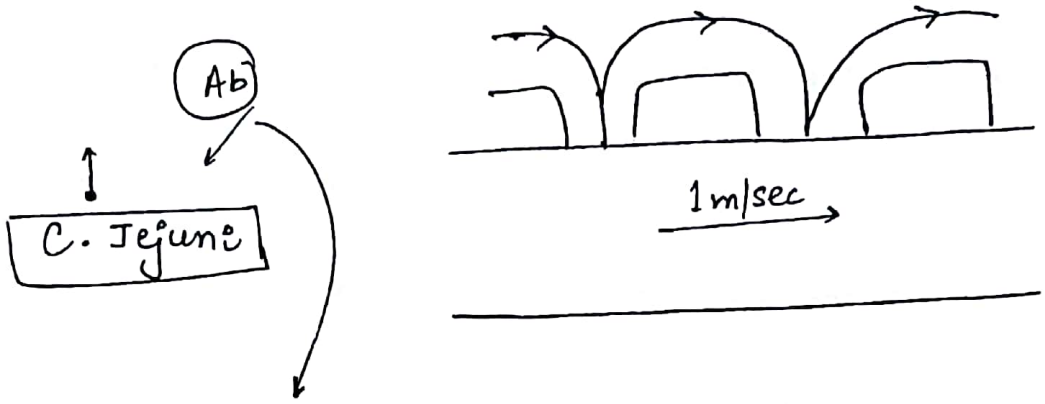
PRAZIQUENTAL

OTHER TYPES OF GBS

AIDP (<4wk)	AMAN	AMSAN
Motor Sensory	motor only	M=S
>90% children mostly	children young adult	Mostly adult ⋮ Worst Prog.
GM_1 Ab +ve	GD_{1a} Ab	

CIDP >9wk.

GUILLAN BARRE SYNDROME



Schwann cells → ↓ schwann cell
↓ myelin
↓ conduction

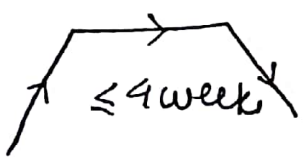
→ Post Infectious
→ Demyelinating
→ Poly neuropathy

VACCINES causing GBS :-
RABIES (neural)
Influenzal

C/F

ASHBURY CRITERIA

→ Ascending Paralysis → Symmetrical
≤ 4 weeks
Distal → Proximal



Areflexia
Minor sensory
Bladder - spared

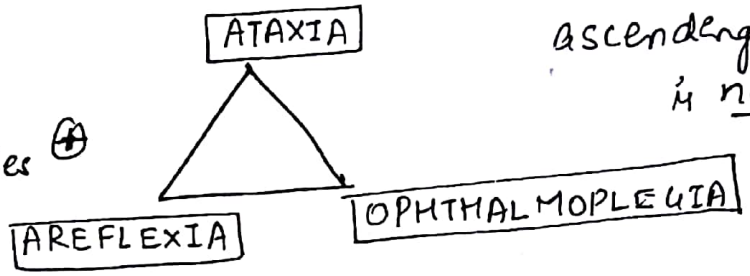
M/c cranial N/v involved = VII th (B/L, LMN)

ACUTE INFLAMMATORY DEMYELINATING POLYNEUROPATHY (AIDP)

VARIANT OF GBS

MILLER FISCHER VARIANT / SYNDROME

GQ1b Antibodies (+)



ascending paralysis is not seen.

MILLER FISCHER TEST (DNB)

Done In Normal Pressure Hydrocephalus

CSF Drained (30 ml)

↓

Cognition

↓

Improved

↓

then go for V-P-Shunting

GUD

Inv For GBS

1) Nerve Conduc" Study

↓ N/v conduc" velocity

↓ A.P.

2) CSF

↑ Albumin
No pleomorphism
] Albumino cytological Dissociation.

Rx

1) IVIg ~~2mg~~ 2gm/kg over 5 Days.] Both are equally effective
2) Plasmapheresis

Best in 1st 14 Days

Steroids is not recommended

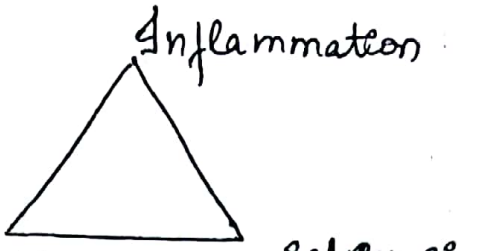
PROGNOSIS

Recovery occurs in 85% [IVIg & Plasmapheresis will not alter the sequlae]
Sequlae → 10%
Death → 5%

INFLAMMATORY MYOPATHY

	DERMATO MYOSITIS	POLY MYOSITIS	INCLUSION BODY MYOSITIES
AGE	Any	>20yrs	>50yrs
MUSCLE INVOL.	Proximal	Proximal	Distal
SKIN Changes	+	−	−
Ass ū malignancy	+ (15%)	−	−
EYE	(N)	(N)	(N)
	Creat. Kinase ↑↑	↑↑	↑↑

MULTIPLE SCLEROSIS



DISSEMINATED
- ↗ Time
- ↘ Space.

C/F

1> SENSORY

1st M/C symptom

↑ Exposure to HEAT ⇒ UTHOFF SIGN

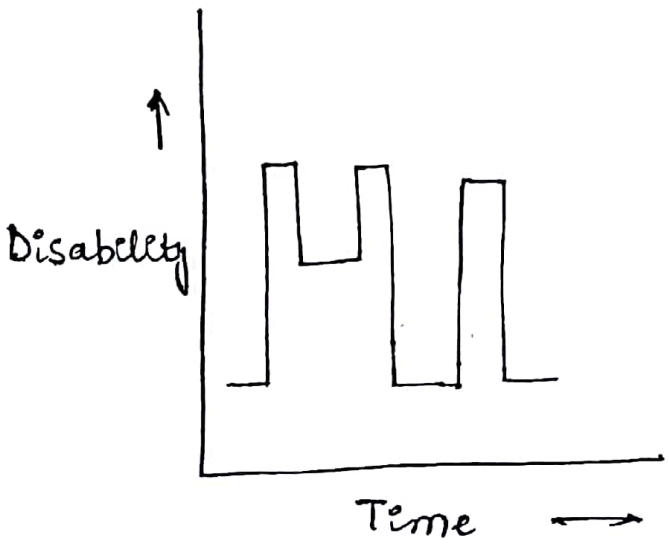
ICE PACK TEST

Cold ⊖ ACHE ⇒ ↓ in MG pts.
Weakness ↓

② OPTIC NEURITIS

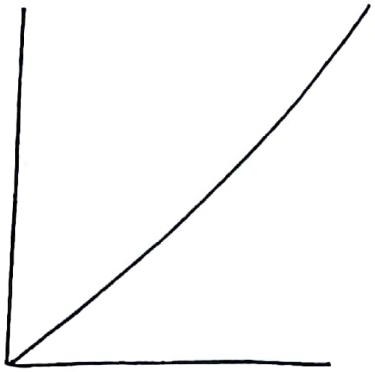
③ SPASTICITY

TYPES

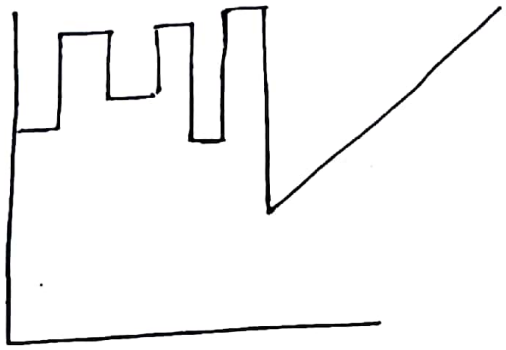


RELAPSING REMITTING (85%)

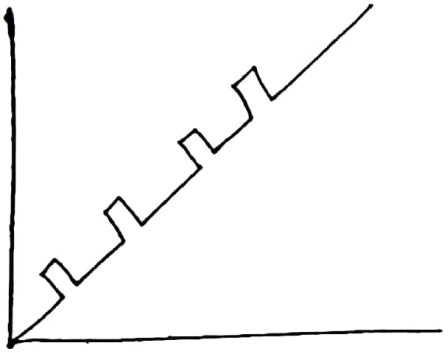
[RRMS]



1° PROGRESSIVE 15%
M/S (PPMS)



2° PROGRESSIVE
MS (SPMS)



PROGRESSIVE RELAPSING
M/S (PRMS)

STAGING

MS = EXTEDED DISABILITY SCORING SCALE (EDSS)

SAH = HUNT & HESS SCALE

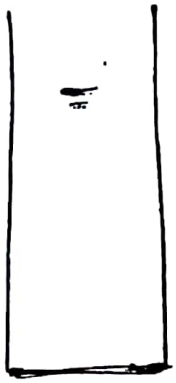
MG = OSSERMAN GRADING

INV

MAC DONALD CRITERIA

MRI → Demyelination → Plaque → Periventricular

CSF



Oligo Clonal Bands ⇒ IgG

Liquid Chromatograph

Rx

ACUTE ATTACK

METHYL PREDNISOLONE (DOC)

DISEASE MODIFYING AGENTS

1) IFN β → β1a, β1b ← DOC

2) Glatiramer

3) Fingolimod [ORAL]

4) Natalizumab [BEST] ⟶ S/E = PML

D/D of DESCENDING PARALYSIS

Botulism

Polio, Porphyria

Diphtheria

ENDOCRINE

– Dr. Achin

PROLACTIN

Secreted in Ant Pituitary

Prolactin making cells LACTOTROPH

FUNC":-

1> Induce, maintain the process of lactation

2> prolactin hormone $\xrightarrow{\ominus}$ GnRH → LH ↓

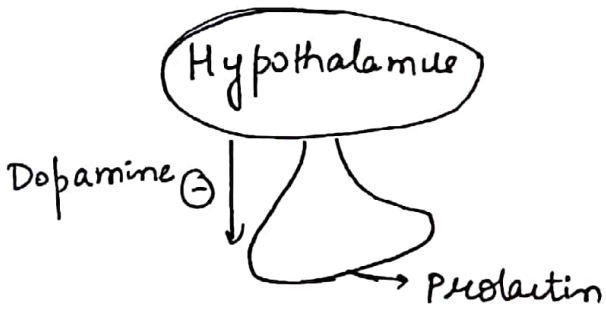
↳ ↓ ovulation

↓

sexual drive ← ↓ Testosterone ↳ ⊖ menstruation

↓

Spermato genesis



HYPEPROLACTINEMIA

ETIOLOGY-

A) PHYSIOLOGICAL

1> Lactation

2> ♀

↑ estrogen $\xrightarrow{+}$ ↑ PL

3> Sleep [NREM sleep]

4> Chest wall stimulation

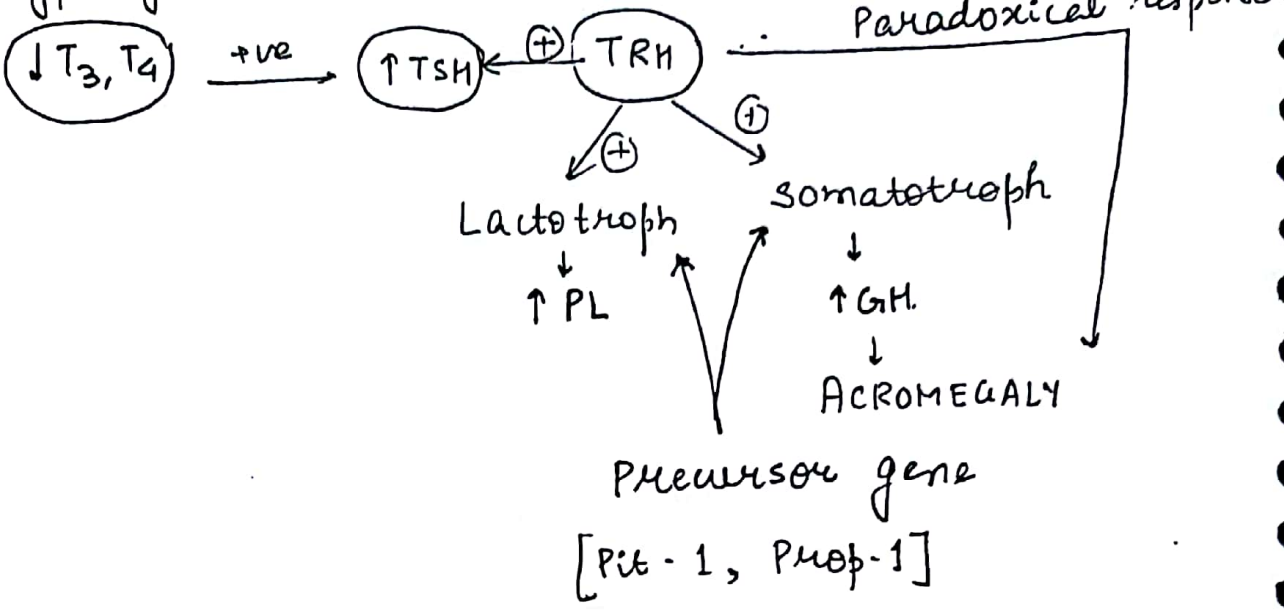
→ nipple stimulation

→ chest trauma or surgery

→ herpetic lesions

5B) SYSTEMIC DISORDERS

1) Hypothyroidism



2) CKD

→ ↓ excretion of prolactin

3) SEIZURE

Post Ictal (30 mins)

C) DRUGS (Iatrogenic)

Dopamine ⊖

→ Typical Antipsychotics
  - Haloperidol
  - CPZ

→ Atypical Antipsychotic
  - Risperidone

→ Metoclopramide

Dopamine Depletors

CH_3 Dopa

Reserpine

CCB - verapamil

H_2 ANTAGONIST

Ranitidine

Cimetidine

⇒ These drugs cause hyperprolactinemia due to blockage of Infundibular Pathway

D> PITUITARY ADENOMA

PROLACTINOMA → M/c type

<10mm
MICRO (90%)
F:M = 20:1

>10mm
MACRO (10%)
F:M = 1:1.

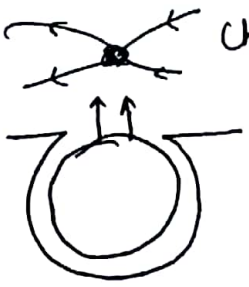
C/F → ♀ → Galactorrhoea - 80%
↳ B/L.

Amenorrhoea → Infertility (M/c presentation)

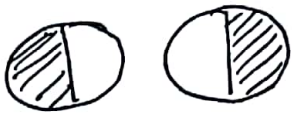
↑ PL → ↓ LH → ↓ ovulation

↓ estrogen → osteoporosis

♂ → ↓ Libido
Azoospermia
Infertility



⇒



Compressive
MACRO > MICRO

S. PROLACTIN

(N) = 5 - 25 µgm/L

- PHYSIOLOGICAL → 25 - 40
- IATROGENIC → 25 - 100
- PRACTINOMA → >200
- MACRO PROLACTINOMA - >250

Stop offending drug
Reasses PL after 72 hours

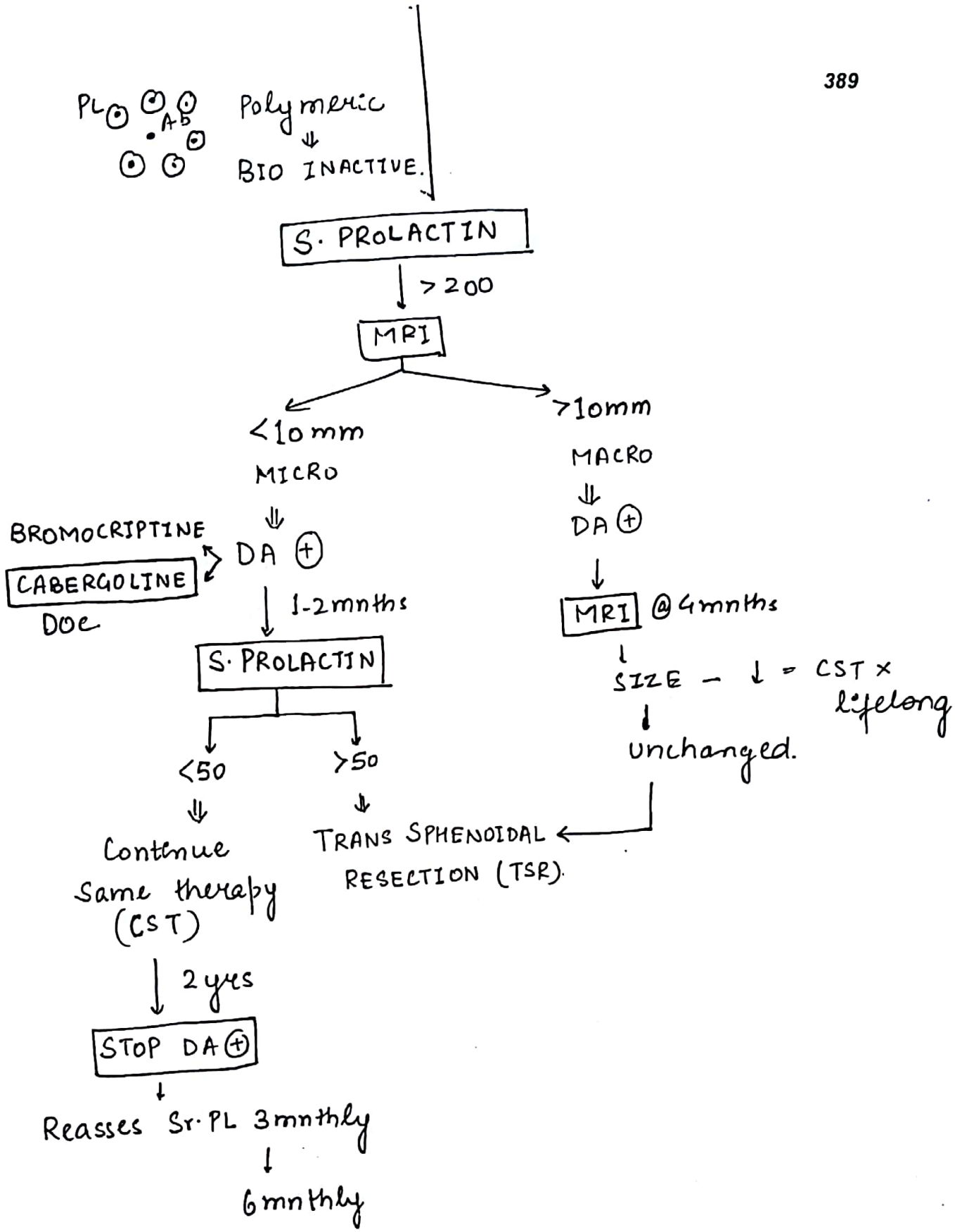
MACROPROLACTIN

Symptoms ⊖
Prolactinoma ⊖
S. Prolactin ↑↑↑
[FALSE HIGH]

PROLACTIN = Peptide hormone (198 A.A)
↳ 85% monomeric

HOOK EFFECT

Symptoms ⊕
Prolactinoma ⊕
S. Prolactin (N)
[FALSE (N)]



Always 1st Line = Medical Rx

PROLACTINOMA ON DA ⊕ WANTS TO CONCEIVE

↓

allow 3 Ⓝ cycles

↓

Stop DA ⊕ → Teratogenic precious ♀.

↓

♀ → Assesment

Rare ← [Headache, ↓ Vision] DA ⊕ [BROMOCRIPTINE]

↓ no response

SURGERY (TSR)

Prolactinoma is ♀ are asymptomatic

DOC for Prolactinoma = CABERGOLINE

Long acting

Convenient Intake

↓ nausea

Better effect

In ♀

↓

BROMOCRIPTINE

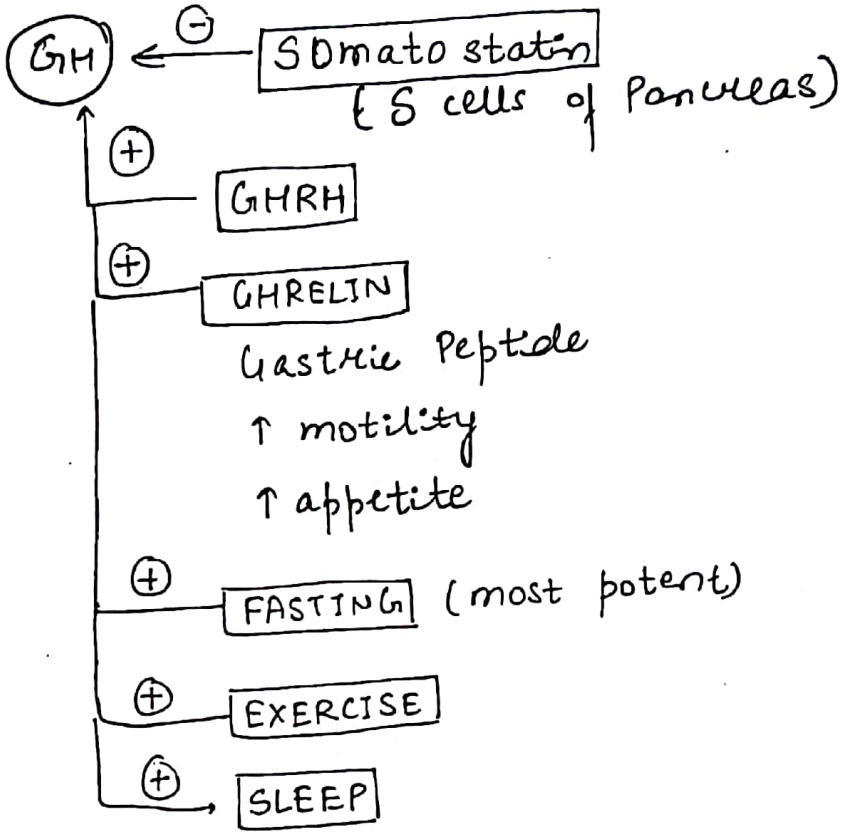
FERTILE ♀ → BROMOCRIPTINE

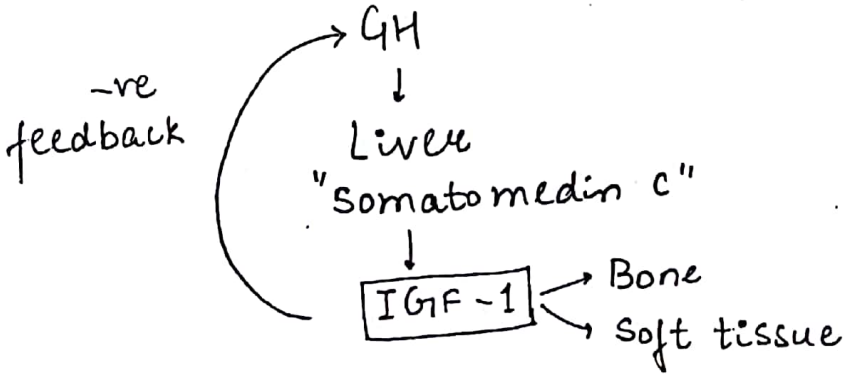
GROWTH HORMONE

→ Released from Ant. Pituitary

→ By SOMATOTROPHS (Most abundant cells) 50%)

> Lactrotrophs > Gonadotrophs
(20 - 30%) (10 - 20%)





	GH	IGF-1
CARBOHYDRATE	Diabetogenic	Anti diabetic
PROTEIN	ANABOLIC	ANABOLIC
FAT	LIPOLYTIC	ANTILIPOLYTIC

GH $\xrightarrow{(+)}$ Lipase → ↑FFA → Insulin Resistance → Diabetogenic

↑GH
↳ Epiphyseal fusion.
↳ BEFORE = GIGANTISM
↳ AFTER = ACROMEGALY

ACROMEGALY

ETIOLOGY

↑GH

PITUITARY
↳ Somatotrophic Adenoma (M/cc)
↓
Loss of feedback
↳ MAMMO SOMATOTROPHIC ADENOMA → ↑PL ↑GH

↑GHRH

HYPOTHALAMUS
HAMARTOMA

ECTOPIC
BRONCHIAL CARCINOMA

ECTOPIC

ISLET CELL CA of PANCREAS

C/F

CVS → LVH
Diastolic Dysfunc"
HTN
CAD

H/cc of DEATH
ACUTE M.I.

Resp → Nasal turbinate Hypertrophy
obstructive sleep apnea (OSA)

GIT → ↑ Liver & spleen (Hepatosplenomegaly)
Q **Colonic Polyps** >> Cancer
↓
Benign

ENDOCRINE → DM (Insulene resistance)
Goitre

SKELETAL → Tall Stature
Large Digits
Prognathism
Jaw malocclusion
[↑ space bet" lower Incisors]
Fleshy nose.

INVESTIGATION

1> GH ASSAY → not useful test

2> IGF-1 ASSAY
Best screening Test

3> GH SUPRESSION TEST → confirmatory Test

$$\left[GH \propto \frac{1}{\text{glucose}}\right]$$

75 gm glucose (oral)

GH → (N) → ↓

ACRO → unchanged

Rx

TSR – [RxOC] F/B → ADJUVENT THERAPY

[Initial therapy]

Somatostatin
octreotide
Lanreotide

GH ⊖
Pegvisomant

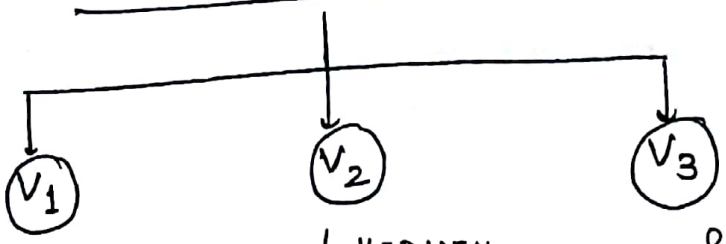
INSULIN STIMULATION TEST

$GH \propto \frac{1}{\text{glucose}}$ → on giving Insulin.

glucose ↓ → GH ↑ (N)

Dwarfism → GH unchanged

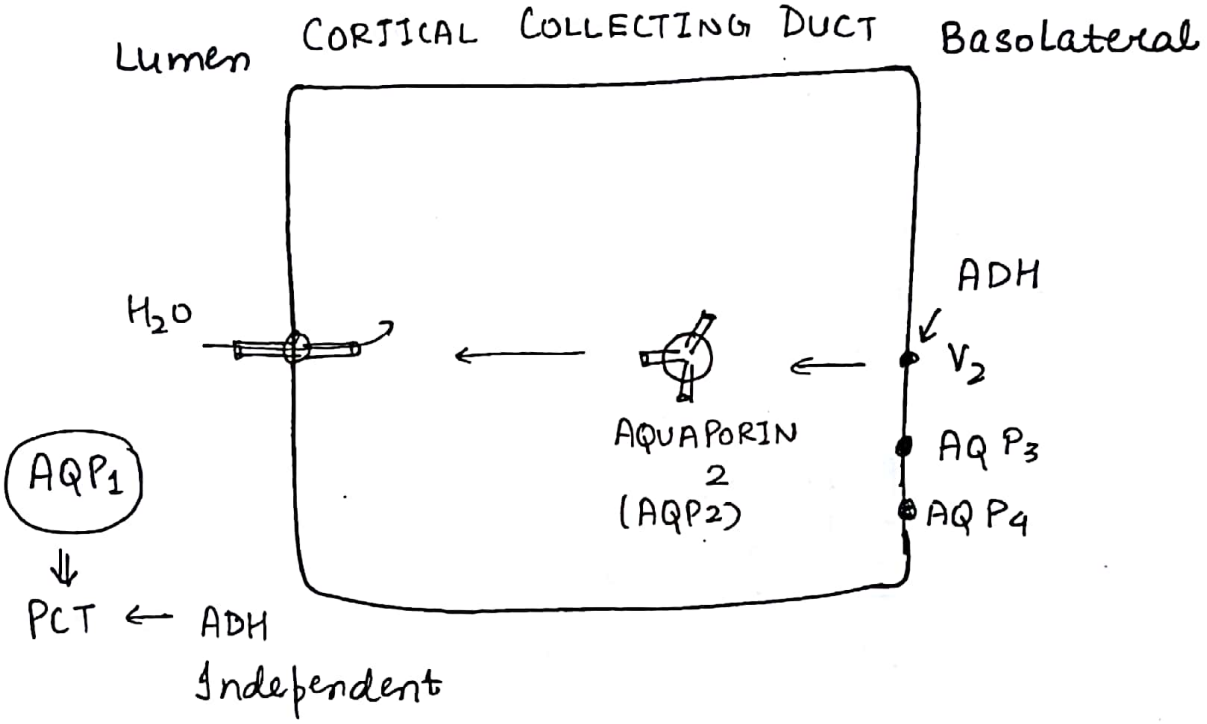
ADH / VASOPRESSIN



V_1
BLOOD VESSELS
Vaso constriction
SMOOTH MIS
(contraction)

V_2
↳ KIDNEY
↳ vascular ~~smooth~~ endothelium
(VWF)

V_3
Pituitary
ACTH (+)



(N) values

S. Osmolality = 275 - 295 mosm/L

Urine osmolarity = 300 - 1000 mosm/L

Sr. Na^+ = 135 - 145 meq/L

Sr. K^+ = 3.5 - 5 meq/L

POLYURIA

> 50 ml/kg/day

> 3L/day

↑ Solute = ↓ H_2O

Isosmolar

SOLUTE/OSMOTIC DIURESIS

⇓

Glucose

Mannitol

Ca^{2+}

Urine osmolality

> 300 (N)

DILUTE

H_2O > Solute

Ur. osm < 300

→ DI

→ Psychogenic Polydypsea (PP)

H_2O Deprivation Test

Ur. osm. ⟶ (↑) = P.P.

↳ unchanged = D.I.

ADH stimulation Test

Ur. osm → (↑) = ADH Def.ⁿ

↳ unchanged = ADH resistance

nephrogenic DI

Phys

Psychogenic Polydipsia

Lumen

$H_2O \rightarrow H_2O$

- $\uparrow$ S. osm $\xrightarrow{+}$ Thirst $\rightarrow$ No dehydration
- $\uparrow$ Sr. Na^+

Polyuria

$\downarrow$

Ur. osm $\rightarrow$ (N)

solute diuresis

$\downarrow$

DI

PP

26

CEREBRAL SALT WASTING DISEASE

$\uparrow$ICT $\rightarrow$ BNP

$\downarrow$

$\downarrow Na^+, \downarrow H_2O$

Hyponatremia $\rightarrow$ Hypovolemia

natriuresis

$\leftarrow H_2O$

Na^+

$\uparrow$ICT $\rightarrow$ $\uparrow\uparrow$ ADH — SIADPH

$\downarrow$

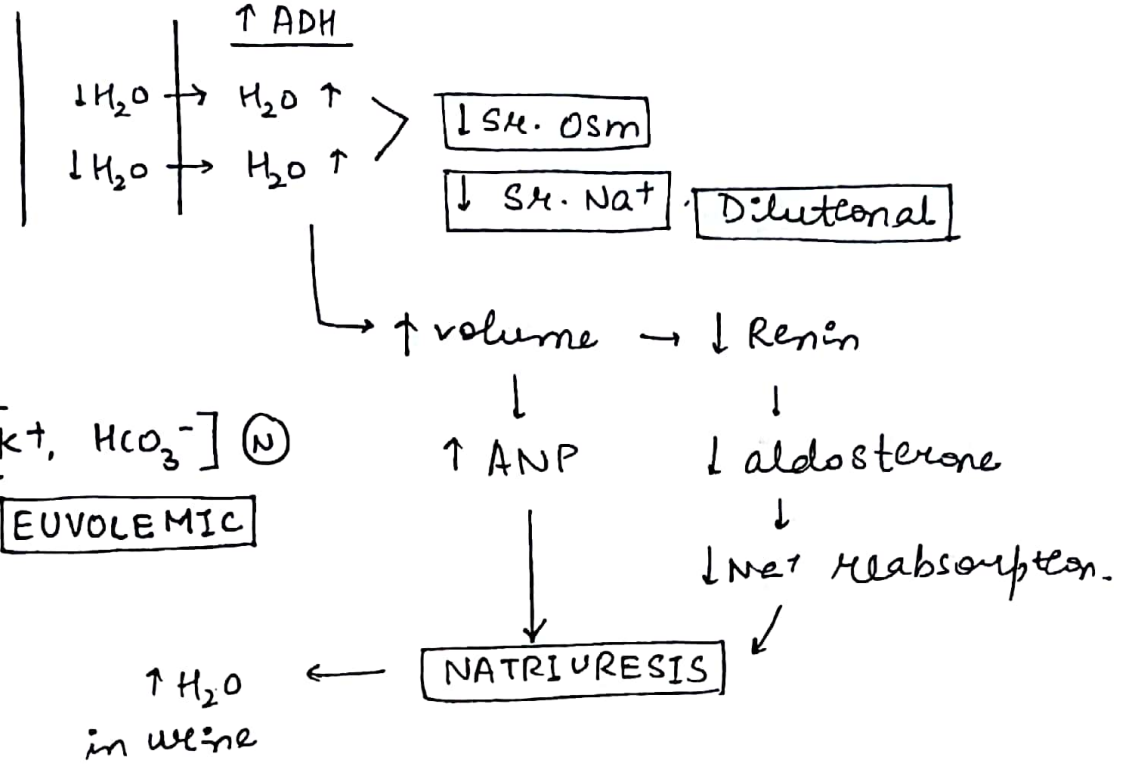
$\downarrow$ ADH (DI)

Mannitol $\leftarrow H_2O \rightarrow \uparrow$Sr. osm

$\rightarrow \uparrow$Sr. NaT

High output due to diuretics

SIADH [Syndrome of Inappropriate ADH]



HYPONATREMIA

HYPOVOLEMIC	EUVOLEMIC	HYPERVOLEMIC
Cerebral Salt Wasting Disease	SIADH ⇓ H_2O Loading Test	CCF CKD Chr Liver Disease

Pt. produce less urine than N pt

R_x = H_2O restriction Rx oc

ADH ⊖ ⇒ DEMECLOCYCLINE

↳ VAPTAN (DOC)

Na^+

[(N) = 135 - 145 meq/L]

>120 = Asymptomatic

110 - 120 = GI symptoms
↳ nausea

100 - 110 = mild CNS symptoms
giddiness
Ataxia

Seizures → <100 ≠ cerebral oedema

PARATHYROID HORMONE

↓ Ca^{2+} → ↑ PTH
↳ Bone = Resorption
↳ Intestine = Absorption
↳ Kidney = Reabsorption

↑ PTH

2° → CKD
Vit D deficiency
Malabsorption.

1° → Parathyroid → Hyperplasia
Adenoma [M/C/C]
↓
M/C type = solitary
M/C site = Inf. Pth lobule.

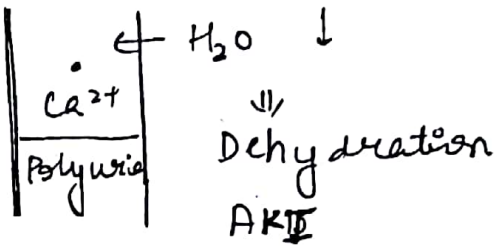
3° = PTH hyperplasia → ADENOMA (3°)

2° ↙ ↘ 1°

HYPERCALCEMIA

C/F -

- → nausea, vomiting
- → Constipation
- → Bony pains ⊕
- → Renal calculi
- → Abdominal Pain
- → depression
- → Psychosis



℞.

1) Hydration.

2) Diuretics
   Caliuric → Loop Diuretics

3) Bisphosphonates
   ⊖ osteoclastic activity
   DRONATES.
   [Delayed onset of Action]

4> GALLIUM]
5> PLICAMYCIN] → Osteoclast ⊖

6> CALCITONIN

7> DIALYSIS

PSEUDO HYPO PTH

↓ Sr. Ca^{2+}

Sr. PTH ↑

PTH resistance

ALBRIGHT HEREDITARY OSTEODYSTROPHY (AHO)

Short stature

Round Face

Short 4th / 5th metacarpal. (Brachydactyl)

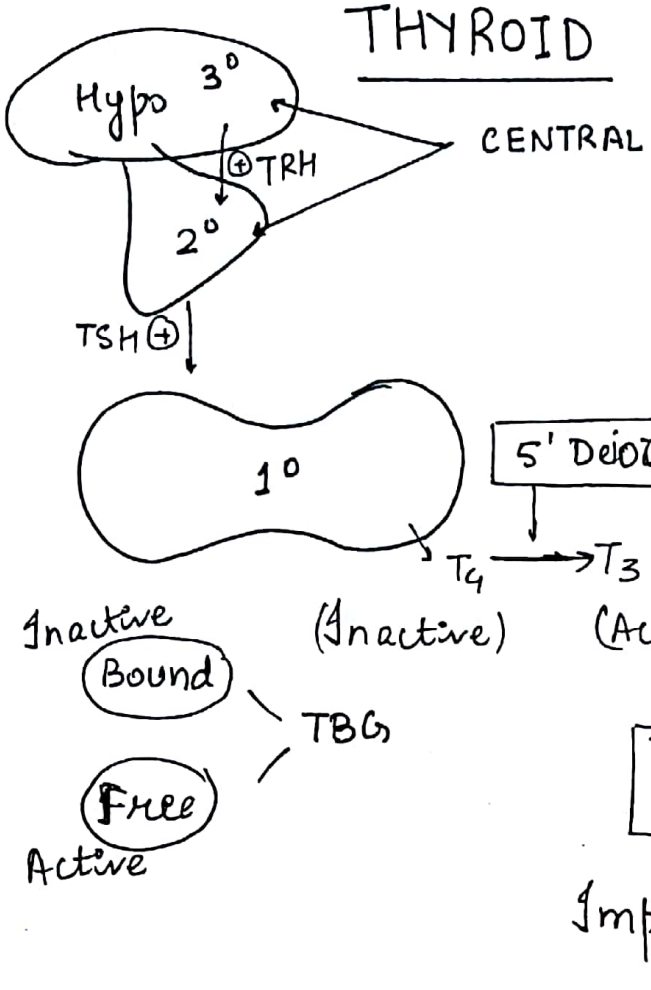
PSEUDO PSEUDO HYPO PTH

Sr. Ca^{2+} = (N)

Sr. PTH = (N)

AHO Phenotype (+)

THYROID



	TSH	FT_3	FT_4
HYPOTHYR (1°)	↑	↓	↓
HYPERTHYR	↓	↑	↑
2° HYPOTHYR	↓	↓	↓
SUBCLINICAL HYPOTHYR	↑	Low (N)	Low (N)

HYPOTHYROID	HYPERTHYROID
Weight Gain	Weight Loss
Fatigue	Anxcety
Cold Intolerance	Heat Intolerance
Constipation	Diarrhoea
Menorrhagia	Amenorrhoea
M/C Amenorrhoea	
↓ H.R.	↑ H.R.
mild Diastolic HTN	↑ S.B.P. / ↑ D.B.P.
Delayed Relaxation of Jerk [HUNG UP REFLEX]	Fine Tremors
	Exophthalmos

Rx HYPOTHYROIDISM

L-Thyroxine [1.6 µg / Kg / Day]

↓ DOSE = elderly, IHD

↓

TSH after [6 weeks]

[(N) = 0.35 - 5]

[Target = 0.35 - 2.5] → L-Thyroxine × Lifelong

↓

TSH 6 monthly

TSH	L-Thyroxine
10	75 µgm / day
↓	↓ +25
8	100 µgm / day

SUBCLINICAL HYPOTHYROID

↑ TSH, [FT_3 , FT_4] low (N)

Rx-

TSH >10 ⇒ Start L-thyr

↓

[5-10] L-Thyroxine.

- ♀ → Infertility
- ♀ → TBG↑ → ↓FT_3 , ↓FT_4 → ↓ +ve → ↑ TSH
- TPO Antibodies

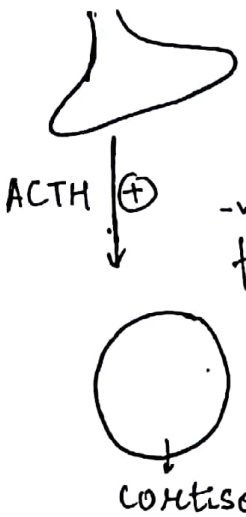
ADRENALS

CUSHING SYNDROME

Loss of -ve feedback

ETIOLOGY

A> EXOGENEOUS / IATROGENIC [M/C/C]



B> ENDOGENEOUS

↓

ACTH

- DEPENDENT (90%)
  - Pituitary Adenoma 75% [F:M = 4:1] — M/C endogenous cause
  - → ECTOPIC ACTH 15% [F:M = 1.1]
    - M/c malignancy → small cell Ca of Lung
    - medullary Ca of thyroid
    - Phaeochromocytoma
    - CARCINOIDS → Bronchial, Thymus, Pancreatic
- INDEPENDENT (10%)
  - ↳ ADRENAL [F:M = 4:1]
    - Adenoma (5-9%)
    - CA (1%)
    - Hyperplasia (<1%)

M/C/C → CUSHING DISEASE

Cushing Syndrome due to Pituitary Adenoma.

C/F :-

↑ CORTISOL → ↑ Gluconeogenesis

1) PROTEIN → MYOPATHY (proximal)

↳ s/c Tissue Tear = STRIAE Purplish colour due to rupture of vessel.

↳ THIN SKIN

↳ EASY BRUISING.

2) FAT Redistribution of fat

CENTRIPETAL OBESITY

↳ BUFFALO HUMP

↳ MOON LIKE FACE

3) DM

4) HYPERNATRENEMIA

Cortisol —(11 β.-OH Dehydrogenase)→ Cortisone

Cortisol ↓ activity → G.C. & M.C

Cortisone ↓ activity → G.C.

- ↑ Na^+ reabsorpn ⇓ HTN
- ↓ K^+, alkalosis ectopic ACTH pts.

5) ♀

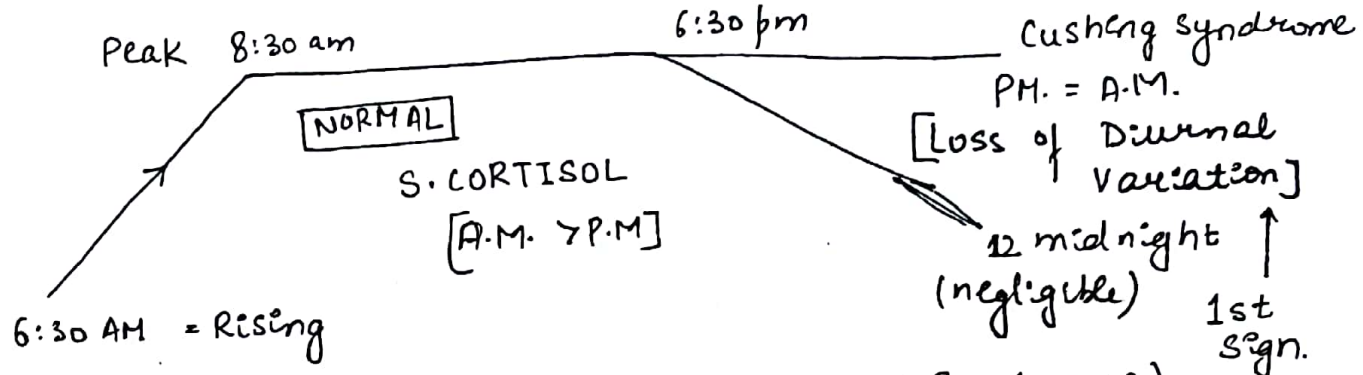
Oligomenorrhoea ⟶ Amenorrhoea

Hirsutism

6> CNS -

↑ appetite Euphoria

↓ sleep [Psychosis]



PSEUDO- CUSHING (mimic cushing Syndrome)

Chronic ~~atka~~ alcoholics

Cirrhotic pts.

Pts c Hyperthyroidism

Pt c Depression.

CLINICAL SUSPICION OF C.S.

WEIGHT GAIN (80%) = Thin skin > HTN
(80%) (75%)

1st M/C symptom

> central obesity (50%)

> ↓ K^+, alkalosis (15%)

↓

SCREENING TEST

SCREENING TEST

- 24 HR. URINARY CORTISOL ↑↑
- MIDNIGHT S. cortisol ↑
- ORAL DEXA CHALLENGE TEST [BEST]

1mg DEXAMETHASONE @ 11:00PM
(oral)
↓
S. CORTISOL @ 9:00AM
↳ (N) = (N)
↳ C.S. = ↑ (due to loss of -ve feedback)
↓
CONFIRMATORY

4mg 0.5mg DEXA I/V 6hrly x 2 days
↓
SH. cortisol → (N) = C.S. ⊖ ⊖
↳ ↑ . C.S ⊕ ⊕
[LOW DOSE DEXA TEST]
↓
ETIOLOGY H/O - exogeneous
↓
↑ ACTH ↓/(N)
DEPENDENT INDEPENDENT
↳ PITUITARY ADENOMA ↓
↳ ECTOPIC ACTH. ADRENAL ADENOMA
[CT Abdomen]

MRI can't visualize pituitary adenoma (2-5mm)

1) INF. PETROSAL SINUS SAMPLING (IPSS)

(CRH)
↓⊕
ACTH
↓
Sample → Petrosal sinus (PS
→ Peripheral vein (PV)

RATIO

$\frac{PS}{PV}$ ↑ ⇒ Increased

$\frac{PS}{PV}$ ↓ = Decreased.

PITUITARY ADENOMA

ECTOPIC ACTH

2mg DEXA I.V. 6hrly × 2Days

↓

S. ~~cholesterol~~ Cortisol

↓ = Pituitary Adenoma

Unchanged = Ectopic ACTH.

2) High Dose DEXA TEST

	PITUITARY ADENOMA	ECTOPIC ACTH
C/F		
ONSET →	Insidious	Acute
PROGRESSION →	Slow	Rapid
HYPERPIGMENTATION →	⊕	⊕ ⊕ ⊕ ⊕
IPSS	$\frac{PS}{PV}$ ↑	$\frac{PS}{PV}$ ↓
HIGH DOSE DEXA TEST	+ve response	Unchanged.

℞

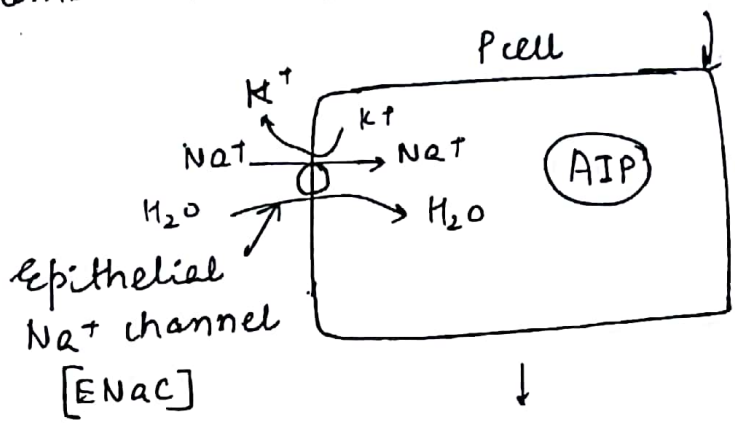
- Ketoconazole
- Metapyrone
- Etomidate
- Mitotaine

⊖ cortisol Synthesis

HYPER ALDOSTERONISM

2°

↓ volume → ↑ Renin → ↑ Aldosterone



AIP = aldosterone Induced Protein.

↓

↑ Na^+ → ↑ H_2O

↓

volume (N)

1° ← H.C.C. → Idiopathic cortical Hyperplasia (60%)

1) B/L

2) Adrenal Adenoma (40%)

↑

M/C/C – CONN SYNDROME

↑ Aldosterone

↓

(transient) ↑ Na^+

↓

↑ H_2O

↓

↑ volume (↓ Renin)

↓

↑ ANP

↳ NATRIURESIS → Polyuria

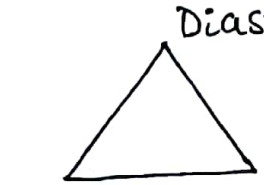
[ESCAPE PHENOMENA]

Cardiac Remodelling → Diastolic Dysfunction → Diastolic HTN

↓ K^+, alkalosis.

[No edema]

CLINICAL SUSPICION



↓

[SCREENING TEST]

ALDOSTERONE RENIN RATIO (ARR) >20

↓

[CONFIRMATORY TEST]

2 Litres of Normal Saline x 4 Hours

↓

↑Volume → ↓ Renin → ↓ Ald. ⇒ (N)

↓

NO Suppression of Aldosterone

or [SALINE INFUSION TEST]

↓

ETIOLOGY

↓

CT Abdomen

↓

ADENOMA

↓

Age

<40yrs → U/L ADRENELECTOMY

>40yrs → Adrenal venous sampling

↓

ALDOSTERONE

HIGH → U/L ADRENELECTOMY

(N) = wait watch

↓

Medical Therapy

HYPERPLASIA.

Rx - Aldosterone (-)

↳ spironolactone

↳ eplerenone

[Incidentilinoma]

D/D

1) Syndrome of apparent Mineralocorticoid excess [SAME]

Cortisol —(Deficiency of 11 β OH dehydrogenase)→ Cortisone

↑ Na^+

↓ K^+, Alkalosis

R_x = STEROIDS → ↓ ACTH → ↓ cortisol

2) Glucocorticoid Remediable Aldosteronism [GRA]

Zona → glomerulosa → aldosterone
Zona → Fasciculata → cortisol (ACTH +, +)
Zona → Reticularis

R_x - STEROIDS → ↓ ACTH → ↓ Aldosterone

3) LIDDLES SYNDROME

↑ Functioning of ENaC → ↑ Na^+
↓ K^+, alkalosis

R_x - ENaC (−) → TRIAMTERENE
→ AMILORIDE

ADRENAL INSUFFICIENCY

- 1° → ADDISON DISEASE → ADRENAL
  - Autoimmune (MCC In world)
  - TB (MCC In India)
- 2° → PITUITARY
  - Surgery
  - Trauma
  - Radiation
  - Apoplexy

↓ CORTISOL

↓

DEFECIENCY

- ↓ G.C. ← Activity → M.C ↓
  - ↓ G.C.
    - ↓ GLUCOSE
      - ↑ Protein Breakdown
        - ↓ Lot. loss
          - ↓ Thin
            - ASTHENIA
              - lethargy
              - Fatigue

M/C & 1st symptom

- M.C ↓
  - ↓ Na^+ ← Salt craving
    - ↑ M/C Biochemical Ab (N)
  - ↓ ECF
    - ↓ BP
      - [↑ K^+, alidosis]

↑ ACTH

Hyperpigmentation. (localised)

↳ Oral mucosa
Conjunctiva
Palmar crease
Nipple & areola region
moles, scars

ACTH administration

- (N) → CORTISOL ↑
- Addison's pt → CORTISOL (unchanged)

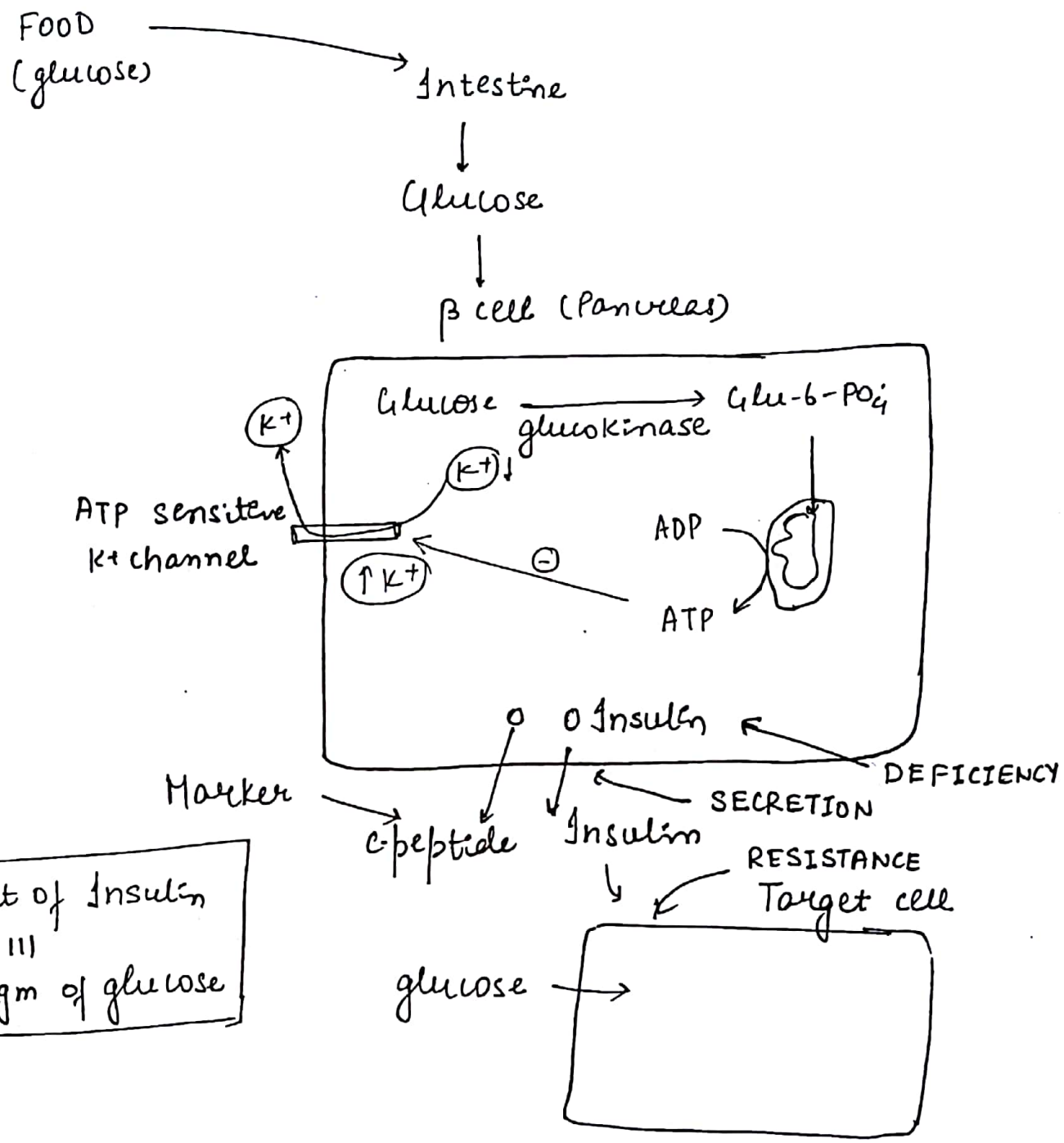
[ACTH STIMULATION TEST / COSYNTROPIN / SYNACTHEN TEST]

~~Dig~~ Diagnostic Test

℞ = STEROIDS

Hydrocortisone (DOC)

DIABETES MELLITUS (DM)



1 unit of Insulin
≡ III
2.5gm of glucose

Deficiency = TYPE-I

Secretion
Resistance
→ TYPE-II

Insulin t½ → 4

TYPE-I

- β cell Destruction (>90%)
- HLA Mediated

Aninsulinemia

Age of onset	<30yrs
Habitus	Thin
Family H/o	⊕
HTN	⊖
Dyslipidemia	⊖

DKA

TYPE-II

Secretory Defect

Insulin Resistance

Hyperinsulenemia

>30yrs

obese

⊕ ⊕ ⊕ ⊕

⊕

⊕ [↑ TG → ↓ HDL]

Hyperosmolar Non-Ketotic coma

20yrs ⟶ 25 yrs

RBS ↑↑↑

K.B. ⊕

Obese

Insulin (Type 1)

RBS - controlled.

Insulin ↓↓

(OHA)

(Type 2)

KETOSIS PRONE DIABETES (KPD)

30yrs ⟶ 35yrs

RBS ↑↑↑

Thin

K.B. ⊖

OHA (Type 2)

RBS ↑↑↑

OHA ↑↑↑

Insulin (Type 1)

1.5 DM

LATENT AUTOIMMUNE DIABETES IN ADULTS (LADA)

MATURITY ONSET DIABETES IN ADULTS (MODY)

Onset 5-15yrs of Age.
Thin
OHA Response
AD Inheritance
DKA ⊖
HTN ⊖

6 types of MODY
↓
TYPE 3 (Mlc type)
↓
HNF -1 α Deficiency

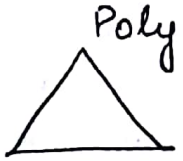
TYPE-3 DIABETES / BRAIN DIABETES / ALZHEIMER

Insulin Resistance. , Deficiency
↓
PPt the Cond"

TYPE-4

Elderly >60yrs.
OHA response (minimum dose)

DIAGNOSIS



± Polyphagia
± non-healing wound.
+ RBS ≥ 200 mg/dL

or.

Fasting 8hrs ← Fasting BS ≥ 126 mg/dL

or

Oral GTT
75gm glucose (oral)
↓
2hr BS ≥ 200 mg/dL.

or

HbA1c > 6.5%
[glucose + globin]

ACUTE COMPLICATION of DIABETES

DIABETIC KETOACIDOSIS

Type-1

(I) RBS = 250 - 600 mg/dL.

(II) Ketone Bodies → Blood → KETONEMIA (Reliable)
→ Urine → KETONURIA (Best Bedside)

(III) ↓ pH

C/F

1> nausea, vomiting (persistent)
K.B. (+) CTZ

2) Abdominal Pain ± Tenderness

3) ↑ HR

4) ↑ RR [KUSMALL BREATHING]

Metabolic acidosis ⟶ Resp. alkalosis

CO_2 → ↑ acidosis
↘ ↓ alkalosis

5) Fruity Odour → due to acetone

6) **Dehydration** (severe)
M/c C of mortality

Rx -

1) I.V. fluids (4-6 L)
↓
Most effective Rx.

0.9% NS ⟶ To prevent ↑ Na^+, ↑ Ca^{2+} ⟶ **0.45% NS**
4-6 hrs

To prevent hypoglycemia ↓
5% Dextrose
RBS < 200

× ~~RL~~ ×
×

2) Insulin
Regular → 10 units/ IV Bolus
↓
0.1 U/Kg/hr

3) KCl @ 20-40 mEq/hr.

4) $NaHCO_3$
pH < 7.

HYPEROSMOLAR NON-KETOTIC COMA

TYPE=2

RBS = 600 - 1000 mg/dL

↑ Sr. Osm.

KB ⊖

Altered sensorium

Rx =1) IV fluid (6-10L)

2) Insulin

CHRONIC COMPLICATION

DIABETIC NEUROPATHY

(A) POLYNEUROPATHY

Distal symmetry sensory (M/c type)

→ glove
→ Stocking
} (S) Loss

1st (S) lost Vibration [128 Hz Tuning Fork]

PARAESTHESIA → ANAESTHESIA

Rx

1) Improved Glycemic control

2) Pain ↓

AED = Prebagalin

TCA: Amitryptiline

(B) MONONEUROPATHY

M/c cranial N/V

III > VII

[Pupillary sparing]

Mononeuritis multiplex = Patchy involvement of

↳ M/c/c – metabolic = DM [(B) in India & world]

Infective = LEPROSY

Vasculitis = POLYARTERITIS NODOSA

(C) ~~AUTOIMM~~ AUTONOMIC NEUROPATHY

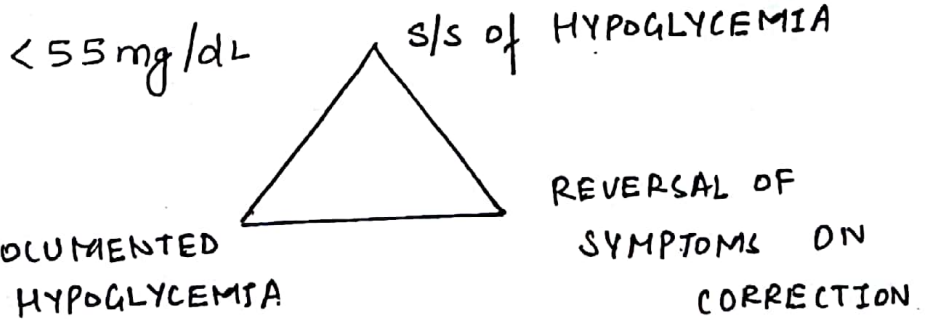
Hypoglycemic Unawareness

β ⊖ avoided in diabetic pts.

Intensive control is avoided ⇒ ↑ Risk of hypoglycemia

HYPOGLYCEMIA

WHIPPLES TRIAD



1) ↓ Insulin
2) ↑ Glucagon
3) ↑ cortisol
   epinephrine
   GH

EXTENSIVE FASTING × 72 hours

↓

↓ GLUCOSE

↓

↑ INSULIN

HYPER-INSULINEMIA

↑ Insulin ↑ C-Peptide → ENDOGENEOUS

only ↑ Insulin → EXOGENEOUS

Insulinoma → Radiological

Insulin : glucose ≥ 0.3

Sulphonylurea Induced

↳ SU Levels

SOMOGYI EFFECT

(40) **3-5 A.M.** Hypoglycemia [↑ night Insulin]

counter regulatory hormones

(240) **8 AM** Hyperglycemia

℞ = Long Acting Insulin.

DAWN PHENOMENA

(240) 3-5AM Hyperglycemia
- Insulinopenia
- Insulin resistance

↓

(340) 8 AM Hyperglycemia

Rx = ↑ night Insulin + Insulin sensitiser

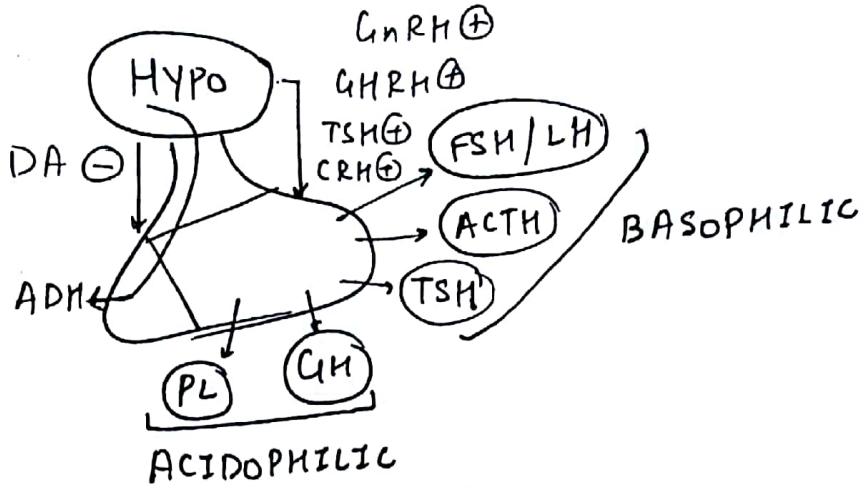
Rx of TYPE-2

FBS

126-200
Diet
Exercise

>300
Insulin

200-300
Obese metformin.
Non-obese - Sulfonylurea
[GLICAZIDE]
↓
10-14 Days
↓
[GLIPTIN]



STALK LESIONS

↑ Prolactin

Hypothyroidism (central)

↓ glucose

↓ BP

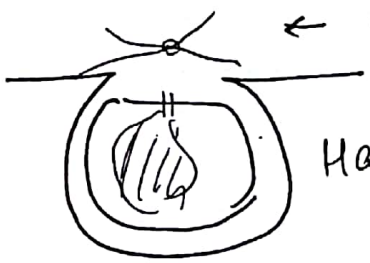
Central DI

PITUITARY APOPLEXY

↳ SHEEHAN SYNDROME

↑ Incidence = Sickle cell Disease
DM
HTN
] Predisposing Factors

← ↓ vision → progressive
Decompression.



Haemorrhagic necrosis

GH → LH → TSH → ACTH

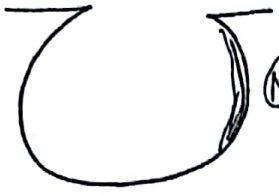
↓

↓ cortisol → ↓ BP

⇓

STEROIDS

↓ after few months



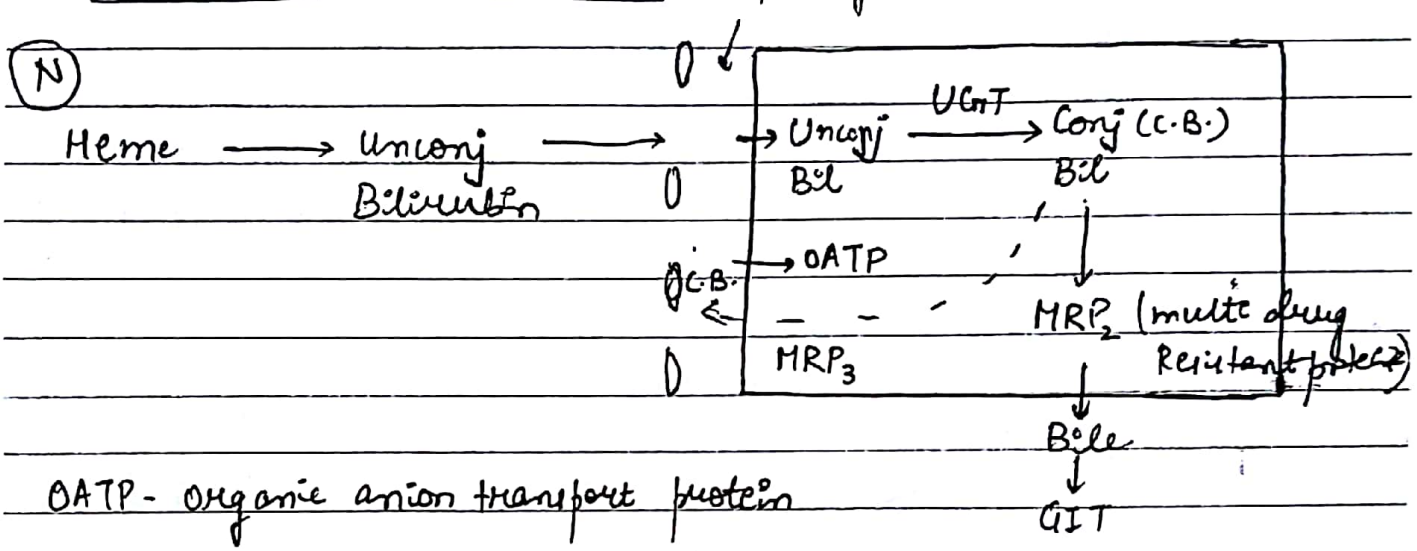
Ⓝ functioning Pituitary

EMPTY SELLA SYNDROME (Incidental finding)

MEDICINE (GIT)

Liver	Intestine
* Disorder of Bilirubin met	* Malabsorption syndrome
* Acute Viral Hepatitis	* Diarrhoea
* Chr. hep / cirrhosis	* GI infec"
* Comp" of Liver failure	* IBD
	* IBS

BILIRUBIN METABOLISM



OATP - Organic anion transport protein

DISORDERS OF BILIRUBIN METABOLISM

I ↑ Unconjugated Bilirubin

1> Increased synthesis -

a) Hemolytic anaemia → ↑ premature destruction of RBC in periphery

b) Ineffective erythropoiesis → ↑ premature destruction of RBC in Bone marrow

Cause

- Thalassemia
- Megaloblastic anaemia
- Severe Fe def.
- Pb poisoning

c) Large haematoma

d) Lobar pneumonia (↑ RBC destruc" in d exudate)

II²) ↓ Uptake :-

Cong	Acquired
Gilbert Syndrome-	Drugs- Rifampicin Probenecide (prophylaxis for gout) Ribavirin (for Hep C virus)

3) ↓ UGT :- (UDP glucuronyl Transferase)

* Cong. causes-

	Crigler Najjar I	CN II	Gilbert Syndrome
UGT activity	0%	10%	33%
Mode of inheritance	AR	AR	Both (AR>AD)
S. Bil (Total)	>20	6-20	<4
Kernicterus	(+)	Rare	(−)
Mortality	Before 1 year @ about t/t-	Adulthood	Not ↑.

Imp

	CN I	CN II	Gilbert Syndrome
Inv.	N	N	Lipofuscin pigment = Brown colour
Liver B_x			
R_x	Liver Transplant	Enzyme inducer Phenobarbital ↓ 25% ↓ in S. Bil. ⇓ If no response then go for Liver Transplant	No T/t Needed

*Acquired causes :-

1) Drugs – Gentamicin
Chloramphenicol
Pregnandione

2) Breast Milk Jaundice (Self-Limiting)
:
FA ⊖ → UGT of neonate →
No need to stop feeding

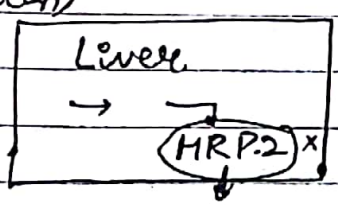
3) Lucey Driscoll Syndrome :- (Self Limiting)
Maternal serum Ab ⊖ UGT of neonate

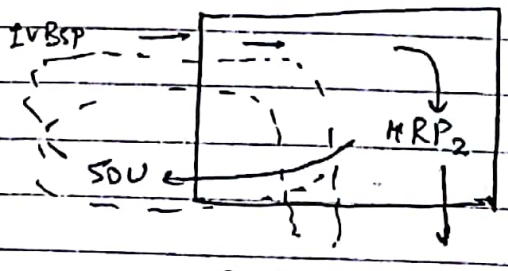
(II) ↑ Conjugated Bilirubin (Isolated).

Liver enzyme (N)

	Dubin Johnson Syndrome	Rotor Syndrome
Mech	⊖ Mutation of MRP_2.	⊖ Mutation of OATP
Mode of inheritance	AR	AR.
S. Bil.	< 4	< 4
Kernicterus	⊖	⊖
Mortality	not ↑	not ↑
Inv		
Liver Bx	Black Pigmentation. (Epinephrine metabolite (N) excreted by MRP_2)	Normal.
BSP clearance test (Bromsulphlein)		

I.V. BSP →





(N) BSP clearance ≤ 90 min

∵ MRP_2 absent, hence no clearance of BSP_2

Delayed clearance of BSP.

Rx not Req — Not Req.

Q. ∈ feature will suggest cause of ↑ of unconjugated Bil except :-

a) GB pigmented stones (H. anaemia) True
b) P/s → spherocytes (H. anaemia) True
c) Acute hep C viral infection Enzyme ↑ + conj bil ↑↑
d) H/o gout . True (Probenecid)

ACUTE VIRAL HEPATITIS

caused by hep A to E

Hep A	Hep E
① Mode of Transmission — H/c Feco-oral	H/c Feco-oral → sewer line
② Transmission to — common close contact	Rare ↓ community spread. ↓ 'New epidemic in community'
③ Rare - • Blood Transfusion Viremia during late incubation period • Sexual	Vertical
④ Not a mode of transmission — Vertical	BT Sexual

	Hep A	Hep E
C/F	M/C cause of Ac. Viral Hep. in children. [M/C of viral Hep - B]	M/C of Ac Viral Hep in adults. M/C of Ac. Viral Hep. in. ♀ [M/C of viral Hep in ♀ = B]
	Relapsing Hepatitis 2 clinical episodes by same virus in ac. phase (<6mnth)	Cholestatic hepatitis. Swollen hepatocytes cause obstruction to intrahep. Bile flow. [ALP also T].
Inv		
Serology	IgM Anti HAV = Acute Hep. A infn	IgM Anti HEV = Acute Hep E infn
	IgG Anti HAV - Pt is immune	IgG Anti-HEV - Pt is immune
	↓ Possibilities.	
	• Post vaccination ✓	±
	• Remote recovered past infn ✓	✓
	• Chronic infection. ✗ (virus ⊕ >6mnth)	✗
Complications.	1) Fulminant hepatitis - 0.1% (encephalopathy < 2wks of Jaundice)	♂ // non ♀ → 1-2% ♀ → 10-20%

2) Chronic Hep (viral ↑ +ve for >6mnth + Liver damge ⊕)	0%	0%
3) Carrier (virus + >6mnth Liver damge ⊖)	0%	0%

LMP Topic

Hep B

1. Mode of Transmission
   - ① M/c - vertical
     - Mother HbeAg ⊕ → Risk - 90%
     - Anti Hbe Ab → Risk - 10%
   - ② Percutaneous
     - Needle → 6-30% risk; viability of virus 7 days
     - BT → 1 in 2 lacs of BU transfused

M/c BT related virus = (B)

Hep C

① M/c - Percutaneous
- Needle → 1.8-6% risk; viable < 4 days.
- BT → 1 in 18 lacs of Blood units transfused.

MOT	HIV	RISK.
Needle	IV drug	0.6%
	accidental	0.3%
BT		1 in 22 lacs

	MOT	HEV	Risk
(Some donors have low level HBsAg & it NOT detected by routine lab method).		Vertical - 5% risk	
③ Sexual	Variable	Sexual	5% risk
Rare. MOT			
secreted into saliva = yes		yes.	
Human Bite	yes	yes.	
Not MOT			
• Virus secreted into ~~sal~~ stool	yes.	yes.	
• Feco - oral transmission (destroyed in stomach)	No	No.	
• Breast milk secreted	yes	yes	
• " " transmission	No	No	

• ~~Secreted~~ :

Q. All are transmitted by blood except

a)	Hep A	a)	Hep A	a)	Hep A
b)	B	b)	B	b)	B
c)	C	c)	C	c)	C
d)	E	d)	HIV	d)	G

Q. All cause AVH, transmitted by blood except
a) Hep A
b) B
c) C
d) G. → never cause AVH.

Q. M/c mode of transmission of hep B
1) Vertical vs ~~Horizontal~~
2) ~~Vertical~~ vs Percutaneous vs Sexual vs Human Bite

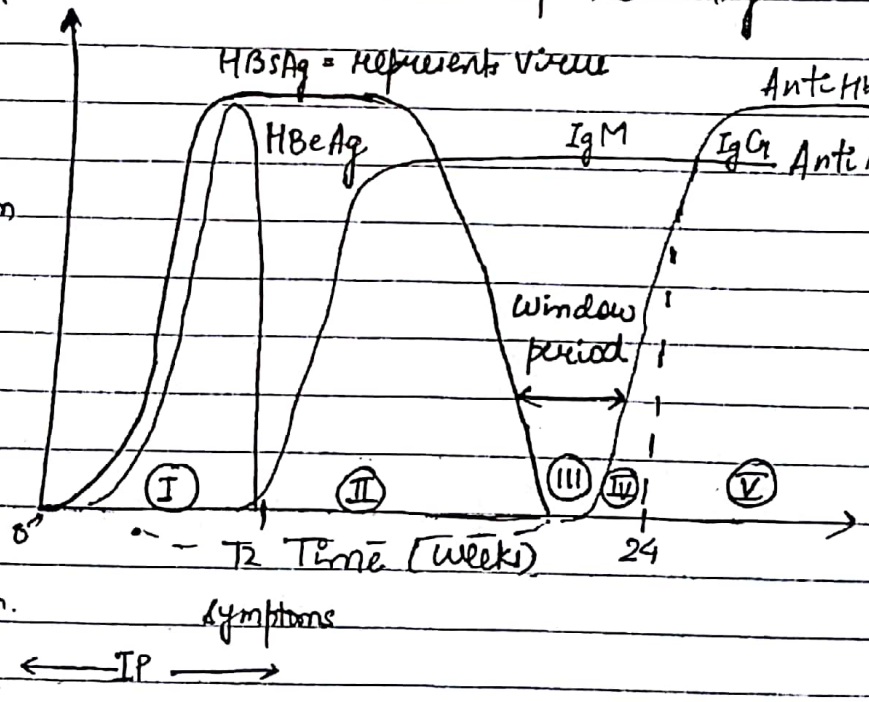
Q. Hep B not transmitted by
a) Saliva
b) Semen
~~c)~~ Feco-oral
d) Breast feeding.

C/F	Hep B	Hep C
	Mcc of viral cause of HCC	Mcc viral cause of cirrhosis
	↓	
	express HBxAg	[Mcc of cirrhosis = Alcohol]
	↙ ↘	
	⊖ p53 ⊕ Viral Replication	
	Mcc viral cause of chr. Hep (Prevalence wise)	Mcc AVH leading to chr. Hep. or Max. Risk of chronicity
	Mcc of Carrier	

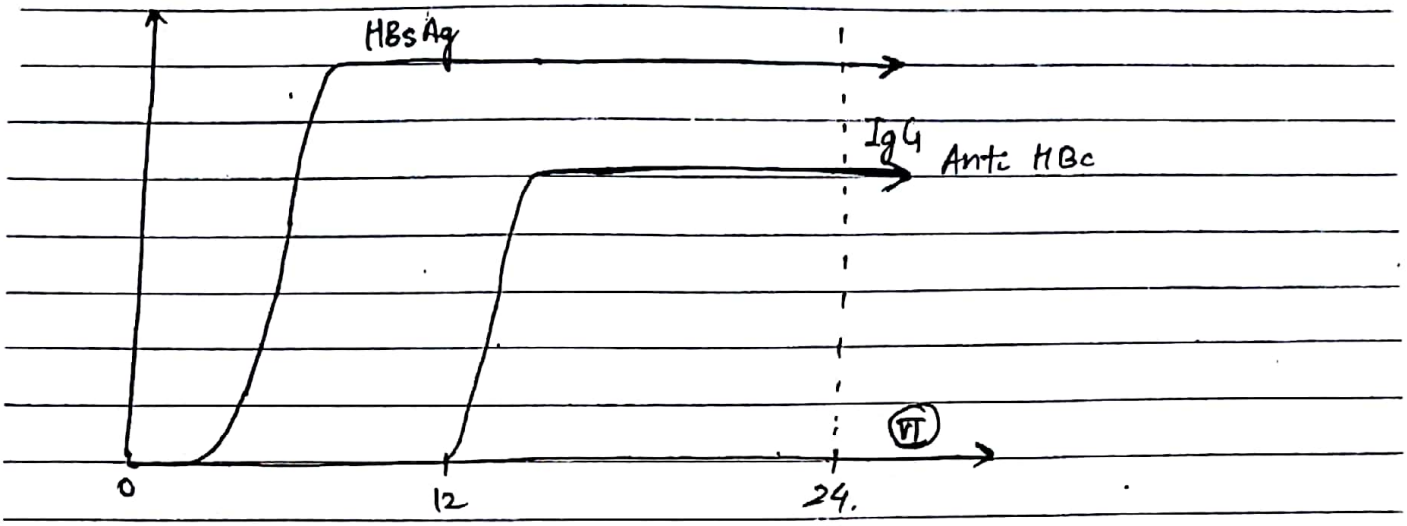
Serum sickness like illness ↓ HBsAg + Ab Joint pain + rashes In children = LN + Hepatosplenomegaly + Rash Gianotti Crosti Syndrome	Insulin Resistance by ⊖ insulin action ↑ Risk of T_2DM

* Serology of Hep B Infec^n

1) If Hep B limited to Acute phase only



2) If hep B converted to chronic infection



Phase	Marker
① I.P.	HBsAg, HBe Ag. Earliest marker of HBsAg.
② Acute (symp) Hep B infection	HBsAg, IgM Ante HBc Most reliable marker of Ac Hep B infection.
③ Window period	IgM Anti HBc
④ Recovery period of Ac. Hep B	IgM Ant HBc, Ante HBs
⑤ Remote past infection	IgG, Ante HBc, Ante HBs ± (disappear after yrs)
⑥ Chronic infection	HBs Ag + IgG Ante HBc

Chr. Hep B

- **Carrier** — Bx Liver Damage (−)
- Chr. Hepatitis — Liver Damage (+)
- Cirrhosis — Fibrosis + Nodules

HAI (Histological Activity Index) ~~$\frac{1}{3}$~~ 3

- ≤ 3 → **Active** — Replication (+) → DNA copies. ≥ 1000 /mL
- > 3 → **Inactive.** (−) — < 1000/mL

Replication markers :-

1) Quantitative marker → DNA copies ← Most reliable replication marker

2) Qualitative marker → HBe Ag.

Exception Pre core Mutants of hep B virus

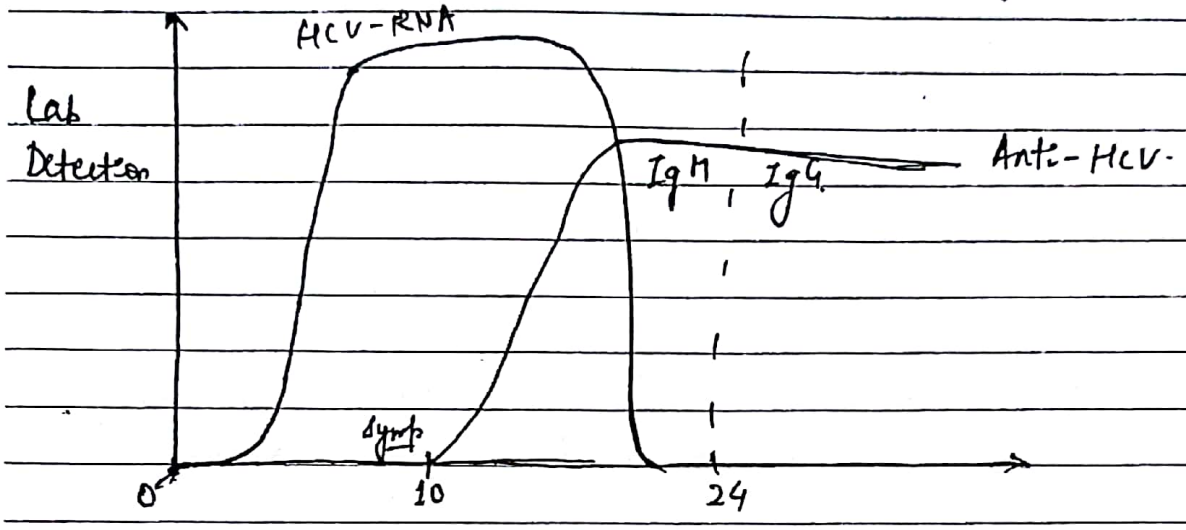
↓

Unable to make HBeAg but replication (+)

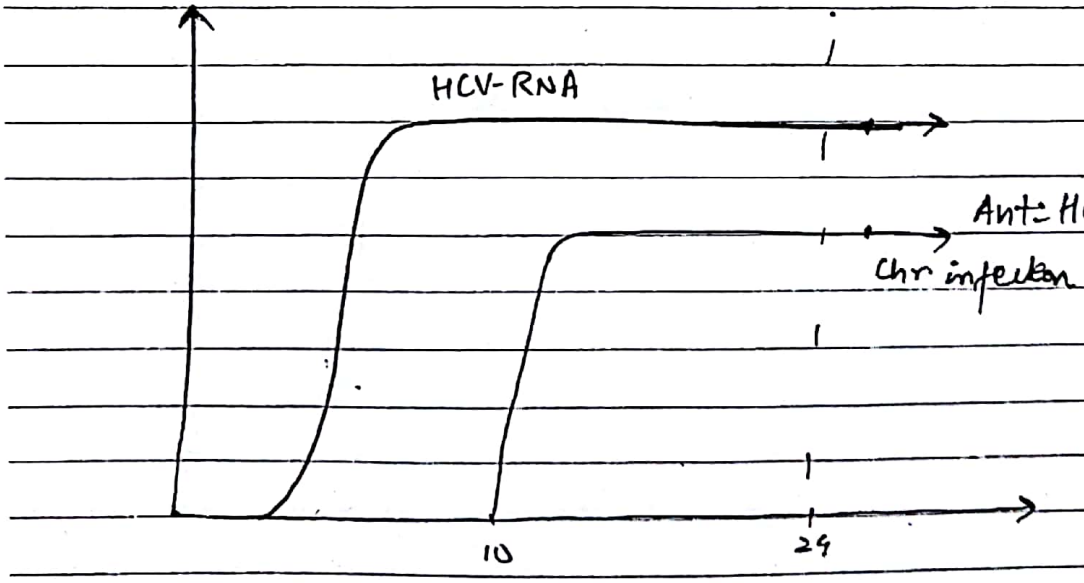
	DNA	HBeAg	Δ
①	(+)	(+)	Replicative phase of (N) hep B virus
②	(+)	(−)	Pre-core mutants of hep B
③	(−)	(−)	Non-replicative phase

* Serology of Hep C Infection :-

1) If Hep C limited to Acute phase only



2) If Hep C converted into Chronic Infection



Complications	Hep B	Hep C
① Fulminant Hepatitis	0.1 - 1%	0.1%
② Chr. Hep	1 - 10%	85%
③ Carrier state	0.1 - 30% Mean - 15%	1.5 - 3.2% Mean - 2.5%

Hep D

Mode of transmission - ① Percutaneous (Non-endemic Inda zones)
② Close contact (endemic zones)

C/F-

① M/c AVH leading to Fulminant Hepatitis ⇒ D or max risk

② Always associated w Hep B

Serology

? co-infection. = Acute hep D + Acute hep B
↓ IgM Anti HDV
↓ IgM Anti HBc

2) Superinfection. Acute hep D + chronic hep B
↓ IgM Anti HDV
↳ IgG Anti HBc

% Comp^{n}

① Fulminat Hep. 5% in Co-infection.
20% in Superinfection

② Chr. Hep } → depend on Hep B.
③ Carrier }

T/t

① AVH

i) Supportive care (mostly self limiting)

↓

I.V. fluid of choice = Dextrose as hypoglycemia risk

Min. Dextrose Req. = 150 g/day.

If 5% Dx = 3000 mL/d
(5g/100mL)

If 10% Dx = 1.5L/day → Fluid of choice

If 25% Dx = 600 mL/day. ⇒ may cause thrombophlebitis.
↳ not used for maintainance
reserved for emergency

ii) 2) Antivirals.

for Acute Hep C

↓

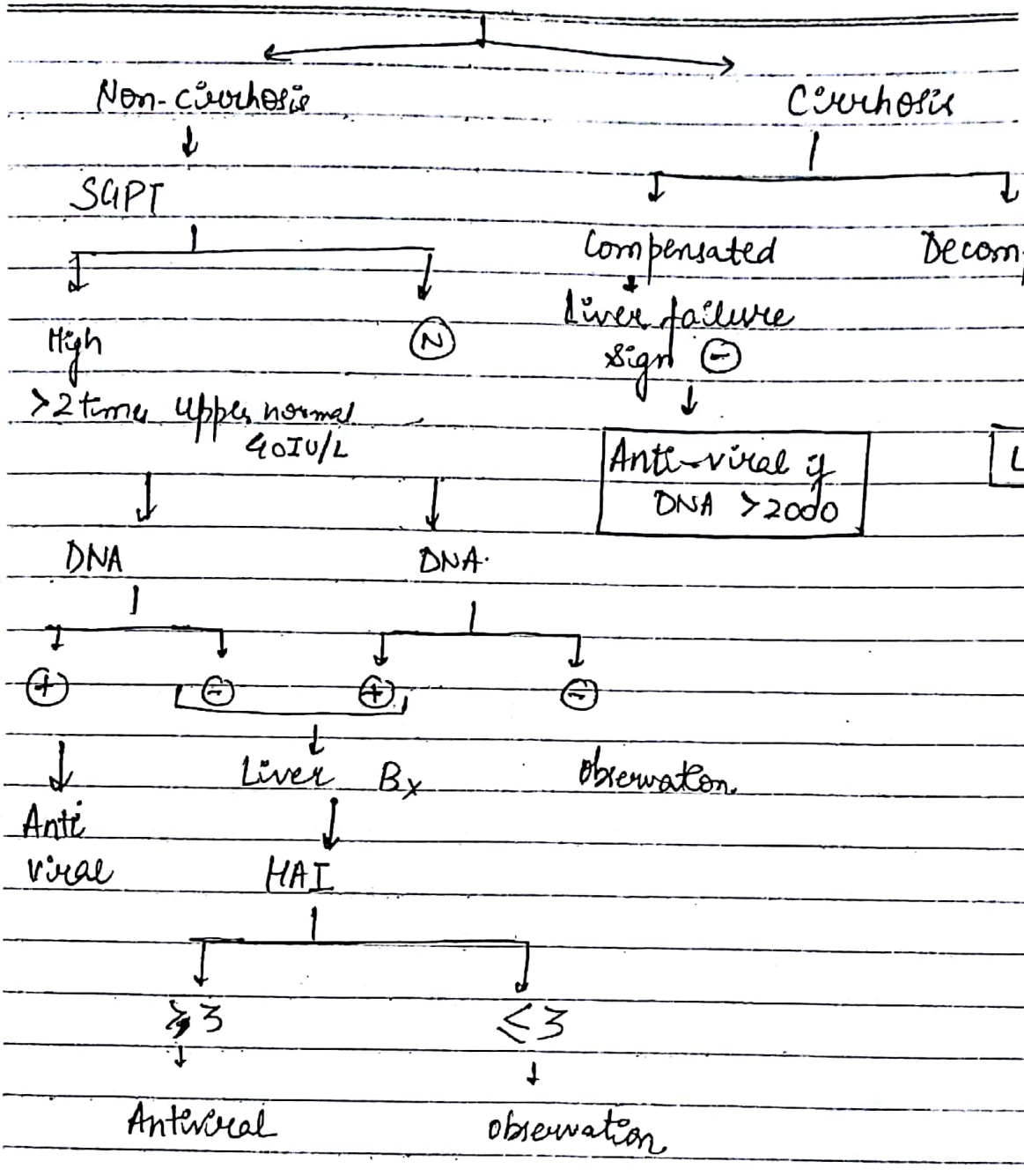
Interferon α. 12-24 wks

LMP Topic

II Chronic Viral Hepatitis

Approach to Chr. Hep B infection

↓



DNA is ⊕ for Anti-viral if ≥20,000 IU/mL. in HBe Ag ⊕

if ≥ 2000 IU/mL in HBeAg ⊖
(Pre-core mutants).

Anti-viral for Hep B

① Initiate ∴ **Monotherapy** from 1st Line agents

1) Interferon α -
- oldest
- Less effective in Cirrhosis

2) Entecavir -
- Most potent
- ↓ effectiveness in lamivudine resistant cases

3) Tenofovir → (DOC)
- Safest + effective even in Lamivudine (R) cases

Duration ≥ 1yr

(II) Chr. Hep. C Infection

Non-Cirrhosis
↓
Start Anti-viral if
1) HCV-RNA detetable
2) Bx - mod-sev hepatitis [HAI > 3]

Cirrhosis (Fibroscan)
- Compensated → Anti-viral
- De-compensated → LT

Antiviral for Hep C

Initiate ∴ (Dual) therapy (oral combination therapy)

INFα → outdated nowadays

Sofosbuvir + Velpatasvir → effective in all 6 genotypes.

>

Sofosbuvir + Daclatasvir

Duration – 12 wks. for all genotypes.

FATTY LIVER

Alcoholic Liver Disease

Patho

Dose → 40-80 g/d = fatty Liver

80 – 160 g/d = cirrhosis

↳ Duration 10-20 yrs

♀ → Dose is half.

Stages — **Mech**

① Fatty Liver ← Ethanol ⊖ → ↓ (N) FA metabolism → ↑ free FA → TG → TG deposit

② Hepatitis ← TNFα

F.L + Enzymes ↑

Non-Alcoholic Liver Disease

Dose of alcohol → 0-20 g/d.

cause – Insulin Resistance

Stages — **Mech**

① Fatty Liver ← TG deposit ← ↑ TG.

Insulin Resistance → Lipolysis → ↑ free FA → ↑ TG.

② Hepatitis ← oxidative injury

③ Cirrhosis ← → ③ Cirrhosis

Stellate cell

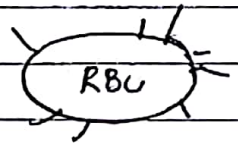
↑

Chr. Hepatitis

C/F

1) Peripheral Neuropathy
   - direct alcohol effect
   - Pure sensory Pyridoxine def. induced by alcohol.

2. Zieve's Syndrome.
Deep Jaundice due to additional effect of haemolysis induced by alcohol



= irregular Acanthocytes

1) Causes of Insulin Resistance
   (1) H/c obesity
   (2) Type 2 DM
   (3) Steroid (⊖ insulin action)
   (4) Hep C

Q. C C/F suggest alcohol as a cause of cirrhosis
- (a) Spider angioma } due ↑ Estrogen → ↓ Catabolism in Liver
- (b) Gynaecomastia }
- (c) Loss of deep tendon reflex
- (d) ascites.

Ix

(1) SGOT / SGPT > 2 Highly specific for ALD
(SGPT synthesis need pyridoxine)

(1) SGOT / SGPT ≤ 1.

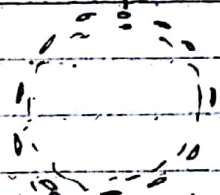
② γGT - ↑ ← (ER) Site = Bile duct + ER Fat Squeeze ER to release γGT.	③ γGT - ↑
③ Peripheral Neutrophilia (+) TNFα recruits if neutrophil > 5500/mm³ = Poor Prognosis	(-)
Rx.	
① Fatty Liver. = Reversible after cessation	FL = Reversible ∵ Rx of underlying cause → obesity
② Hepatitis Doc - Steroid ↓ act on TNFα. Indication if MADDREY's alcoholic discriminant func^n. > 32 = 4.6 x [PT of pt. - PT of control (12sec)] + S. Bil	Vit E. ↓ act as ante-oxidant
③ Cirrhosis Best Rx → Liver Transplant Recurrence of 1° disease after LT = Nil if underlying cause Remain treated	Cirrhosis Liver Transplants

AUTOIMMUNE

Autoimmune Hepatitis	1° Biliary Cirrhosis
Patho	
Direct Ab damage to the hepatocytes. (Type II HS)	Autoimmune fibrosis of intrahepatic Bile duct → Bile accumulation → Damage hepatocytes
C/F ♀	♀
Age 20-40 yrs	40-60 yrs
Recurrent (Recur over years)	Pruritus Xanthelesma (cholesterol deposit in the eyelids)
Inv Ab depends on type of AIH	MC/Most sensitive/Most specific Ab → Anti mitochondrial Ab
I - M/c → ANA Most sensitive Ab → Smooth ms cell P-ANCA	
II → Anti LKM I (Liver kidney microsome) ↓ (also +ve in Hep C infection)	
III - Least common, most severe Ab → Liver soluble antigen Most specific	

Regenerating hepatocytes

Bx



'Rosette pattern'

Non-suppurative inflammation of intrahepatic Bile ducts

Rx

① Hepatitis = Steroids (DOC)

② Cirrhosis

Decompensated → LT

Recurrent after LT → (common upto 50%)

① Compensated cirrhosis
Ursodeoxycholic Acid (UDCA)
(solubilise bile to non toxic)

② Decompensated cirrhosis
LT.

Recurrence after LT → rare

LHR Topic

GENETIC

WILSON'S DISEASE	HAEMOCHROMATOSIS
Patho: AR mut^{n} of ATP7B ↓ ↓ Cu excretory protein in Liver ↓ Cu overload in the body	AR muta^{n} of HFE ↓ ↓ Hepcidin [⊗ ↓ Fe absorp^{n}]. ↓ ↑ Fe absorption ↓ Fe overload
4F: Liver	Most c or earliest organ: Liver
age < 20yr	>40yr
Chr. Hepatitis +	+

Cirrhosis - Macronodular	Mixed or Micronodular
HCC +	++ (M/C cause of death even in t/td. pt.)
2nd organ affected — CNS → Basal Ganglia	CNS → Hypothalamic pituitary axis
M/C CNS manifestation — Tremor	Hypogonadism
Frontal lobe → neuropsychiatric abnormalities.	
Cr. N/v → XII (M/C Cr. N/v affected) (Dysarthria)	
Autoimmune dysfunction → Postural Hypotension.	
Not affected → 1. Sensory system 2. Motor power. (Pyramidal pathway)	
3rd Colour Change — Eyes	Skin.
↓ daytime vision = sunflower cataract	due to Fe + melanin deposits ↓ Bronze Pigmentation.
Kayser-Fleischer Ring (Vision (N)) — Peripheral	

④ Functional Effect

Kidney

↓

Proximal Tubular Dysfunc^{n}

↙ ↘

RTA - 2 | Fanconi Syndrome

Pancreas

↓

β cells affected

↓

Bronze DM

↓

* Reversible after tt of haemochromatosis unlike other

⑤ Structural Damage

RBC Membrane

↓

Haemolytic Anaemia

Joints (2 & 3rd MCP jt)

↓

Fe in joints ⊖ Pyrophatase

↓

Ca Pyrophosphate ↑

↓

Pseudogout

⑥ ×

CVS - Fe infilterate inside myocyte

↙ ↘

Myocyte Contraction ↓ | Myocyte relaxation ↓

↓ | ↓

DCMP > RCMP

M/c cause of death ⇒ CVS in untreated pt.

Inv

Ⓝ Free Cu + Apoceruloplasmin

↓

Ceruloplasmin (Bound Cu)

Ab(N) ↓ binding of free Cu ē apoceruloplasmin

1. S. Free Cu → ↑
2. S. ceruloplasmin → ↓
3. S. Total Cu = ↓ (mainly in bound form)
4. Urinary free Cu levels - ↑
5. Bx - Liver Cu > 200 µg/g dry liver wt

Rx

Hepatic → Zn (DOC) [50mg tds]
↓
⊖ Cu absorption

2> Cirrhosis -

According to NAZER SCORE

- SGOT
- S. Bil
- PT.

<7 | 7-9 | >9

Zinc + Trientine

LT

Pt. will be lifelong Zn therapy

Recurrence after LT → NIL

1. S. Fe ⇒ ↑
2. % Transferrin saturation → ↑
3. S. Ferritin ↑
4. TIBC ↓
5. New UIBC ↓↓ = TIBC - S. Fe ↓ ↑
(unsaturated)
↑ Most sensitive Inv

6. Bx → ↑ Fe.
Prussian Blue Stain

Hepatitis →
Rx OC → Phlebotomy

- 1mL Blood will remove → 0.5mg Fe
- Single phlebotomy → 500mL Blood. (250mg Fe removed)
- Fe overload. >/20g
↓
8o phlebotomy Req.

Cirrhosis → Liver Transplant

Recurrence after LT → rare <10%

Q. ⊆ causes ↑ Cu in Liver ∴ KF ring -
a) autoimmune cholangitis
b) 1° Biliary cirrhosis
c) 1° sclerosing cholangitis
d) All
} Ch. cholestasis condition

Q. After Phlebotomy manipulation of haemochromatosis ?

Reversible
- Hepatomegaly
- Skin pigmentation
- Diabetes
- CHF

Irreversible
- Cirrhosis
- Arthritis
- Hypogonadism

Q. HFE mutation ↑ risk of ⊆ cancer = Breast
Colon cancer

COMPLICATIONS OF LIVER FAILURE

1) HEPATIC ENCEPHALOPATHY

Mech - ↓ Urea cycle
↓
↑ NH_3 .
↓
Astrocyte Damage

C/F - West HAVEN's Grading

Restless I Earliest symptom = altered sleep cycle
" sign = altered handwriting (constructional apraxia)

Drowsiness II

↓

Trail making test
join to (1) to (25) numbered circle

Stuporous III

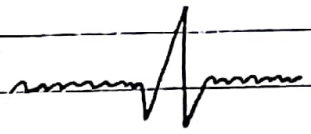
(N) time 15-30s.

Coma IV

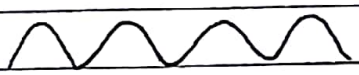
Deep coma V

Inv

EEG → (1) most characteristic Triphasic large amplitude wave (Grade II IV)



(2) S Wave - Grade V
(1-4 Hz)



Rx

1> Rx | ppt. cause | Mech. | Rx

(1) GI infection | ↑ bacterial proliferation | Ab of choice Rifaximin. (550 mg BD)

(2) Upper GI Bleed (ruptured oesophageal varices) | Blood protein ↓ reach gut bacteria i.e. ↑ NH_3 | If vitals Hobble → Ryle's tube aspiration.

Rx OC → Endoscopic Band Ligation of Varices
DOC → Octreotide
2° prophylaxis - β blocker (never in acute bleed)

③ S. K^+ ↓ — ↓ Peristalsis → ↑ Bacterial Proliferation — I.V. KCl infusion 10-20 mmol/hour.

④ Metabolic alkalosis ↑ vomiting (HCl loss) — $NH_3 + H^+ \rightleftharpoons NH_4^+$ (toxic) (Non-toxic)
if pH ↓ → eq. shifts to ®
if pH ↑ → eq. shifts to ©
— Rx underlying cause

⑤ Constipation — Bacterial proliferation ↑ — Laxative of choice : Lactulose
causes acidic pH. ↓
Target 2-3 stools/day
otherwise may cause diarrhoea

⑥ Hypovolemia — ↑ Renin → ↑ aldosterone ⇓ S. K^+ ↓ & Met. alkalosis — CI → RL
Lactate → Liver → HCO_3^- ↓ Met. alkalosis
So, IV. fluid → NS

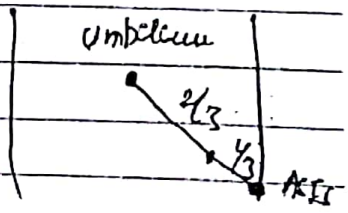
2) ASCITES

*Mech. ↑ Sinusoidal pressure (compression by nodules)
+
Na & H_2O retention ← Aldosterone ↑
↑ NO synthase (N degraded in liver)
↓
↑ NO
↓ Systemic vasodilatation (Blood pooling in systemic circulation) → Renal perfusion ↓ → Renin ↑
↓ Pulmonary vasodilatation
↓
Hepato-Pulmonary Syndrome
Hepato-Renal Syndrome

*C/F

Sign	Min fluid needed
Min PUDDLE	← 120mL
Shifting dullness	← 500mL
Fluid Thrill	← 1500mL

*Inv Ascitic fluid
• Preferred site → (L) lower quadrant

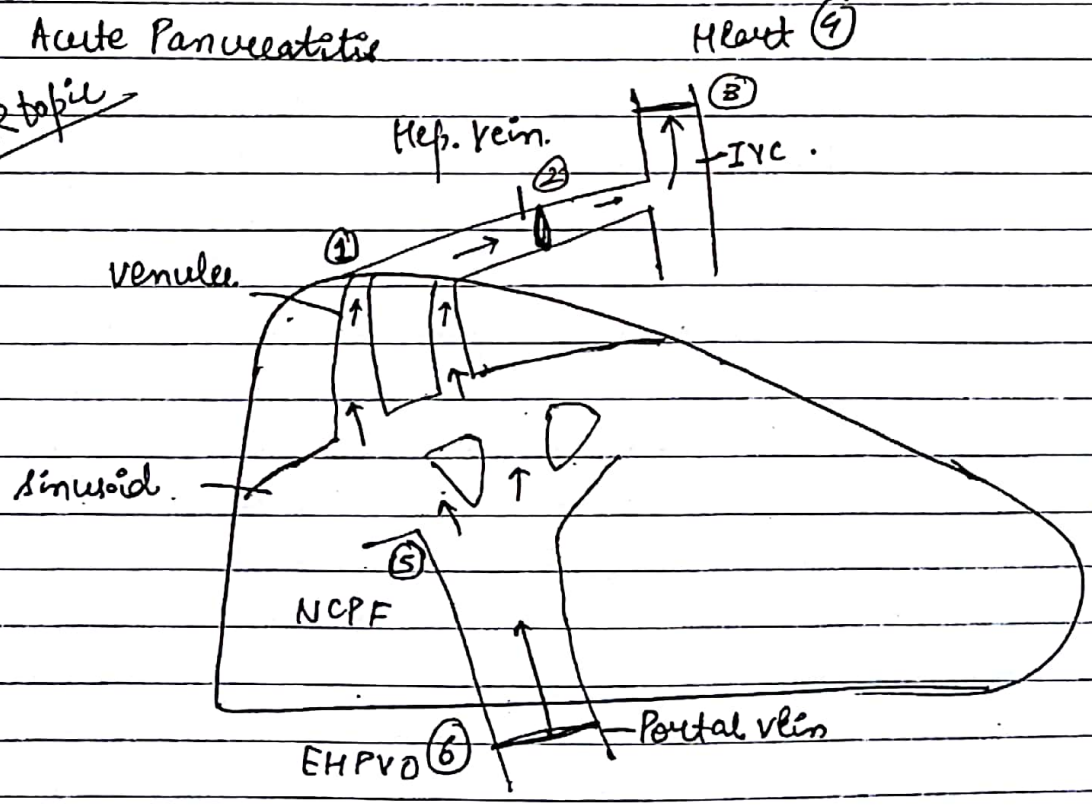


• Needle Size = Diagnostic 20-22G
Therapeutic 15G

Step ① S. albumin - Ascitic Albumin (SAAG)

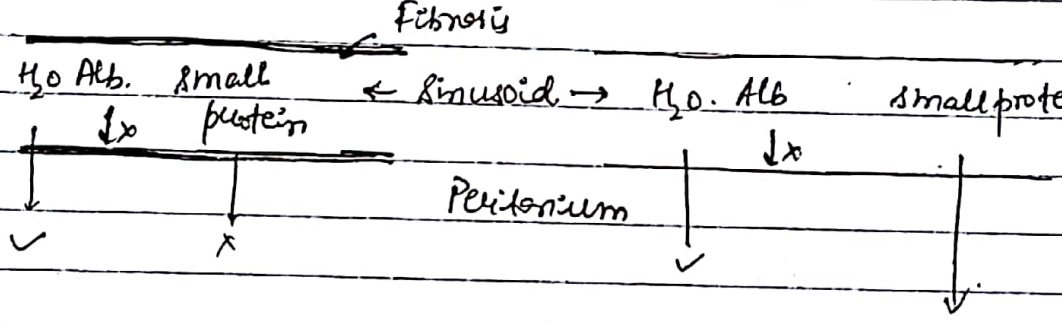
< 1.1	> 1.1
(N) Sinusoidal pressure)	↑ Sinusoidal pressure
1) ↓↓ S. albumin ↓ eg. Nephrotic Syndrome	1) ↓↓ Ascite albumin ↓ • ↑ Sinusoidal pressure. • Sinusoidal wall is impermeable to albumin leak.
2) ↓↓. Ascite albumin ↑ due to ↑ Peritoneal vessel permeability eg. TB peritonei Cancer Acute Pancreatitis	

LHR topic



Step 2 - Ascitic Total Protein ← if SAAG > 1.1.

- Cirrhosis < 2.5
- Non-cirrhotic (Post-sinusoidal obstruction) > 2.5
  1. Veno-occlusive Disease
  2. Budd-Chiary
  3. IVC obstruction
  4. CHF / Constrictive Pericarditis



Rx

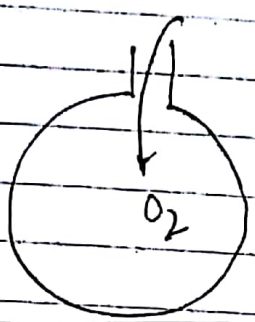
Grade	Defn	Rx
I = Mild Ascites	No clinical signs	salt restriction
II = Moderate "	clinical signs +ve Respiratory distress -	Add Diuretics spironolactone (max - 400mg/day) Furosemide (max - 160 mg/d)
III. Severe	Resp. Distress +	Large vol. paracentesis (5-6L removed) + I.V. albumin (to retain I.V. fluid)

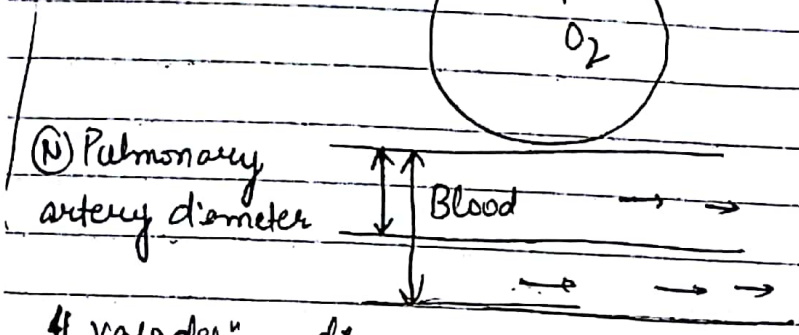
IV Refractory Ascites	No response >7 days of Max dose of Both diuretics	Same as Grade III

⑤ Non-Cirrhotic Portal Fibrosis	⑥ Extra-hepatic Porta vein Occlusion
Age >20 yr	<20 yr.
c/f upper GI bleed + ↑	+
Portal HTN + ↓	+
Spleen + >7cm below Costal margin	+ <7 cm below costal margin
Jaundice ⊖	⊖
Encephalopathy ⊖	⊖
Ascites ⊖	
Rx - Endoscopic Band ligation +	+

3. HEPATO - PULMONARY SYNDROME.

Mech. Pulmonary vasodilatation





↑ vasodil" = diam ↑ occurs

mixing ē deoxygenated blood on Ⓛ side

R to L shunt

C/F

Platypnoea - dyspnea ↑ on standing [diaphragm moves down ↓ shunt open ↓ hypoxia ↑]

Inv

① ↓ in O_2 saturation by 3% on standing from supine
Orthodeoxia

Rx -) Sclerosis of dilated vessel

2) Rx Oc = Liver Transplant

INTESTINAL

MALABSORTION DISEASES

due to SI disease

Proximal	Distal
↑	↑
Fe, FA, Ca, Mg	Bile, Vit B_{12}
Fat, CHo, Protein ++	+

Tests for malabsorption

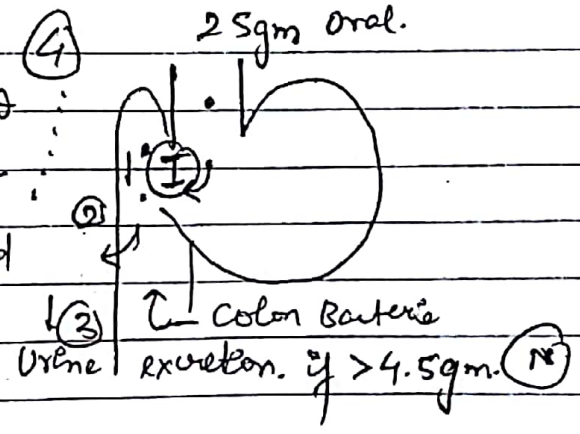
I) For Fat :-

① Gold Std → 72 hour Stool fat estimation.
if fat excretion >6% ⇒ Steatorrhoea
↑
M/C abnormality seen in any malabsorption syndrome

② Spot Ix → Sudan III stain.
+ve if stool fat > 10%

II) For Carbohydrate :-

① Most specific Ix → D xylose Test



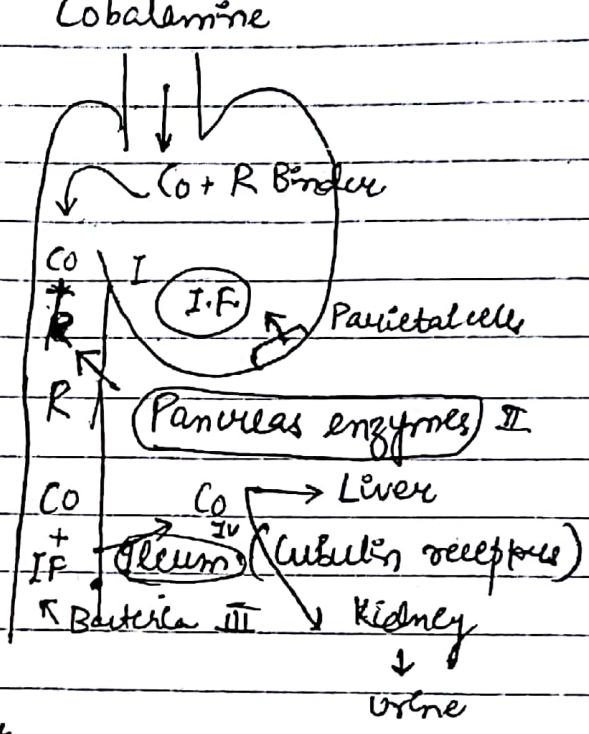
Causes of <4.5gm excretion
1) Pyloric stenosis
2) Proximal SI disease
Eg. Celiac sprue
3) Bacterial overgrowth Syndrome
4) 3rd space Coll → Ascites
Pleural Effusion

⑤ Renal failure

(III) Vit B_{12} malabsorpⁿ:

SCHILLING's TEST

① Oral radiolabelled cobalamine
+
I.M. vit B_{12} (1mg)
to fill Liver
↓
24 hour Urine collection.
↓
↓ <10% → malabsorpⁿ
↓ >10% of excretion → (N) test



If excretion <10% AND becomes >10% after adding.

1) I.F. → Pernicious Anaemia

2) Pancreatic enzyme → Chr. Pancreatitis

3) Ab x 5 days → Bacterial overgrowth syndrome
↓
if remains <10% → Ileum disease

Q. In dietary deficiency of B_{12}, schilling test (N)

Q. Mut' of cubulin (R) ⇒ IMERSLUND GRIESBEECK's SYNDROME

IV Intestinal Biopsy
Gold Std. Ix or Most Specific Ix for malabsorption.

Etiologies of Malabsorption-

CELIAC SPRUE	TROPICAL SPRUE.
Cause GLIADIN Hypersensitivity (+ve in gluten) ↓ Local contact HS	Bacterial Toxins. + Folic acid deficiency (↓ mucosal repair)
Prox SI > Distal SI	Distal SI > Prox SI.
G/F * Age- Typical 6-12 months can occur at any age Spontaneous remission - 2nd decade	Adults
* Steatorrhoea (large vol, foul smelling) leading to ↓ Chronic >4 weeks. Non-inflammatory (No blood or pus in stool)	✓
* Extra-intestinal manifestation. M/c- Dermatitis Herpetiformis Other - T1DM, IgA deficiency	

	COELIAC SPRUE	TROPICAL SPRUE
Inv		
① Serology	+	−
Most specific Ab = Anti-Endomysial Ab.		
Most sensitive Ab = Anti tissue Transglutaminase (TTG)		
Most sensitive + specific Ab/MC/Best = Anti TTG		
② Biopsy		
• Loss of villi	+ (reversible after gluten free diet)	+
• Flat mucosa	+	+
• Lymphocyte infiltration	+	+
③ HLA DQ2	(+) in 100% cases.	−
HLA DQ8	but non-specific	−
Rx		
1. Gluten free diet		Antibiotics → Doxycycline or Rifaximin. + Folic acid. Duration of Rx → 6 months
2. Steroid. Indications		
1) Refractory sprue		
2) (no response upto 12 months) of gluten free diet		
2) Celiac shock (↑ gluten load)		
3) SI Lymphoma		
M/c cause of death		

WHIPPLE'S DISEASE

~~Ato~~ Cause - Tropheryma Whipelii

C/F

Acute	OR	Chronic (HS reaction)
1) Acute GE		1) Mc presentation = migratory Poly/oligo arthritis
2) Pneumonia		

2) CNS
M/c → Dementia
Most characteristic CNS manifestation
Oculo Masticatory Myorhythmia
(conv./diverg. nystagmus.)

Other CNS manifestation.
- Cerebellar ataxia
- Myoclonic seizure
- Encephalopathy
- P. Neuropathy

3) CVS - Pancarditis
M/c - Pericarditis.

4) Eye - Uveitis

5) Polyserositis = Ascites
Pleuritis

Q. organ not involved in whipple's
① ~~kidney~~
② Lung
③ CVS
④ CNS

Inv Bx - PAS +ve macrophage containing

D/D → TB

Bacilli	TB
AFB ⊖	AFB ⊕

Rx ① GIT → Ceftriaxone (2wk) → Cotrimoxazole (1yr)

② CNS/CVS → Ceftriaxone (2wk) → Doxycycline + Chloroquine or Hydroxychloroquine (1 year)
(↑ risk of recurrence)

BACTERIAL Overgrowth Syndrome

Proliferation of colonic bacteria in prox SI

Causes -

Communication bet" LI & SI	Anatomical stenosis of SI	Functional Stenosis of SI
↑	↑	(↓ Peristalsis)
fistula	stricture	↑
	+ Intussepteon	DM
		systemic sclerosis

CF -

1) Steatorrhoea — Bile is deconjugated by bacteria in S.I.

Inv.

1) 72 hour stool test. >6%

2) D-Xylose Test
excretion <4.5 gm

3) Schilling Test ab (N)

4) S. Folic acid level ↑ (Synthesis by bacteria + reabsorbed by Prox. SI mucosa).

5) Lactulose Breath test or H^+ Breath test.
↓
+ve in Breath 2-8 hour after giving lactulose as Bacteria in SI metabolise.

6) Endoscopic jejunal aspirate culture
↓
M/c organism E.coli $>10^5$/mL

Rx

1) T/t underlying cause

2) Cyclic ~~Ab~~. antibiotics [Co-amoxyclav.
Ab x 1 week
↓
gap 3 wk.
↓
Ab 1 wk

APPROACH TO DIARRHOEA

Essential Criteria for Diarrhoea
Stool vol. > 200 mg/d
Stool wt. > 200 mg/d

Duration.

Types

< 2 wk	2-4 wk	> 4 wk
Acute	Persistent	Chronic
90% Due to infections Acute & Persistent		≥ 90% due to non-infectious

If Infectious Diarrhoea

	Toxin induced (↑electrolyte + H_2O secretion)	Inflammation induced (exudative
• Fever	⊖	⊕
• Pus in stool	⊖	⊕
• Blood in stool	⊖	⊕

If Toxin induced

Preformed	Enterotoxin
I.P. ~ in hours	1-2 days
1) Bacillus cereus (Chinese Restaurant diarrhoea	1) Vibrio cholerae (↑ HCO_3 in stool - Rice ~~stool~~ watery stool

2) Staph. aureus.

2) Enterotoxic E.Coli
M/c c of Traveller's diarrhoea

3) Clostridium Perfringes

If inflammation induced

I. Mild = mucosa limited. (blood in stool ⊖)

II. M/c Viral diarrhoea in adults = Noro virus
" " " children = Rota virus

II Mod. = submucosa

1) Salmonella → involves ileum
↓
Bile reabsorpⁿ ↓
↓
Bile in stool.

III Severe

2) Yersinia → Severe ileum inflammation
Pseudo appendicitis

(3)
II Campylobacter J. M/c infectious cause of GBS

III Severe = Deep layers

1) Shigella → Toxic encephalopathy
Ekiri Syndrome

2) E. histolytica → flask shaped ulcer

Rx - acute/persistent diarrhoea

① Essential - Rehydration

I.v. fluid of choice → RL contains

	mmol/L
K+	4
Na^+	130
Ca^{2+}	2
Cl^-	109
Lactate$^-$	28
Osmolarity	273

slightly hyposmolar

② Antibiotics

Indication - Mod to severe inflammatory infectious diarrhoea

If ≥ 1 of 3 criteria (+)

a) Fever >101°F

b) Blood in stool

c) Pus in stool

Empirical = Flouro quinolones.

Chronic Diarrhoea

↓ Non-inflammatory
eg. Malabsorption Syndrome

↓ Inflammatory
LMR
Topic
Ulcerative colitis } IBD
Crohn's Disease

	UC	CD
*Risk/associated		
① Smoking	↓	↑
② appendicectomy	↓	↑
③ Drugs		
OCP	↔	↑↑
Methyldopa	↑	↔
Ab use in 1year	↑	↔
④ Infections	↔	↑ MC = Mycobacterium Para TB.
		Infection & MC of CD - H. Pylori
⑤ Turner's	↑	↑ NOT DOWN SYNDROME
⑥ IL-10 Receptor deficiency	↑	↑
↓		
ⓝ anti-inflammatory		
→ Early onset IBD.		
C/F Intestinal		
M/c site →	Rectum + Sigmoid > Rectum only	M/c site → SI + LI > SI only.
		M/c isolated site - Ileum.
M/c isolated site - Rectum		Rectum is usually spared
Site not involved → SI.		

① Malabsorption Synd	⊖	⊕
② Bleeding PR (Tenesmus)	⊕	⊖
③ Fistula formation	⊖	⊕ (Transmural involvement)
④ Toxic Megacolon (dilatation of colon >6cm)	⊕	⊖ Bowel wall or thick resist dilatation
Ulcer → Collar Button ulcer (non-creeping)		Cobblestone ulcer (Creeping)
Inv		
① Stool Examn. Lactoferrin correlate ī disease activity	⊕	⊕
Calprotectin Predicts ~~relapse~~ relapse	⊕	⊕
② Serology. M/c → ANCA		Mc Anti Saccromyces cerevisce Ab
Role → ↑ risk of Pancolitis		Role - ↑ risk of early complication
③ Confirm	Bx	Bx

Rx of Ulcerative Colitis

(I) Mild to mod. severity (stool freq. < 6/day)

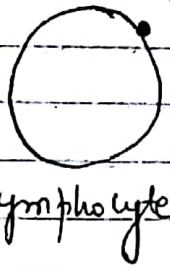
- Distal Dis
  - DOC.- Per Rectal ASA
  - Mesalamine
- Pancolitis
  - DOC - Oral ASA
  - Mesalamine + Sulfasalazine
  - ↓ If no response in 4 wks.
  - Oral steroid therapy

II Severe IBD (Stool frequency > 6/day or shock).

DOC - I.V. Steroid

- Steroid response
  - ↓ Taper + Stop
- ~~Taper + Stop steroid~~ Steroid Dependent
  - ↓ Steroid sparing agent
  - Azathioprine
- Steroid resistant (no response in 5 day)
  - ↓ TNF α Ab or cyclosporine
  - ↓ if unresponsive
  - only for CD - Anti - Integrin

Only in Crohn's Disease (Resistant steroid)



Integrin (N) helps in vascular adhesion

β_1 ↙ ↘ β_7 subunit

Lymphocyte ↓ specific for GIT vessels

Ab against β_1 & β_7 = NATALIZUMAB.
(used in Multiple Sclerosis)

↓

S/E → Reactivate JC virus

↓

Progressive multifocal leuko encephalopathy

Ab against β_7 = VEDOLIZUMAB

Rx of Crohn's Disease

I. Mild to Mod. IBD

↓ ↓

Ileum limited

DOC - Ileal Release Budesonide

Small + Large Intestine

DOC - Oral prednisolone

↓ no response in 4wks

Methotrexate.

* Miscellaneous Points :-

1) MC cause of death → Cancer

2) Colonic cancer risk → Ulcerative colitis = Crohn's Disease

3) Colonic Ca risk ↓ → Folic acid, ASA agents.

4) Extraintestinal Manifestation of IBD (usually more in CD)

Correlated with Bowel activity	Independent of Bowel activity
Skin - ① Erythema Nodosum (Red, hot, tender, nodules on shin)	N - neutrophil infiltration N - non-infective N - necrosis of skin, ① Pyoderma Gangrenosum
Joints - Migratory Polyarthritis (Peripheral joints)	Ankylosing spondylitis
Eye - Episcleritis	Uveitis
Liver - Non-alcoholic fatty Liver Disease	1° Sclerosing Cholangitis → Risk factor for Cholangio Carcinoma

Q. M/c extra-intestinal organ affected in IBD - Joints

Q. M/c " " manifestation. → Erythema Nodosum

Q. C " " " more in UC → Pyoderma
1° sclerosing cholangitis

Addition Harrison selected.

Part I → Involuntary wt. loss – Defn
Causes
Inv (Table)

Ascites

Table of causes of diarrhoea

Part II – Table of T/t of Hepatitis C
(exclude doses or regimen)

Table of intestinal Biopsy findings

Protein losing enteropathy
(1st 2 para - causes
inv)