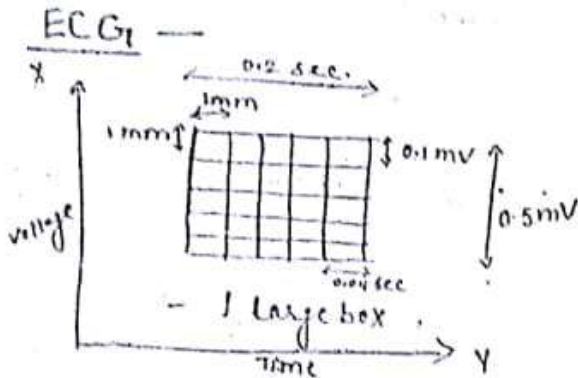


(2)

— CVS —

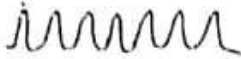


Speed — 25 mm/sec. → it is std.

But it can be changed acc. to need.

* 50 mm/sec — used in case of tachycardia
& in blw & wave we can see small changes

25 mm/s



5 mm/s



Waves :-



P = atrial depolarization.

* SA node firing doesn't produce any wave in ECG
it is the chamber depolarizⁿ which produces wave

Segment

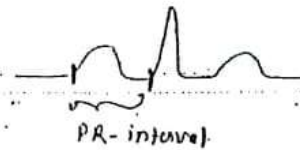
Interval

- No wave in segment

- include wave

measured in: vt. (y) axis

- Hz (x) axis



AV nodal delay

0.3 m/sec - speed of atrial conducⁿ

0.5 m/sec = ventricular conducⁿ

1 m/sec = Bundle

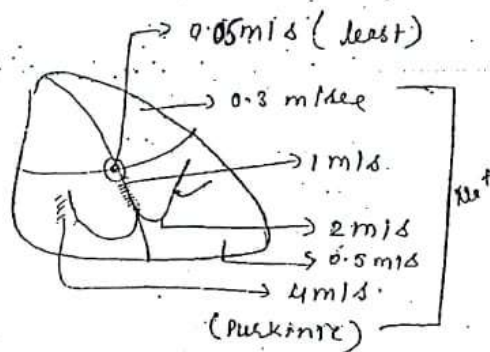
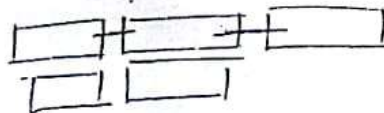
~~SA node~~ 0.05

why AV node has least speed of conducⁿ -

1) Ca^{++} dependent depolarizⁿ

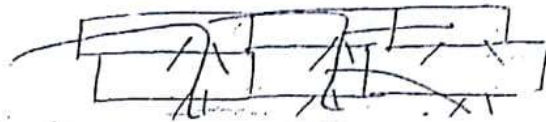
Rest all are Na^{+} dependent

2) $\downarrow$ gap juncⁿ -



(3)

* Rest all not dependent → 1 gap juncⁿ



→ impulse will spread fast

* AV node conducⁿ is slow b/c if AV node also fire at same rate, atria & vent. both will contract simultaneously.

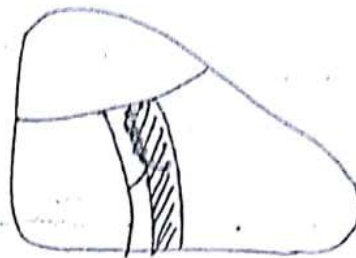
↓
1 press in ventricle
↓
closure of tricuspid & BC valve
↓
regurgitⁿ of blood to veins.

QRS wave — diff ventricular depolarizⁿ.

T wave — ventricular repolarization.

U wave — * m/c cause papillary muscle / Purkinje fiber repolarization. → physiological

* Hypokalemia → pathological.



* Lt. side & the middle of the IV. septum is first to depolarize (b/c Lt bundle br. has more fibres & depolarize faster)

- middle area depolarize 1st b/c in upper part there is Bundle of His which doesn't depolarize ventricle.

* Last site for depolarizⁿ —

• posterobasal portion of Rt. ventricle.

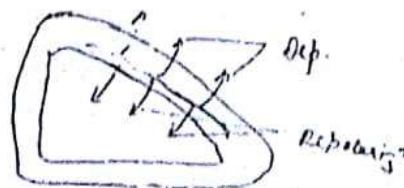
* 1st site for repolarizⁿ — PB. LV.

Rule — last site to depolarize will be 1st site to repolarize.

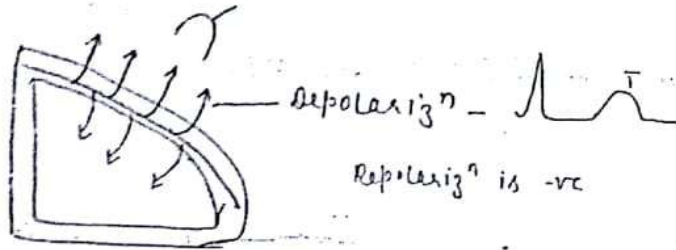
* last site to repolarize → LV endocardium.

Depolarizⁿ → endo → epicardium.

Repolarizⁿ → epi → endo.



(4)



Subendocardial ischaemia —

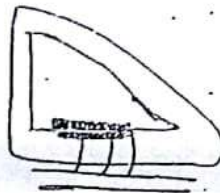
Repolarizⁿ from endo → epi.

→ Flipped / inv. T wave.



* Subendocardium is least perfused area & very prone to ischaemia.

Endo → can take blood from ventricle also.



* Father of ECG = ^{William} Einthoven

* Father of Stethoscopy — ^{Rene} Laennec

* Father of EEG — Hans Burger

* Father of modern medicine — Osler

* Father of medicine — Hippocrates

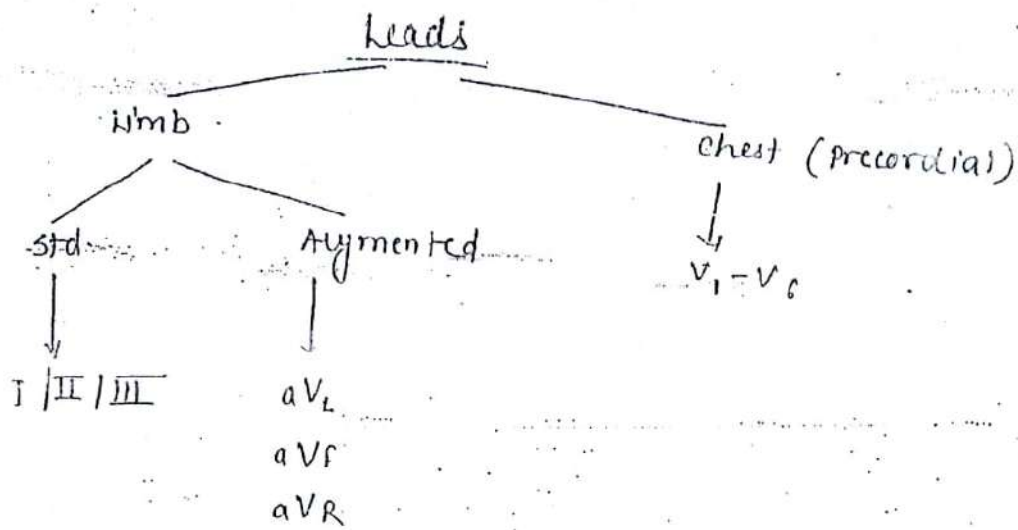
* Father of evidence based medicine — Sackett

* Father of BP — Potain

* Father of diastolic B.P — Korotkoff

* Father of mercury sphygmomanometer

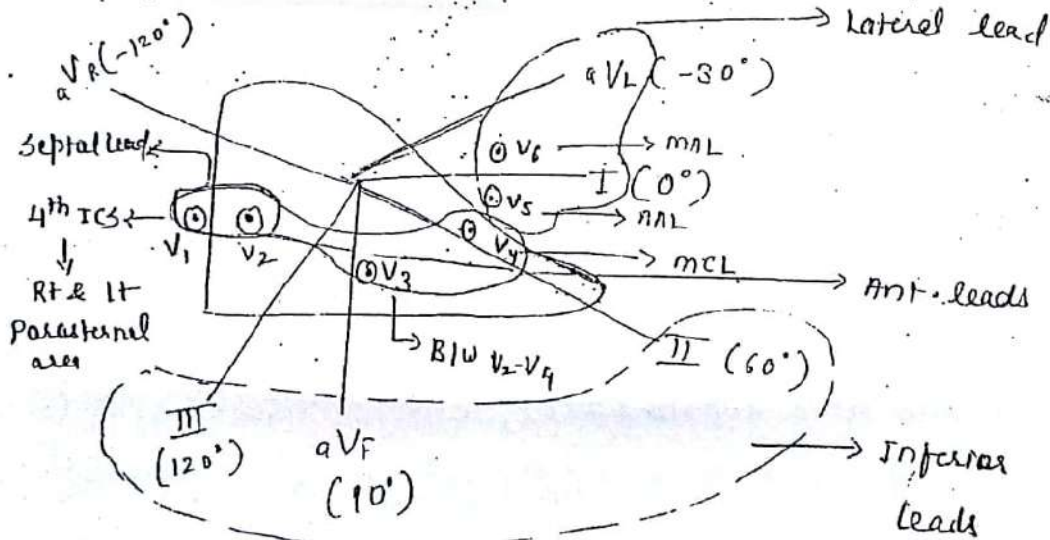
(5)



* min. 2 leads required for ECG.

* max^m leads = no limit

* std. - 12 lead.



STEMI! — ST $\uparrow$ $\rightarrow$ can be localized

<u>STEMI</u>	ST $\uparrow$
Inf. wall MI	I / II / aVF
Lat. wall MI	I / AVL / V5 / V6
AWMI	V1 - V4
Septal	V1 + V2
AL MI	V1 - V6 I / aVL
ext. AWMI	V1 - V6

Disadv. of 12 lead system —

- Not able to see Rt. ventricle
- can't see post. wall.

* Specialized leads —

- whenever there is inf. wall MI, we suspect Rt. ventricle & post. wall MI also as all of them have common blood supply (RCA)

so we take Rt. side ECG using same leads

- $\left. \begin{matrix} V_{4R} \\ V_{5R} \\ V_{6R} \end{matrix} \right\} V_1 - V_6 \text{ are attached on Rt side.}$

(6)

Post leads — V_7, V_8, V_9 } V_1, V_2, V_3 are kept on L-side in
infrascapular region.

→ can detect post-wall MI.

STEMI — minimum >1 mm elevⁿ in 2 contiguous leads. — V_5, V_6, V_1, V_2 , not V_4, V_5

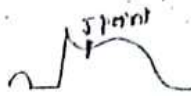
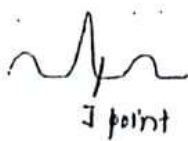
exception — Rt ventricle / post wall MI — 0.5 mm

Stages —

I — Hyperacute stage → • Tall T wave.



II — Acute stage → • ST elevⁿ / J point elevⁿ

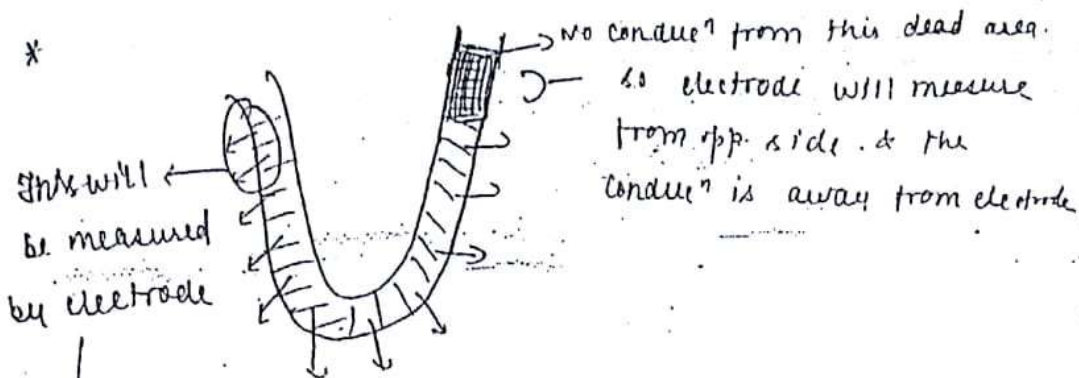


III — Subacute → ST ↑ + T inversion.



IV — Chronic → path. Q wave → >1 mm.
(infarct)

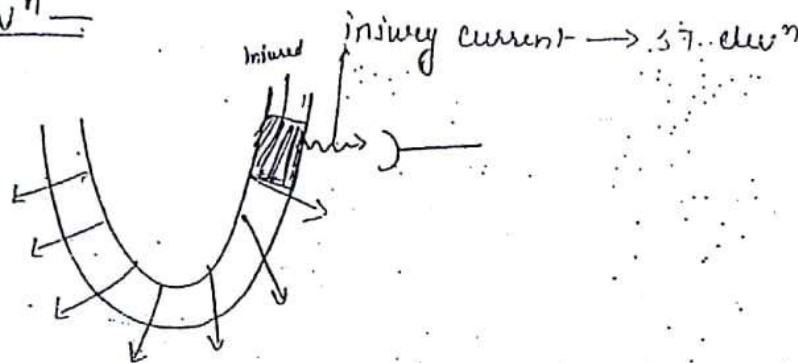
→ Hallmark of STEMI



↓
pathological Q wave

↓
signify that myocardium is dead.

* ST elevⁿ —



ST elevⁿ signify —

- myocardium is live
- Salvageable
- Immediately do thrombolysis, Reperfusion:

* If ST ↑ + Q wave → Reperfuse to salvage live myocardium.

7

ST elevation —

- 1) Acute STEMI
- 2) Acute pericarditis

Difference —

STEMI

- 1) IMI

Pericarditis

- 1) mcc- viral

• H10 viral infection

(mcc of adult GE — Norwalk virus
children GE — Rotavirus)

• mcc of GE — viral > bacterial

- 2) Chest pain → Ischaemic pain

- locⁿ — central

- character — crushing

- 3) Radiation — • Radiate to T₁ - T₅ dermatome.

• Radiaⁿ to jaw, neck,
↓ shoulder

Phrenic N. (C3-5)

↓
irritated b/c of diaphragm.

- Can mimic GERD in case of inf. wall MI which irritate GE junction.

- 2) Non ischaemic pain

- Central

- Pricking

- Radiate to trapezius

4) On examinⁿ—

• Can be unstable

• • ⊖

ECG!—

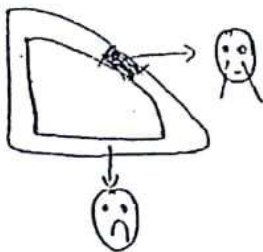


similar sign—



Toombstone appearance

• Reciprocal ST ↓



pericarditis

• stable

(no pur. edema, shock)

• Pericardial rub.

Global ST ↑



concave (convexity facing down)

90 real time ECG - ST ↑ seen in inf. & lateral wall.

⊖

• PR segment ↓

• TP segment downsloping
↓
spodick sign



(8)

STEMIST $\uparrow$ — ~~1st line~~ — NSAIDPericarditisST $\uparrow$ — NSAID 1stColchicine 2ndsteroids 3rdST $\uparrow$ — causes

- 1) Ac. STEMI
- 2) Acute pericarditis
- 3) vasospasm —
 - I) Prinzmetal angina (1st)
 - idiopathic vasospasm
 - mc RCA affected
 - II) Takotsubo cardiomyopathy
 - III) cocaine
 - vasospasm
 - ST $\uparrow$
 - DOC — NTG + diazepam
 - CI $\rightarrow$ inotropics are CI in all

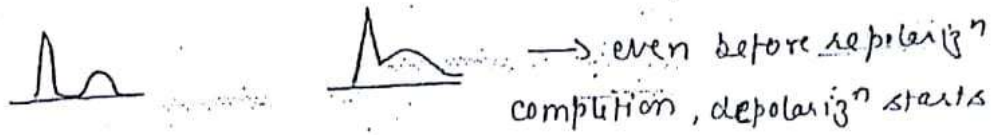
4) LBBB / RBBB

- 5) spectral :-
 - ① Brugada Syndrome (SCN 5A)
 - ↓
 - can die during rest
 - this channel is involved in Brugada
 - this gets mutated

finding — Atypical RBBB $\pm$ ST $\uparrow$
 - seen in $V_1, V_2 \pm V_3$

② ERS (early repolarizⁿ syndrome) —

— occur in adult



③ LV aneurysm → Persistent ST ↑ even after t/t of STEMI.

④ myocarditis → usually ST ↓ & T inversion
L rarely — STEMI.

Causes of ST elevⁿ! —

E — electrolyte imbalance like hyperkalemia

L — LBBB, LVH

E — early repolarizⁿ variant

VA — ventricular aneurysm

T — Trauma (pericardiocentesis), Takotsubo

I — injury like AMI

O — Osborne waves (hypothermia)

N — non occlusive spasm (Prinzmetal angina)

of B — Brugada

P — Pericarditis

⑨

Heart rate —

$$\frac{300}{\text{no. of large boxes b/w 2 R-R interval}} = \frac{1500}{\text{no. of small boxes}}$$

Bradycardia = > 5 box

Tachycardia = < 3 box.

P wave — 1) (N) — 0.1 sec.

2.5-mm = on both x & y axis



1) width ↑ →
in left atrial
enlargement

→ P mitrale
[LAE previously — MCC RF
now — MCC syst. HTN]

2) length ↑ (1.2-5)



→ P pulmonale

* MCC Pul HTN

2) Best lead to see P wave — II > V₁

PR interval — • 0.12 – 0.25 sec. (3-5 small square)

< 0.125 (< 3 small square) → short PR → caused by tachycardia

> 0.25 (> 5 small square) — Prolonged PR
— mce. bradycardia

QRS duration — (M) — < 0.11 sec. (3 small sq.)

< 3 small sq.

↓
narrow QRS

↓
Normal

stimulates
faster conduction.

> 3 small square

↓
wide QRS

↓
Pathological

→ conduction through ventricle
bypassing (M) conducting pathway.

cause — ① BBB

② ventricular origin of
QRS.

QT interval —

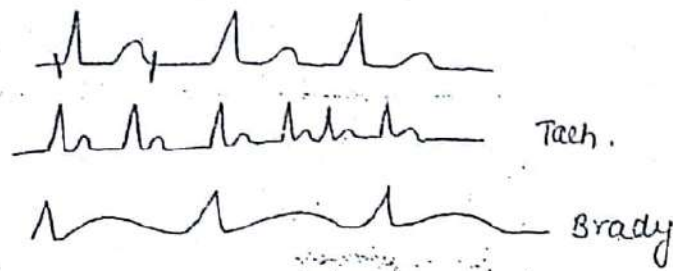
• (contain 2 waves)

• QRS complex + T-wave.

• Depolarizⁿ + Repolarizⁿ
(ventricle)

• Bias : — qt changes ∝ heart rate.





Corrected QT $(QT)_c = \frac{QT}{\sqrt{R \cdot R}}$

Bazett's formula — $\frac{QT}{\sqrt{R \cdot R}}$

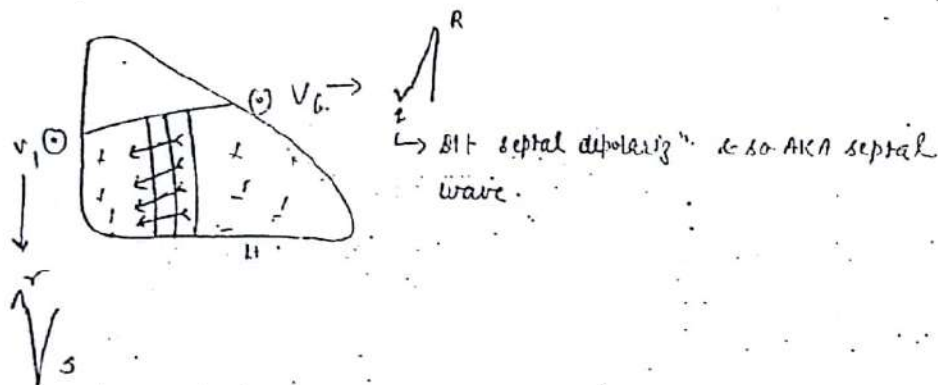
$QT_c = 0.35 - 0.45 \text{ sec.}$

< 0.35

Short QT

> 0.45

Long QT → sudden death



* Any +ve wave — R

* Any -ve wave — $\begin{cases} \text{Bit +ve R} - Q \\ \text{Att +ve R} - S \end{cases}$



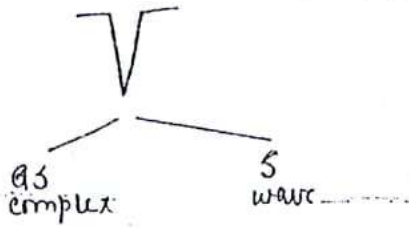
R5



aR



V5



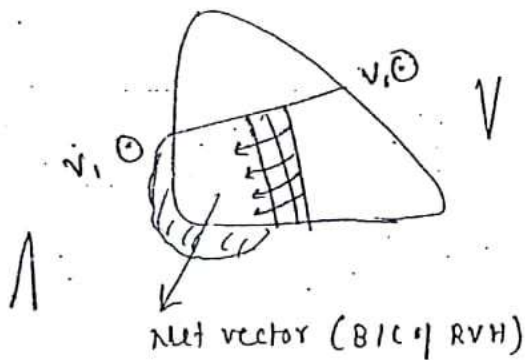
* Septal hypertrophy $\rightarrow$ Pathological Q wave $\oplus$
(α -HOCM) (≥ 2 mm)

This is pseudoinfarction pattern.

Sokolov Lyox —

* $SV_1 + RV_1 \geq 35$ mm = Lt. ventricular hypertrophy.

* $RV_1 + SV_6 \geq 25$ mm = RVH.



(11)

RBBB → wide QRS ← LBBB
 $> 0.11 \text{ sec}$
 $(> 3 \text{ small sq.})$

① see V_1

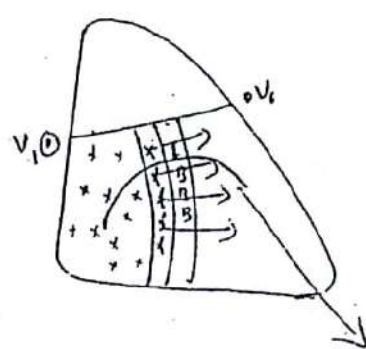
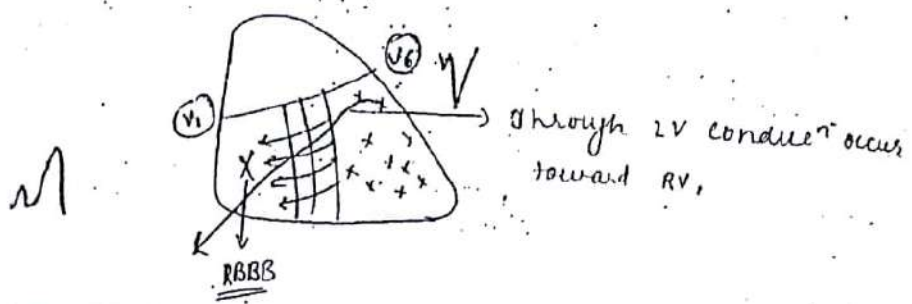
② 
 ↓
 RBBB

$\sqrt{\text{③}}$
 ↓
 LBBB

④

WILLIAM
MARRON

⑤



Here R1. side of septum
depolarize 1st b/c there is
LBBB.

RBBB → Both BB supplied by
LDC artery

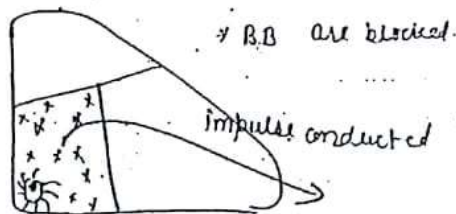
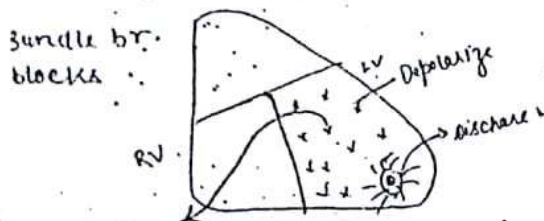
LBBB

- ① old age
- ② IHD
- ③ Acute MI
- ④ Severe heart failure
↓
DCMP
- ⑤ RVH causes
↓
RBBB

- ① old age
- ② IHD (mc)
- ③ Acute MI (mc)
- ④ Severe heart failure
↓
Dilated cardiomyopathy
- ⑤ LVH causes
↓
LBBB

⑥ Vent. tachycardia / Ventricles
premature contracⁿ

⑦ VT / VPC



This pattern of vector mimics
RBBB ⇒ wide QRS

- mimics: RBBB
- wide QRS

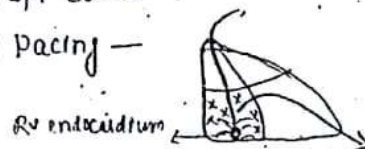
(even the rate of discharge is less but speed of conducⁿ is less)

⑧ Spl. causes —

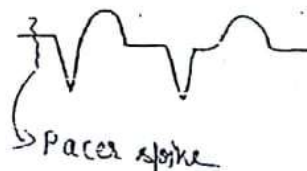
⑧ spl. causes

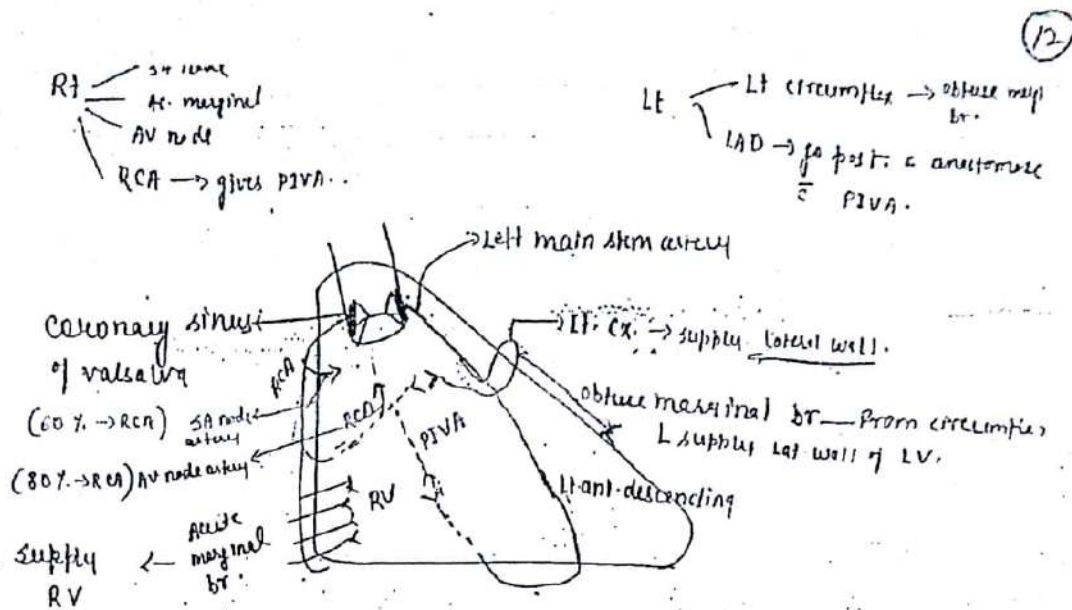
1) Brugada syndrome — atypical
RBBB +
ST elevⁿ

1) Pacing —

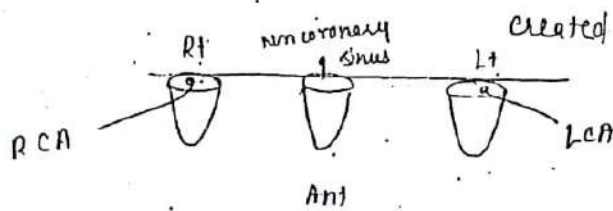


2) Ac. pulmonary embolism —





* When aortic valve open — 3 cusps open & 3 sinus



* RCA + PIVA → supply post. wall
• AV node

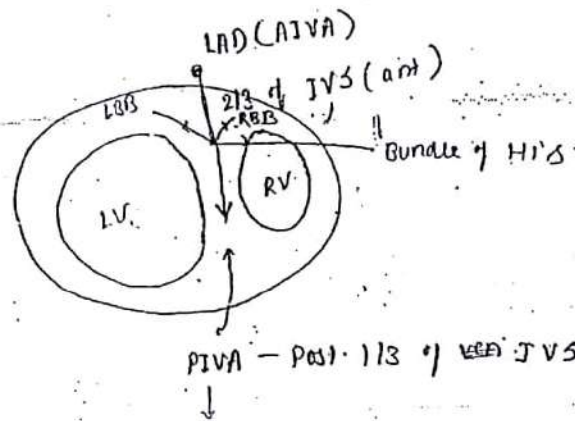
* Acute marginal br. → supply inf. wall.

* LAD — Ant. wall + apex of LV.

↳ more apt to harbour atherosclerotic plaque

* LCx → least to harbour atheroscl. plaque

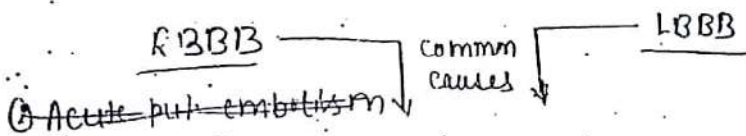
↓
so isolated it - wall m. is least common.



90-95% pt. PIVA is Rt. dominant

~25% pt. PIVA is Lt. dominant i.e. from
Left ant. descending

~5% PIVA is from both RCA & LCA, it
is codominance.

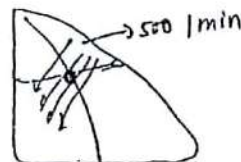


① ~~Acute pulmonary embolism~~
① Hyperkalemia

(not caused by Hypokalemia → it doesn't cause any
problem in conducⁿ)

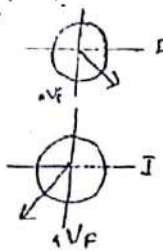
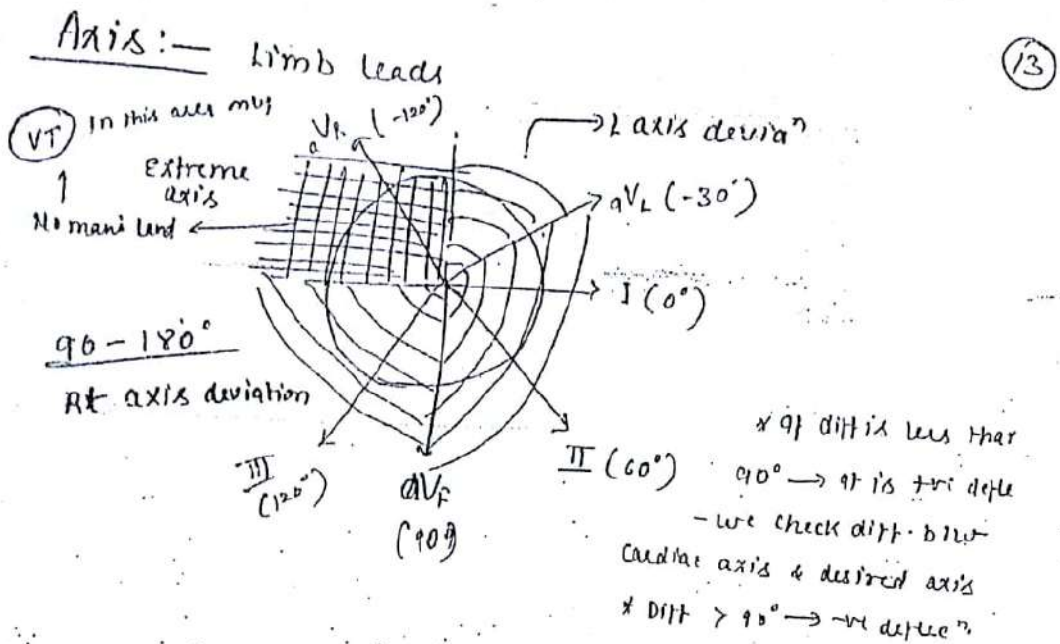
② Ashmann syndrome → occurs in atrial fibrillation.

Some BB go to
refractoriness to
prevent ventricle
arrhythmia.



RBBB >>>>>> LBBB → 91 has 2 fascicles & so it

Can't ~~cause~~ compensate more efficiently & so LBBB is ↓ common.

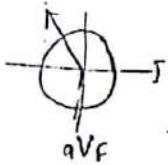


I
+

aV_F
+

(N) axis

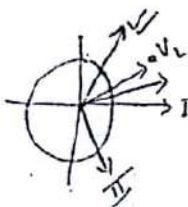
Rt axis



-

-

N-W axis



+

-

Lt axis

+

-

(N) axis

L axis $\leftarrow$ -ve

(II)

$\rightarrow$ check lead II & aV_L

(N) axis $\leftarrow$ +ve

if L b/w aV_L & II is $> 90^\circ$ - Lt axis

L b/w aV_L & II is $= 90^\circ$ - (N) axis

Causes -

Rt-axis devia?



- All causes of RBBB

Lt-axis devia?



- All causes of LBBB

Not anatomical
shifting of
heart
physiologically

- Dextrocardia
- Tall & thin individual
- Pediatrics

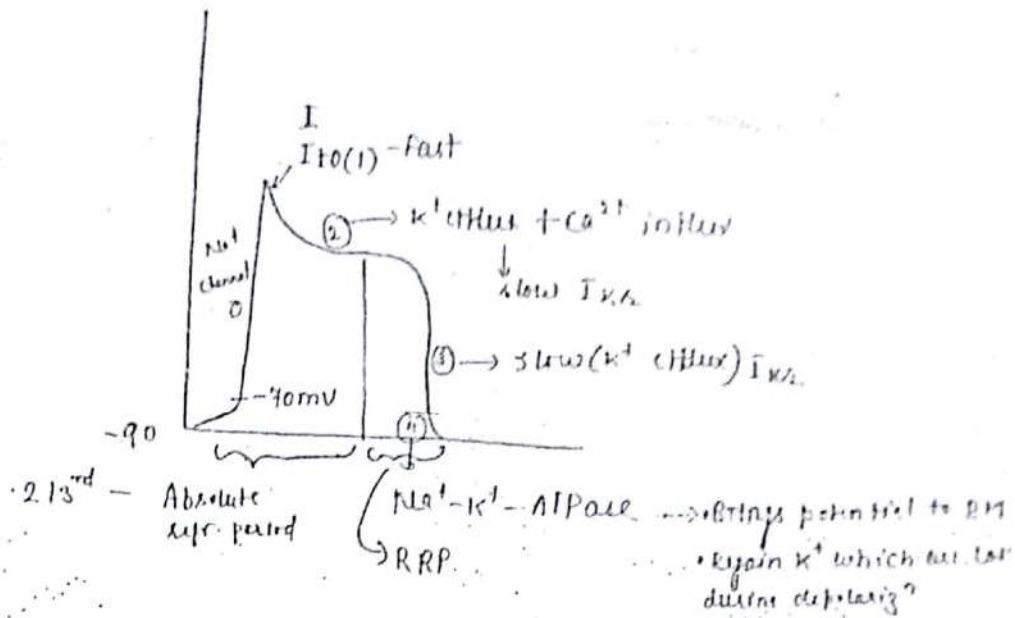
• massive pleural
effusion / pneumothorax
of Lt side.

Rt side

- ← Pleural effusion
- ← pneumothorax.

(14)

QT interval



Channel - Holes in cell along which ions move across conc. gradient.

Pump -> Na⁺-K⁺ pump - work against gradient using ATP. At pump K⁺ inside & Na⁺ outside.

-> 3 : 2 Na⁺ K⁺ in -> so inside cell there is net -ve
out
↓
so it is aka hyperpolarizing pump.

⊖ of pump - (1) Digitalis.
(2) ouabain

* ERP = ARP + RRP -> suprmaximal stimulus can trigger new depolariz?



Phase 0 - QRS

Phase 1-2 - ST segment

Phase 3 - T wave

* RRP is vulnerable period. i.e. any supramaximal stimulus will cause action potential.

* vulnerable period in ECG - T wave

R' on T wave - Dangerous

• Depolarizing wave formed during RRP & myocardium can stimulate leading to malignant arrhythmia.

QT interval - = ERP = ARP + RRP

- From begining of QRS complex to end of T wave.

* on QT → ~~the~~ ↑ the RRP there is more RRP
i.e. more vulnerable period & so sudden cardiac death can occur.

- Here proportionately ERP also ↑ing.

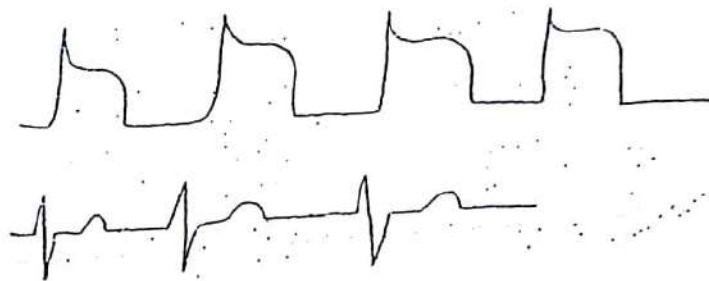
(15)

Congenital long QT syndrome — take long period to repolarize

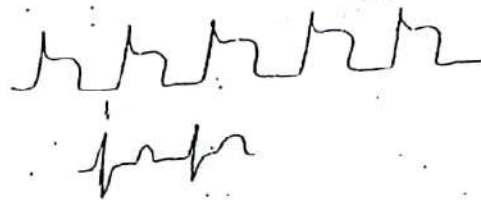


↓
so ↑ RRP
↓
sudden death

(N)

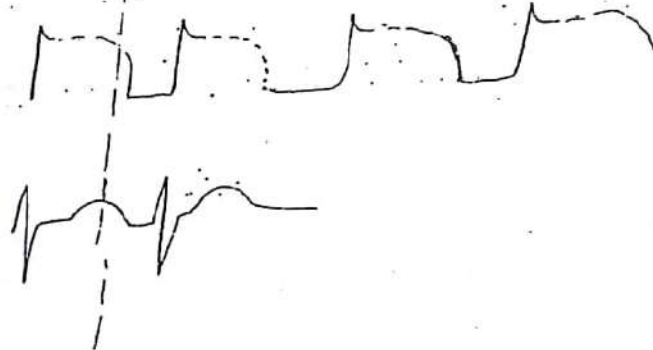


Tachy



(N) pacem
can shorten
AP.

QT ↑ —



These pt. can't shorten AP & so impulse fall on RRP.

β_x — T02 is β -blocker $\rightarrow$ q7 control heart rate.

Long QT — causes

① Cong. long QT syndrome —

Jervell Lange Nilson $\rightarrow$ c deafness

Romano ward syndrome

② 4 Hypo's —

- Hypokalaemia
- Hypocalcaemia
- Hypomagnesaemia
- Hypothermia

③ Drugs —

- ① Antihistaminic (Terfenadine banned)
- ② Quinolone $\rightarrow$ later generⁿ (gatifloxacin banned for systemic use)
- ③ Antipsychotics $\rightarrow$ later generⁿ
- ④ macrolide — newer generⁿ
- ⑤ Antiarrhythmic — Ia / Ic / III (max^m risk)

✓
affects
Ito
(transient outward
channel)

↓
affects I_{Kr}

(16)

* charact. arrhythmia $\bar{c}$ QT prolongⁿ is Torsades
pontis / poly. ventricular tachycardia.

* Amiodarone is very broad spectrum, can be used
in any tachyarrhythmia except Torsades pontis.

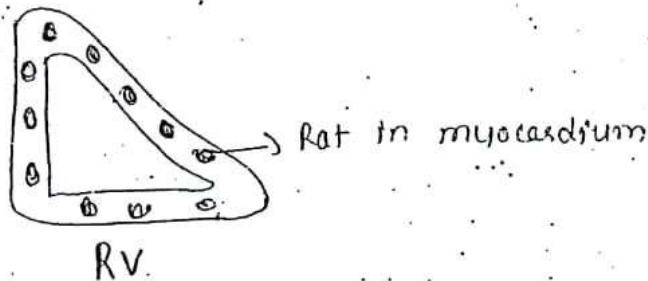
Here Doe is $MgSO_4$

- Short QT —
- 1) Cong. short QT syndrome
 - 2) Hypercalcaemia
 - 3) Hyper K^+ (early)
 - 4) digoxin

Sp. waves —

- 1) J wave / Osborn wave — seen in - Hypothermia
- Hypercalcaemia
 - 2) S wave — WPW syndrome
 - 3) E wave — ARVD (ARVA) (arrhythmogenic RV dysplasia)
- * Pat in myocardium:

sis → MRI



* ARVD + cong. palmo/planta hyperkeratosis
(Naxos syndrome)

↓
IOC- MRI

(17)

- Bradycardia -

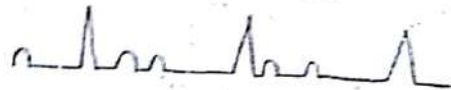
- No of large boxes ≈ 5 .

→ AV bradycardia can sometimes cause $\odot$ H.R.

AV block — 1° AV block —

On ECG PR interval shows activity of AV node.

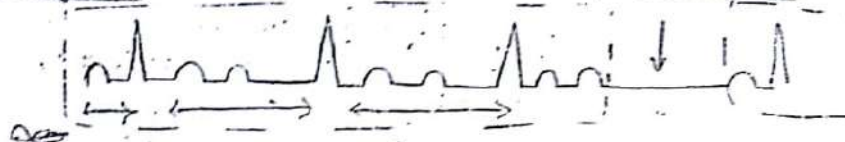
- PR interval prolonged.



2° AV block — Mobitz (I) / Wenckebach

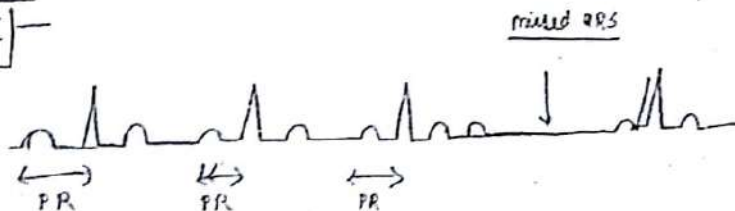
Mobitz (II)

Mobitz I → Grouped beat



→ progressively PR interval ↑.

Mobitz II —



- 3 PR interval remains constant only 1 of the impulse is not conducted.

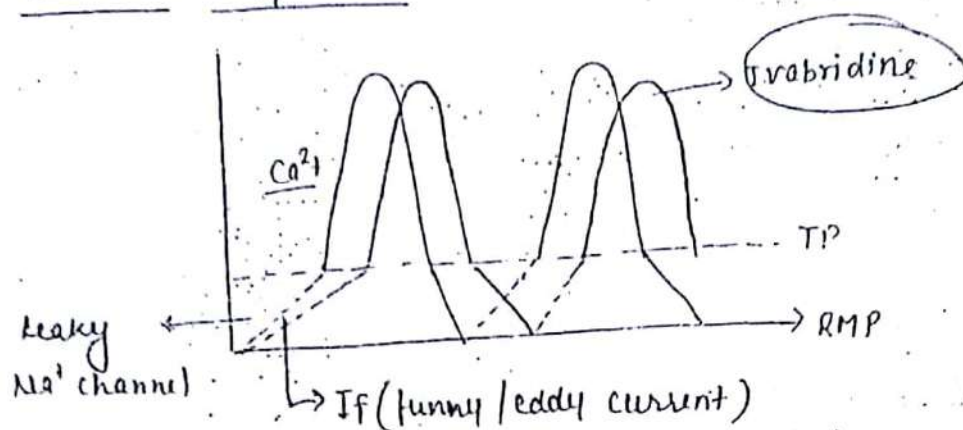
3° AV block — (complete heart block)

- SA node continue to send impulse even though AV node is not functioning.



Sequential P wave at P-R interval

Pacemaker potential —



* Funny channel $\ominus$ by — Ivabridine $\rightarrow$ + 1 time to reach TP.

uses — 1) sinus tachycardia

H.R should be > 70 before only then Ivabridine can be given.

2) 3rd line — chronic stable angina.

3) 4th line CCF

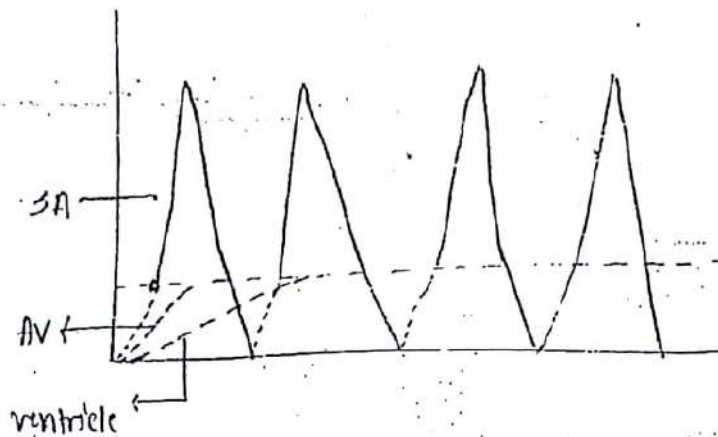
C/I — Bradycardia

S/E — • Vision problem

• Bradycardia

(18)

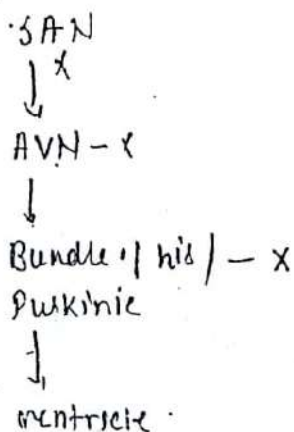
- * (N) SA node generate impulse & rest of the fibres modify to perform conduction function only.



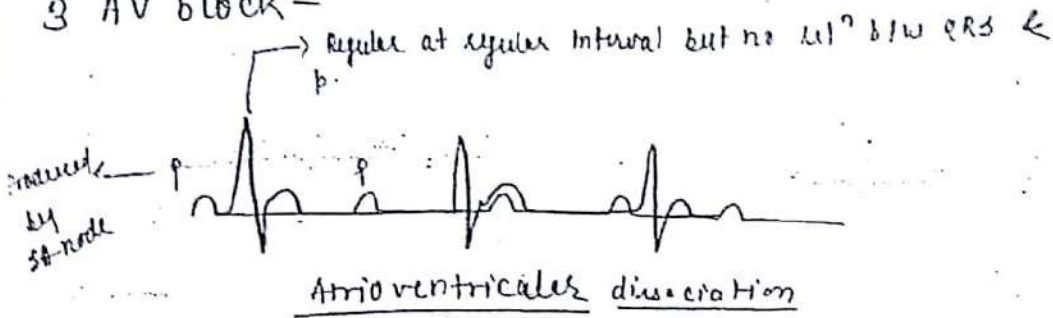
- * SA node is therefore dominant node bcz when SA node has reached TP, AVN & ventricle still not reached TP.

- Thus SAN inhibits the ^{pacemaker} activity of AVN & ventricle.
↳ causes overdrive suppression → any pacemaker $\bar{c}$ max^m rate of firing will be dominant.

- * escape rhythm → They produced when one pacemaker fails the other pacemaker takes over.



3° AV block -



→ As AV node is not working → separate P & QRS waves formed. + there is no relⁿ b/w them.

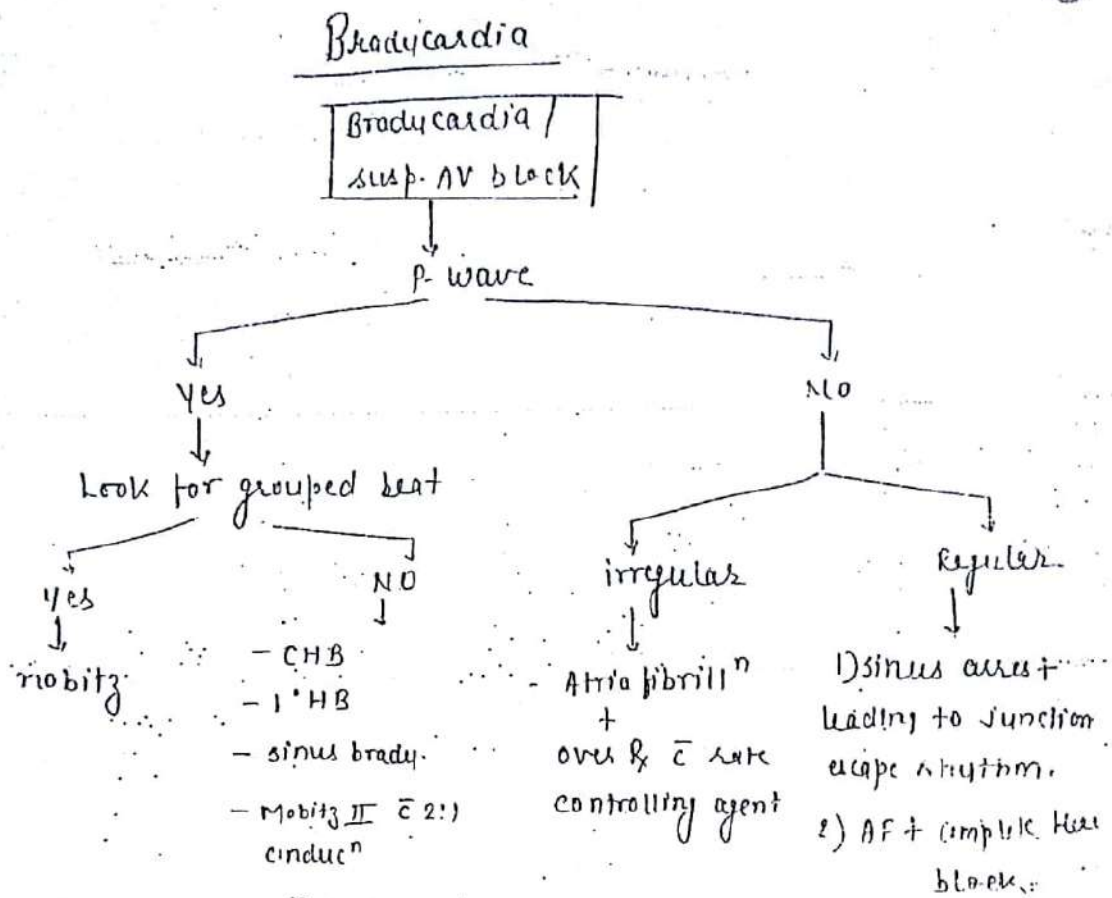
SA node — at high rate → produce P wave
QRS complex → dit ventricle / bundle block.

* Digitalis can't produce Mobitz II.

→ it can produce any type of arrhythmia.

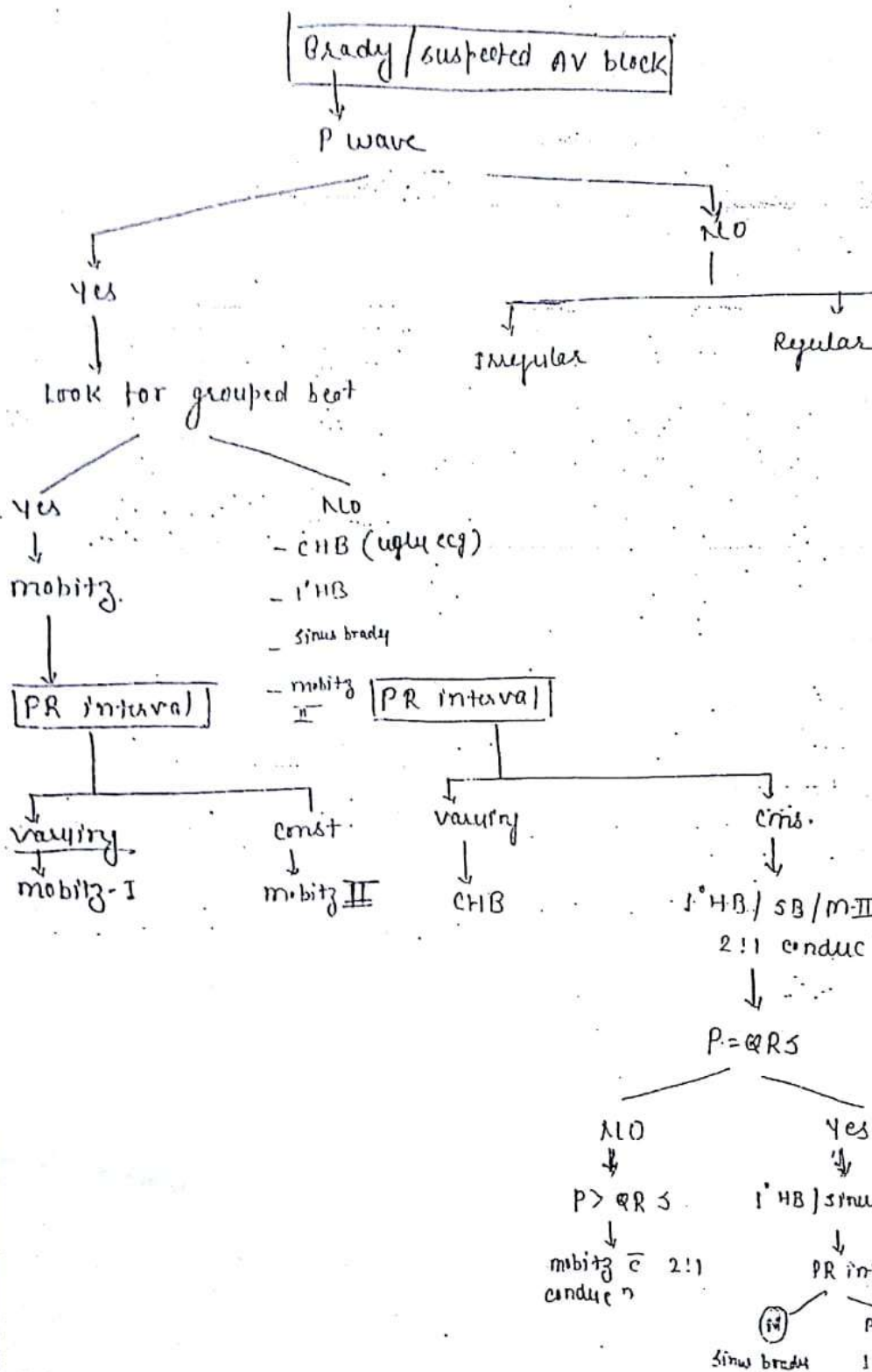
~~watch back~~ →

(19)

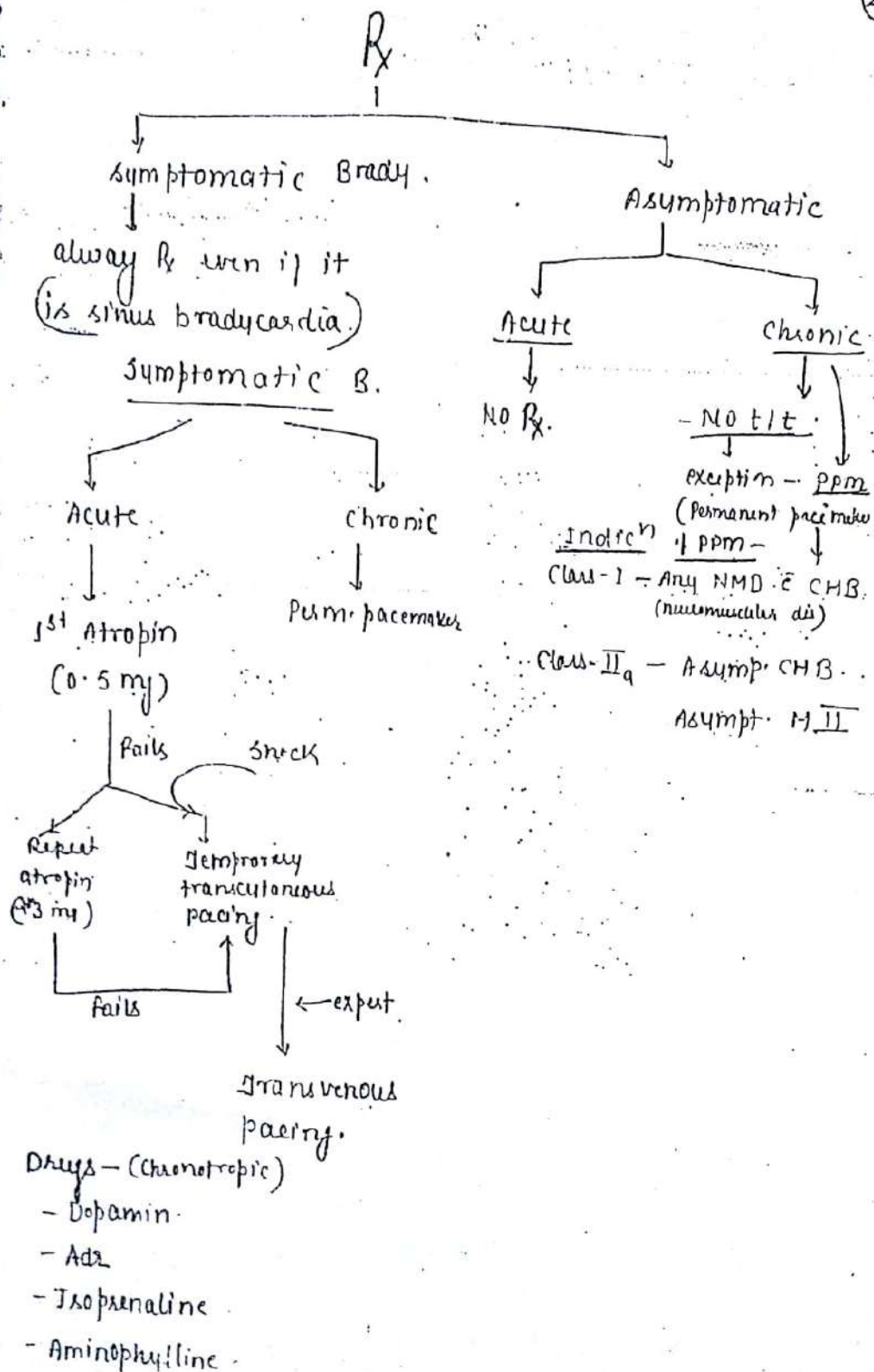


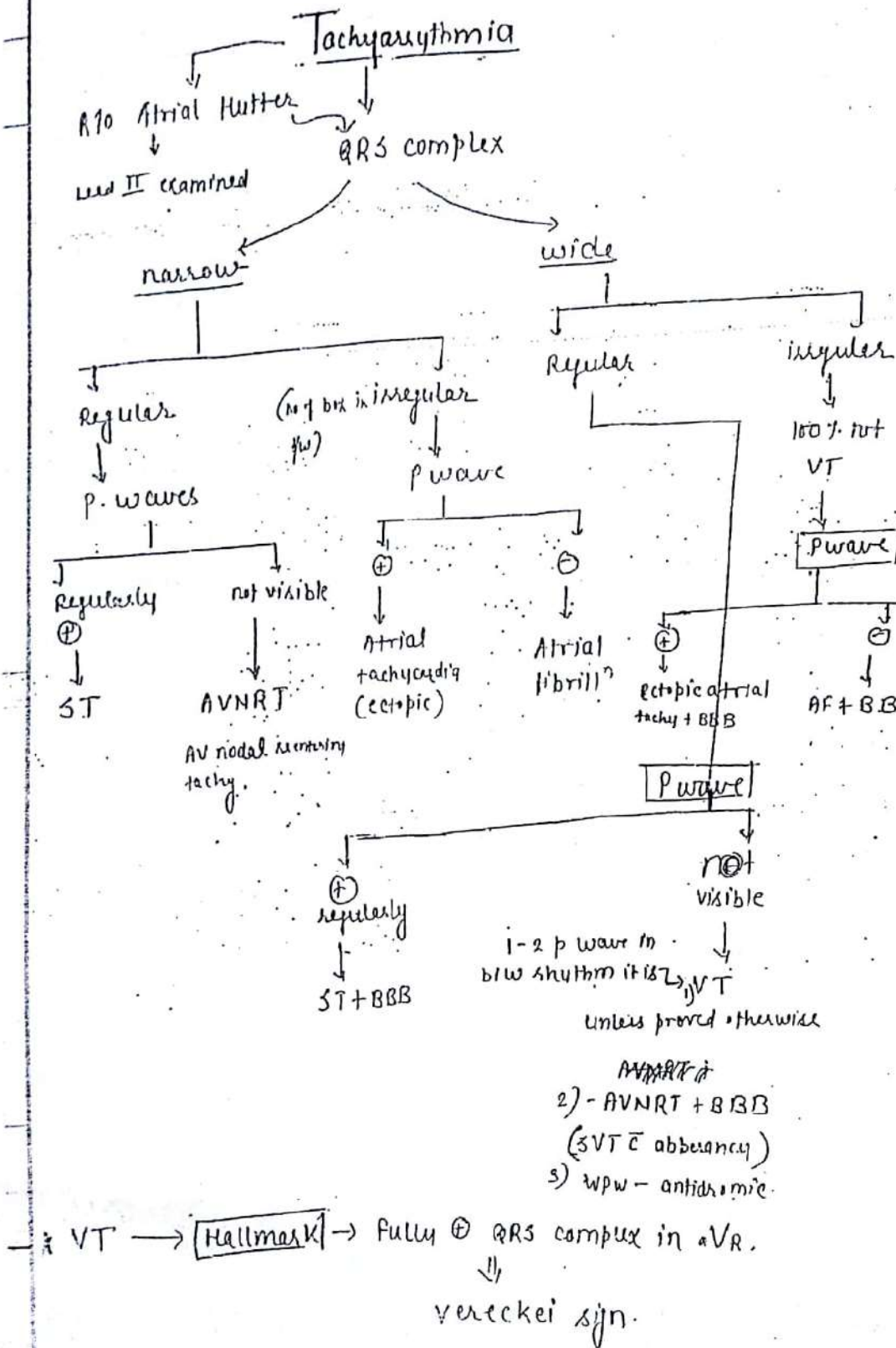
* After Atrial fibrillⁿ if there is regularizⁿ of rhythm it signifies there is complete heart block & its cause is over the $\bar{c}$ digoxin.

3:1 →



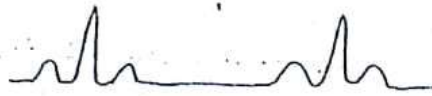
(20)





(21)

* QT-



→ B/w 2 R-R interval draw a line

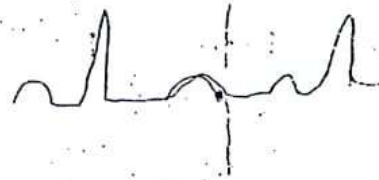
↓
at end of T wave

Inside this
midline

↓
(N) QT

outside
midline

↓
(M) QT



(M) QT

→ Pt should not have tachycardia

while calculating QT from this method.

* Atrial flutter —

saw tooth wave / -ve p waves / F waves —



* Hallmark of Torsades —

- Can't differentiate b/w +ve & -ve complex.

- Alternate bigger & smaller ^{group of} wave.

* monomorphic tachycardia —

- Here +ve & -ve complexes can be seen.
- Notching seen. here & not in polymorphic VT.
- Nothing give direct of complex. $\uparrow \uparrow$

— AVNRT — ascending

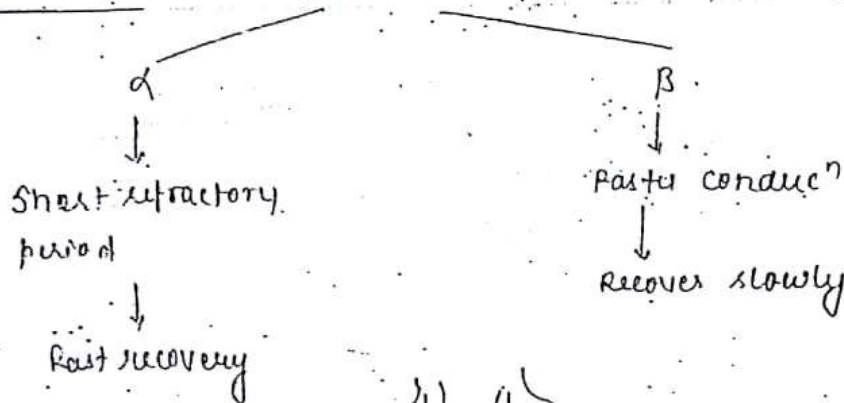
• mc mechanism of arrhythmia — Reentry.

- AVNRT is prototype of ~~AVRT~~ reentry.

Pre requisit for reentry —

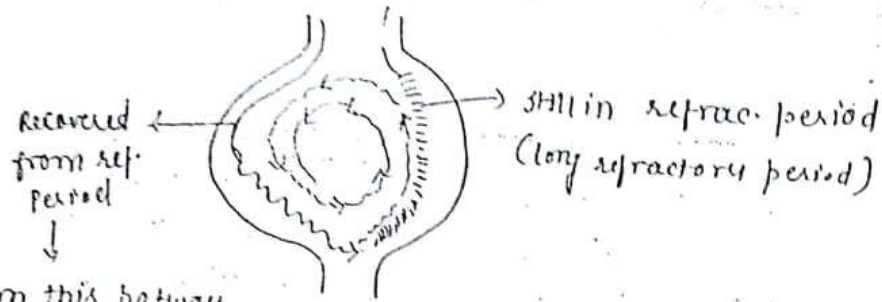
2 different circuit & 2 diff. physiological property.

AV node — 2 pathway.



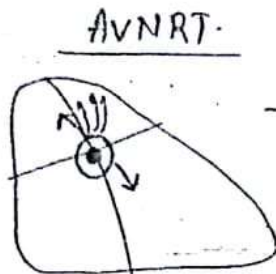
(22)

- * PAJ - premature atrial impulse.
- it is a m. imp. trigger for AVNRT
- it comes before next heart impulse



So from this pathway
PAJ will travel.

↓
PAJ will travel slowly
as it is a slow impulse & by this time the β pathway
will be recovered from refractory period, so impulse
will go along this pathway.



- Impulse is thrown simultaneously to Atria & ventricle.

1) * This circuit is very short & so less time is taken for completion of 1 ^{Impulse} ~~cycle~~ so there is tachycardia.

- Rate = 140-180 b/min.

2) * Impulse is conducted through ^(N) pathway in ventricle.

AVN
↓
Bundle of His
↓
Bundle br.
↓
Purkinje fibre

3) Impulse is trans. to SA node & it get suppressed (as rate of impulse = 140-180/min)

4) Atrium is depolarizing & so even though SA node is not working 'p' wave^{all} produced dlt atrial depolarizⁿ. but they are not visible as they are buried in QRS complex.

5) There is retrograde depolarizⁿ of atrium & so p waves formed are inverted.

(23)

CIF — • Benign rhythm — doesn't cause much problem

• mc complain — palpitation (resting palpitation)

Prox sign — simultaneous contracⁿ of atria & ventricle

↓
tricuspid valve close

↓
blood from atria goes to great vein

↓
Prox sign: $\leftarrow$ JVS $\uparrow$ each beat

— similar to cannon A wave.

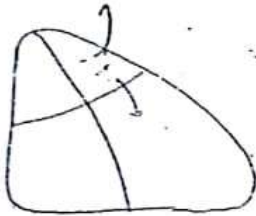
* in any tachycardia — Diastole time ↓

↓
less time for filling

↓
1) — less filling of ventricle

↓
↓ output

↓
— shock, hypotension, syncope



2) Blood go to pul. vein.

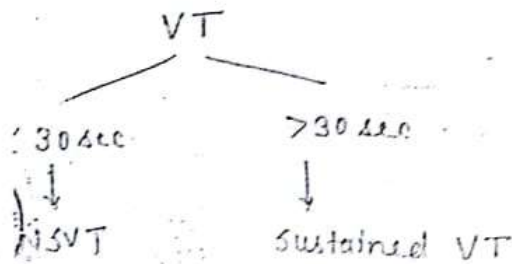
↓
pul. edema

3) coronary blood flow ↓

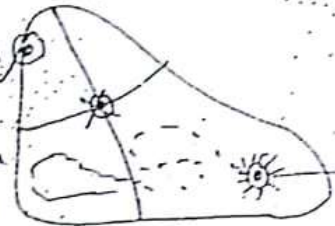
↓
MI

VT

Defⁿ - ≥ 3 VPC's at rate of 120/min
consecutive



Hallmark of VT -

working $\leftarrow$ SA  Rate = 200/min
SA node works bcz
none of the ventricle
impulses has reached
to atria & so, SA node doesn't know anything.

$\downarrow$
P wave produced bcz of atrial depolarizⁿ & they are also
produced regularly.

$\downarrow$
~~vent~~ none of the P wave conducted to ventricle as
the AV node is blocked.

$\downarrow$
 $\therefore$ There is A-V dissociation.

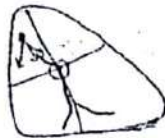
$\downarrow$
① P wave seen buried in QRS.



(24)

② Verrecks sign - fully ⊕ aVR

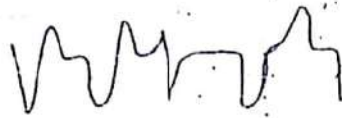
③ Capture beat - very rarely for a fraction of microsec



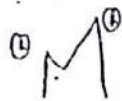
SN node impulse trans. through
④ conduction pathway when
bundle br. are in refractory period

* only 1 normal wave seen on ECG.

→ Fusion beat - q is in b/w sinus impulse &
VT impulse.

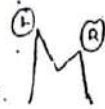


④ Rabbit ear (LV VT)



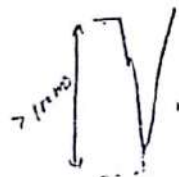
Gal R
↓
RBBB / VT

~~Bugada sign (RV VT)~~



Gal L
↓
A → VT

⑤ Bugada sign - RV VT



Dist b/w starting pt. of QRS & nadir
is > 100 ms → it is VT

* seen in V₁.

Permanent AF →

- multiple attempts have failed & pt. & doctor both accepted that AF is the rhythm.

(26)

A Flutter

- RA
- mc - PHTN
↓
RAE

- Single big macroentry circuit is there.
- Is running in counter CW rotation → 30 - 40
- P wave seen.
- Rate - 350 - 450
- Less resistant to Rx

Fibrillation

- LA
- mce - 300 - 400
↓
LAE.

- Multiple (microentry)
- 500
- more resistant to Rx.



(27)



(28)

- Pill in pocket —
- young pt
- no risk factor
- recurrent paroxysm AF
- literate people
- no comorbidity
- CHA₂DS₂ — 0

— whenever they feel that the pulse & H.R. become irregular → they take the drug.
↓
Continue their activity.

* Doc. for pill in pocket → Flecainide
propafenone.

Warfarin

Novel anticoagulants

Adv -

monitoring
(INR)

⊖] disadv

Disadv -

Drug interaction

Heparin bridge

⊖] Adv.
⊖]

Adv -

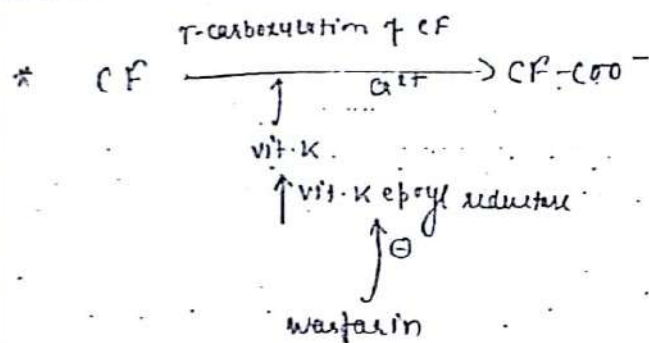
Reversal easy

Difficult (disadv)

↓
DOC - Acute → prothrombin
conc. complex (PCC)

mild-moderate → vit-K

MOA of warfarin



Uses -

AF

valvular

Non valvular

↓
warfarin

↓
warfarin / novel oral anticoagulant

(29)

Anticoagulants :-

Vit-K antagonist → coumadin derivatives →
• warfarin
• Acitrom

Thrombin Θ → Indirect → Heparin → UFH
→ Direct → Hirudin
→ Direct → Lepirudin
→ Direct → Bivalirudin
→ Direct → Argatroban
→ oral
• Dabigatran
• Ximelgatran

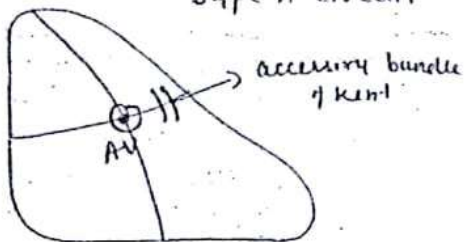
Factor X Θ → Indirect → PE → Fondaparinux
→ Direct → oral → Apixaban
→ Direct → Rivaroxaban
→ Direct → Edoxaban

WPW syndrome if suspect of pre-excitation there is pre-excitation of AV node & AV node delay

- B/w Atria & ventricle apart from AV node there is one more communication $\rightarrow$ accessory bundle of Kent.

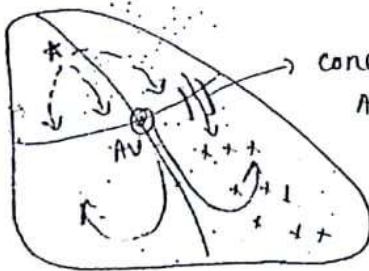
- $\rightarrow$ it is fast
- $\rightarrow$ not dependent
- $\rightarrow$ there are routine conducting fibres

Type A circuit



Type B circuit

B/w RA & RV
there is accessory bundle



conduct impulse immediately & not AV delay.

impulse will directly go to ventricle

& ventricular conduction is slow

1) Short PR ~~segment~~ interval

2) S wave $\rightarrow$ wide QRS for some period

* After some time when AV nodal delay has completed it will conduct impulse around (N) pathway

QRS complex formed

(30)



Precordial leads are used to see this nicely.

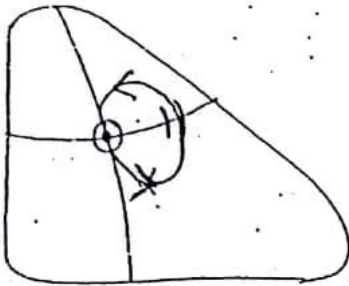
① short PR

② s wave

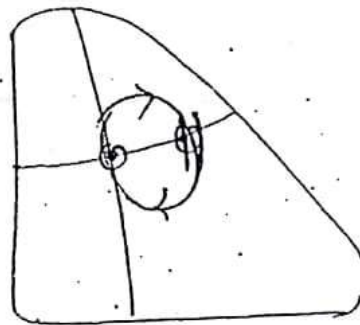
③ T inversion → seen in precordial

→ they are seen only in sinus rhythm, & get lost when there is tachycardia.

*

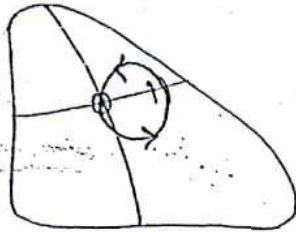


Orthodromic
conducⁿ



Antidromic
conducⁿ

— AVRT → (Atrioventricular reentrant tachycardia,
an pt. w/ WPW → the reentry circuit may cause
tachycardia.

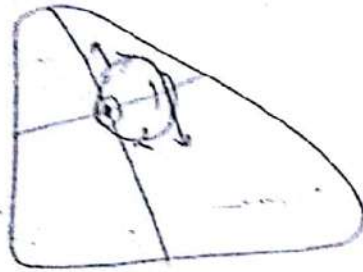


Orthodromic

- 1) → tachycardia → As the circuit is short.
- 2) Narrow QRS — As the impulse from passes from AV node it follows (N) curve.
- 3) SA node suppressed → As the impulse reaches atria, it has very high rate as compared to SA node & so SA node get suppressed.
- 4) Atrium depolarizⁿ → It will occur & can cause p wave which get buried in QRS.
- 5) This type of patientⁿ is seen in AVNRT & can't be differentiated on the basis of ECG.
- 6) T/t — They are treated as AVNRT.
 - A - Adenosine
 - B - P-blocker
 - C - CCB
 - D - Digoxin

— They block AV node & so circuit is broken.

(31)



Antidromic

- 1) Tachycardia
- 2) wide QRS $\rightarrow$ as impulse pass through bundle, it take abn. path
- 3) SA node suppressed
- 4) "Atrium depolarizing" $\rightarrow$ Buried P in QRS
- 5) & like VT as it mimics that

R_x like AVNRT

R_x like VT



Sinus rhythm
achieved



Then only classical manifestation will be
seen like S wave, short PR, T inv.



Then only it can be confirmed as WPW.

R_x - A known case of WPW & AVRT can be
treated with

A

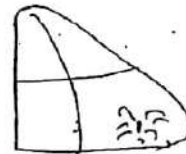
B

C

D

* In case of VT we avoid ABCD b/c impulse

lie in ventricle & there is no
benefit in blocking AV conduction.



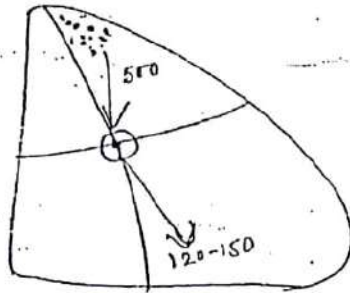
- other than this if we give

CCB it will cause hypotension & pt is already
in shock.

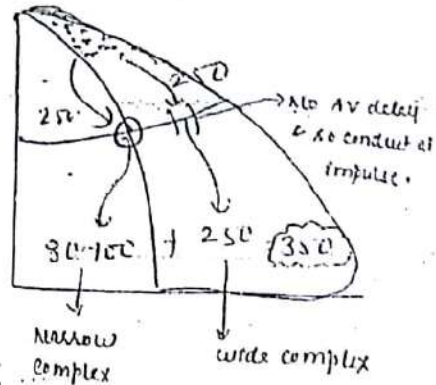
22

WPW in atrial fibrillation

(A) Heart



WPW Heart

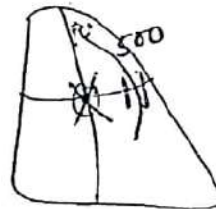


- The waves are mixture of narrow & wide QRS complex.

- There are also haphazard & irregular rhythm.

* $R_x \rightarrow ABCD \rightarrow$ absolutely C.I.

if u give ABCD -



* Doc $\rightarrow$ Na^+ channel blockers
procainamide.
Amiodarone.

* Radiofrequency ablation — done if pt. come repeatedly with AVRT.

LGL syndrome → abandoned.

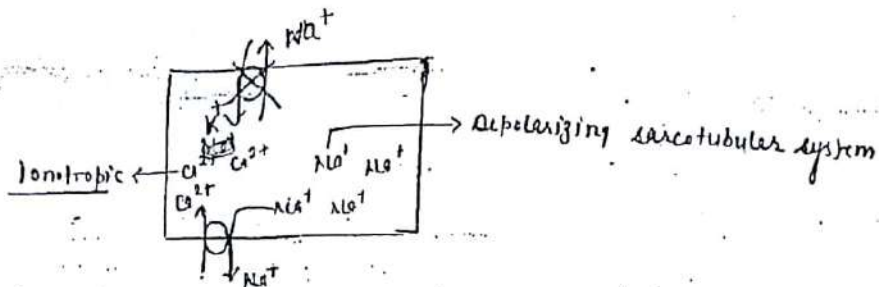
* James fibers ⊕

Mahaim fiber —

Fibers directly conduct from A-V node to ventricle, bypassing ⊕ pathway.

(33)

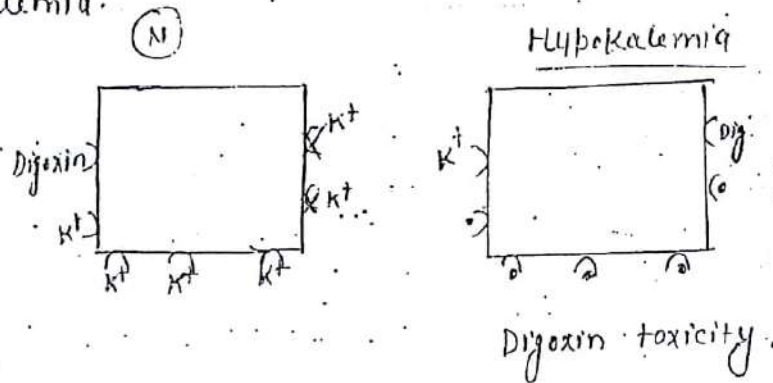
- Digoxin -



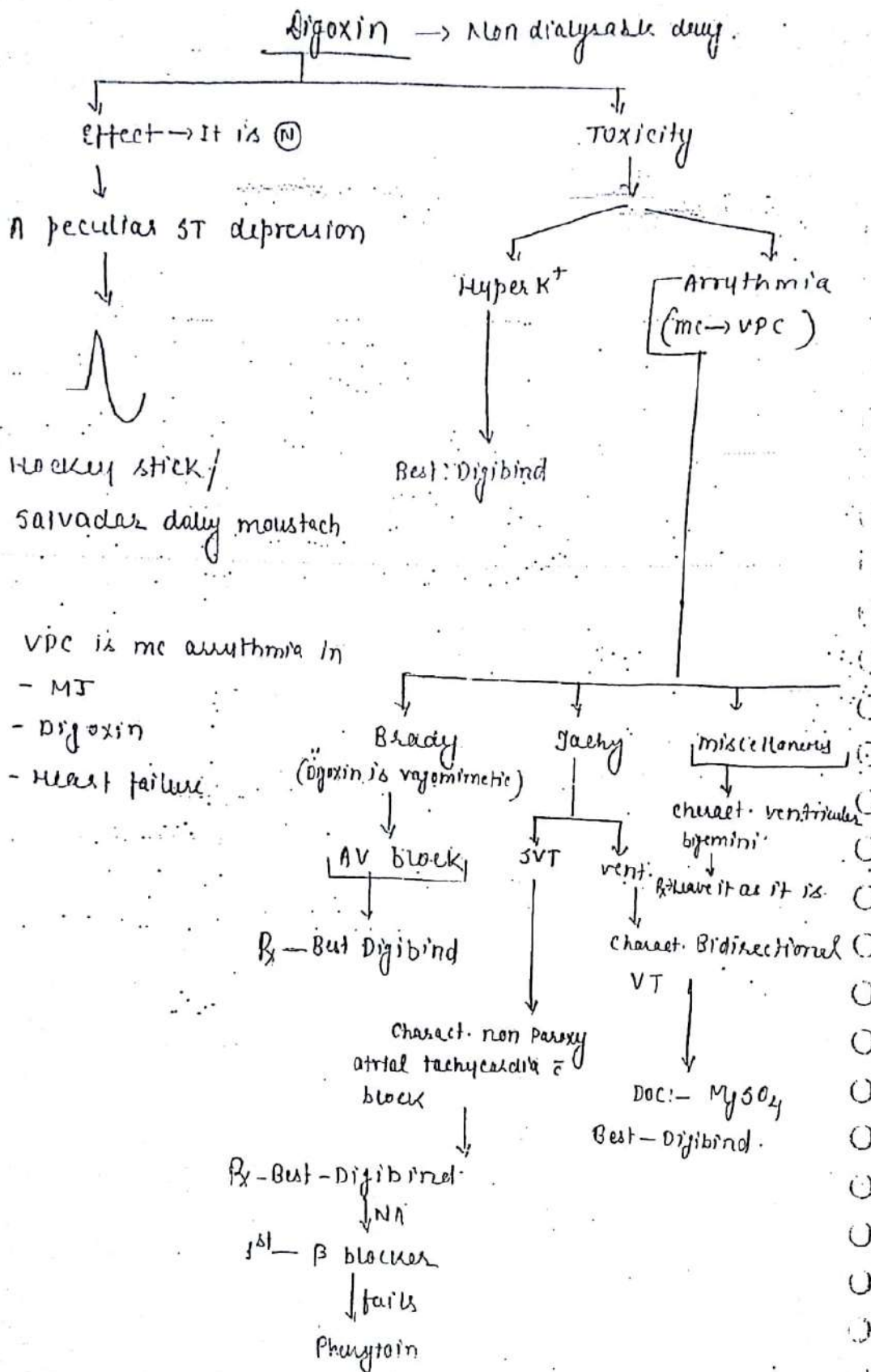
- Digoxin bind to Na^+-K^+ ATPase & block it.

* Digoxin bind to extracellular site of Na^+-K^+ ATPase

→ Digoxin toxicity occur ~~at~~ ~~in~~ in case pt. has hypokalemia.



* In case of Hyperkalemia - if Digoxin is given it further aggravates Hyperkalemia.



(34)

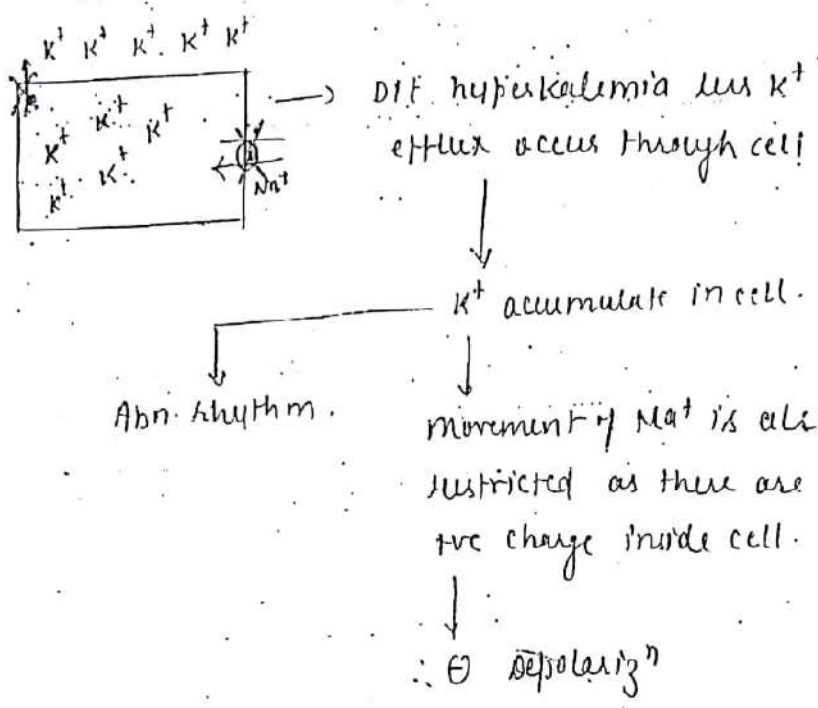
miscellaneous — ventricular bigemini

Electrolyte

1) Na^+ → Not cause any problem

2) K^+

Hyperkalemia — * Blocks depolarization.
* Triggers arrhythmia.



ECG:- R's poorly correlate to ECG

t) ^{1st} — Tall T wave — $\begin{cases} > 2 \text{ large box} - \text{chest lead} \\ > 1 \text{ large box} - \text{limb lead} \end{cases}$

→ Atrium depolarizⁿ affected

↓
p wave - wide

↓ Later

p wave - nt (atrial paralysis)

→ Нуклон K^+

↓
can cause any type of block.

-BBB

- fasc. block

- AV block

→ ventricular depolarization affect → QRS widening

→ sine wave (pre death)

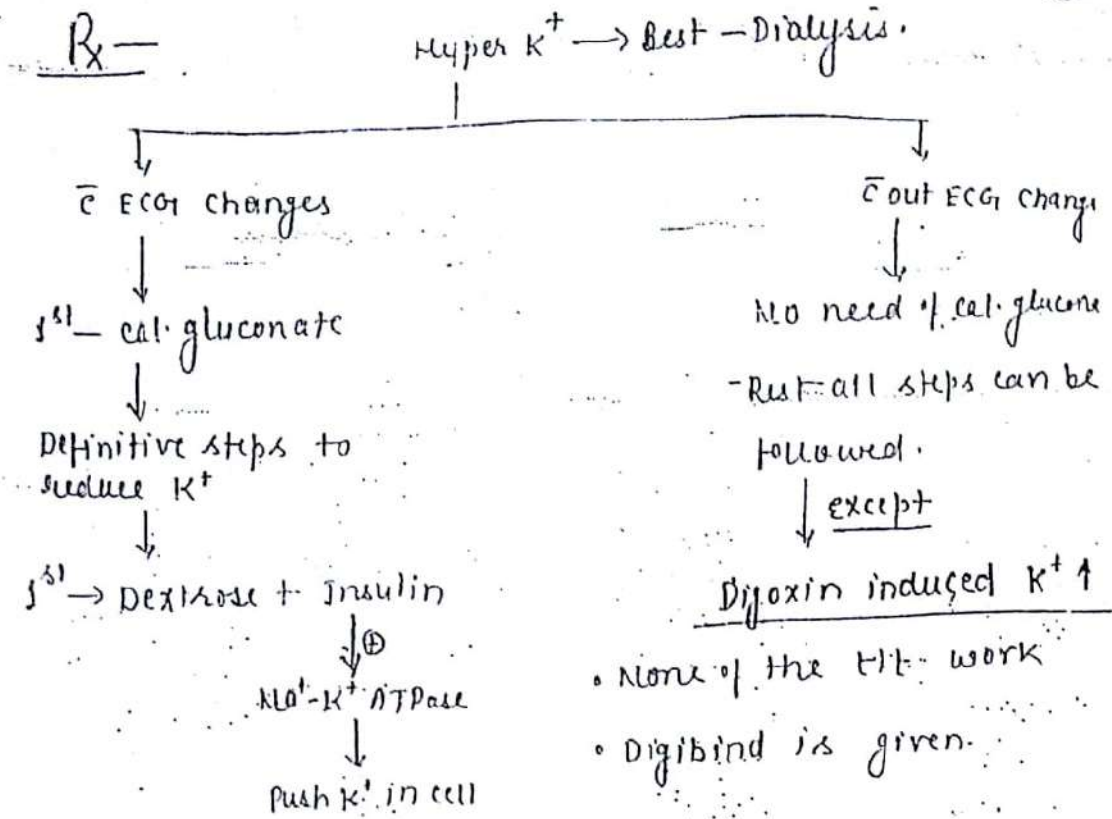
↓ leading to

Arystole

Arystole
(Diastolic arrest as there is no depolarizⁿ, no contracⁿ will occur)

→ Any Hm. there can be VT/VF.

(35)



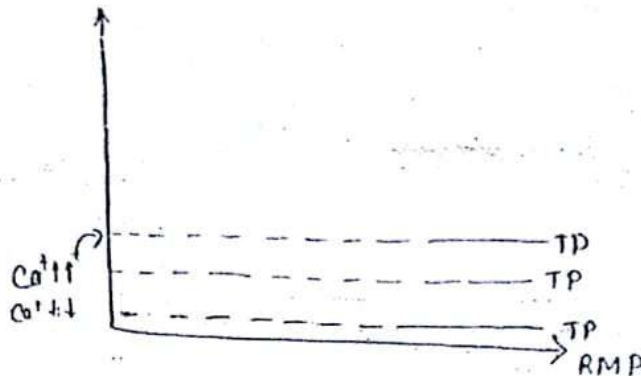
- None of the Ht work
- Digibind is given.

Other → Repeat β_2 agonist nebulizⁿ

• $NaHCO_3$

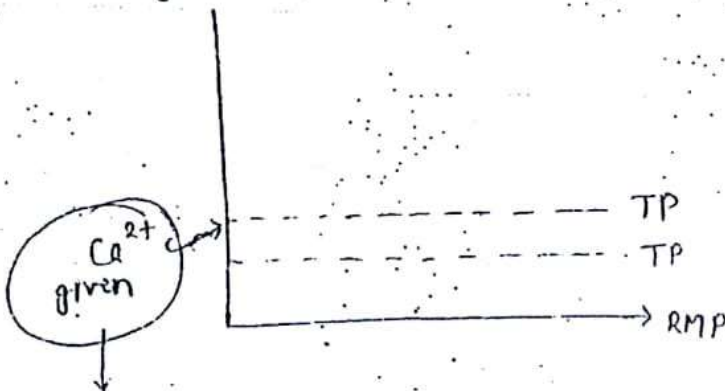
• SPS (K^+ binder)

↓
an higher doses carbonic needsis /
perforation occurs.



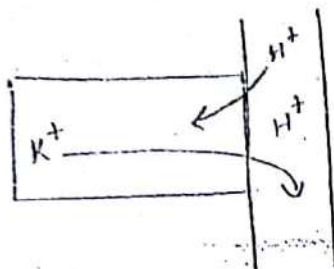
∴ Hypo Ca^{2+} causes tetany.

* Why Ca^{2+} given in Hyper K^+

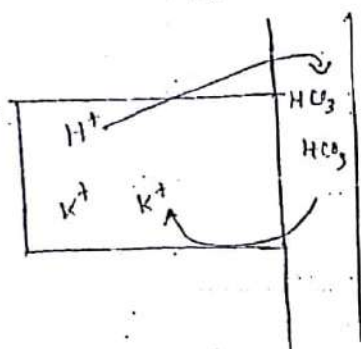


This can shift TP & so we get time to stabilize membrane.

(36)



Acidosis
↓
causes Hyperkalemia



Alkalosis
↓
Hypokalemia

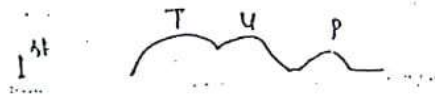
Hypokalemia → mce diarrhoea
* colon secretes K^+

EKG change —

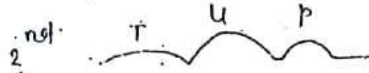
1) 1st → 'u' wave (pathological)



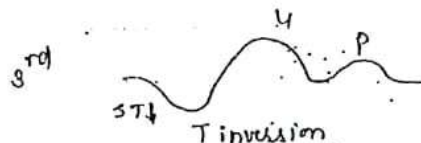
Normal



Pathological



Flattening of T

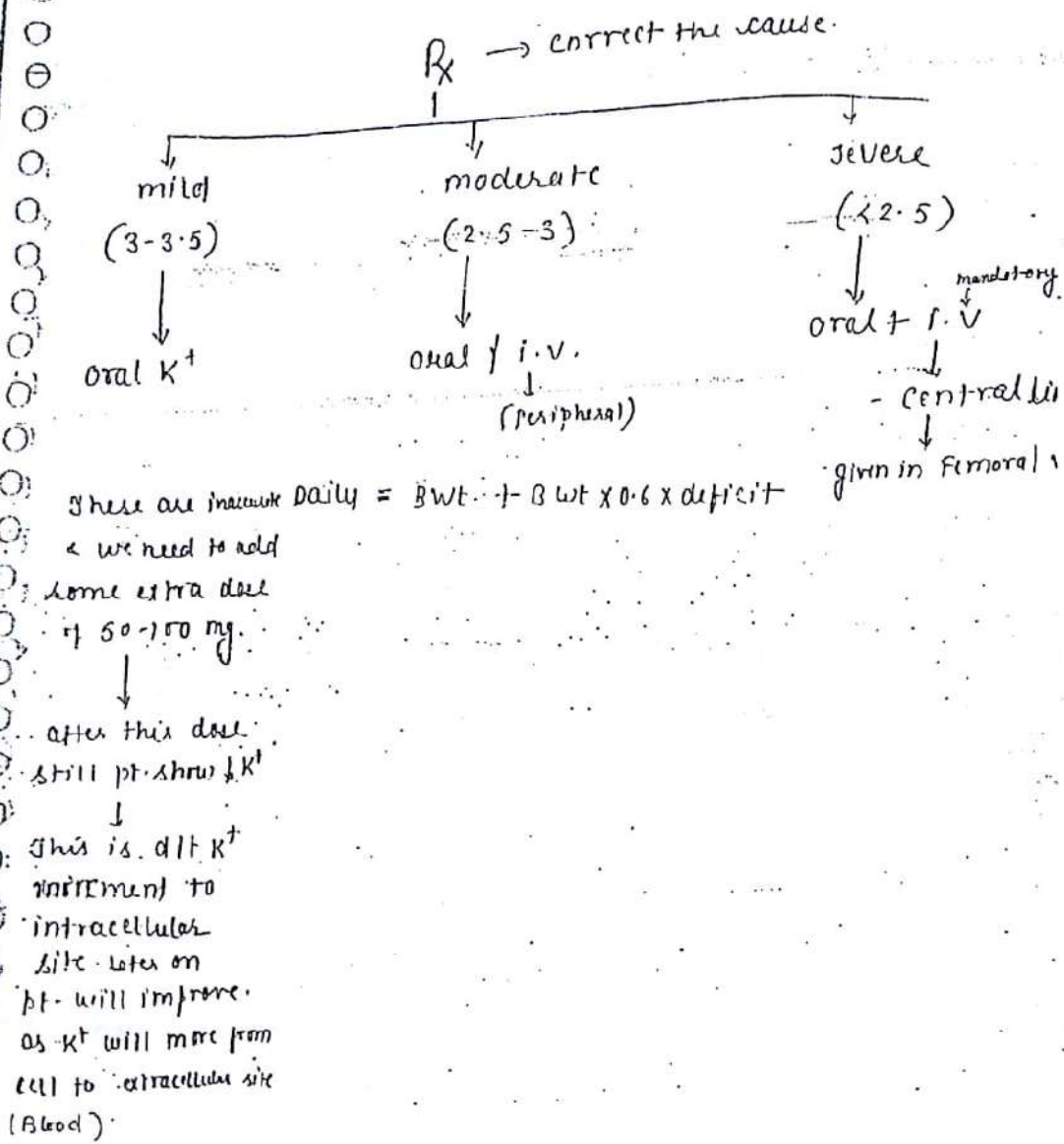


Biphasic

4th - VT / VF → Long QT
↓
Torsades

* mce arrhythmia in Hypokalemia is APE (atrial premature contracⁿ).

(37)



28

- Cardiac tamponade -

- Acute pericardial effusion causes cardiac tamponade.
- There occurs defective filling of heart.

Compression



↓ filling of heart



1) ↑ in diastolic pressure in heart



2) compression occurs in all 4 chambers

so there is equalization of diastolic pressure



3) Also there is ↑ intrapericardial pressure

CIF - ① ↓ filling → ↓ output



↓ B.P.

② ↑ JVP → veins not emptying

③ muffled heart sound

Beck's triad

IOC:- Trans-thoracic echo. → Helpful in management also.

even removal of 15-20 ml drastically improves.

ECG! —

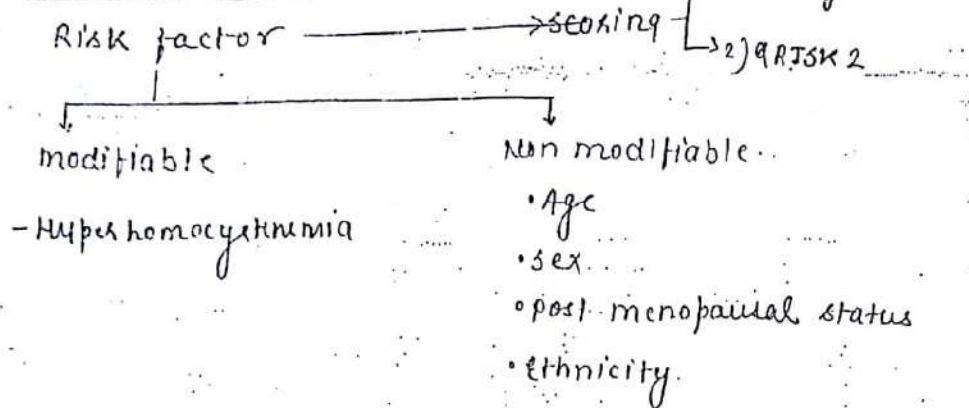
- ① Low voltage complexes in chest lead b/c of fluid interface.
- ② Tachycardia
- ③ Electrical alternans — Alt. long & short QRS



(39)

Ischaemic heart disease

Coronary artery disease



Risk predictors

- | <u>Lipid</u> | <u>non-lipid</u> |
|---|----------------------------|
| 1) Best = $\frac{\text{Total cholesterol}}{\text{HDL}}$ | 1) But: High sensitive CRP |
| < 3.5 — Low risk | < 1 — Low risk |
| 3.5 - 5 — Normal | 1 - 3 — (M) risk |
| > 5 — High | > 3mg/dL → High |
| 2) non HDL cholesterol (Apo B) | 2) MPO |
| $\frac{\text{apo B}}{\text{apo A}}$ | 3) Fibrinogen |
| 3) LDL cholesterol | 4) Interleukins |
| 4) HDL cholesterol | |
| 5) TC & triglyceride alone. | |

* While testing

Fasting

Req.

↓
LDL

TG

not req.

↓
HDL

Total cholesterol

* In MI — lipid profile taken immediately.

↓
after 24 hr

↓
There is false ↑ in lipid volume.

↓
In case if failed to get lipid profile in 24 hr

↓
Same after 4 wk (≈ 30 days)

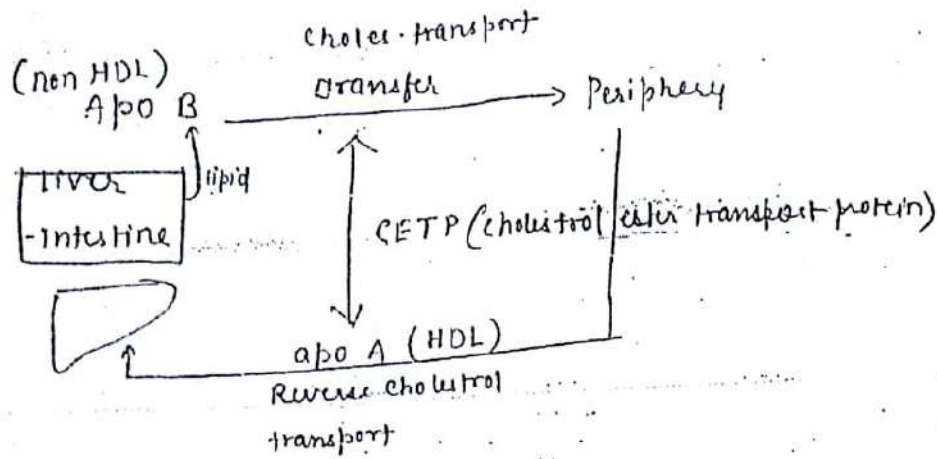
* Friedewald formula —

$$LDL = TC - HDL - \frac{TG}{5}$$

$$VLDL = \frac{TG}{5}$$

$$LDL = TC - HDL - VLDL$$

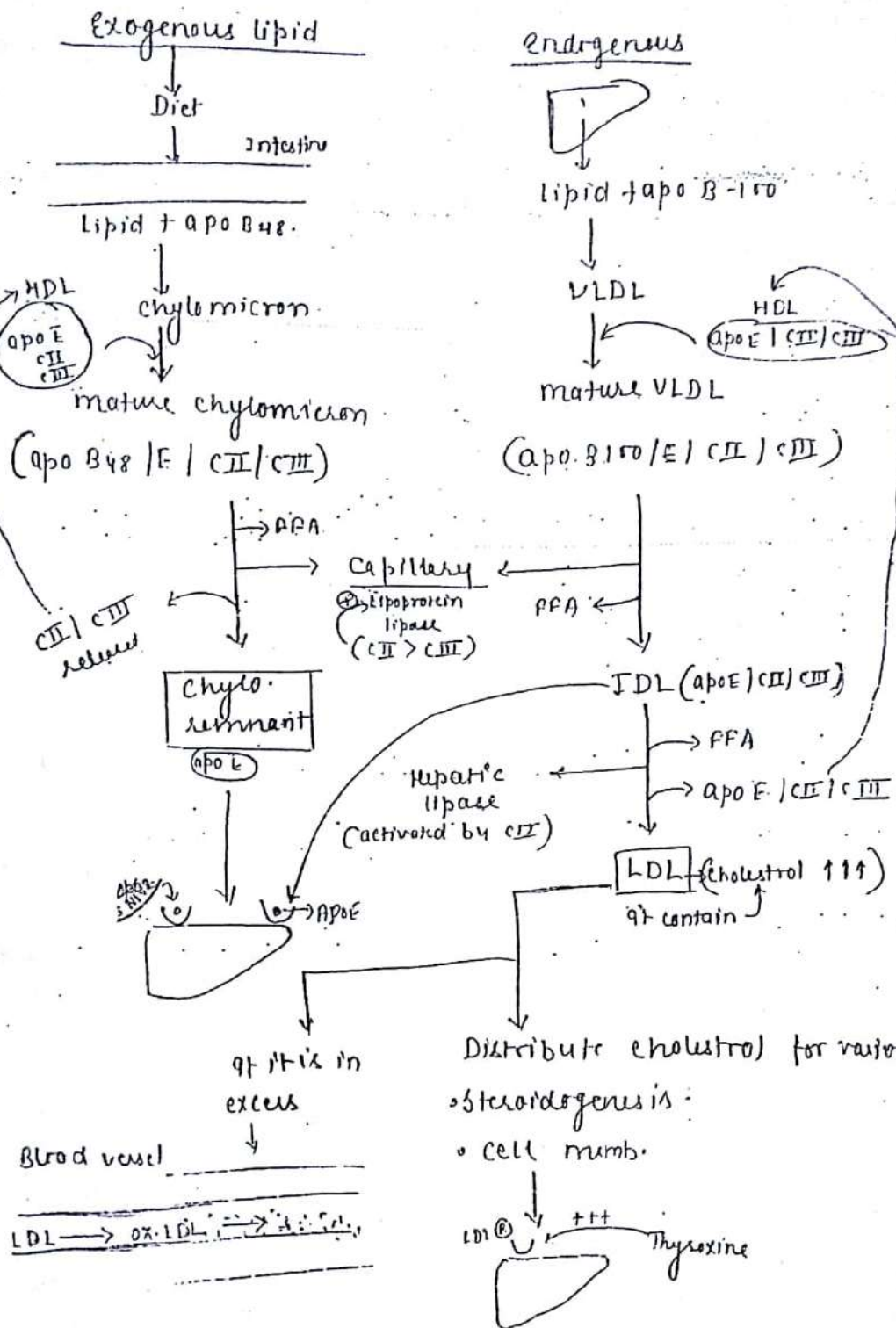
(40)



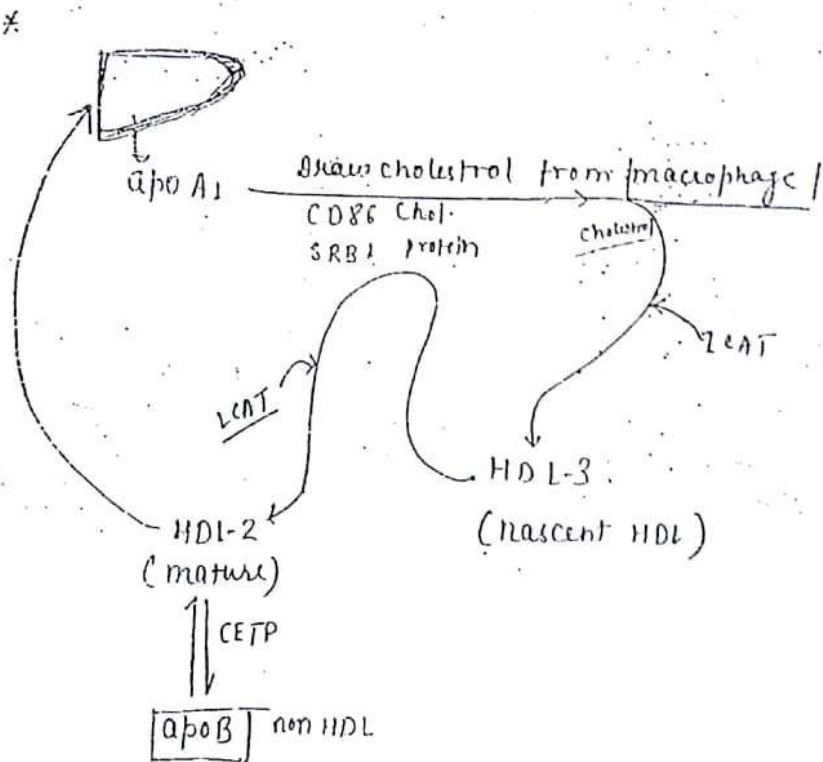
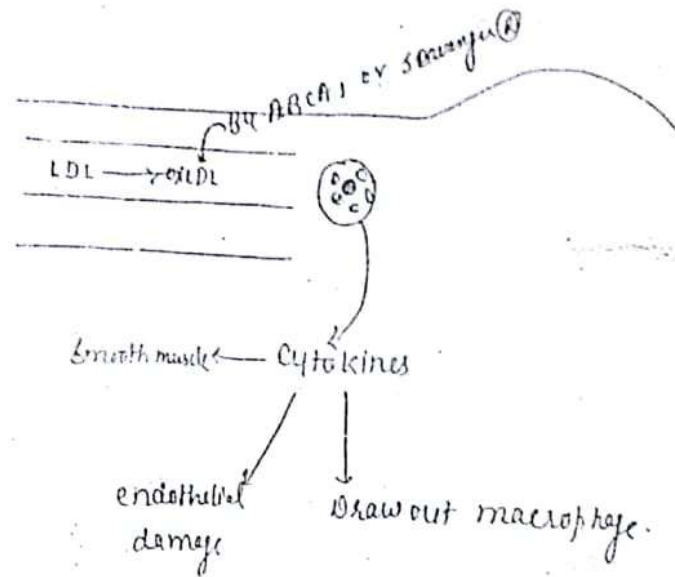
$\frac{apo B}{apo A} = \uparrow$ - Bad $\frac{apo B}{apo A} = \downarrow$ - good

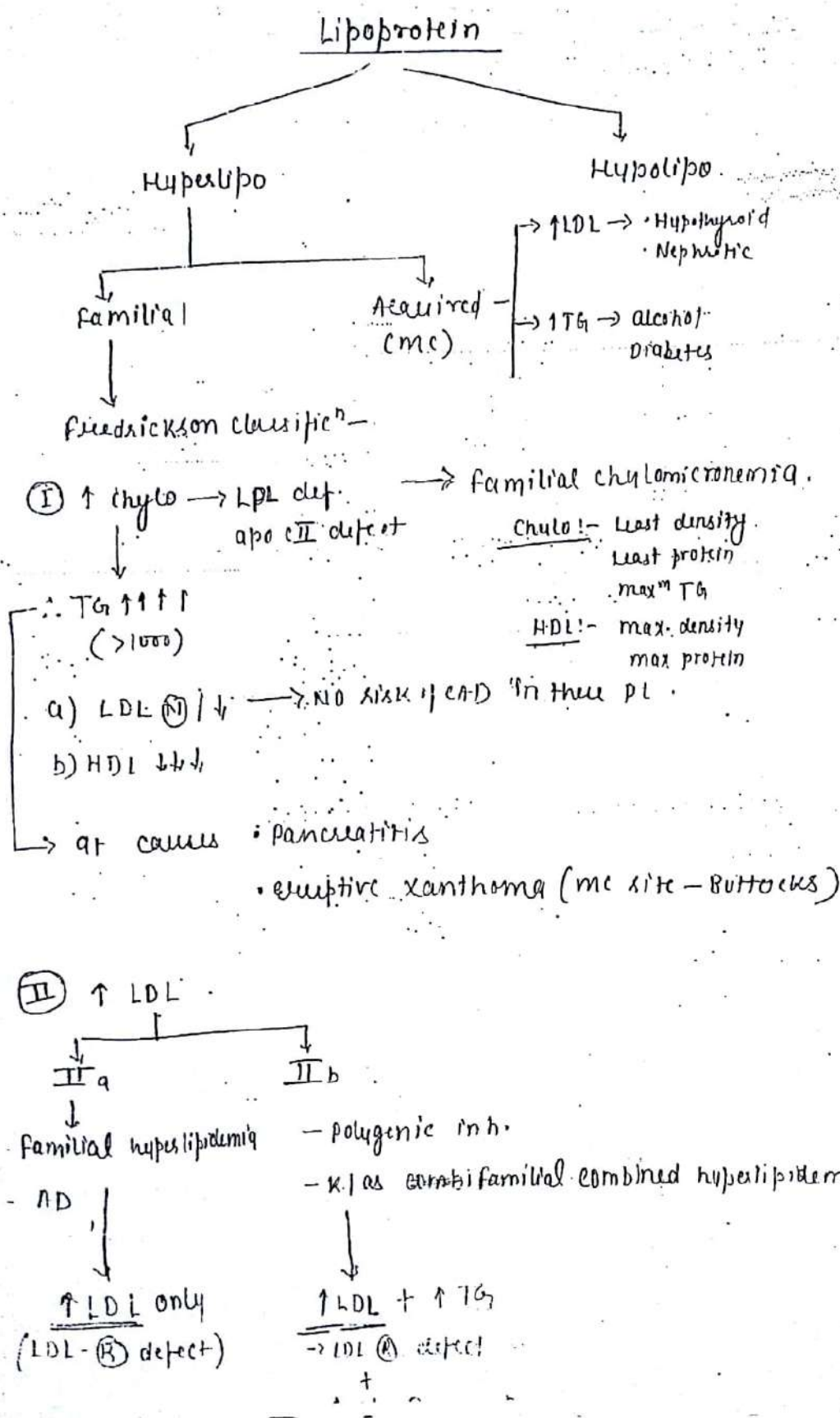
exogenous lipid
↓
Diet

endogenous lipid



(41)



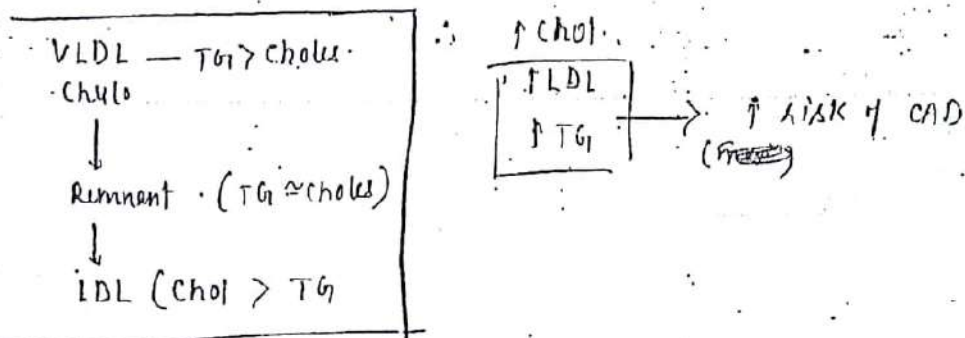


* Due to ↑ LDL, both of them will have ↑ risk of CAD. (42)

C/F- tendon xanthoma
xanthelasma
Arcus juvenilis } Seen in Familial hyperlipidemia
+ not in combined hyperlipid.

③ ↑ remnants (Remnant disease)
(Fam. dysbetalipoproteinemia)

→ apo E defect (apo E takes up remnants)



④ ↑ VLDL productⁿ (Familial hypertriglyceridemia)
↓
↑ TG (not like type - I)

⑤ 1 + 4 = 5 ⇒ ↑ chyl + ↑ VLDL
↑↑ TG (> 1000)
↓
- pancreatitis
- eruptive xanthoma

x NO risk of CAD

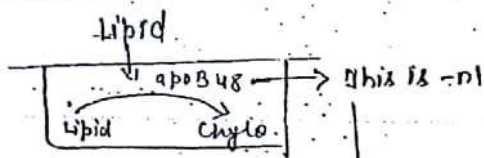
Hypolipidemia

↓
Abetalipoproteinemia

↓ apo B

↓ apo A

Intestine



So lipid accumulates in intestine & further

i) stops absorbing lipid

↓
So intestine loses everything specially

fat soluble vit. (vit E → ataxia)

TOC:- UGI scopy → Bx.

LCAT:- Fish eye disease -

CIF - Anemia (Hemolytic)

Renal failure

corneal lipid deposit.

↓
LCAT deficiency

↓
Familial
(100%)

↓
Partial

↓
Fish eye disease

↓
HDL do not mature

(apo A₁ → little short)

HDL ↓ ↓ ↓

LDL (N) → so no risk of CAD

Coronary artery disease

43

Asymptomatic

Symptomatic

Chronic stable
angina

Acute
Coronary
syndrome

Stable plaque

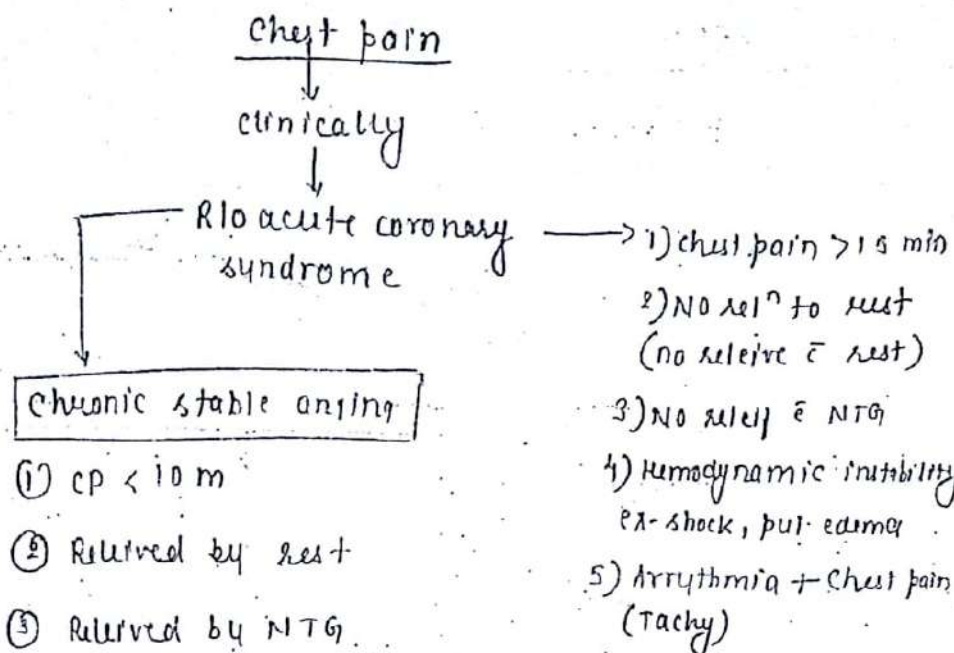
STEMI

NSTEMI

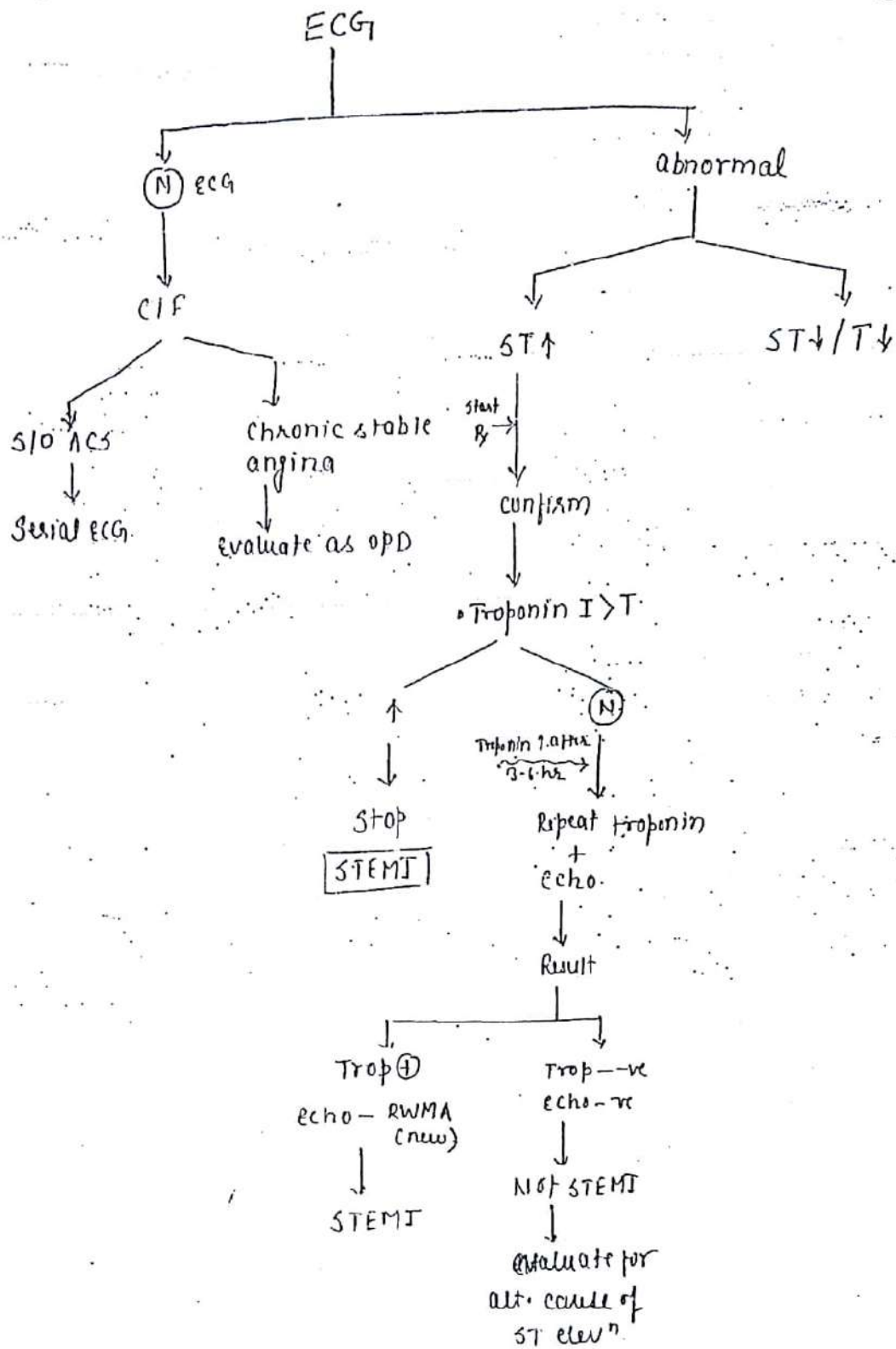
Unstable angina

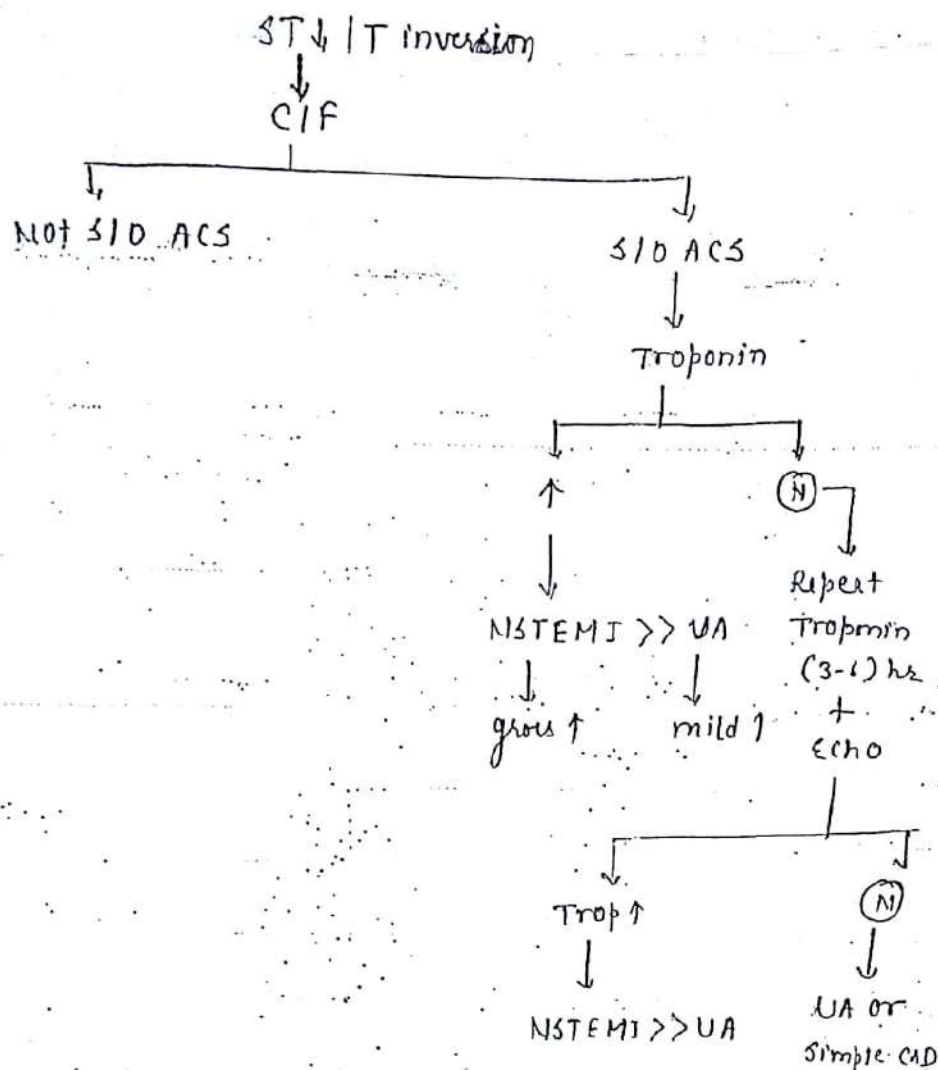
Plaque rupture

Chest pain (cardiac)



- 3/3 - Typical angina
- 2/3 - Atypical angina
- 1/3 - Non cardiac pain





(45)

Chronic stable angina

CSA → unstable angina

- no rest pain

- Rest pain

- 90% CSA → Pt. has stable pain i.e. same magnitude

- Each time the magnitude of pain & frequency both ↑

↓
(Kias crescendo pain)

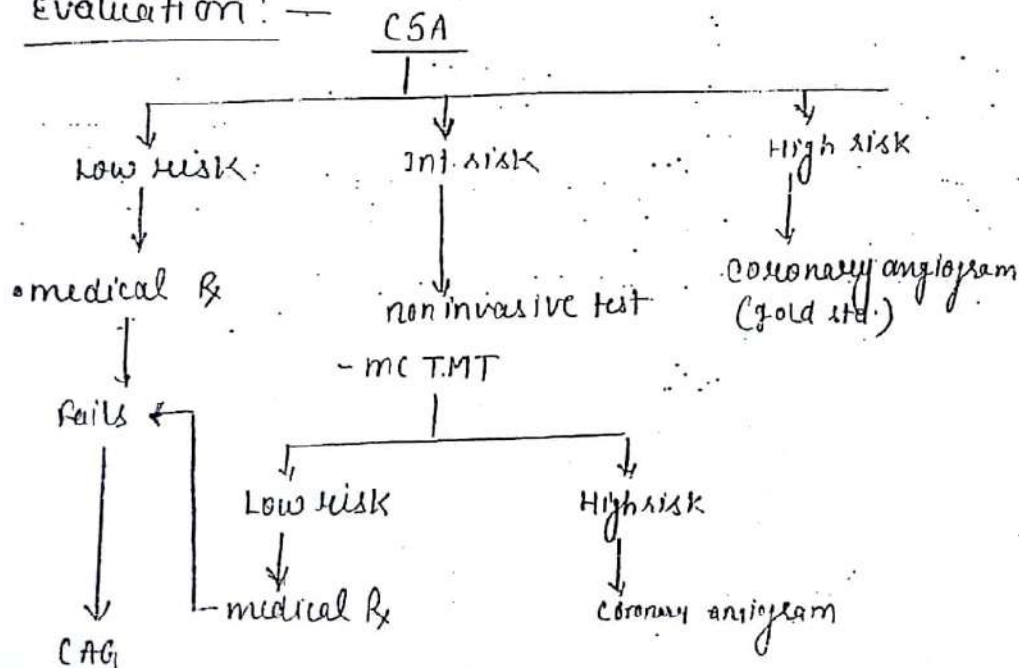
- Here pain & plaque both are stable.

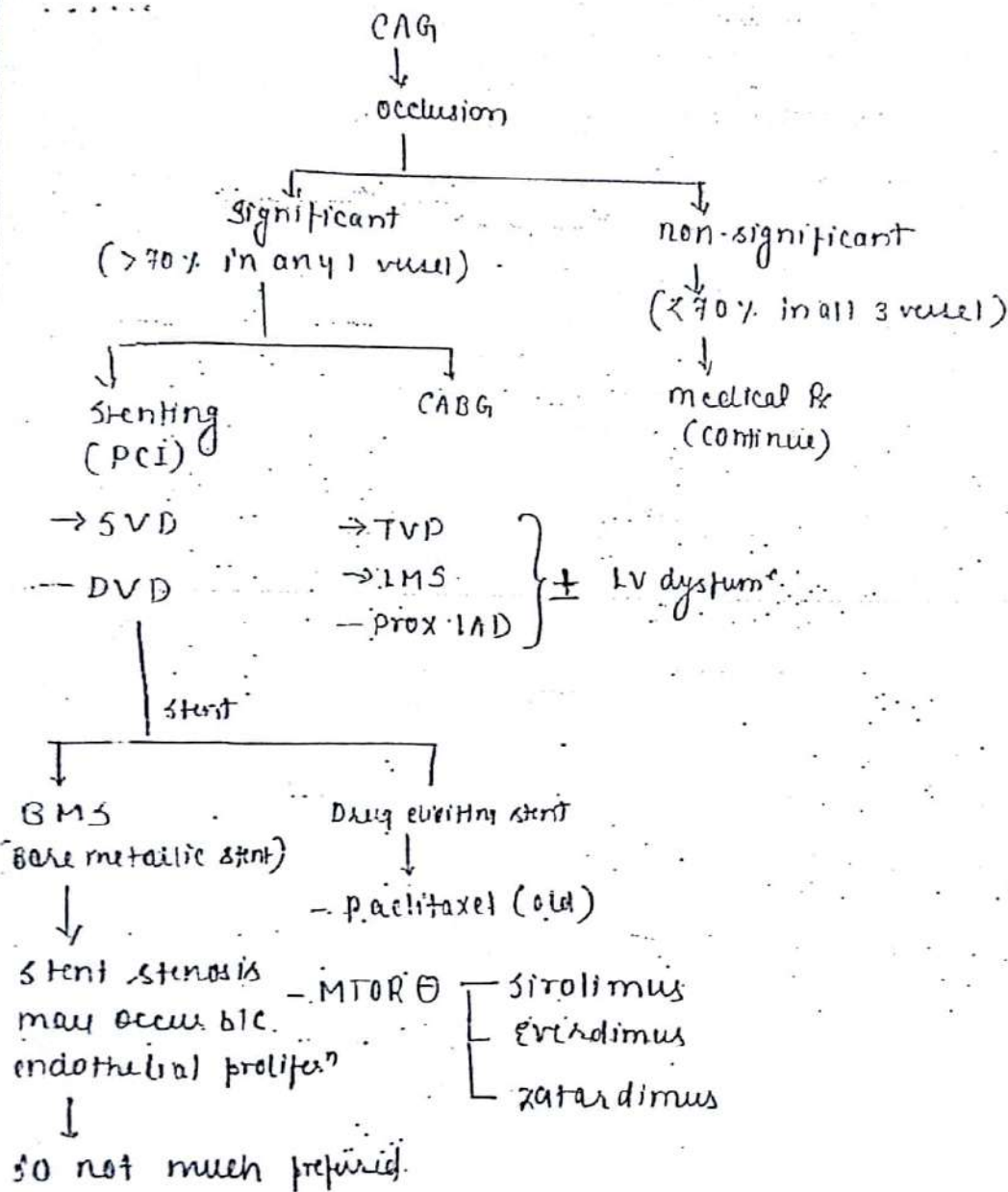
- pain & plaque both are unstable.

- min. 70% occlusion is needed to produce pain.

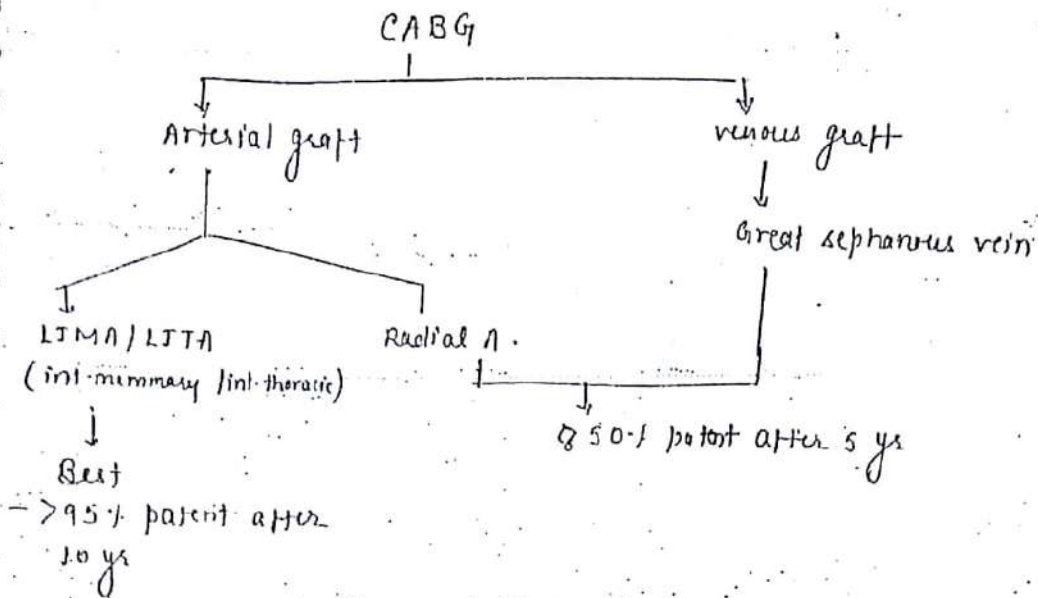
- at least 80% blockage should be there.

Evaluation:





(46)



Medical Rx

1) Acute attack — Nitrates

2) Prophylaxis — 1st line: — Short-acting nitrate + β -blocker.

→ symptomatic benefit

2nd line — calcium channel blockers (NMDHP/DHP)

Plan for CABG

→ fails

not given if previously β blocker was given

3rd line — Ivabridine (when HR > 70)

Ranolazine

Nicorandil

3) Aspirin } mortality benefit

4) statin }

& 90 mg & Heart failure β blockers give mortality benefit

Indicⁿ of TMT—

- ① Chronic stable angina.
 - ② Exercise induced arrhythmias
 - ③ Pacemaker funcⁿ evaluaⁿ (rate modulating funcⁿ)
 - ④ Post discharge M-I risk stratificaⁿ.
↓
sub maximal test
- normal test

Contraⁿ of TMT—

- ① Acute coronary syndrome
- ② Acute pulmonary embolism
- ③ Aortic dissection
- ④ HOCM → sudden death will occur
- ⑤ Severe Aortic stenosis
(mild-mid AS → TMT done)
- ⑥ uncontrolled HTN
- ⑦ malignant tachyarrhythmia
- ⑧ Pregnant
- ⑨ Advanced AV block
- ⑩ Acute pericarditis
- ⑪ Fever
- ⑫ Baseline ECG change

(4)

Protocol for TMT - modified Bruce criteria

We calculate - Duke's TM score

Low risk

High risk

- we have to achieve target H.R (end point)

It is 85% of $\text{max}^m \text{HR}$

$\text{max}^m \text{HR}$ - $\begin{cases} \text{male} = 220 - \text{age} \\ \text{female} = 210 - \text{age} \end{cases}$

When to stop -

- ① Pt. asks
- ② $\uparrow$ B.P. (severe - SBP > 220)
- ③ Brady / AV block
- ④ malign. tachycardia
- ⑤ ST $\uparrow$
- ⑥ ST $\downarrow > 5 \text{ mm}$
- ⑦ Paradox $\downarrow$ in B.P
- ⑧ Pul. edema
- ⑨ when target H.R achieved.

+ve test —

- ① ST $\downarrow$ $\geq 1\text{mm}$ ————— ^{Low} ~~High~~ risk
- ② Pt. reproduce same symptoms which they are having before
- ③ ST $\uparrow$
- ④ ST $\downarrow$ $> 2\text{mm}$
- ⑤ malignant tachy.
- ⑥ AV block
- ⑦ $\downarrow$ H.R
- ⑧ $\downarrow$ B.P
- ⑨ $\uparrow$ QRS voltage (It is showing devⁿ of LV during exercise)
- ⑩ ST $\downarrow$ $\rightarrow$ on rest $\rightarrow$ ST $\downarrow$ persist $> 6\text{ min}$ after rest
- ⑪ Not able to exercise $< 6\text{ min}$. (< 4 metabolic cycles)
[Not even 4 metabolic equivalent person is spending]

High risk

High risk

(48)

Other modalities — Non invasive tests —

① CT coronary calcium scoring. → Agaston score

↓
 <10 — low risk

$10-100$ — moderate

$100-400$ — High

>400 — very high

② CTCA

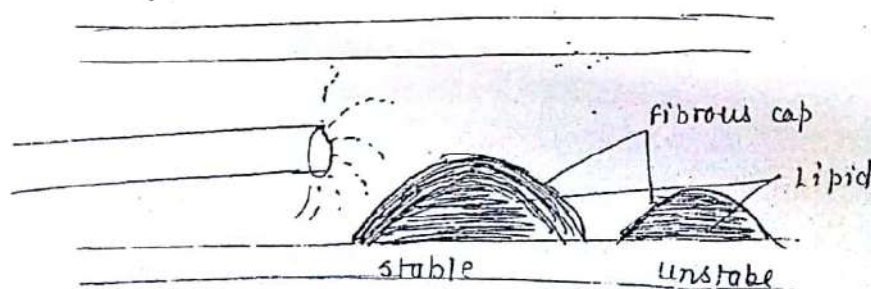
③ Dobutamin stress echo → Done in pt. who can't exercise
 dlt #, injury, dementia etc.

* These test also show % occlusion like CAG but it's non invasive.

* All these test have high -ve predictive value.

Invasive test — IVUS

*



— go check the real nature of plaque we perform invasive test.

OCT

* extent of plaque

* morphology of plaque.
better seen

IVUS

* extent of plaque better
seen

* morphology of plaque can
be seen.

Indicⁿ - Reperient chest pain
despite having (N) coronary
angiogram

(9)

— Acute coronary syndrome —

Universal defⁿ of MI

— Rise & fall of cardiac markers (essential)

+

1/5

A — ischaemic chest pain

B — ST, T changes in ECG

C — a wave formⁿ in ECG

D — imaging

(i) Echo — ~~any~~ regional wall motion abnormality (RWMA).

(ii) viability testing — new loss of viable myocardium

E — prove intracoronary thrombus after ~~Stx~~ A2

Types of MI —

① spontaneous MI → STE CAD (mc)

② ^{DLT} Ischaemic Imbalance.

③ MI causing sudden death

④ Post PCI related MI

⑤ Post CABG related MI

* m. specific marker for MI — Troponin.

* least specific marker for MI — myoglobin.

1st to elevate —

1st to fall —

* Last marker to elevate

come to base line

→ LDH

* Troponin

	Rise	Peak	Baseline
T-I	4-6 hr	24-48 hr	5-7 d
T-II			10-14 d

↑ Troponin —

- ① Acute MI
- ② CKD
- ③ SIRS —
 - severe burn
 - sepsis
 - polytrauma
 - Ac. pancreatitis
- ④ myocarditis (not pericarditis)

- ⑤ Injury to heart —
 - ① Cardiac sx —
 - cardiomyopathy
 - cardiac transplant
 - ② Procedure —
 - PCI
 - LABG
 - ③ vigorous CPR

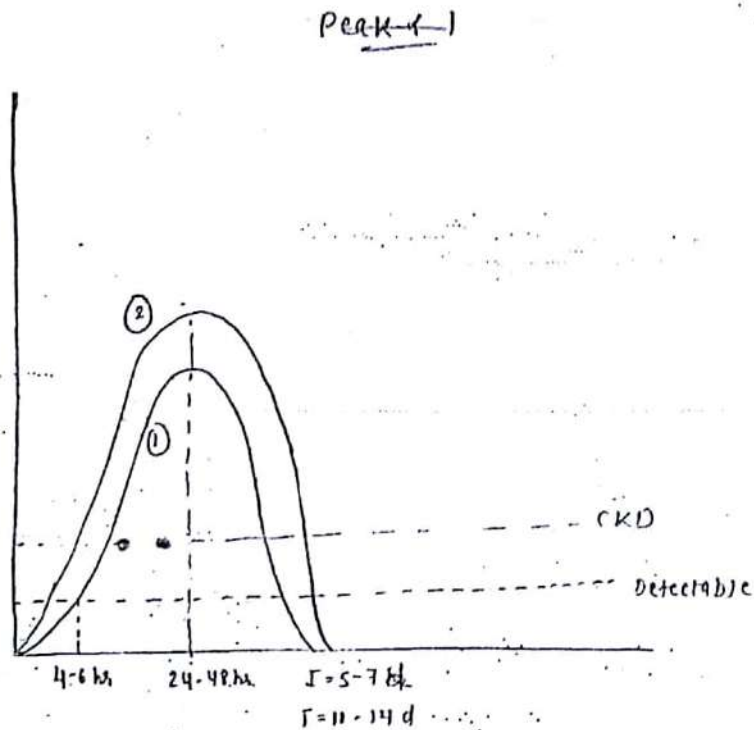
Defibrillⁿ —

- ① ST ↑ — transient (5 min)
- ② (1) troponin

Complicⁿ —

- Arrhythmia (Brady + tachy)
- Burns
- myocardial necrosis (epicardium)
 - ↳ ST elevⁿ

* Troponin is most specific for MI & its dynamics are imp. i.e rise & fall rather than a single value.



* Peak & severity of 1
elevation fraction

* Pt. ② has severe MI

* on CKD — there is static value of troponin

Reinfarction —

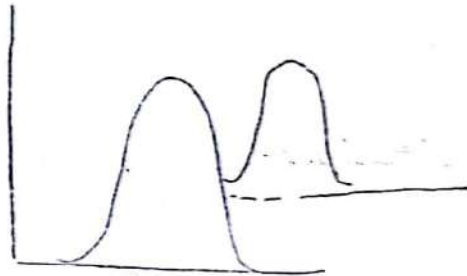
• There is 2nd peak in the curve

• Troponin $\geq 20\%$ of previous is A¹ of MI

* if Troponin reached to baseline & now Reinfarction occur $\rightarrow$ Any rise from baseline shows MI

(5)

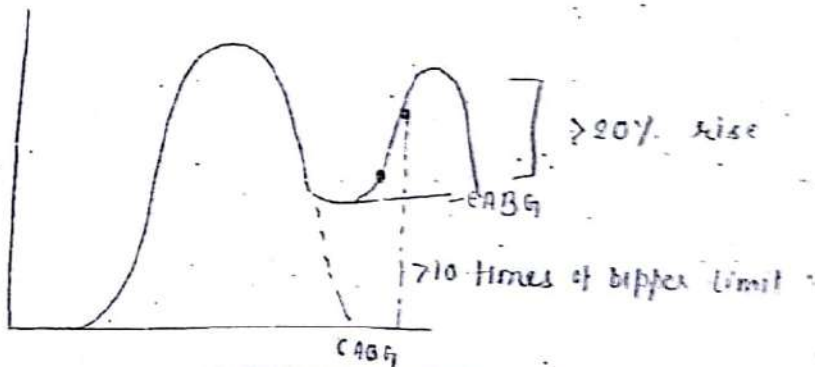
PCI related MI —



9) troponin not reached baseline — 2nd value
↓
≥ 20% of PCI

9) troponin reached baseline → 5 times from upper
limit of (N)

*



	1 st value ↑	1 st value (N)
Reinfarction	> 20 % 3-6 hr	⊕
PCT	> 20 %	5X ULN
CABG	≥ 20 % 3-6 hr	10X ULN

(52)

STEMI

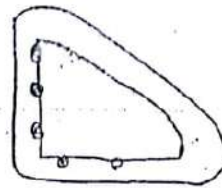
- 100%
- Transmural & focal



- Single vessel occlusion
- very less comorbidity in pt.
- ST ↑
- Localized
- Red clot (contain more fibrin)
 - ↓
 - Fibrinolysis done
- Early mortality (in hospital)
 - ↓
 - MCC - cardiogenic shock
- cause of death even before coming to hospital → arrhythmia.

NSTEMI/UA

- Partial occlusion (>80%)
- Subendocardial & multifocal



- multivessel
- ↑↑ comorbidity
- ST ↓ / T ↓
- Deep symmetrical T inv.



⇒ Wellen syndrome

qt tells that condition is NSTEMI not UA.

- can't be Localized.
- White clot (Platelet)
 - ↓
 - Fibrinolysis C/I
- Antiplatelet drug is beneficial
GP IIb/IIIa ⊖
- Late mortality

MI of STEMI

Stabilize the patient

① Pain control — NTG

POC — morphine

② oxygen

③ Aspirin — 300-325 mg (non enteric coated)

Adv:-

• ↓ O_2 demand
• ↓ Post MI
arrhythmia

CI — • Pul. edema
• Hypotension
• A-V block

← ④ I.V. β blocker — (metoprolol)

Unstable

stop β blocker &
give once pt. become stable

3 doses

↓
stable

↓ 4-6 hr

oral β blocker (metoprolol)

Reperfusion

↓
iPCI > thrombolysis

↓
criteria

↓
pt & chest pain

Time < 12 hr

12-24 hr

Ambulance

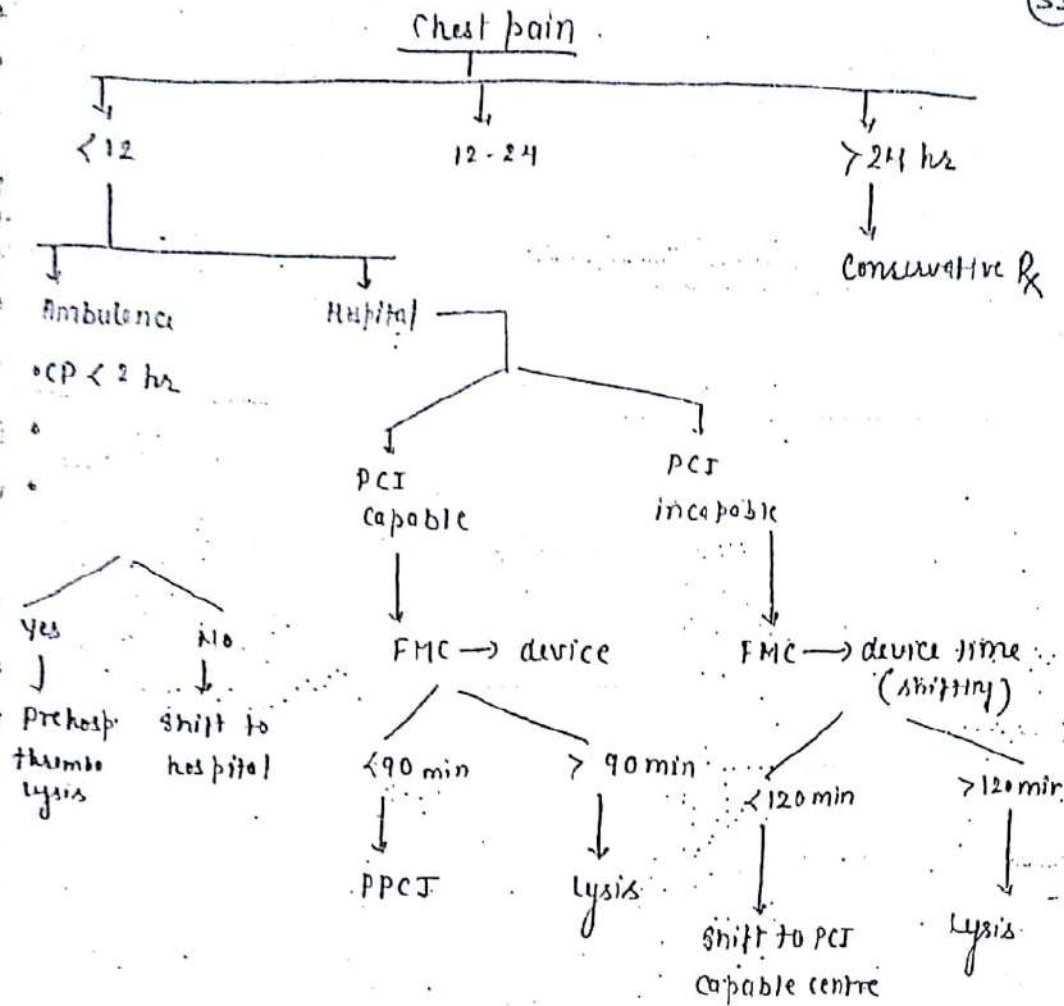
Hospital

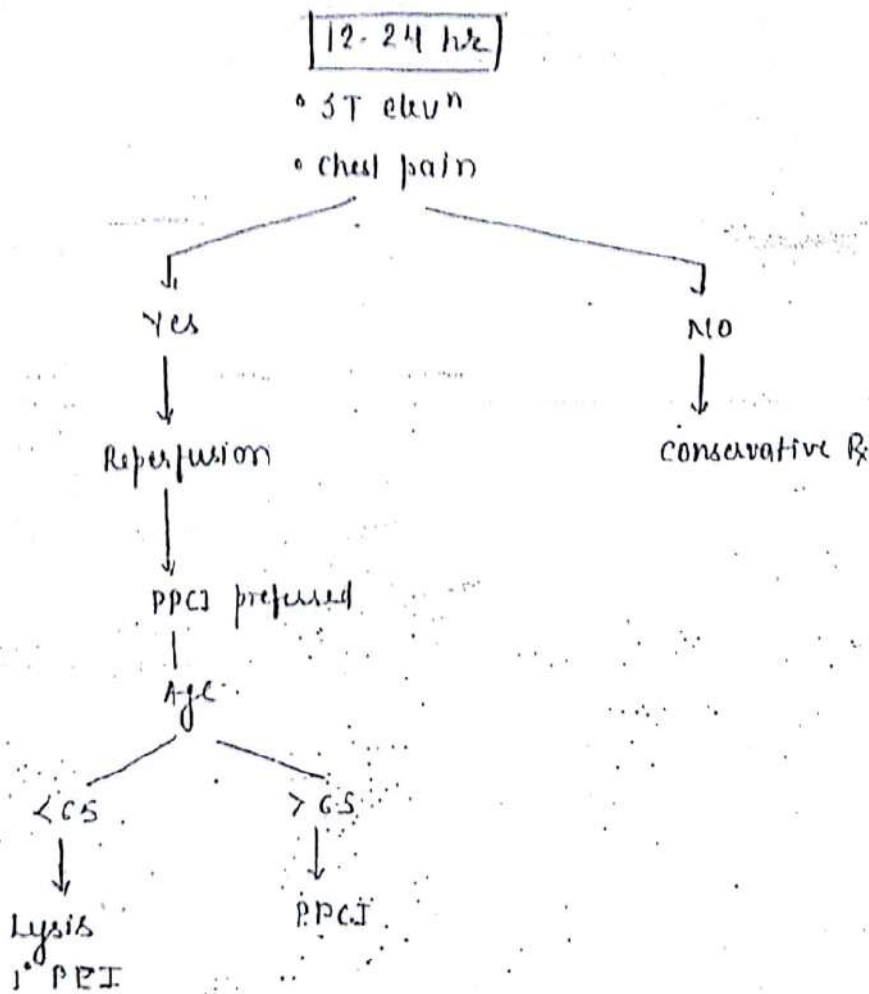
↓ criteria
D.C.P < 2 hr

③ No CI of Thrombolysis

→ 1st medical contact → needle time < 30 min

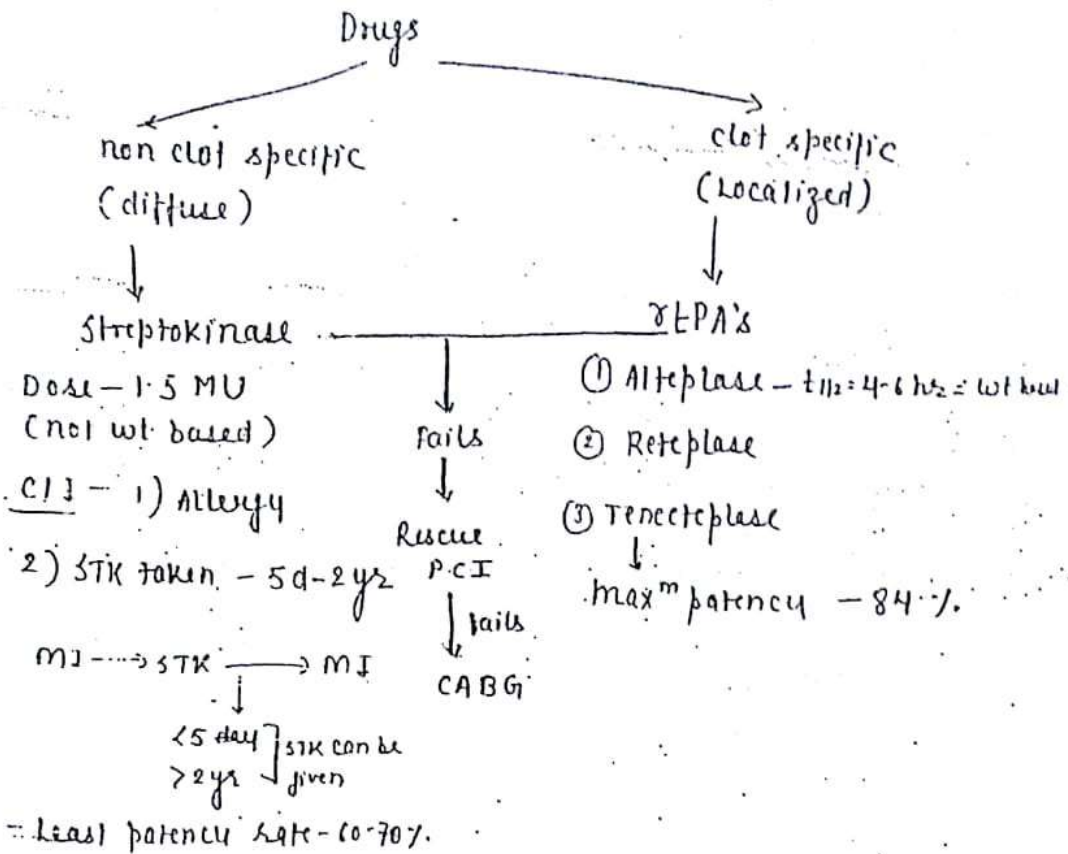
(53)



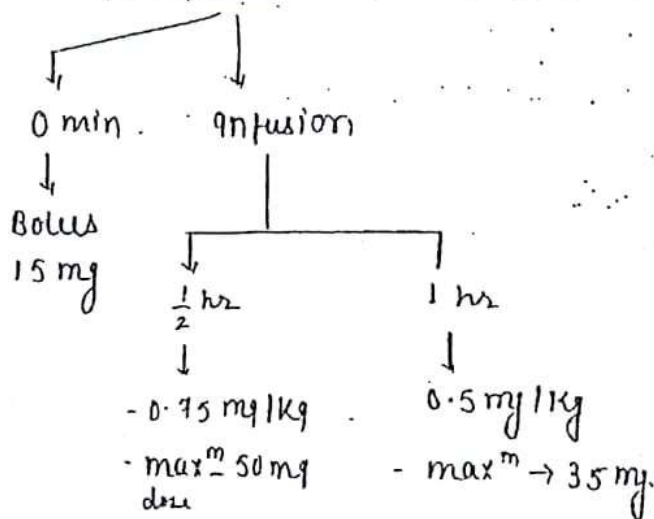


Lysis — most effective $\bar{c}$ in 6 hr (³hr)

(56)



* Alteplase — 3 doses = max^m total dose = 150 mg



Retepase — Dose : Double ~~bolus~~ bolus

0 min 30 min
(18 mg) 10 U + 10 U

• not wt based

Tenecteplase — Dose : 1 bolus

• wt based

> 90 kg — 50 mg (max)

80-90 kg — 45 mg

70-80 kg — 40 mg

60-70 kg — 35 mg

< 60 kg — 30 mg

Scanned by CamScanner

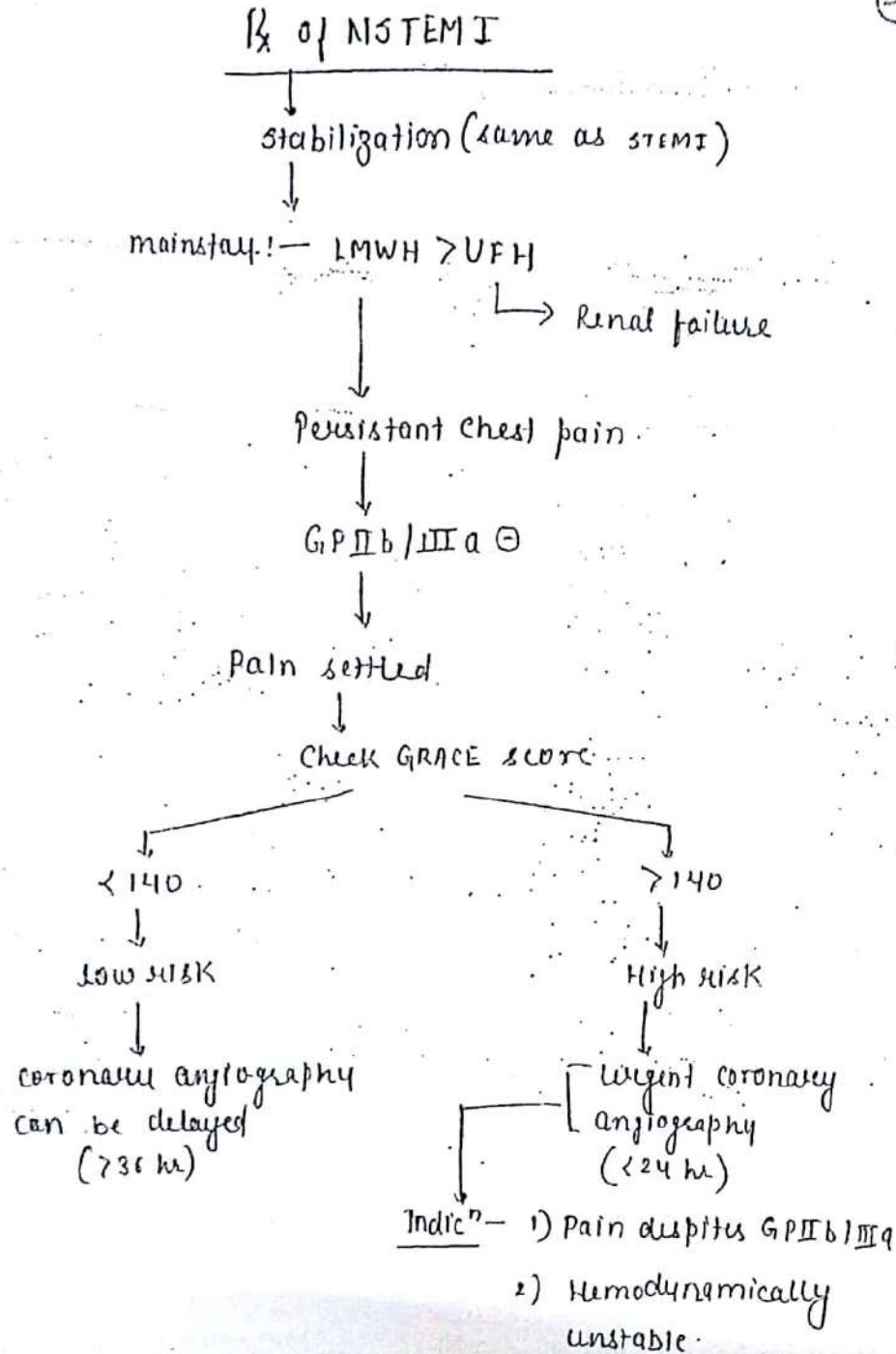
③ statin $\rightarrow$ High intensity statins given:

④ ACE $\ominus$

⑤ β blockers $\rightarrow$ continue

⑥ qf EF $< 35\%$ $\rightarrow$ mineralocorticoid antagonists
• spironolactone

(56)



Post discharge m/m! — 'Same'
- Repeat

Compleⁿ of STEMI —

① cardiogenic shock! —

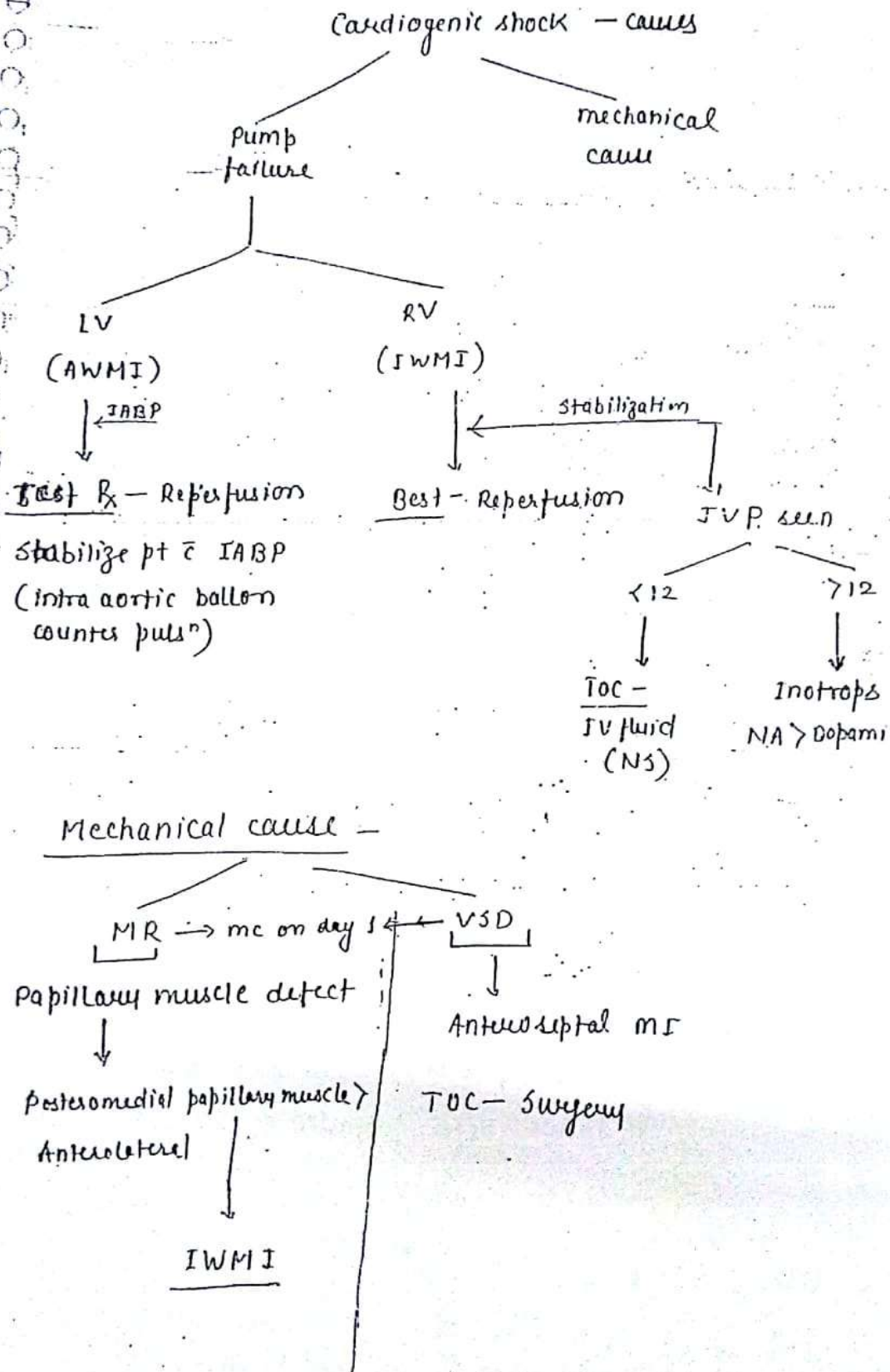
Killip classificⁿ

- | | |
|--|----------------|
| I — no S_3
no creps | — Best |
| II — S_3
creps → lower 1/2 | } Intermediate |
| III — creps → entire lung
(frank pul edema) | |
| IV — shock | — worst |

Forrester classificⁿ — Based on catheter data

	<u>Congestion (PCWP > 15 mmHg)</u>	<u>Hypotension (cardiac index < 2.2 L/min/m²)</u>
I	X	X
II	✓	X
III	X	✓
IV	✓	✓

(52)

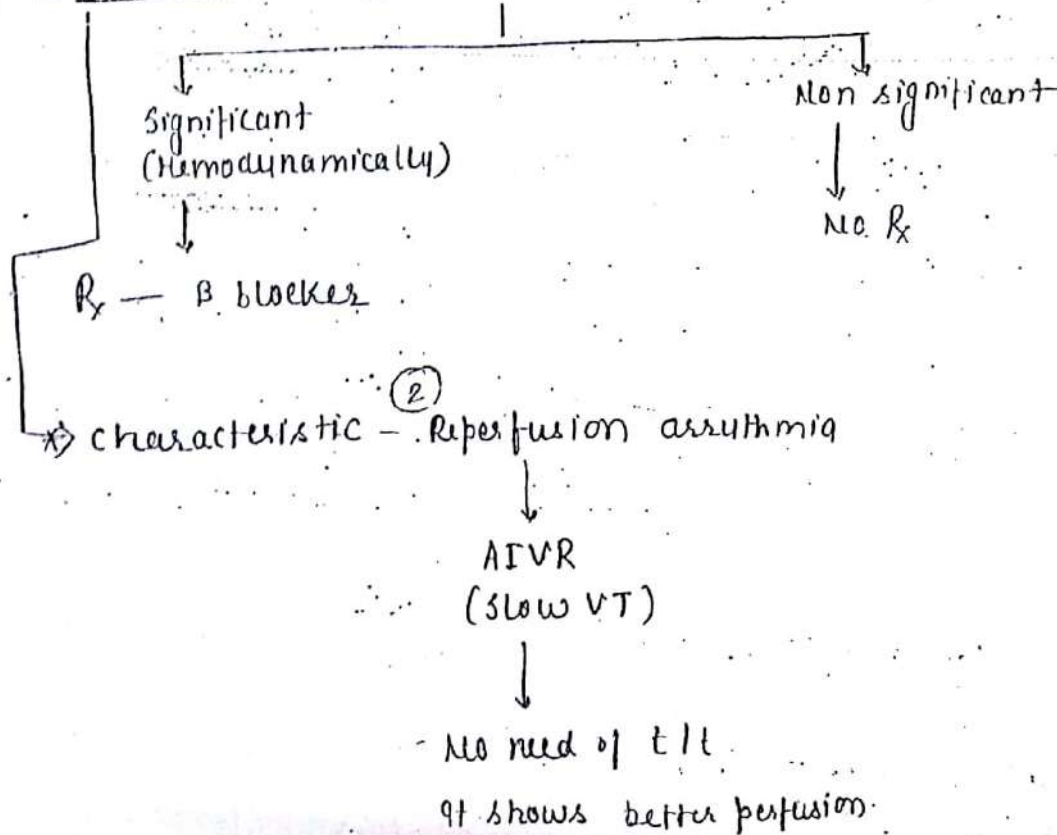


② Free wall rupture - • Rare

Risk factor :- 1) Use of antico drugs (>24 hr, age >65 yr)
2) NSAIDs consumption in M.I.
($\therefore$ NSAID is C/I in M.I.)

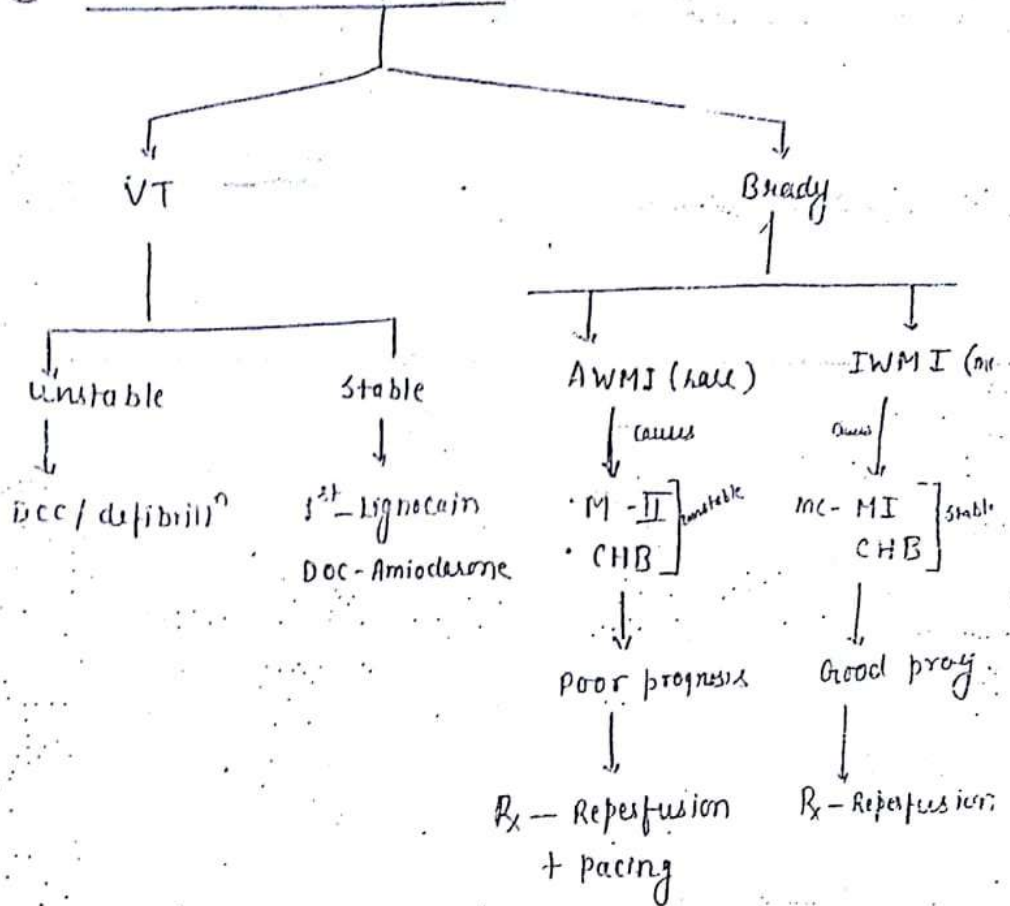
* occurs in < 1 wk.

③ Arrhythmia - (Inc. VPC)



58

③ Problematic arrhythmia



④ Recurrent chest pain —

Recurrent MI

Rx like old MI

Pericarditis

Order statin

Early
(<1 wk)

Late - 2wk -
- 2mth

Transmural
MI (STEMI)

cause is inflammⁿ

Autoimmune

- Pericarditis
- Pl. effusion
- Consolidation
- Arthritis

Rx — Aspirin dose $\uparrow$ $\rightarrow$ 150 mg QID

(59)

Statins Indicⁿ

Pt $\bar{c}$ Atherosclerotic
CVD

Start statin irrespective
of cholesterol level

- Acute coronary sy.
- CSA
- TIA
- Stroke
- PVD

Statins have pleiotropic
effect (↓ fibrous cap)

- statins → anti Inflamm

Plaque stabilizⁿ
(↓ lipid from plaque & foam
cell & ↓ fibrous cap)

* High intensity statins
given ↓
(↓ LDL-C by >50% in 3 month)
ex- Atorva - 40-80 mg } $\uparrow$ mes^m
Rosuva - 20-40 mg }

* If age > 75 → moderate
intensity statins given.

Pt out ASCVD

Based on cholesterol (LDL) level

LDL > 190

statin

High intensity
statin

LDL > 90

+ (1/3)

a) 10 yrs cv risk
> 7.5%

b) Diabetes mellitus

c) Age > 40

statin

mod.

Any 1.

High

Any 2-3

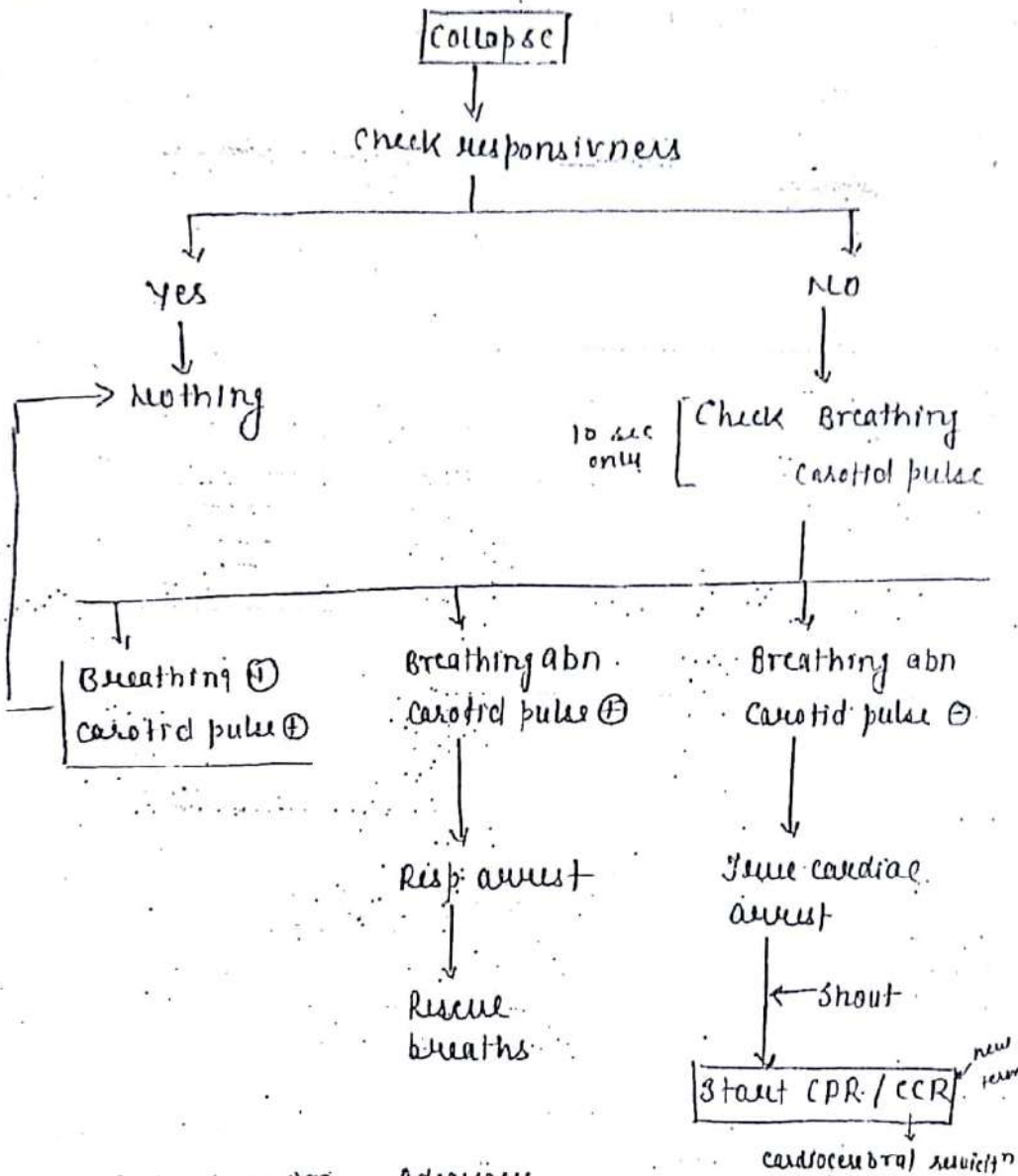
* When TG > 500

Fibrates can be given
overall

• ↑ HDL - niacin

↓
not indicated if many
side effect.

Cardiac arrest



Chest compression - Adult

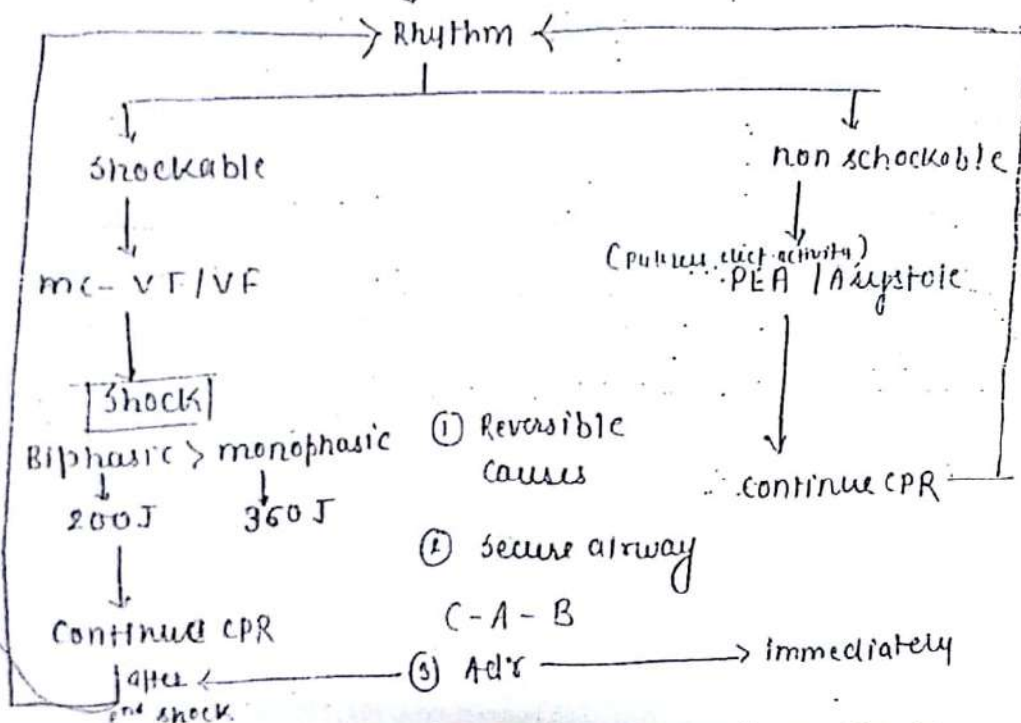
- Quantitative -
- (1) 5-6 cm depth
 - (2) Rate 100-120/min.
 - (3) $\text{ETCO}_2 > 10 \text{ mmHg}$

60

Start CPR

Age	Rescuer	Ratio
neonate	doesn't matter	3:1
Pediatric	single	30:2
	Double	15:2
Adult	Doesn't matter	30:2

↓
Leads applied



* chest compression never stopped. Alone it can tilt pt.
- only in case of shock it is stopped.

(3) Adri

Dose - 1:10000
1 ml
IV

1:1000
0.5 ml
IM } Anaphylaxis

(4) Amlodarsone → not given for non-shockable.
after 3rd shock ← (atropine, lignocaine)

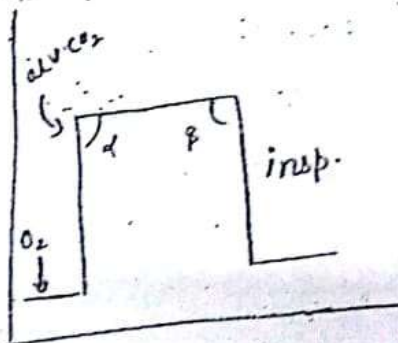
(5) Atropin, vaso X

↓
outcomes

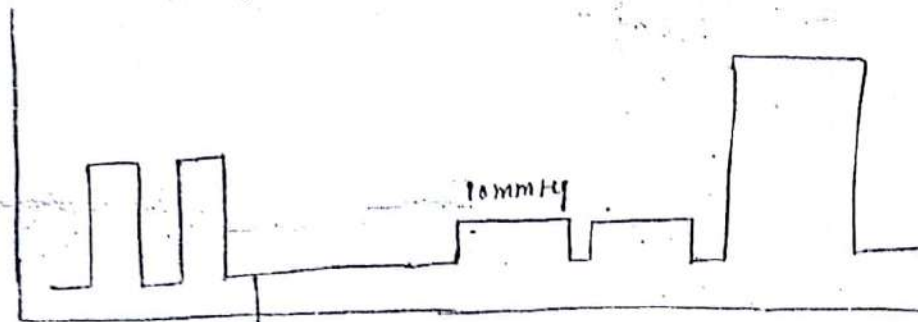
↓
Death

↓
Return of
spont. circulⁿ

↓
gold std - ETCO₂
(measure rise in CO₂)

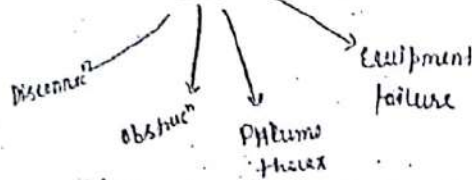


(61)



• Cardiac arrest

• DOPE



ROSC

Benefit → Shunt put to
Hypothermia
(33-36°C)

(after return of ROSC) Ind. of poor prognosis:-

① -nt corneal reflex @ 24 hr

② -nt motor response @ 48 hr

③ Pupilary reflex @ 72 hr

④ EEG:- status myclonus @ 48 hr
Burst suppression — poor

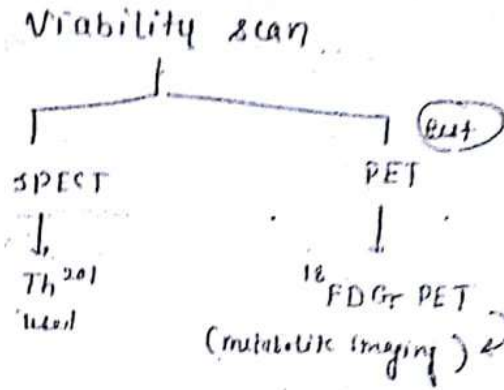
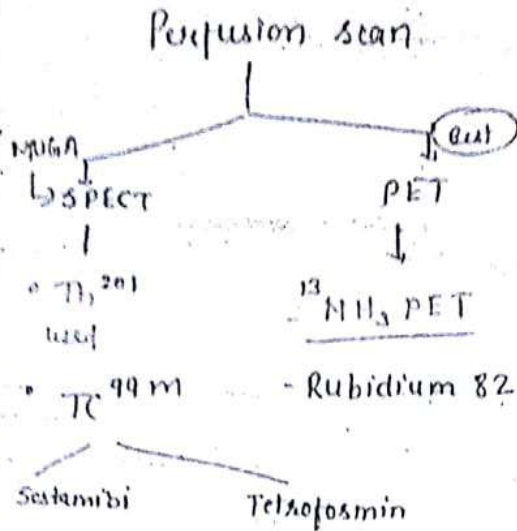
⑤ marker — NBE
3-100 } 1 level show poor prog.

(1) N 20 somatosensory evoked potential —

↓
BII - nt

↓
death (100 %)
specific

(62)



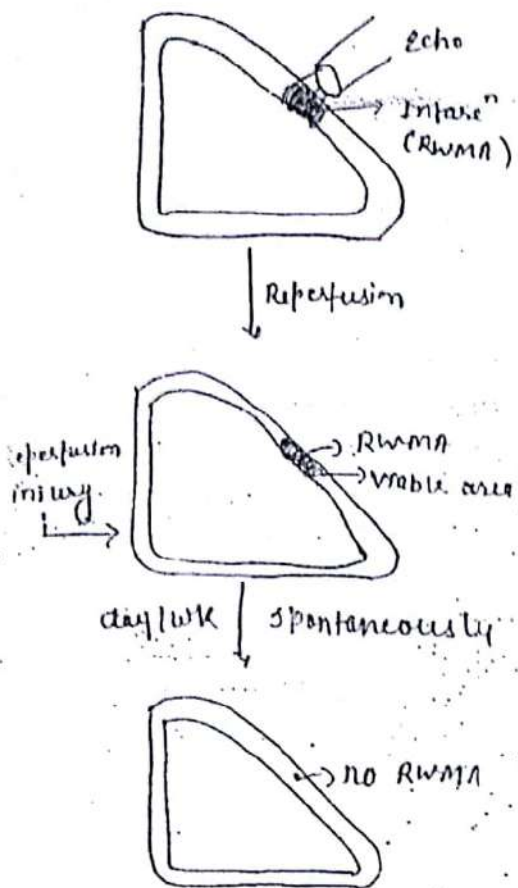
Best - PET —

- accurate
- image quality good
- Radio t1/2 short (5)

Th²⁰¹ — • Better for perfusion study only
• viability can be also be detected in same setting.
though best is PET only

Th ²⁰¹	viable	Non-viable
1 st inj — early	warm	cold
Late	cold	warm
2 nd inj — specific	cold	warm
T ₂ WI MRI	X	Hyperintensity.

Stunned myocardium



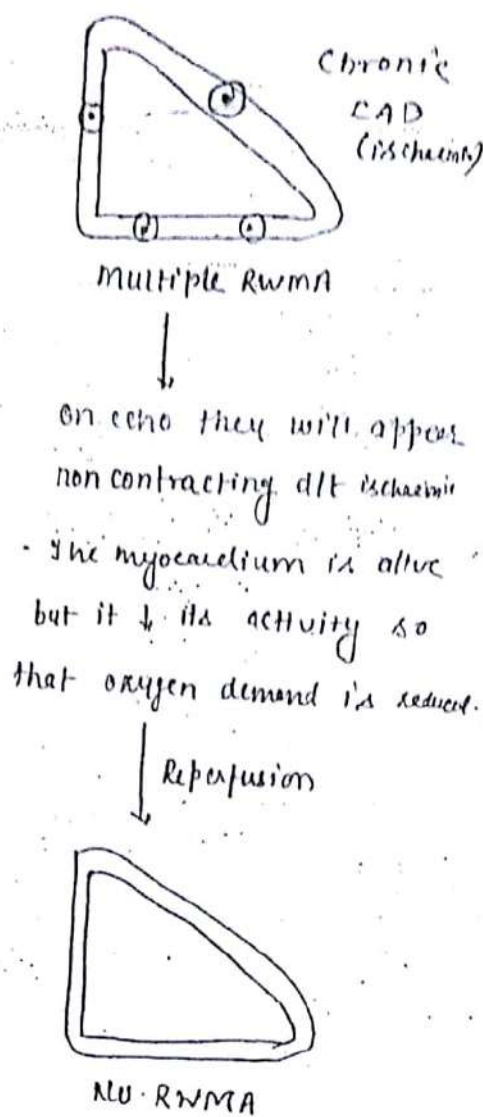
* Stunned myocardium is mostly due to reperfusion injury.

viable myo.

on echo - RWMA

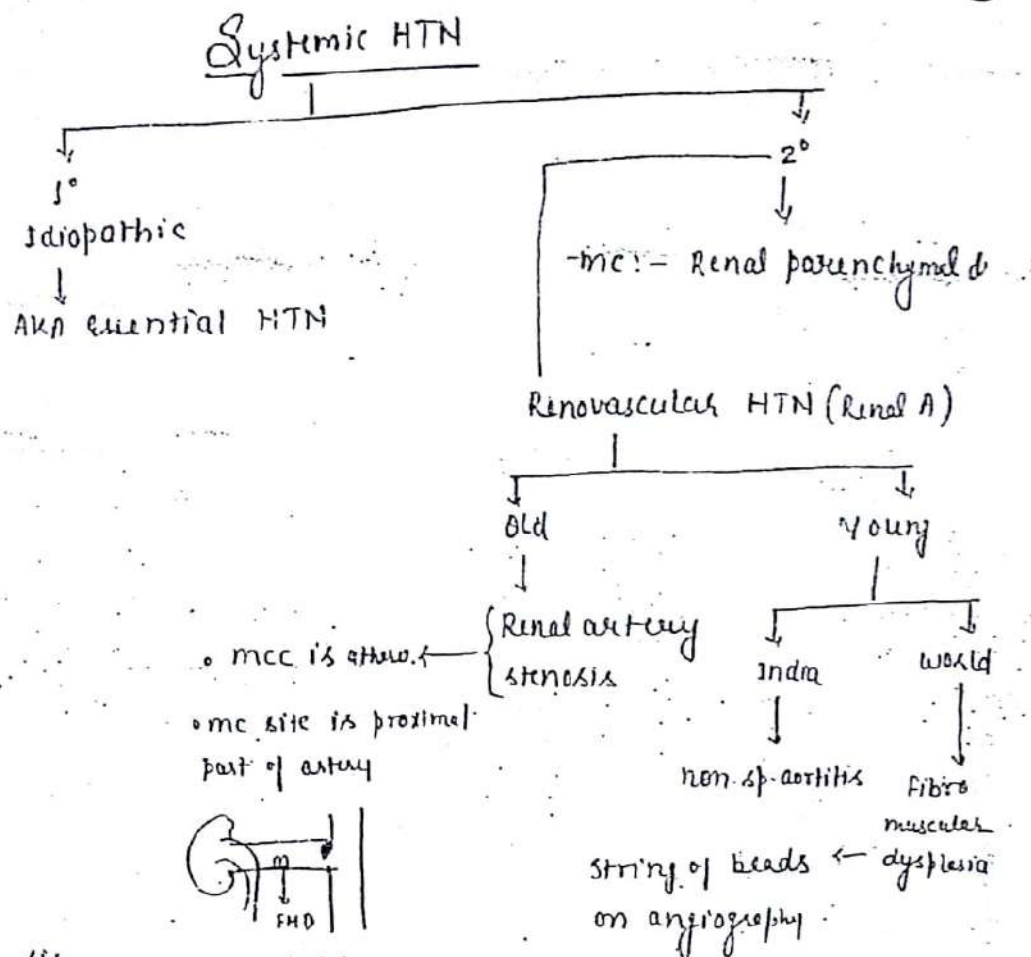
Recovery - ⊕

Hibernating myocardium



* Here it is reperfusion
* Problem is chronic ischaemia.
• viable myo.
• on echo - RWMA
• Recovery - ⊕

(63)



Diagnosis:

• Gold std: - Angiography (invasive)

• Best -

Captopril scan > CT angio > MRA > USG doppler

Mt: - medical. tll of atherosclerosis

- statin

- aspirin

* BIL RAS → ACEI & C/I

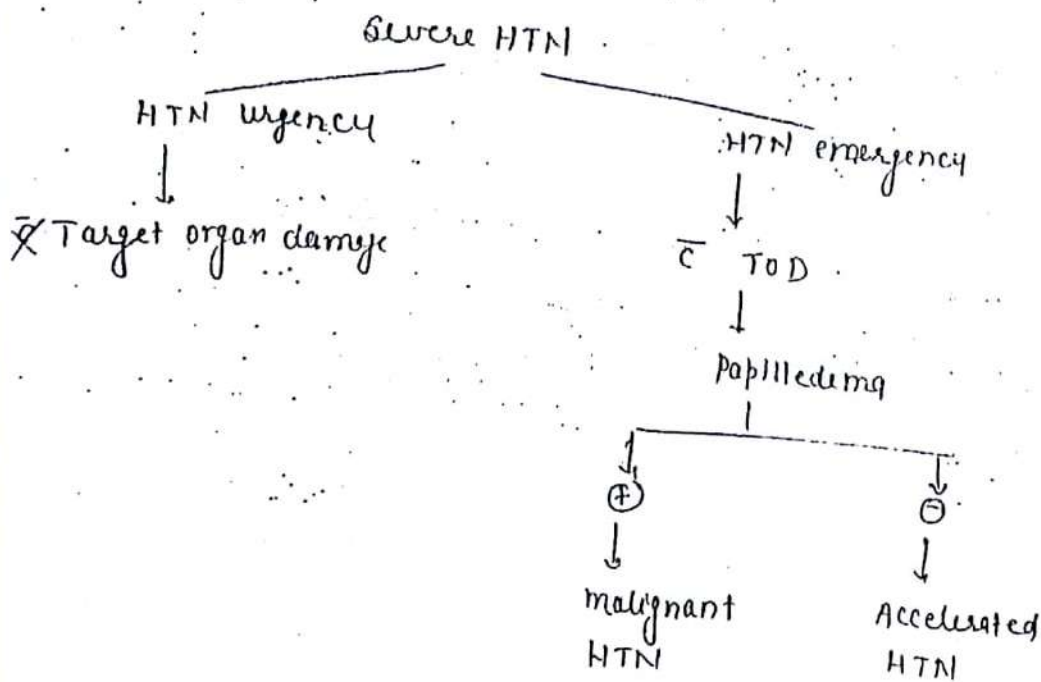
UIL RAS → NO C/I

→ Surgical → Stenting
(Not done b/c difficult to perform)

* Recurrent flash put edema. } ⇒ No stenting ← * only 1 functional kidney
* CKD
* Failure of medical Rx.

JNC-7 — Classification of HTN —

	SBP	DBP
N	< 120	< 80
Pre-HTN	120-139	80-89
Stage-I	140-159	90-99
Stage-II	160-179	100-109
Severe	≥ 180	≥ 110



(64)

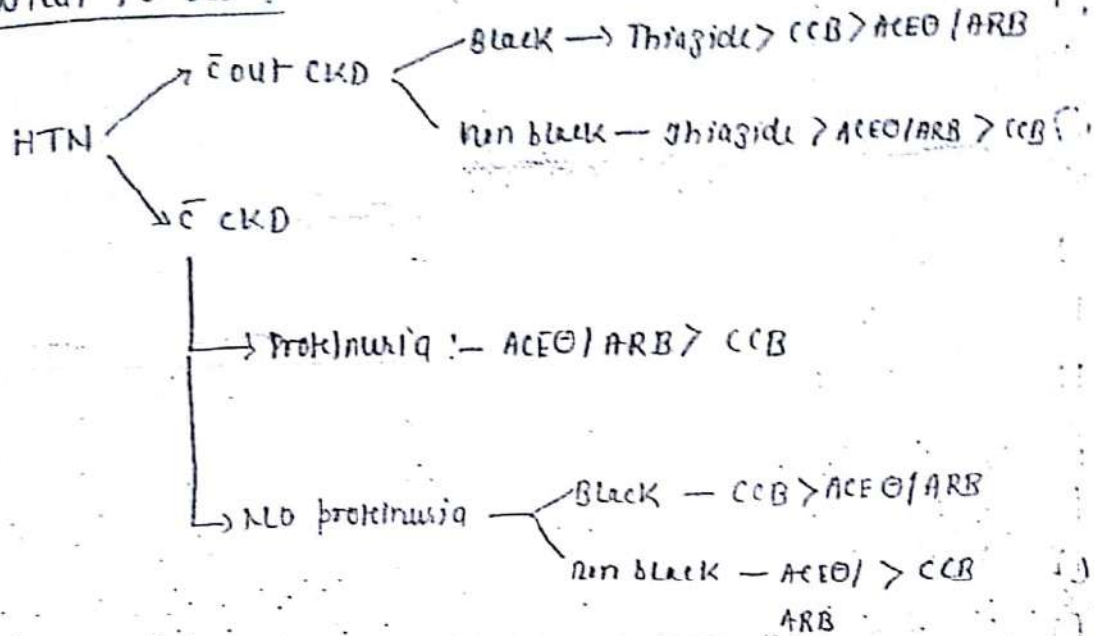
Target organ damage —

- ① CNS — • encephalopathy
• Isch. stroke
• Hem. stroke
• papilloedema
- ② CVS — • Acute coronary syndrome
• Pul. edema
• Aortic dissecⁿ
- ③ AKI
- ④ eclampsia

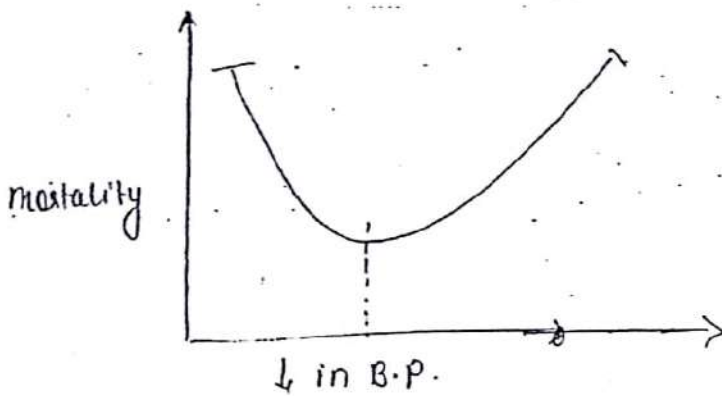
Routine (JNC-8)

	when to Rx	Target BP
① Age > 60 + No comorbidity	BP > 150/90	BP < 150/90
② Age < 60 or comorbidity (DM / CKD)	BP > 140/90	BP < 140/90

What to do?



J curve! — seen in sys. HTN
••••• systolicemia



(65)

Rx - HTN urgency - slow ↓ in B.P. over 24-48 hr.

$$MAP = DBP + \frac{1}{3} PP$$

Emergency -

Initial
1-2 hr

Later
over 24-48 hr

Fast ↓

Slow ↓

Reduce to 25% MAP

ex - 230 / 130

MAP = 165

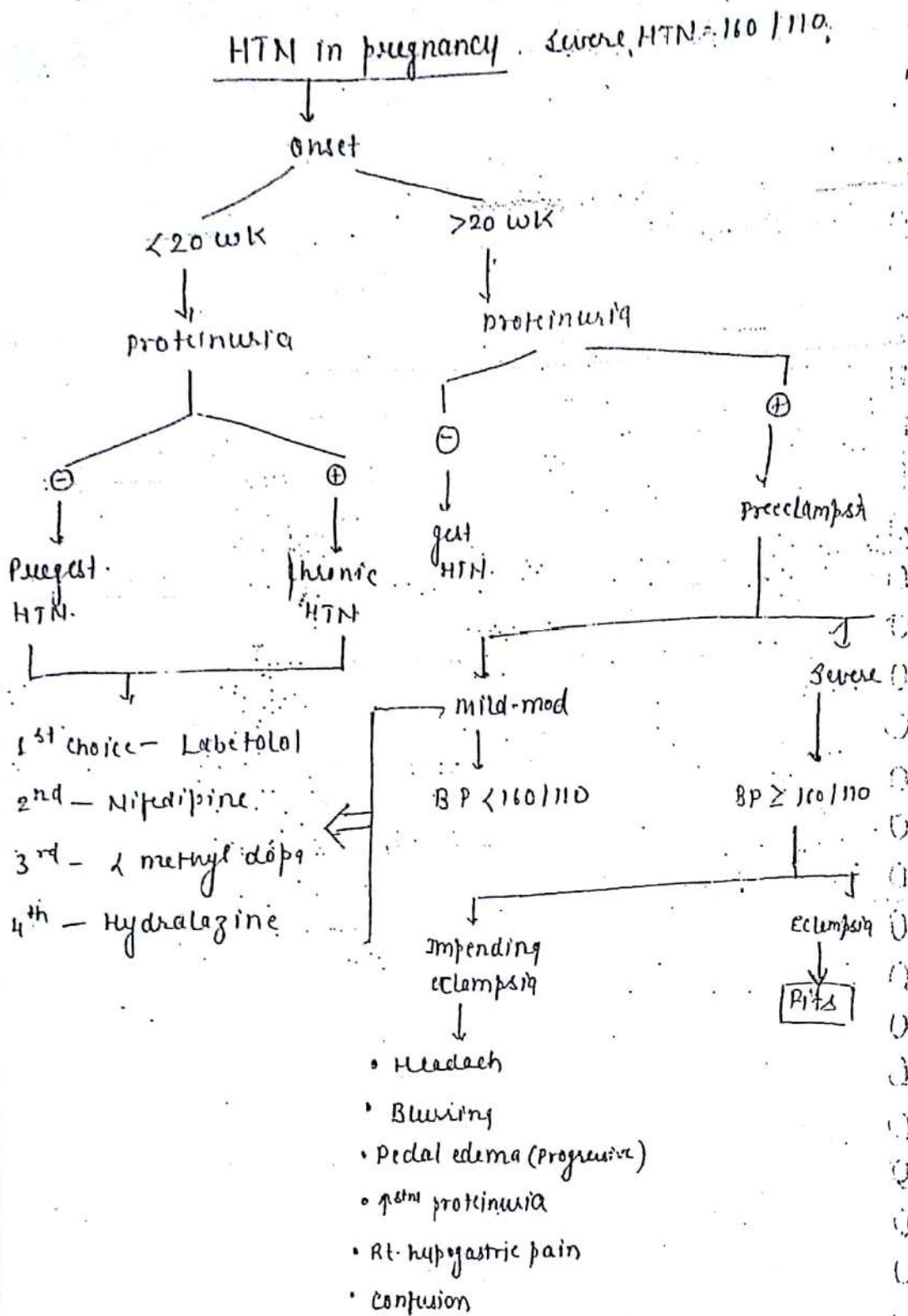
1-2 hr

next
24-48 hr

165 - $\left(\frac{165-125}{100}\right)$

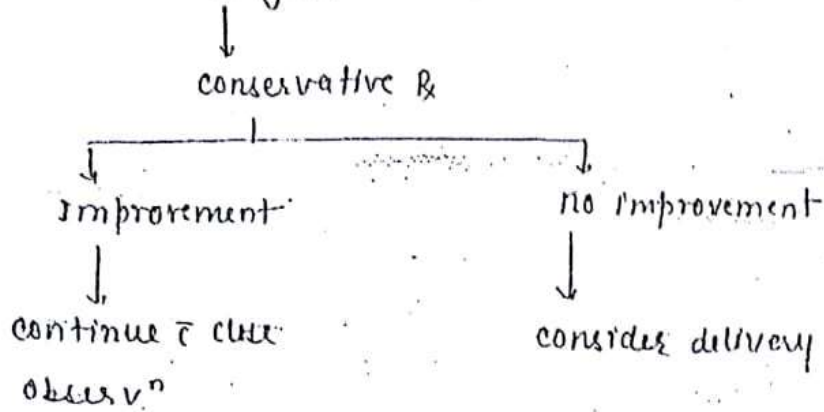
125 target

(N) MAP slowly



(66)

Rx — Impending eclampsia



* at fits (eclampsia)

- ↓
- Delivery
- i/v antihypertensive + MgSO₄ (DOC)
 - ↓
 - 4 gm loading (i/v)
 - ↓
 - 1 g/hr infusion x 24 hr

Other uses of MgSO₄ — • fetal neuroprotection

- Dose — same as previous
- use — anticipate preterm labour in nxl 24 hr

Drugs in HTN emergency - I.V.

1) I.V. NTG → cardiac
• avoid CNS

2) Labetolol → Aortic dissecⁿ

3) { Nicardipine
Nitroprusside

Fenoldopam - (Peripheral Di)

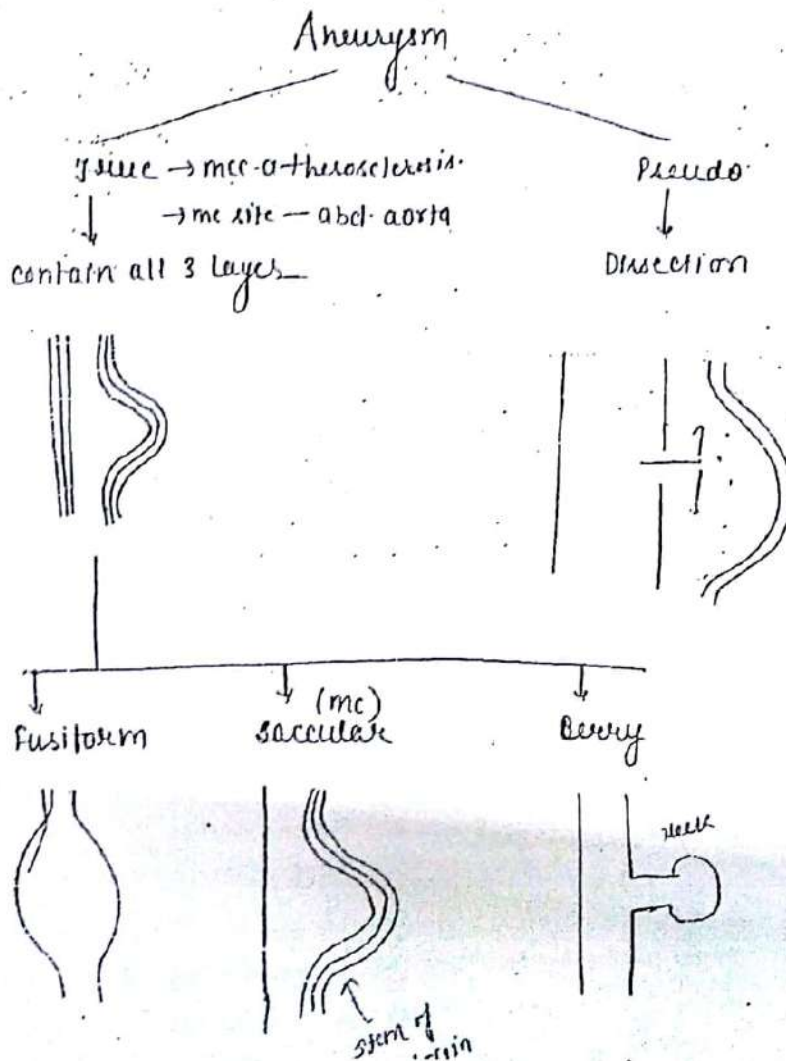
(67)

Risk factor - Aortic dissection -

* mcc - sys. HTN

collagen → marfan / EDS → cystic medial degenerⁿ
 coarctation
 Takayasu
 prior aortic surgery

Pathology - Intimal tear



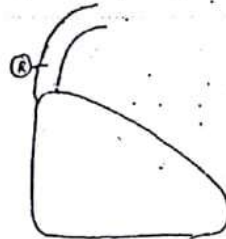
* Mycotic aneurysm — A type of saccular aneurysm
cause is bacterial (mc staph. aureus)

—X—

C/F! — Aortic dissection! —

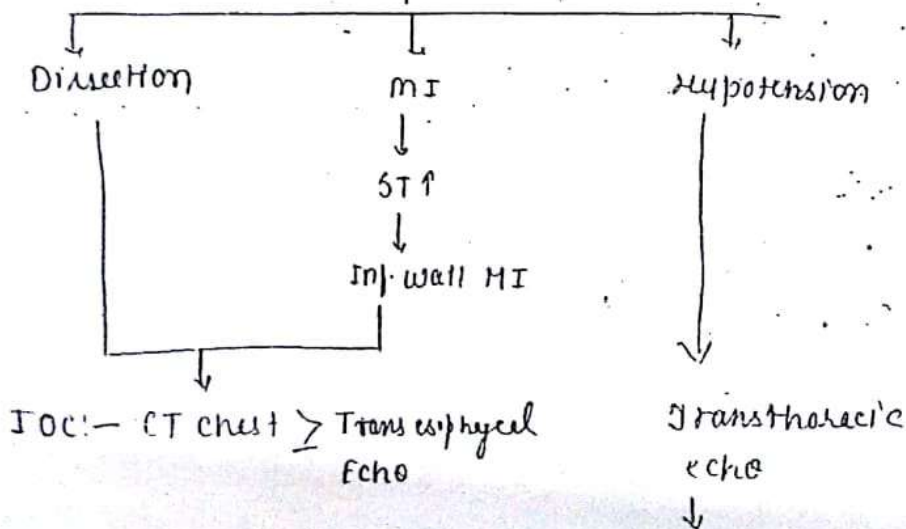
- chest pain radiating to Back (b/w 2 scapulae)
- ↓
- stabbing
- tearing

* mc site! — Rt. lateral tear in first few cm of origin of aorta



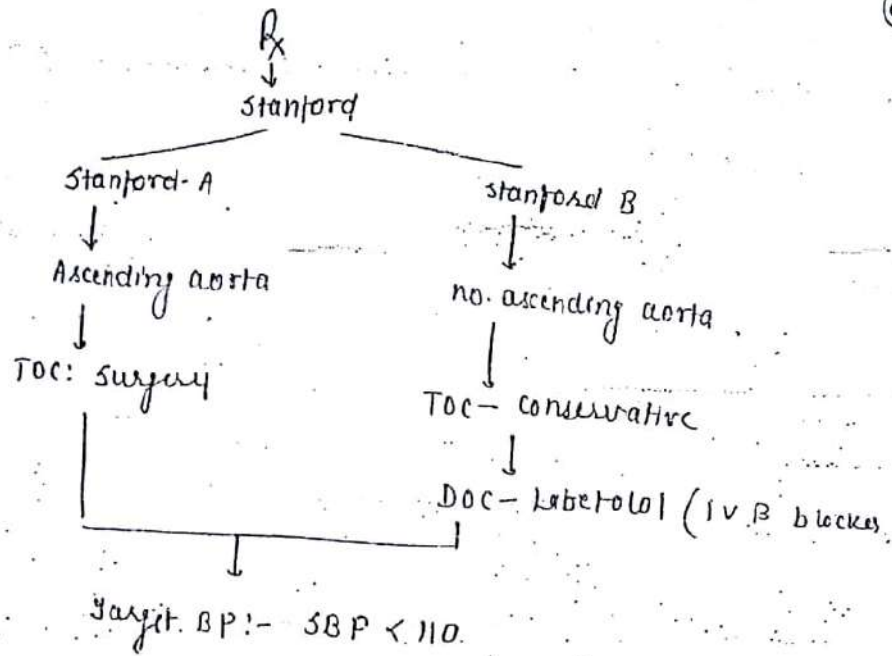
Investig! —

Pt. can presents as



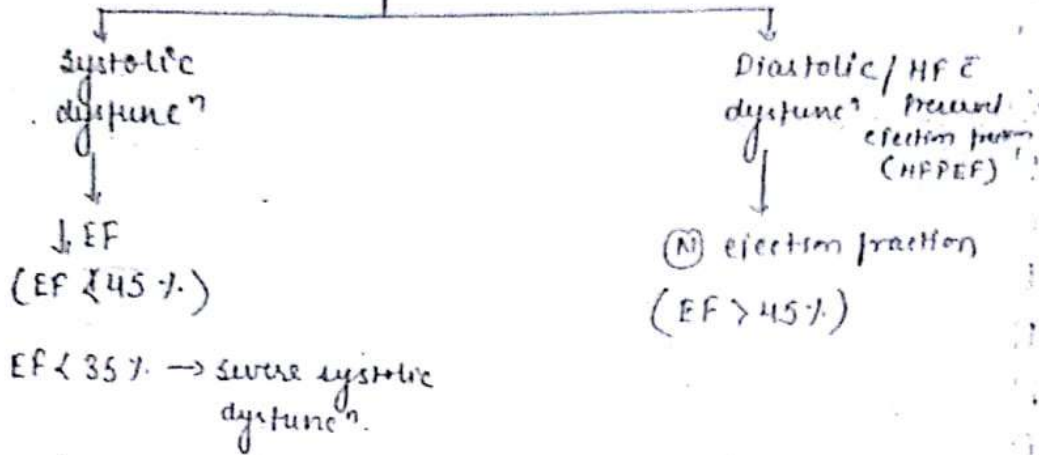
initial part of aorta is in pericardium & when there is tear the leak causes cardiac tamponade.

68



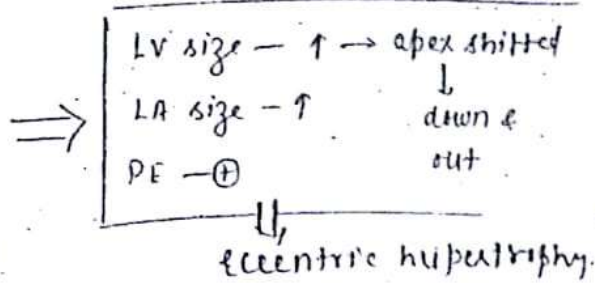
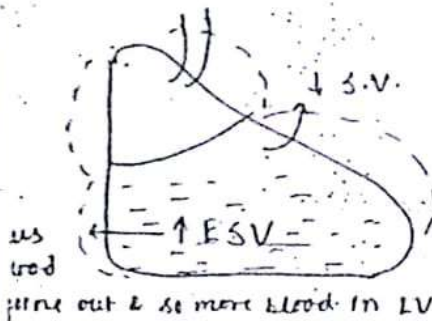
C/I - Anticoagulant are C/I, antiplatelet also C/I.
cause more bleeding.

— Heart failure —



• mce of Syst. dysfunction: —
JHD

• mce — DM / HTN



Blood regurgitate to LA → more blood in atrium
↓
LA & LV enlarged
↓
Pul. edema.

more blood will come to ventricle during diastole.
↓
∴ EDV ↑

$$EF = \frac{SV \downarrow}{EDV \uparrow} = \downarrow$$

(69)

Diastolic dysfunction



↑ afterload d/t syst HTN &
heart has to contract
against this

There occurs hypertrophy of muscle.

↓
Less size of ventricle cavity

↓
Blood go to LA

↓
Less bld will come
to LV

↓
∴ ↓ EDV

↓
Less Bld. in ventricle

↓
∴ ↓ SV

$$EF = \frac{SV \downarrow}{EDV \downarrow} = \text{(N)}$$

- LA size & enlargement
- LV size -
- PE ⊕

• Heart size (N) (only muscle enlarge)

• PE ⊕

• LA enlargement

Concentric Hypertrophy

* EF - ↓

- size - ↑

apex - shifted [D70]

eccentric

* EF - (N)

- size - (N)

- apex (N) (mild lateral shift)

- Apical impulse → Hyperdynamic

Vol. overload

Apical impulse heard for
< 1/3rd of systole as contra-

-tility is poor.

→ A.I. - seen in ≥ 2 inter-

-costal space d/t heart
dilated

* in cond. where there is
vol. overload - same present
(MR, AR, CCF)

* Extra sound - S₃
(mcc CCF)

- S₁ - soft

→ Apical impulse - Heavy

(pressure overload)

> 2/3rd of systole

→ A.I. in one ICS only.

* All other condition in which
there is press. overload, these
features are seen.

(AS, PS, HOCM, sys. HTN)

S₂
(mcc - sys. HTN)

- S₁ (N)

(70)

Inv:- 1) IEC - Echo

Blood:- NT Pro BNP $\rightarrow$ High -ve predictive value

Rx-

NYHA $\rightarrow$ ^{for} shortness of breath only
 $\rightarrow$ functional classifc

- it is not for pul. edema (to prove it there should be crepts/congestion)

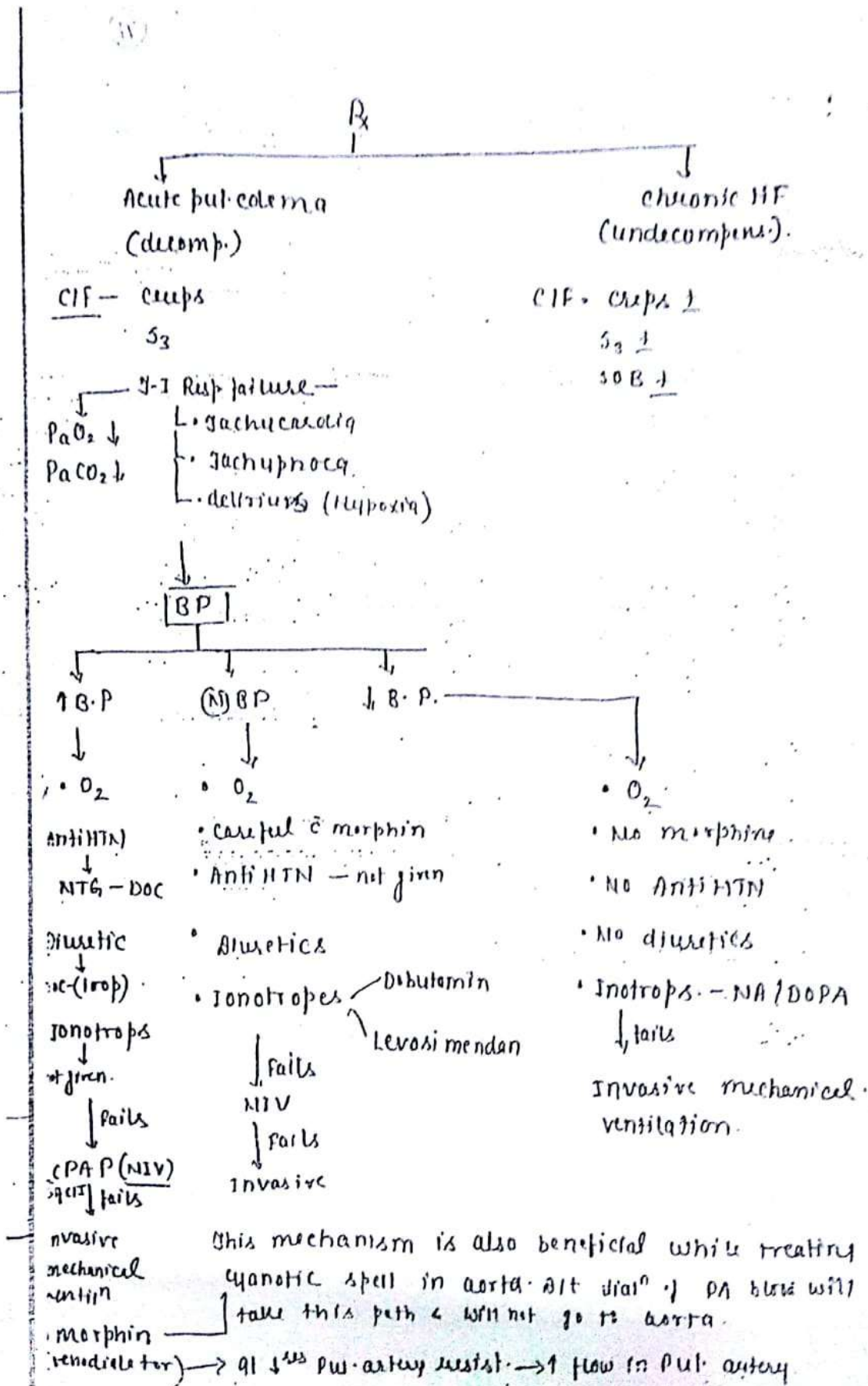
NYHA -

	<u>Limit</u>	<u>Shortness of breath</u>
I	No limitation	severe exertion ($>$ normal)
II	mild	Normal
III	moderate	$<$ normal
IV	severe	Rest

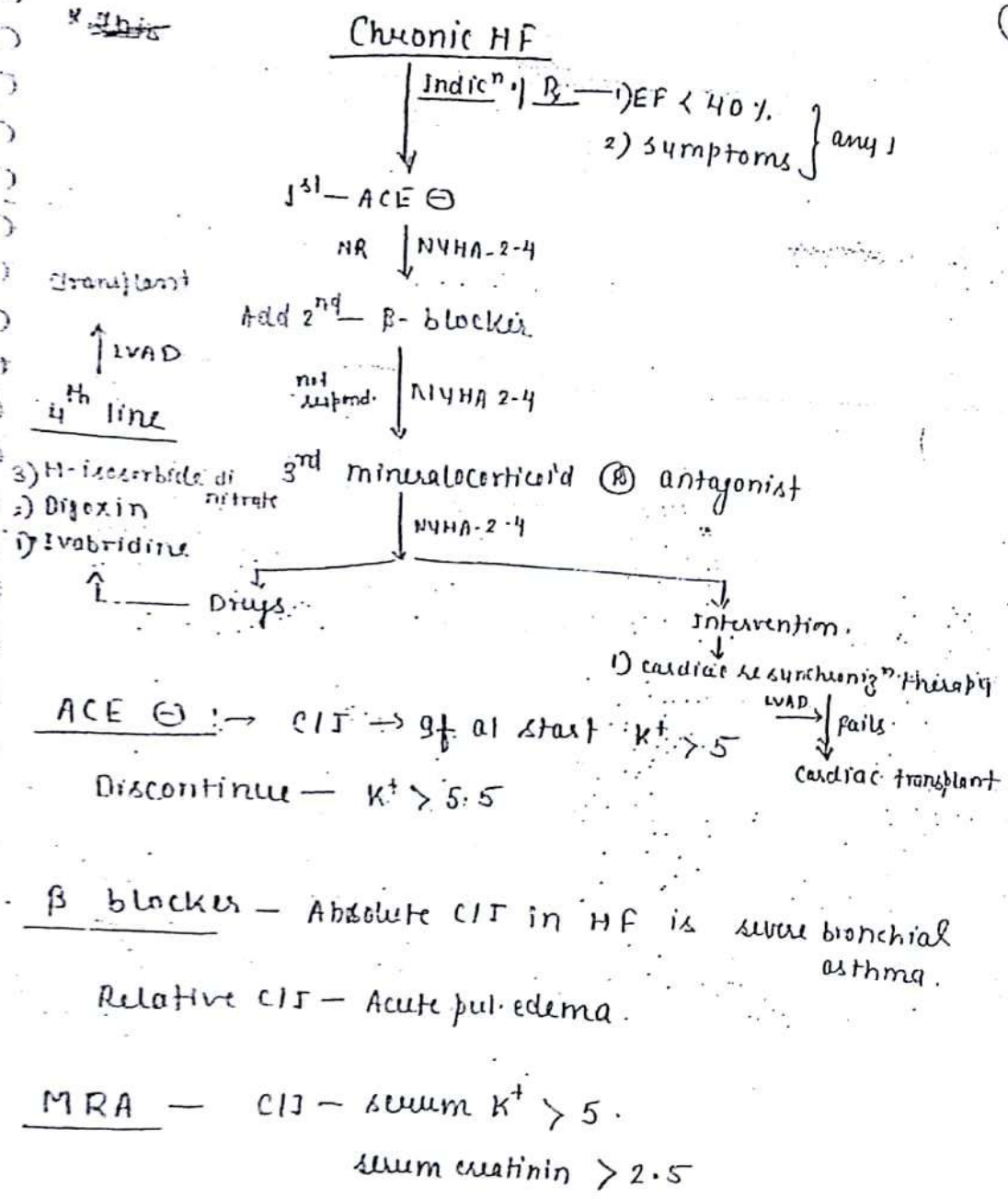
C/I of NIV:-

1) $\downarrow$ GCS

2) Hypotension.



(71)



Acute pul. edema (decomp.)

chronic HF (undecompens.)

CIF - cups
S₃

CIF - cups ±
S₃ ±
S₄ ±

GI Resp failure -

PaO₂ ↓
PaCO₂ ↑

- tachycardia
- tachypnoea
- delirium (hypoxia)

BP

↑ B.P. (N) BP ↓ B.P.

• O₂
Anti HTN
↓
NTG - DOC

• O₂
• careful c morphine
• Anti HTN - nitro

• O₂
• no morphine
• No Anti HTN

Diuretic
↓
furo (loop)
↓
Inotropes
↓
+ furo

• Diuretics
• Inotropes
 Dobutamine
 Levosimendan

• No diuretics
• Inotropes - NA / DOPA
 ↓ fails

CPAP (NIV)
↓
if fails

↓ fails
NIV
↓ fails
Invasive

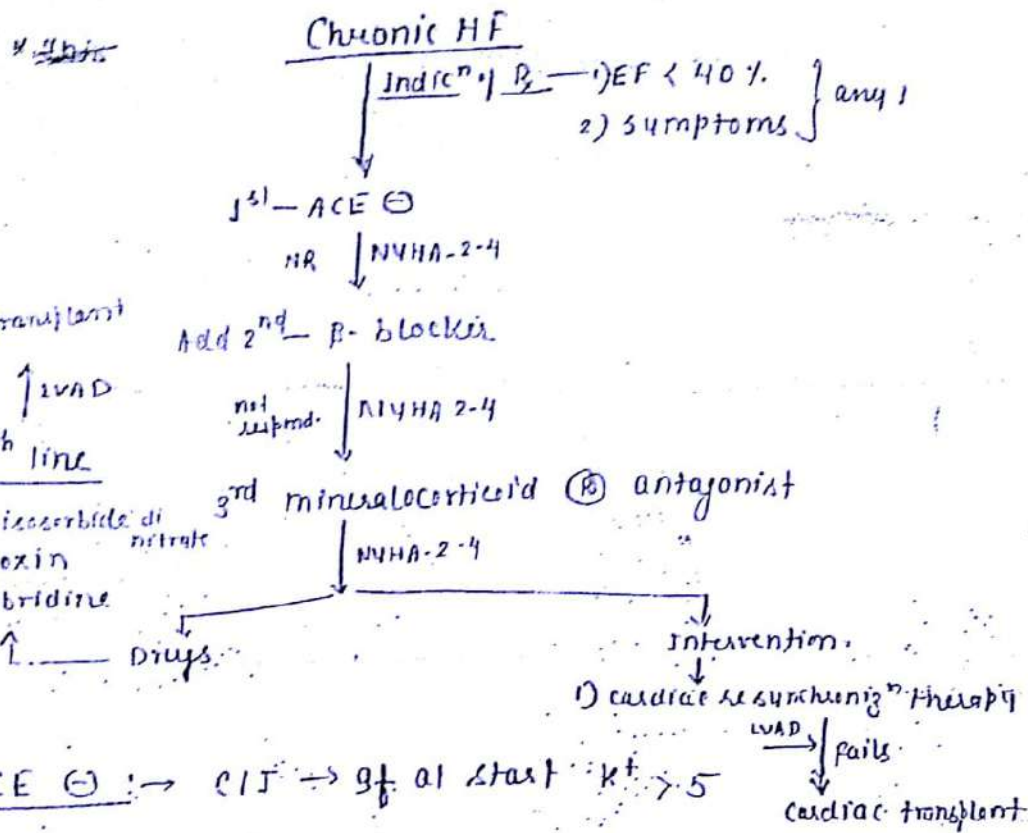
Invasive mechanical ventilation.

Invasive mechanical ventilation

morphine (vasodilator)

This mechanism is also beneficial while treating cyanotic spell in aorta. Ait d'Al. PA blood will take this path & will not go to aorta.
↓
at ↓ PVR - artery resist. → ↑ flow in Pul. artery.

(71)



ACE $\ominus$:→ C15 → 9f at start : $K^+ > 5$
Discontinue — $K^+ > 5.5$

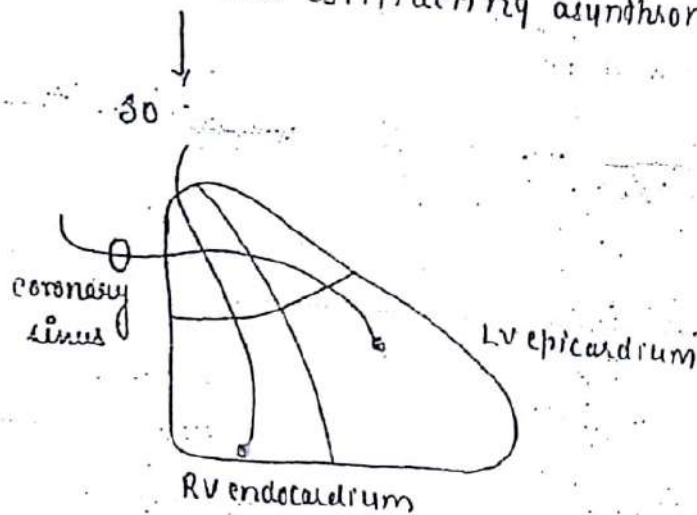
β blocker — Absolute C15 in HF is severe bronchial asthma.

Relative C15 — Acute pul. edema.

MRA — C15 — serum $K^+ > 5$.
serum creatinin > 2.5

CRT! - Cardiac resynch. therapy -

* In Ch. H-F Rt & Lt contracting asynchronously.

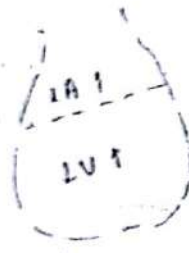


- By placing electrode, both the ventricles are allowed to contract synchronously.

LVAD! - All modalities failed & pt. waiting for transplant.

Indicⁿ -

(72)

CardiomyopathyDilated

→ EF ↓

→ Systolic dysfunction

Causes —

→ 1° DCM — idiopathic

→ 2° DCM — 1) Ischemic heart disease (IHD)

2) Alcohol

3) neuromuscular dis.

DMD

BMD

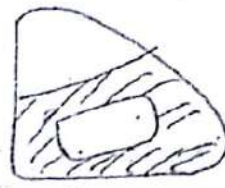
Friedreich ataxia

MD

4) Drugs —

• Doxorubicin

• Anthracycline

HCM

EF (N)

→ Diastolic dysfunction

Causes —HCM

1°

↓
HOCM

2°

ms. - sys. HTN

• Aortic stenosis

• Fabry's disease
(α-galactosidase deficiency)Fabry's disease — drug
which can reverse dis.Fabry's is
cause of
restrictive CMRestrictive

→ EF (N) / ↓

→ Syst. + diastolic
(mainly diastolic)Causes —

① Amyloid

② CTD — Sarcoidosis

RA

SLE

③ Eosinophil → Löffler's

④ Fibro → EMF
(endocardial fibroelastosis)

⑤ Iron — Hemosiderosis

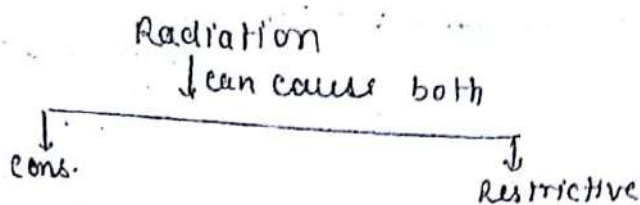
⑥ Fat — ARVD/ARVH

⑦ Miscell — Radiation
Carcinoid

⑧ Glycogen — GSD

GSD II & III (congenital) ↓

Anticari
Pompe's (GSD I)



Special!:-

• Takatsubo CM (Broken heart) - Apical ballooning synd-

- ♀ young → middle age

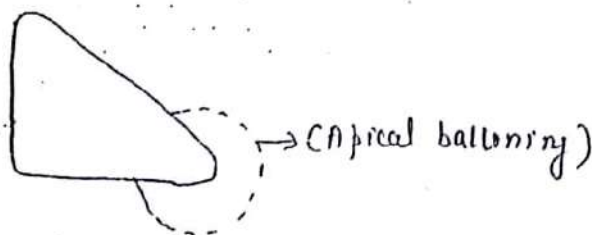
- NO risk factor for CAD

↓ emotional outbreak

chest pain + Heart failure

↓
ECG - ST elevⁿ

* IMV! - Echo



Apex will be selectively dilated

* Rx — NTG + Diazepam — (to reduce anxiety)

Avoid Inotrops

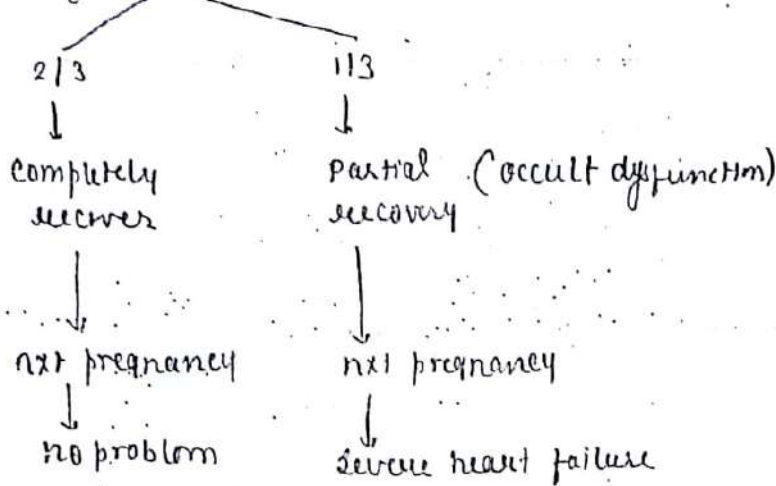
* Excellent recovery.

(73)

Peripartum CM -

- 1 mth before delivery — 5 mth after delivery
- Echo → Dilated CM like features.

Prognosis:-



* excellent recovery

Shape

Disease

- spherical ventricle — DCM
- Spade shaped — apical hypertrophic CM (variant of HOCM)
- Distortion of ventricle — MI / aneurysm / Remodelling
- Banana shaped — hypertrophic CM.

* Commotio cordis —

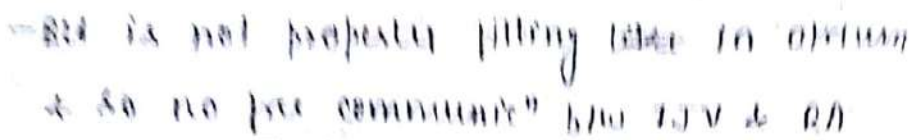
Rx - Defibrillation.

Sports activity → Blunt non-penetrating trauma

↓
Sudden death — VT/VF

Experiment 1

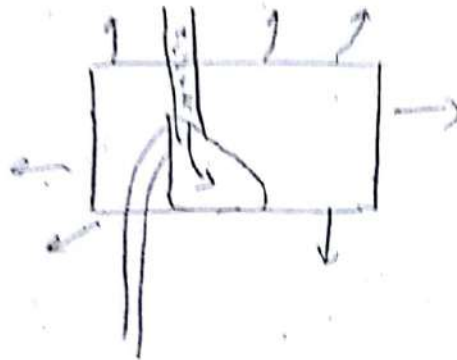
but without error.



93VP

[illegible]

Inspire™



- JVP ↓ $\rightarrow$ as there is release of obstruction.

- waveform - better seen (b/c of better focus)

- * R1 sided events augmented during inspirⁿ
except $\rightarrow$ pul. valvular click (it has τ inspirⁿ)

De curvilinear's law.

(74)

* Lt sided flow $\rightarrow$ $\bar{c}$ expiration

$\rightarrow$ Inspirⁿ

$\downarrow$
Drainⁿ of pul. vessel & drainⁿ of thoracic cavity

$\downarrow$
Stasis of blood

$\downarrow$
~~flow~~ $\uparrow$ blood flow to left side.

$\rightarrow$ so Lt sided event better $\rightarrow \bar{c}$ expirⁿ.
(expirⁿ hold)

* exception of this rule $\rightarrow$

• HOCM

• mitral valve
prolapse

HOEM

↑ Blood → ↑ event in other
↓ HOEM

↓ Blood → ↑ in HOEM
↓ in other

→ 9n HOEM — septum hypertrophy (irregularly)

↓
Blood has to flow through aorta &
there is LV ^{with} obstruct

↓
aortic stenosis

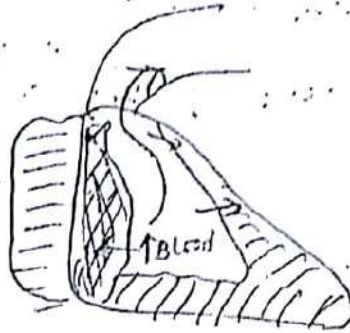
↓
Hypertrophy of muscle

* When ↑ blood in ventricle

↓
stretch muscle

↓
so obstructⁿ get
relieved

↓
↓ murmur



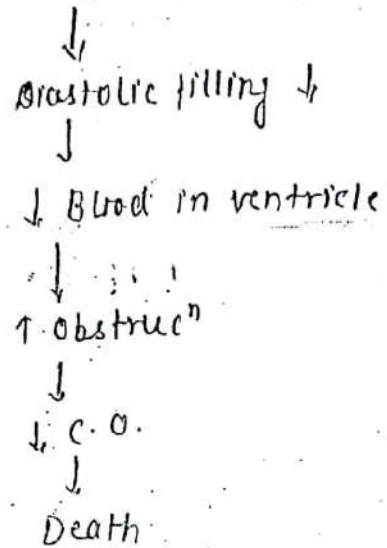
* ↓ Blood

↓
↓ obstructⁿ

↓
↑ murmur

(75)

* on exertion — tachycardia



Preload



obstruction



murmurs



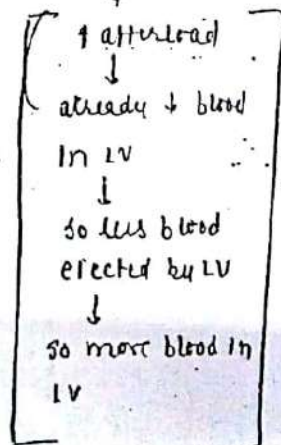
Afterload



obstruction



murmurs



Preload ↑

- Lying down
- Squatting (also ↑ afterload)

Afterload ↑

- Squatting
- Hand grip (isometric exercise)

Preload ↓

- Valvular maneuvers
- Diuretics
- ACE I
- Nitrates

↓ Afterload

- ACE I
- Nitrates

Genes involved in HCM

* β Myosin heavy chain myosin binding protein

→ HCM is multigenetic disorder.

CIF — • Asymptomatic

- Symptomatic during exertion
 - syncope
 - death
- Family H/O • sudden death
- On ECG → VT/VF

ECHO ←

- Asymmetric septal hypertrophy
- LVH
- Systolic ant. motion (SAM) of ant. mitral leaflet (AML)

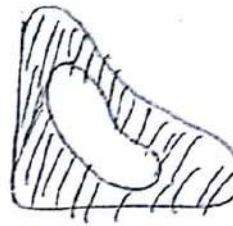
Revert

↓ again ECG

- Bilateral LVH
- Septal hypertrophy
- ↓
- Pseudo-infarct

(76)

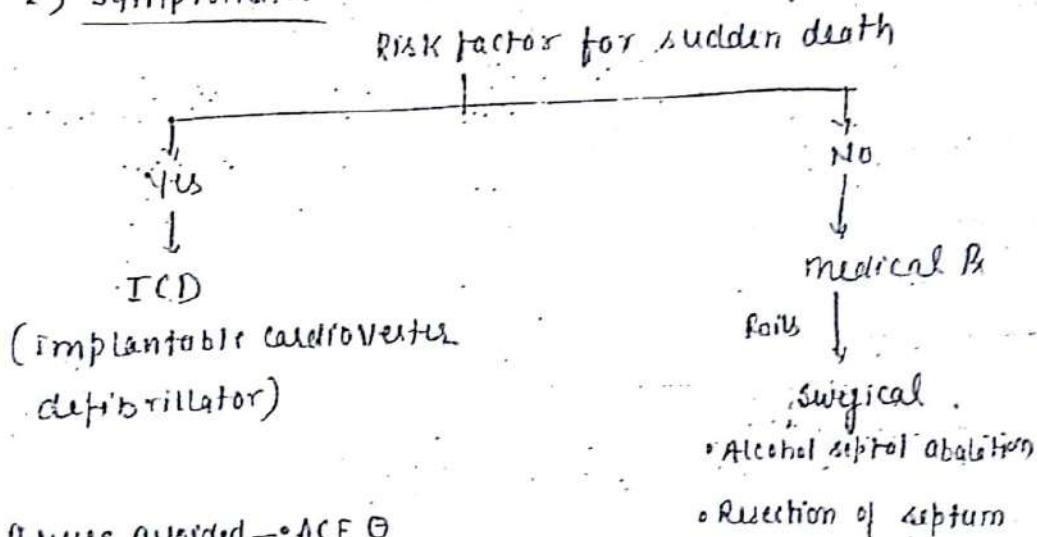
- * Autopsy finding -
 - LVH
 - ASH
 - (asymmetrical septal hypertrophy)
- * Banana shaped cavity



* Bx → Histo. sketch myocyte away
 ↳ Taken from RV, as it is easily accessible (most anterior)

Rx - 1) Asymp - β blockers - ↓ H.R. [stab injury will cause - tricuspid v. - damage]

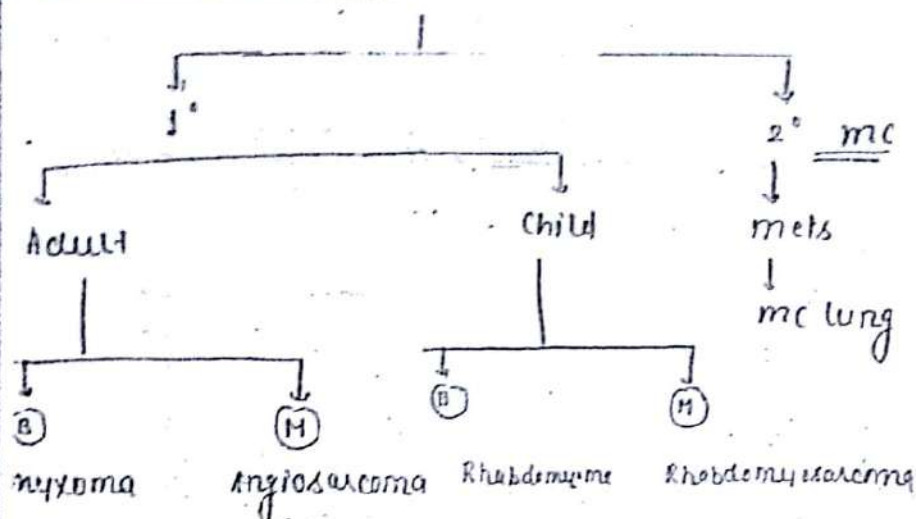
2) Symptomatic -



Drugs avoided -

- ACE I
- Nitrates (↓ PL & AL)
- Diuretic (as they ↓ PL)
- Digoxin (↑ force of contracⁿ of septum & muscle)
 ↓
 then come closure

Cardiac tumor:-



% In acute pul. edema — Pulsus alternans (LVF)

→ LVF → is mcc of chyne stroke breathing

Rheumatic fever —

* Only pharyngitic strain — RF

* Pharyngitic ~~Hept~~ impetigo strain → Glomerulonephritis

C — Carditis

A — Arthritis

S — Sydenham

E — Erythema marginatum

S — sub-cutaneous nodule

* MR → mc valvular HD is acute RF.

(77)

Arthritis - migratory / flitting polyarthritis

- Non erosive

Sydenham chorea - can occur at any stage of disease

- Don't affect course of disease

Risk factor for getting Sydenham chorea -

- preg (
- ocp's

Erythema marginatum - not occur on face

- Erythematous ulcer which are expanding
- commonest site - trunk

S.C. nodule - ext. surface of upper limb

Minor criteria -

P - Prolonged PR

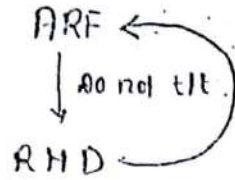
E - elevated ESR

A - Arthralgia

C - ↑ CRP

H - HIV strepto. infecⁿ

Fever



∴ RHD is a cumulative damage.

1st Prophylaxis — Prevention of ARF by treating pharyngitis.

- if in 9 days of pharyngitis give penicilline
- if allergic to penicilline — give erythromycin.

2nd Prophylaxis — Pt. has RHD & we are preventing ARF.

HISTORY

RF.

[no carditis
no valvulitis]

RF

+
carditis

RF

+
valvulitis
+ carditis

Durⁿ

21 yrs age

5 yrs durⁿ (which ever is late)

21 yrs age

10 yrs durⁿ (which ever is late)

40 yrs age

10 yrs durⁿ (late)

(78)

2° Px -

Doc. Penicilline

↓ Allergic

Sulfadiazine

↓

Erythromycin

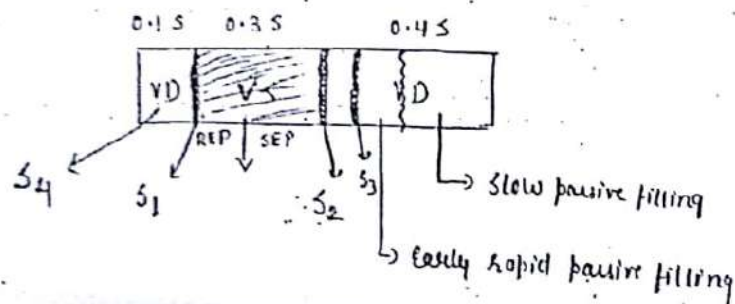
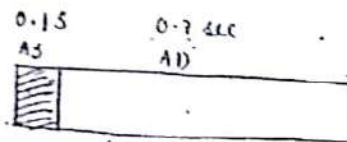
MS

* MCC → RHD

* congenital MS — MS + ASD → Lutenbacher Syndrome

Cardiac cycle -

0.8 sec



S₃ — Prerequisite — 1) Lt. atrial press./LA volume ↑

2)

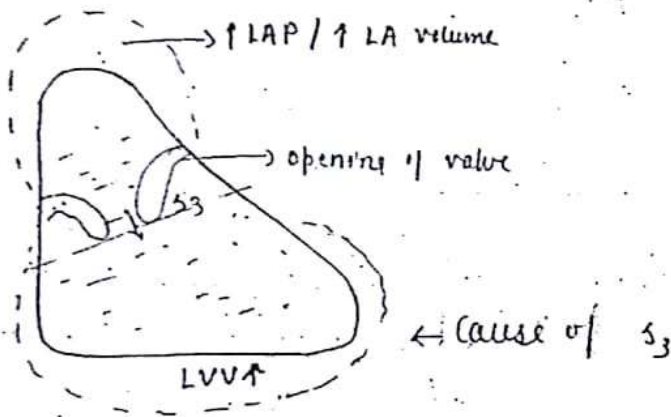
ESV — (N) → Physiological S₃
 ↑ → Pathological S₃ → cause → CCF

* qn MR & VSD → Physiological S₃ is there

★★

Low pitch
S₃
S₄
Tumor plop

Rest all are high pitch sound.



* qn ESV is (N) & there is no failure then it produces physiological S₃

(79)

Physiological S_3 —

- Hyperdynamic state
- Fever
- anemia
- Hyperthyroidism
- Beri-Beri
- A-V. malformⁿ
- children
- exercise
- tachycardia

How to diff. b/w pathological / physio S_3

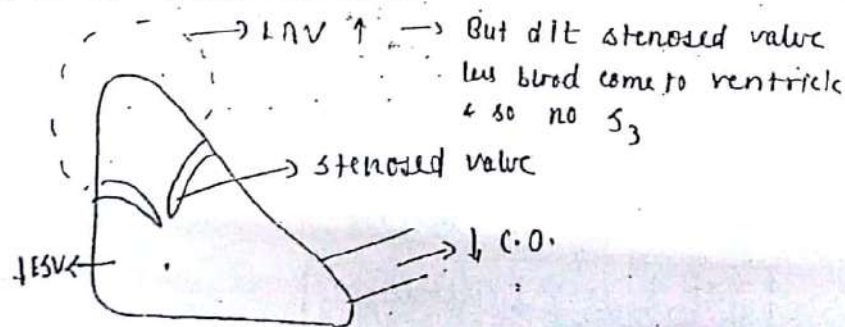
— Allow pt to stand
↓ ↓ venous return

Physiological S_3 abolished

↓

Pathological S_3 persist

✗ In MS → S_3 is not possible



✗ LV never fails in M.S.

✗ In MS → Apex is at (N) place

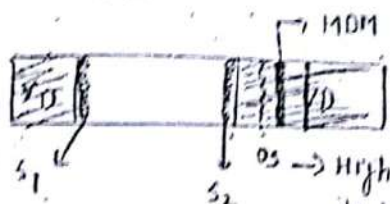
✗ → apical impulse → tapping

* Risk of AF very high in M.S.

* Opening snap:— thickened valves when striking ventricular wall while opening produces opening snap.



* Intensity of 1st H.S → loud.
(valve opening for large dist & closing for short dist)



S₂ → High pitched sound → can radiate to back, neck.

→ close S₂ - 0.5 gap → correlate severity of disease

gap ↑	→	↓ severity
gap ↓	→	↑ severity

80

* Mitral valve orifice $\rightarrow 4-6 \text{ cm}^2$

9) $< 1.5 \text{ cm}^2$

severe MS

Symptomatic

Asymptomatic

TDC-PMBV
(Pmc)

Yes

Risk factor for embolism

NO

Exercise stress
test

(+)

PMBV

(-)

yearly follow
up

C/S - ① LA clot

② MS with mod-severe MR } absolute C/S

③ Fully calcified valve $\rightarrow$ Relative C/S

$\Downarrow$
mitral valve replacement
is done in this cases

→ Criteria of LFT
(pulmonary artery catheter) PASP

at rest exercise ≥ 50

at rest exercise ≥ 60

TMG (trans mitral gradient)

≥ 10

≥ 15

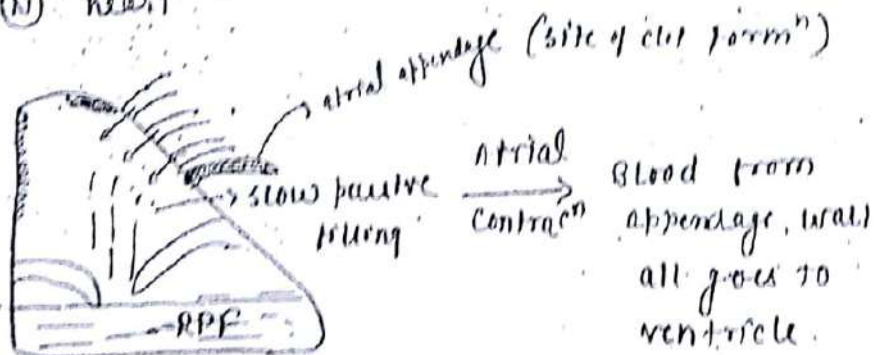
↓
ave test

↓
PMBV

(Percutaneous mitral balloon valvulotomy)

S_4 → (Pressure overload)
occurs at

in heart



→ this atrial contracⁿ pushes 20% blood to LV
80% blood is filled in ventricle by Rapid
passive filling.

(8)

* i.e why pt. w/ AF doesn't die as the 80% blood has already there in ventricle.

* In MS pt. Rapid passive filling

↓
fills 50% of ventricle

↓
So the atrial kick is very much imp. for filling of ventricle.

↓
If there is AF in pt. w/ MS

↓
There will be no 20% blood coming through atrium

↓
Decrease

* S₄ produced due to more atrial kick

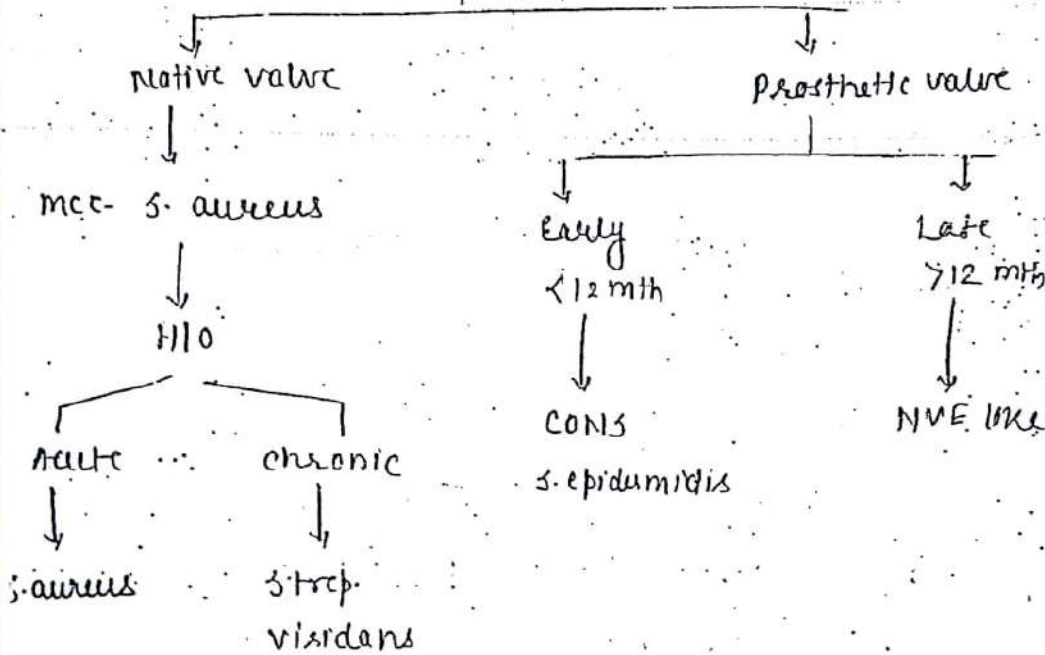
* In MS → atrial kick will be very forceful to push blood

↓
This creates presystolic accentuation
(occurs before ventricular systole)

* No's in AF —

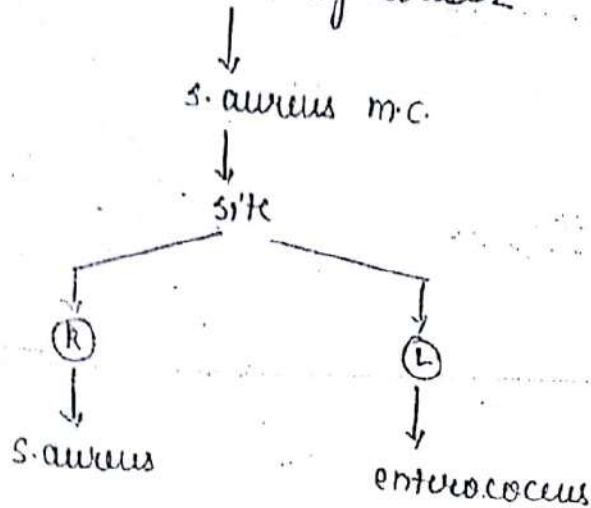
- P wave in ECG
- a wave in JVP
- S₄
- No presystolic accentuation

- Infective Endocarditis -



* JE in IV drug abuser

(82)



* strept. bovis → mc organism causing JE in pt.
c ulcerative colitis / colonic polyp.

Duke's criteria —

Major — (1) Blood culture — yield is 100%

A) 2 blood culture 12-24 hrs apart
↓
Both ⊕
Both show same organism

B) 3-4 culture → gap b/w 1st & last culture = 1 hr
↓
min. 3 culture ⊕ for same organism.

C) For coxiella burnetii single culture is enough.

* Persistently +ve blood culture.

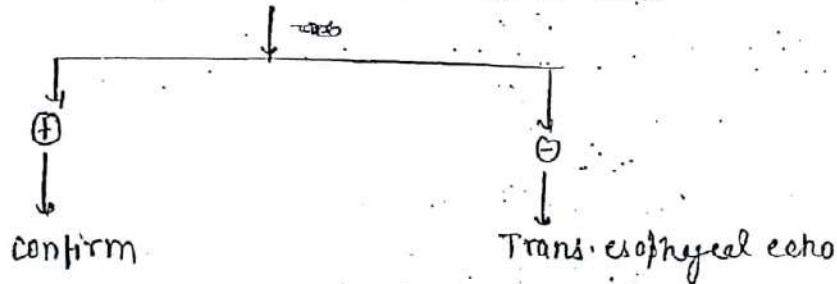
- ② Echo — I) vegetation in valves
II) Intracardiac abscess
III) New valvular regurgitation
IV) New prosthetic valve dehiscence

Minor —

- ③ Immunological —
• Osler's node → Finger tip, Painful
• Roth spot
• Glomerulonephritis
• Rheumatoid factor (+)
Hge ← a → spot

- ④ vascular —
① septic emboli
② Janeway lesion — seen on palm & soles, painless
③ splinter hemorrhage
④ mycotic aneurysm

Inv! — Screening TTE — Transthoracic echo



(83)

Rx:- empirical:-

vanco. + gentamycin $\pm$ Rifampicin (Breaks biofilms)

[5x] Indicⁿ:- ① Large vegetation > 1cm

② Prosthetic valve endocarditis

③ Fungal endocarditis

④ Persistent +ve blood culture even after 1 wk Antibiotic t/t.

⑤ Severe HF dit. valvular regurgitation

⑥ Presence of intracardiac abscess

⑦ Development of new conduction blocks

Prophylaxis:-

Indicⁿ:- ① Person H/O IE:

② +ve of prosthetic valve in body

③ +ve of cardiac transplant $\bar{c}$ valvulopathy

④ Any uncorrected: cyanotic CHD.

⑤ Any cong. heart disease

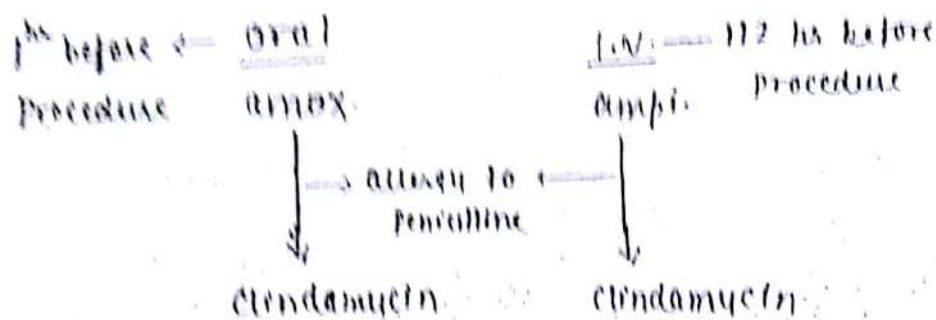
⑥ After correcting CHD, $\bar{c}$ in first 6 mth.

⑦ Any CHD corrected $\bar{c}$ surgery but, still the correction is incorrect.

when to R —

- ① Buccal / oral procedure (involving gingiva)
- ② Invasive deep tract procedure

what to give —



* For fungal endocarditis → Azole Prophylaxis is given life long.

* Max^m risk of IE is C MR.

- MVP C out MR → zero risk

(MVP → AKA Barlow's disease)

- MS → least risk → MVP C out MR > MS

* EHD having max^m risk — PDA & VSD

II — I — min. risk — ASD (secundum)

(24)

% more the gradient of blood flow
↓
↑ damage to valve
↓
↑ RISK

Pericardial cyst — mesite cardiophrenic angle of
Rt. side.

— CNS —

→ Dominance —

Ⓡ handed

Ⓛ handed

Ⓛ hemisphere
is dominant

Ⓛ hemisphere
(> 90%)

Dominant

Funcⁿ: — ① Speech & language

② Judgement

③ Abstract thinking

④ writing

⑤ Calculation

⑥ Verbal memory

Non dominant

① Fantasy

② Creativity

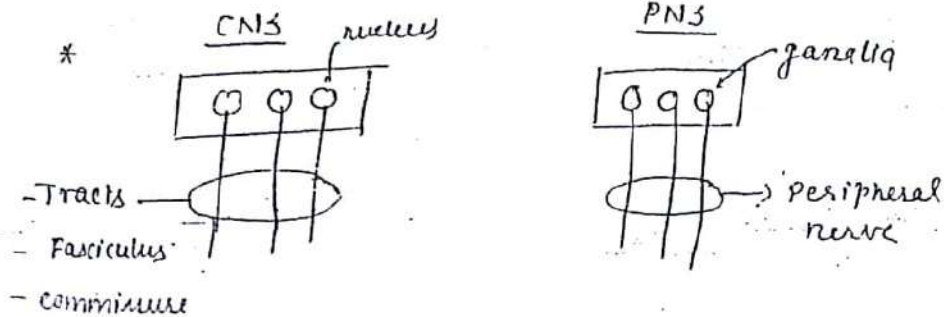
③ Philosophical thinking

④ 3-D activity —

Drawing & constructⁿ

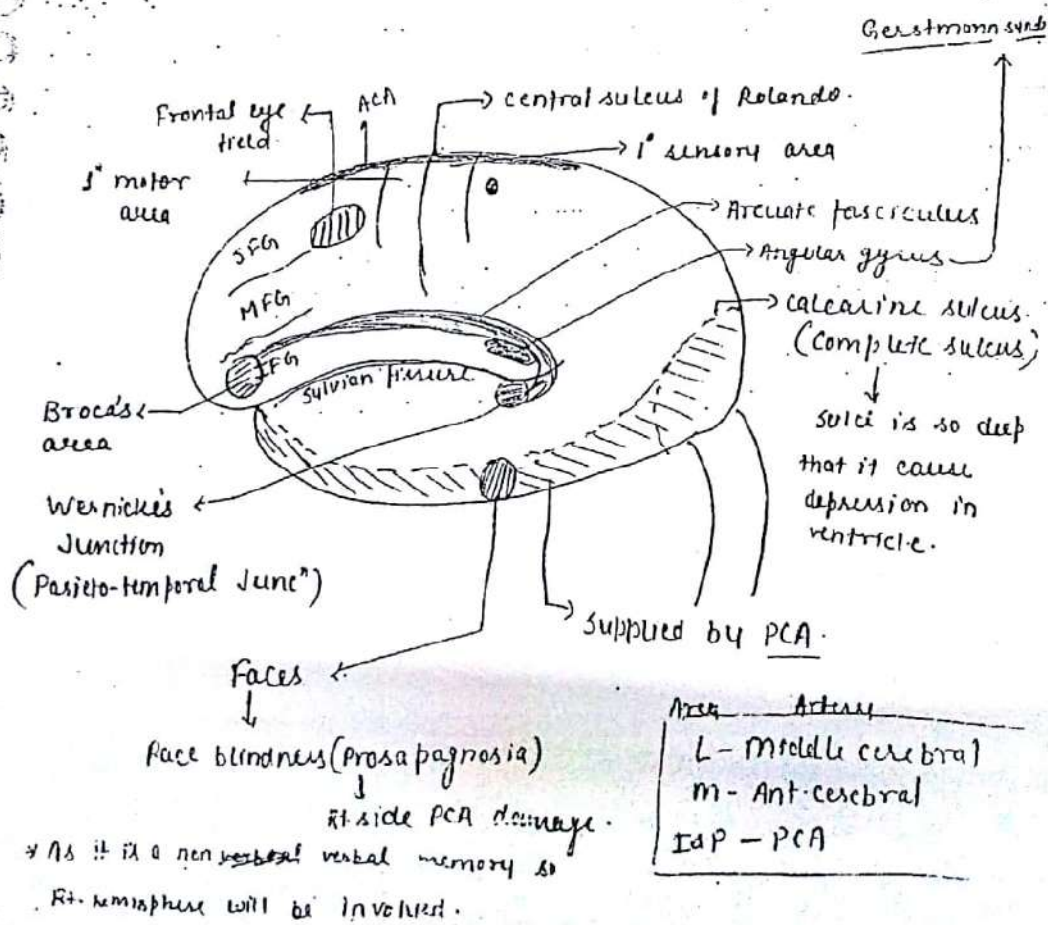
⑤ Non verbal memory

(85)



Fasciculus — connecting 2 ~~case~~ part of same cerebral hemisphere.

Commissure — one hemisphere to other hemisphere.



* medial part of temporal lobe involves in → memory.

Agnosia — • Not able to identify known objects.

Apraxia — • Problem in ~~performing~~ motor sequencing.

Ideational apraxia — Idea itself is lost.

Ideomotor apraxia — idea is intact, but still not able to perform.

→ occur due to lesion of motor ~~association~~ ^{association} area.

→ lesion of sensory association area will cause ideomotor apraxia.

(86)

Lobe	Function	Dysfunction
Frontal	1° motor area	face & arm ↓ mcn ↓ legs - lcl
mcn	- Frontal eye field ↓ (Push buttons)	C/L - Hemiparesis
	- Broca's area	C/L - gaze palsy
		Broca's aphasia
ACA	- Paracentral Lobule	Incontinence (infantile bladder) ↓ cortical bladder
	- Pre frontal cortex <u>Social</u>	Antisocial behaviour
	- Initiate thought	Abulia
	- Suppression of primitive reflex	Release reflexes

Parietal lobe —

Dominant parietal	{	writing	Agraphia	{	Gustmann
Dominant Angular gyrus		calculation	Acaculia		Suratone
		RT/LE orientation	R/L confusion		
			Finger agnosia		

• Arcuate fasciculus → conduction aphasia

Reading → Alexia

Non dominant angular gyrus

construction

(draw circle, connect no. 1-2, 5-6, 3-4)

Deconstruction

Construction apraxia

Deconstruction apraxia

1st sign in hepatic encephalopathy → construction aphasia.

Number connection Test performed.



C/L Hemineglect
(mostly it side is neglected)

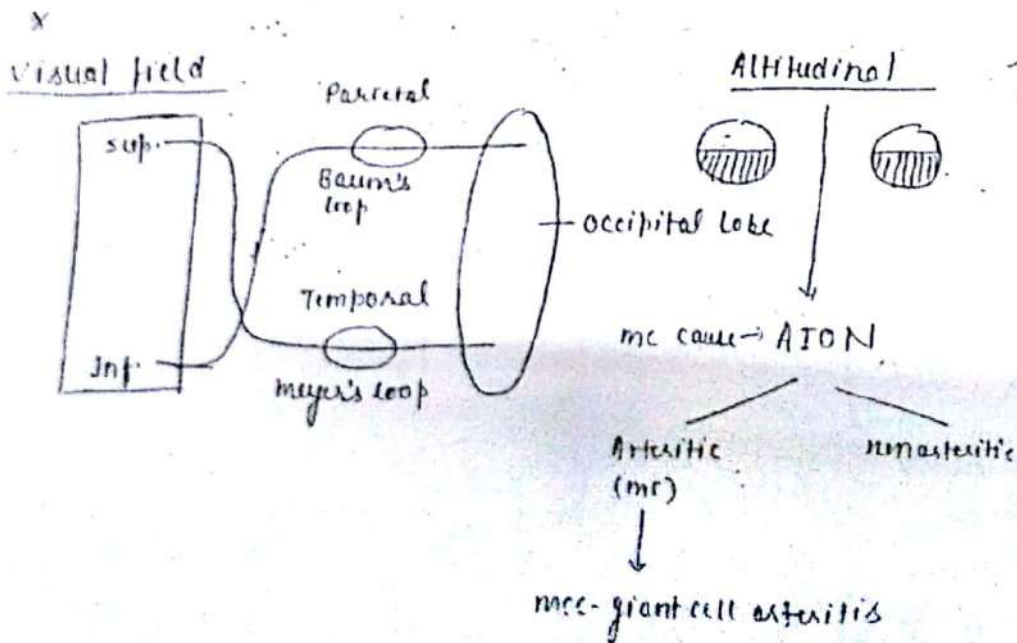
(87)

Dominant temporal	- Wernicke's area	Wernicke's aphasia
	- verbal memory	Pure word deafness
Non dominant temporal	- non verbal memory	Prosopagnosia
	- music	Amusia

Occipital lobe	U/L	• CIL homonymous hemianopia & macular sparing
	B/L	• cortical blindness

Sometimes we can see through subcortical centre also but it only shows face of object, not texture & detail of body.

Anton syndrome → Denial of blindness

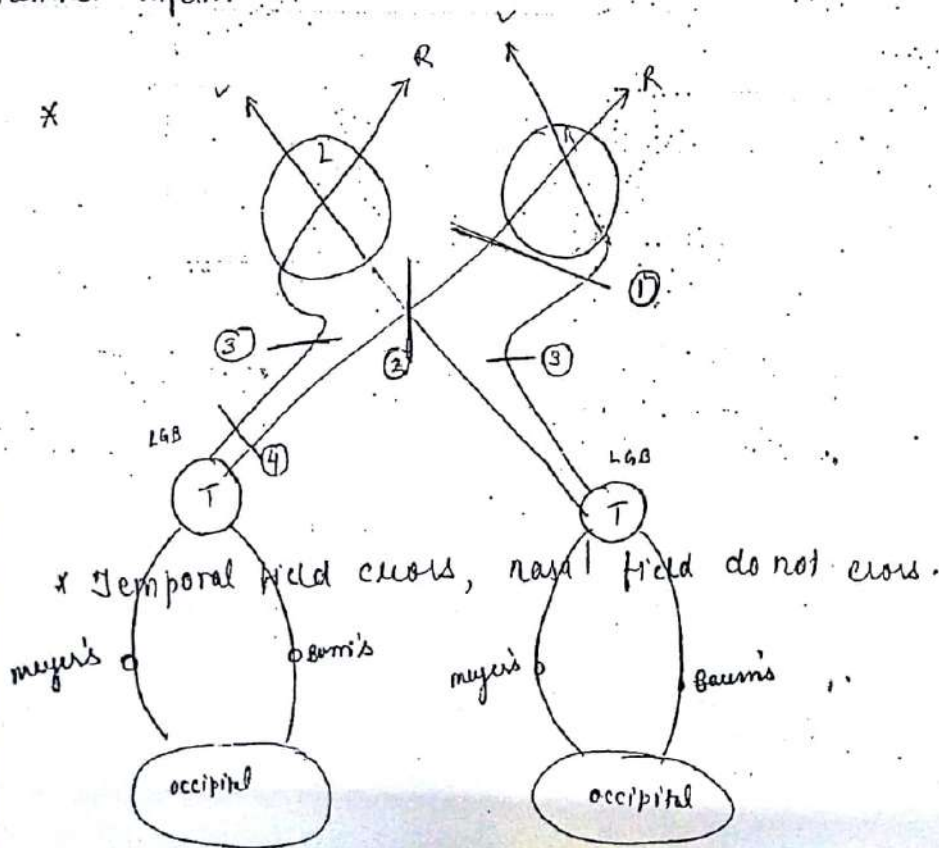


Quadrantanopia defect - lesion of Bomp's; meyer.



Lesion of ~~Bomp's~~ meyer's

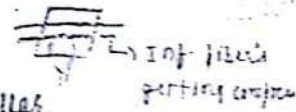
P I T S → Superior
↓ ↓
Parietal Inferior



(88)

1) Optic nerve lesion → I/L blindness

2) Chiasma — Bitemporal hemianopia



Causes: — • Pituitary adenoma

• Craniopharyngioma

Infundibular



Compress optic chiasma

from top as it is suprasellar type.

Sup. quadrant

Inf. quadrant



Pituitary adenoma

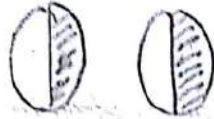
Craniopharyngioma

3) Binasal hemianopia —

Cause — B/L Int. carotid artery aneurysm → middle cavernous sinus thrombosis



(4) 11. optic tract → Rt side vision is lost



Homonymous hemianopic defect

optic tract lesion cause c/L Homing. hemi. defect
& both maculae sparing

(5) Thalamus — Same

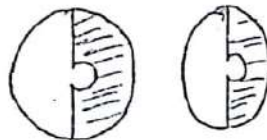
(6) Mayer's / Baum's → Inf quadrant defect of opposite side

↓
Sup. quadrant defect of opposite side

ex- Lt Mayer's — Rt. Sup Quadrantopia.

(7) occipital cortex — Lt occipital lobe damage.

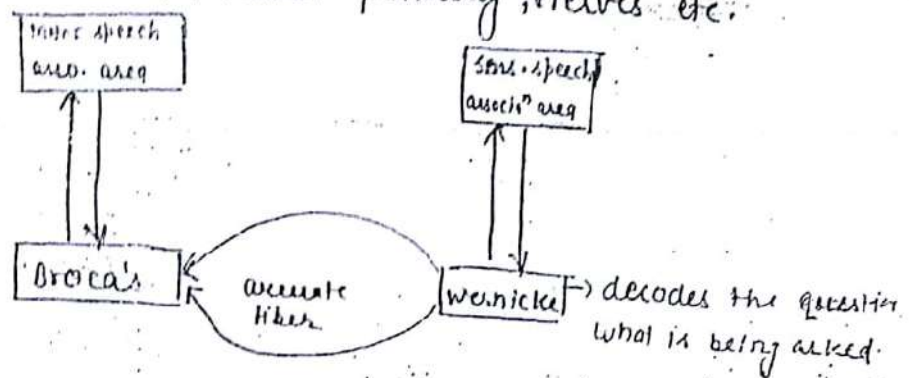
↓
Rt. side field loss & maculae sparing.



(89)

- Aphasia -

- * Problem is in cortical area
- * Dysarthria — Problem is not in cortex. It can be in subcortex, motor pathway, nerves etc.



- * Pose repetition → No need of higher centres.
- * Broca's area → Proper formⁿ of sentences, syntax of speech.

Components of Aphasia

Comprehension Repetition Fluency Naming

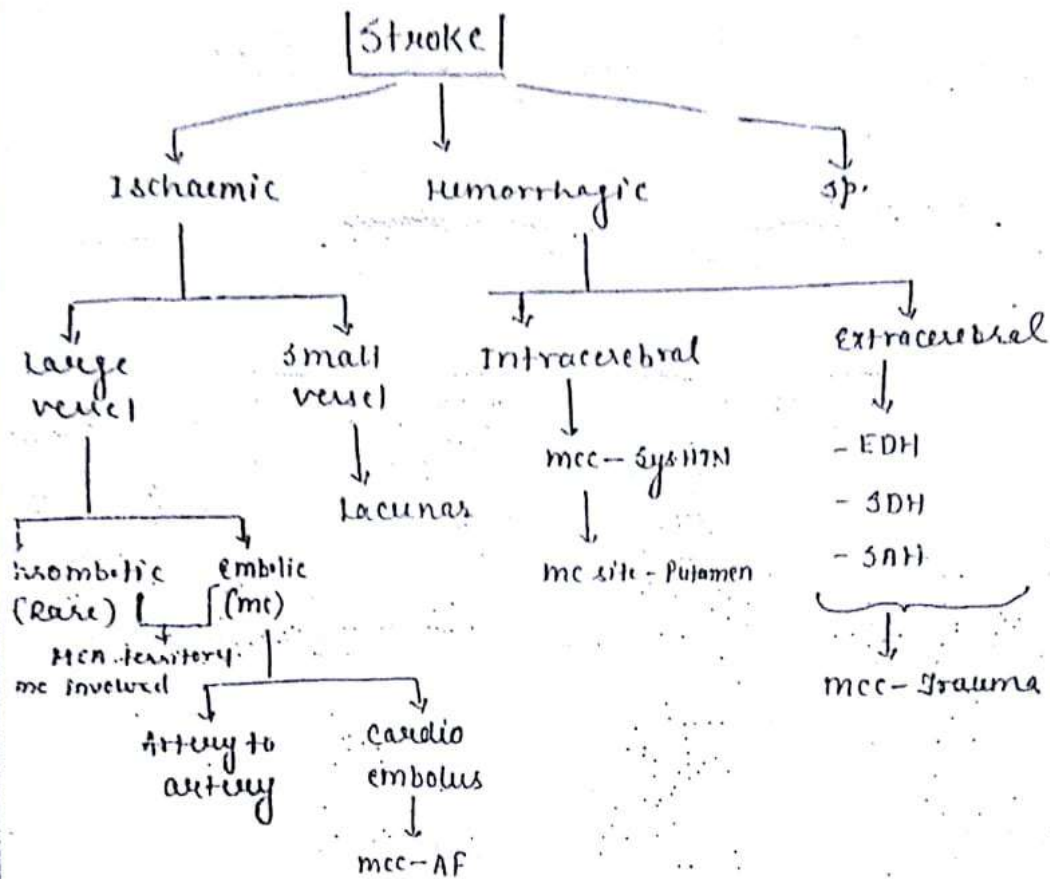
Wernicke's

⊖

	Comprehension	Repetition	Fluency	Naming
1) Wernicke's Neologism (Jargon)	⊖	⊖	↑↑ (Broca loses its inhibition)	⊖
2) Broca's	⊕	⊖	↓↓	⊖
3) Transcortical sensory aphasia	⊖	⊕	(N)	⊖
4) Transcortical motor aphasia	⊕	⊕	↓↓	⊖
5) Isolation aphasia (with TSA + TMA)	⊖	⊕	↓↓	⊖
6) Conduction aphasia	⊕	⊖	(N)	⊖ / ↓
7) Nominal aphasia (anomic aphasia)	⊕	⊕	⊕	⊖
8) Global aphasia	⊖	⊖	⊖	⊖
9) Crossed	- of Rt. sided lesion causes aphasia.			

(90)

Anomic aphasia → Earliest to occur in Alzheimer's
& in metabolic encephalopathy.

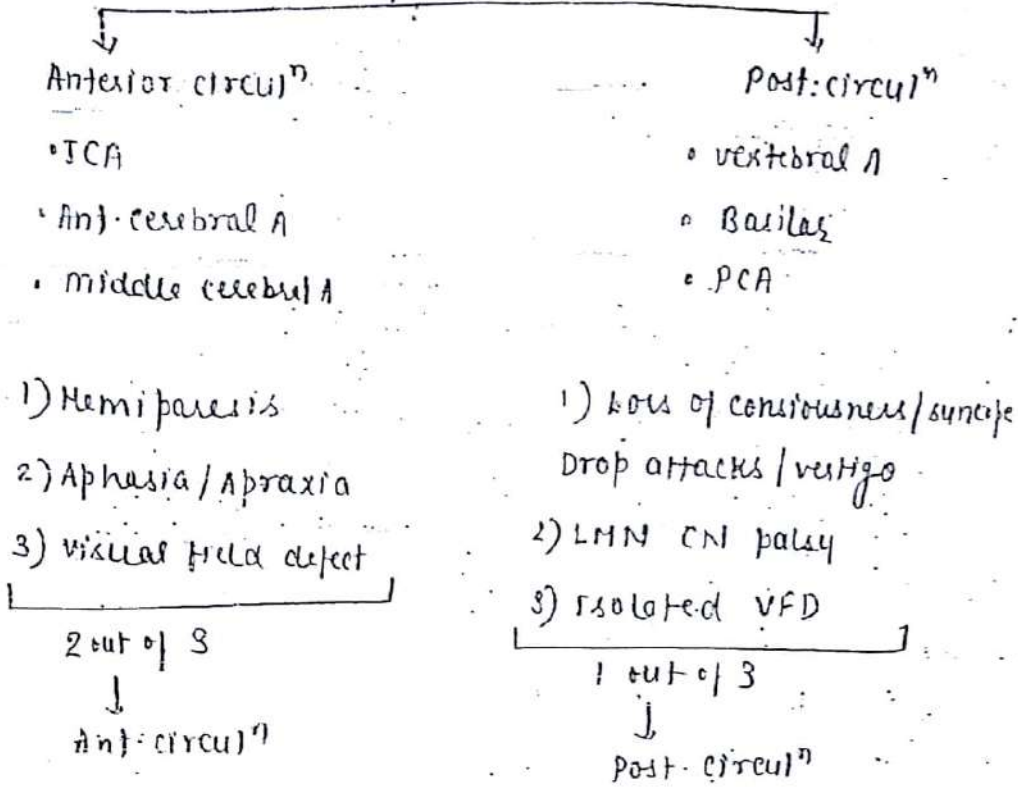


special stroke

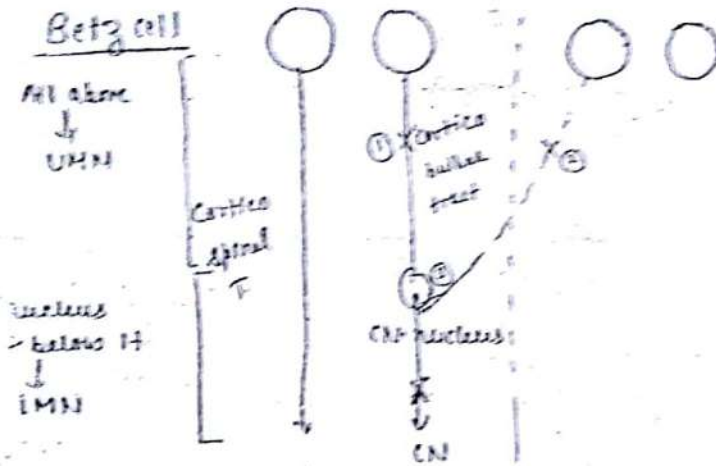
- 1) venous (CVT) → corticovenous thrombosis
- 2) Dissection (VA/ICA) → extracranial
- 3) CADASIL - NOTCH-3 gene mutation

(91)

Localization of Stroke - Oxford Banford classification



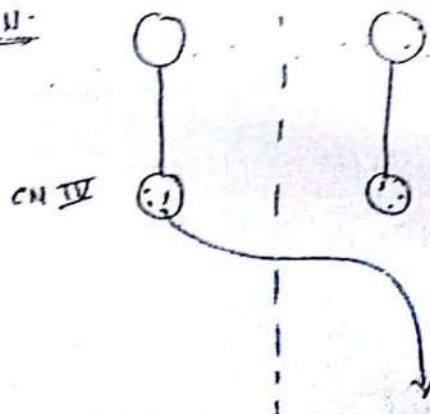
Cranial nerve —



* CN contain fibres from both side.

- 1) So U/L UMN — no problem
- 2) B/L UMN — Problem
- 3) U/L — LMN — Problem

Trochlear N.



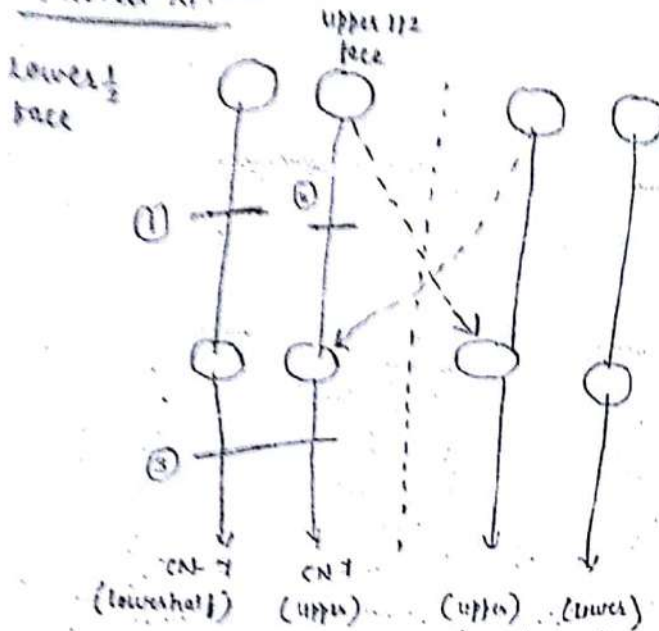
* Complete crossing
occurs in trochlear N.

* partial crossing to
opp side occurs in
Oculomotor N.

except

facial N:

(92)



Lesion ① — UMN + U/L → lower half of face affected

② UMN — UL (upper) — No effect

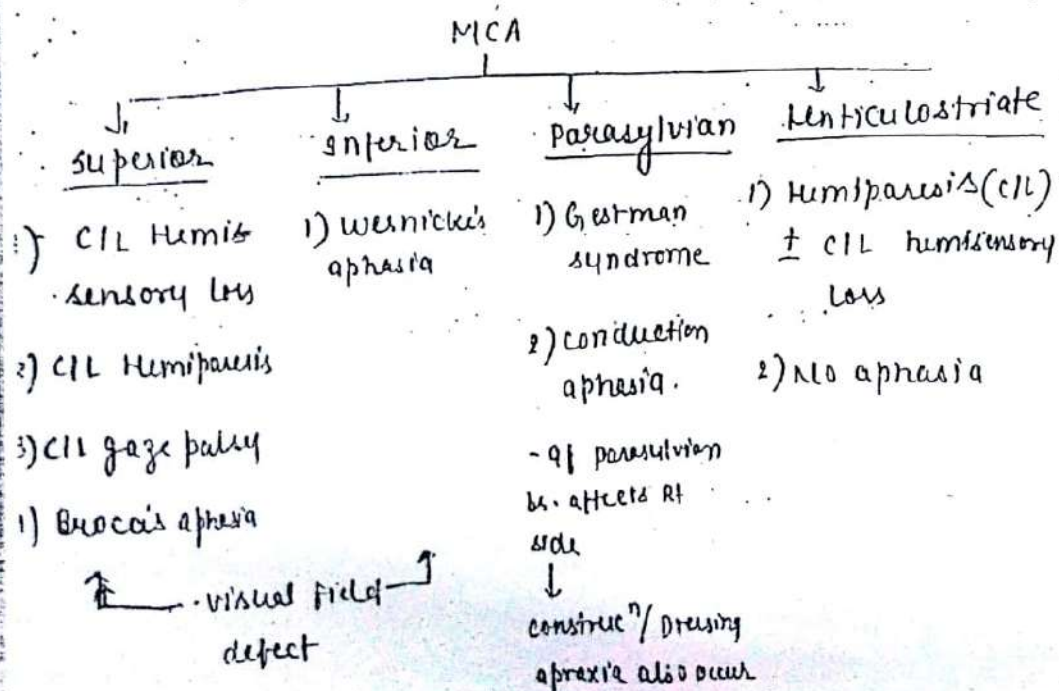
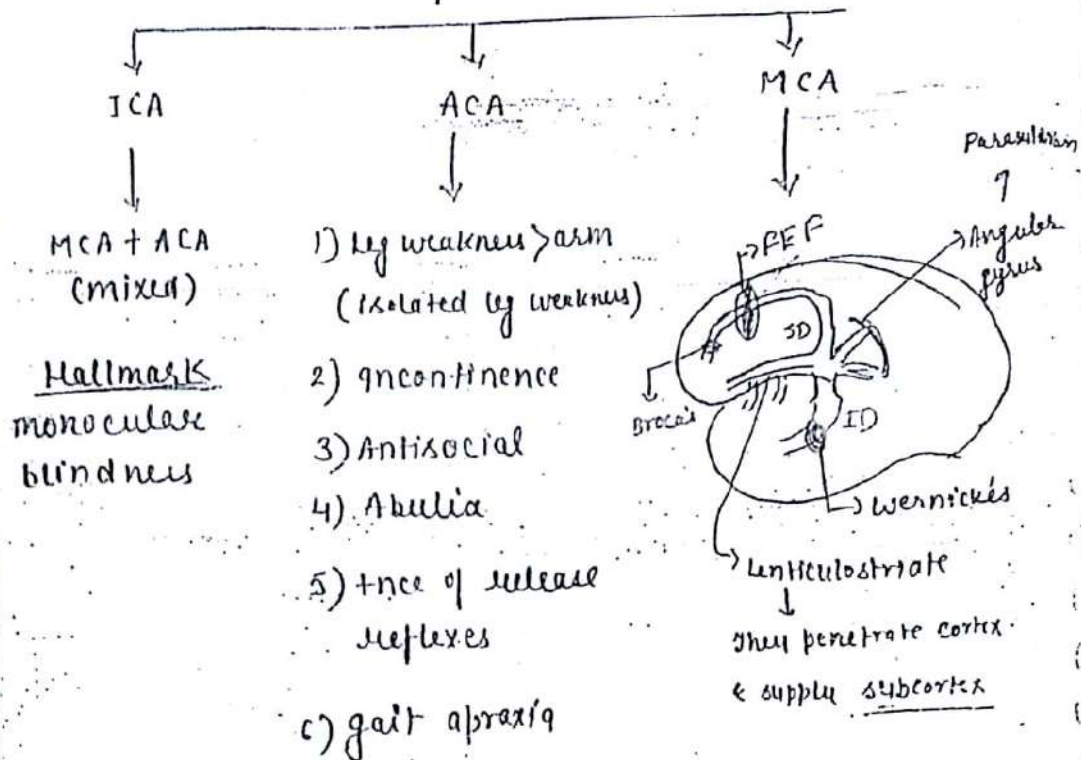
* 1+2 for U/L UMN → only lower half of face affected

③ U/L LMN → Both upper & lower half affected.

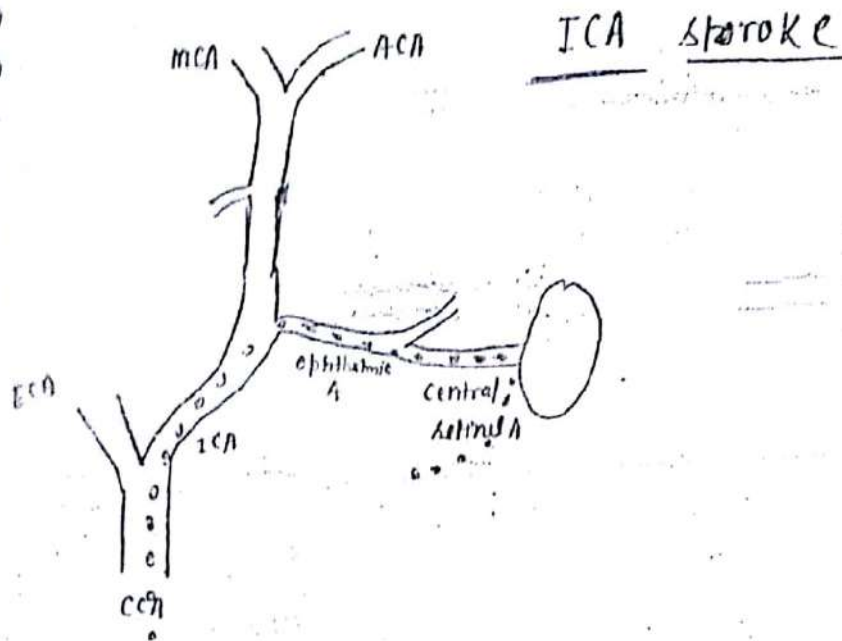
* 9th U/L

Localization -

Ant. circulⁿ stroke



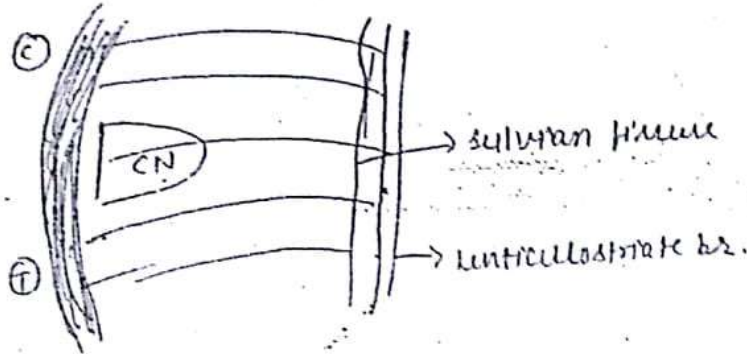
(93)



* MCA
ACA } damage → visual field defect

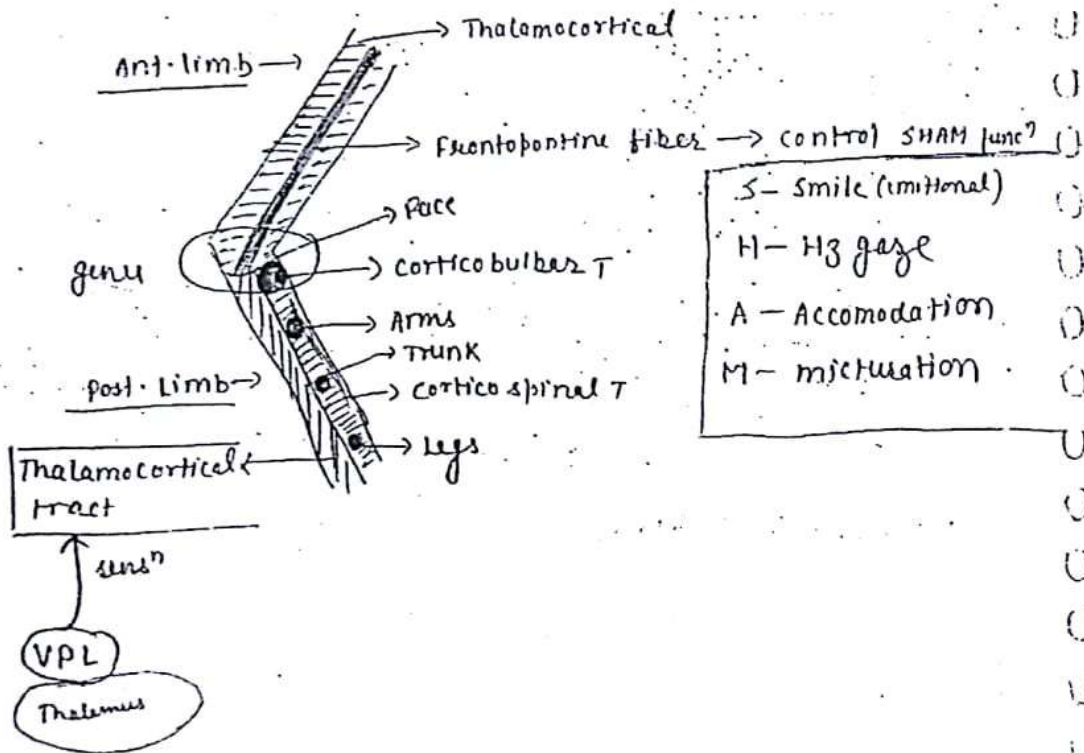
* ICA → damage → central retinal A will not get blood
↓
monocular blindness

* CRAO → There is transient loss of vision i.e., amaurosis fugax.
This occurs when the artery is occluded by atheromatous plaque.



Lenticulostriate br.

Internal capsule —

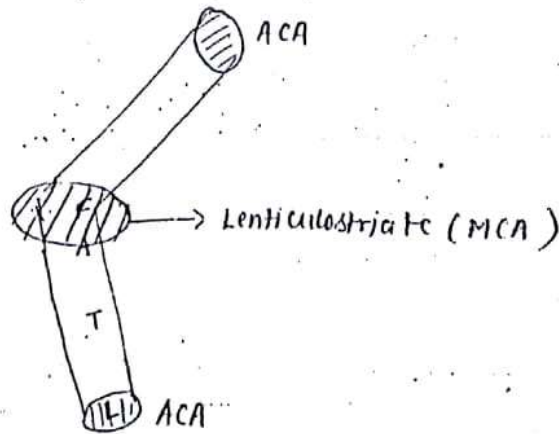


(94)

Thalamocortical tract fiber

Papez circuit — component

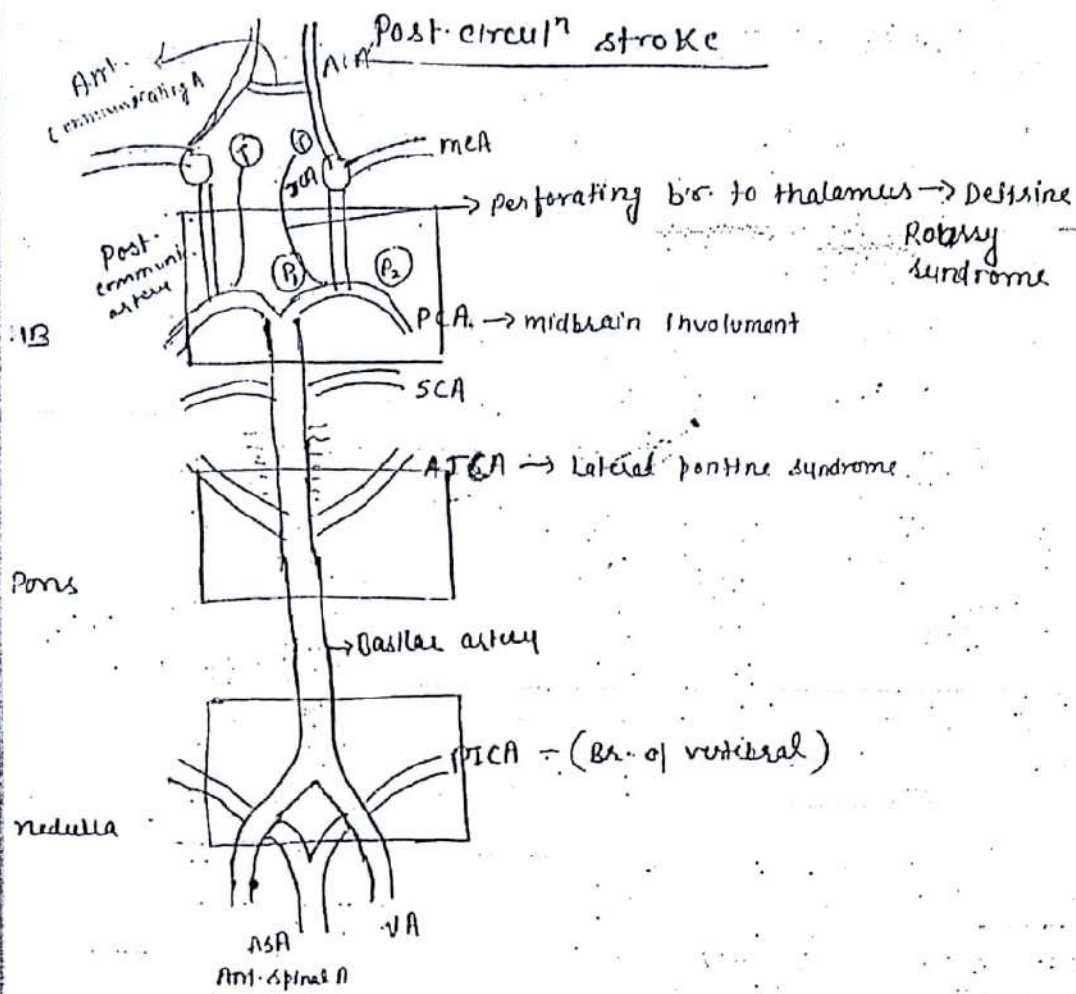
- M — mammillary body
- A — Ant. thalamic nu.
- C — cingulate gyrus
- H — Hippocampus



* Leg weakness — ACA

SHAM funcⁿ ←

* MCA affected — Face
arm



* Wallenberg syndrome — VA > PICA involved

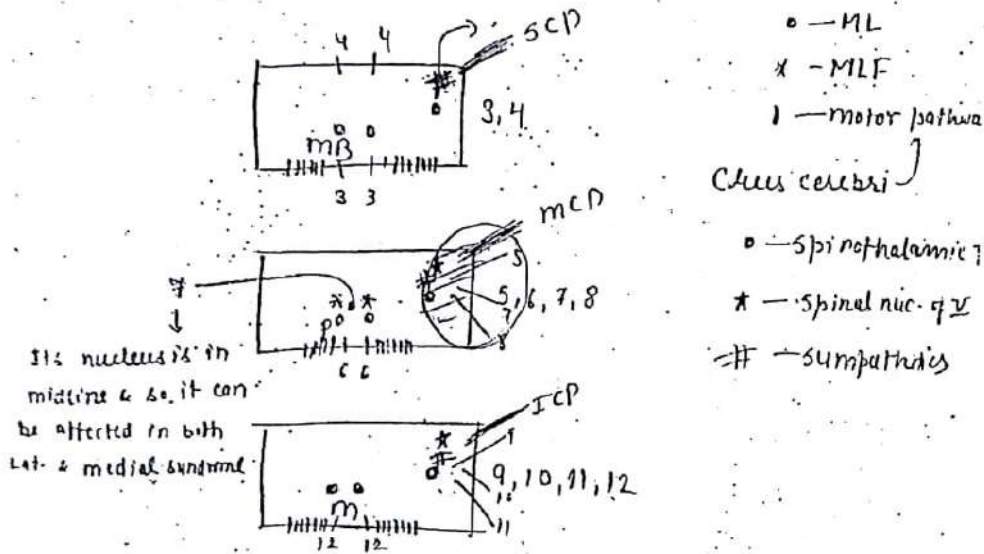
(95)

Dejerine Roussy synd - CIL Hemisensory loss

↓ days - wk
Severe pain
(Burning)

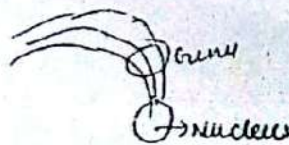
Rule of 4:-

- ① 4 cr. nerve comes from pons, 4 below pons,
4 above pons.



- ② midline cranial N:- 12 — (divide it in no. & no decimal should be there)
i.e. 3, 4, 6, 12

Racral N:-



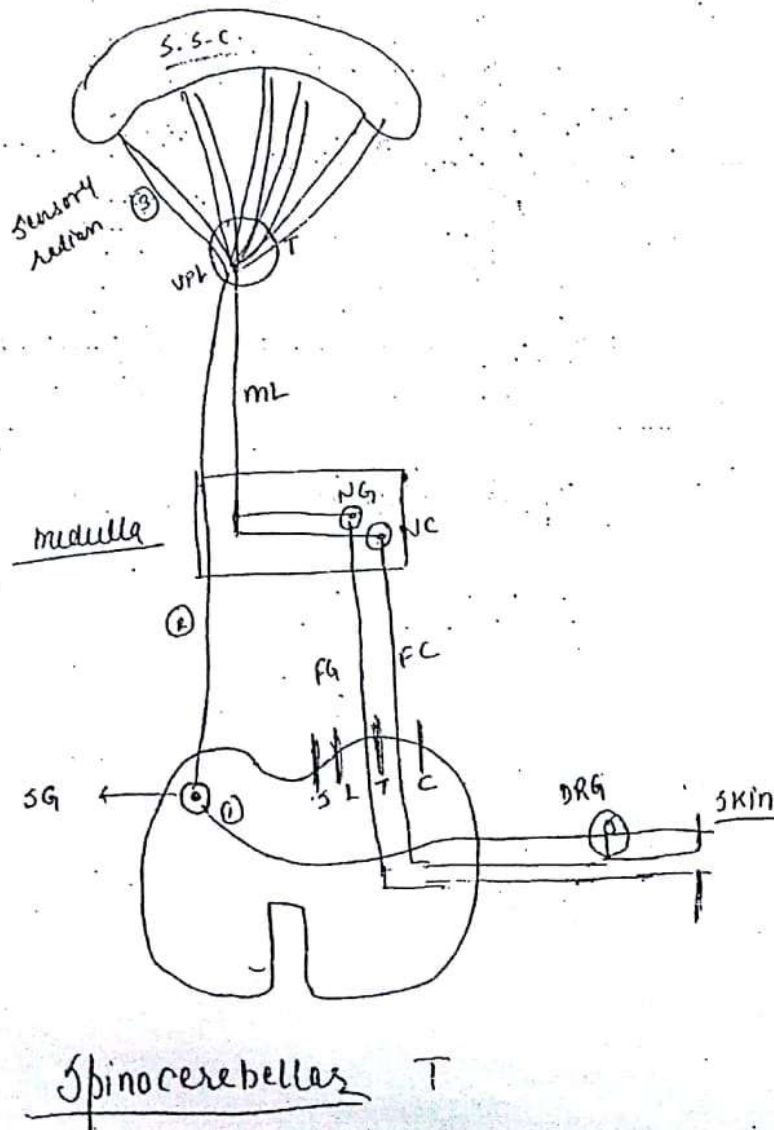
③ 4M - midline

4M — 1) medial lemniscus (dorsal column medial lemniscus pathway)

2) MLF → supplies medial rectus

3) motor pathway (CST)

4) midline CN.



(96)

Funcⁿ of ~~spinal cord~~ Dorsal column

- * Fine touch
 - Pressure
 - Vibrⁿ
 - Position (Joint position)
 - Conscious proprioception → maintaining posture position
consciousness (Romberg's test)
 - Cortical sensⁿ → tactile localizⁿ
 - 1) Stereognosis
 - 2) Two point discrimination
(max^m - lips, finger tips) → at least dist.
 - 3) Graphoesthesia
 - 4) Parechthetia → ability to differentiate
bls & weight
 - 5) Tactile extinction → (not feeling ones own
clothes)

* Loss of position → 1) High stepping stamping type of gait

High stepping gait is also seen in fibular N. injury but here stamping is not there. It is specific for cerebellum.

- 2) Wide based ataxic type of gait (Drunkens gait)
- 3) Pseudoathetosis → It loss position of joint sense & make some movement periodically.
- 4) Romberg's test.

* Dorsal column is highly myelinated tract & are phylogenetically new.

→ ∴ Demyelinating di. first affects dorsal column.

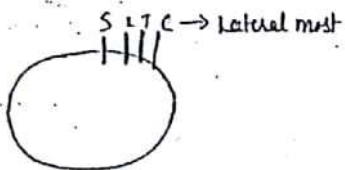
* Spinothalamic T. are older tracts & are less myelinated.

SC

• 1st order neuron have no connection in spinal cord.

• Lesion in DC — same side defect

• Lesion in ML — opp side affected



ST

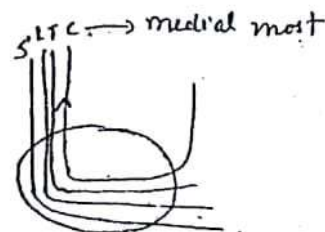
• Have connection

↓
2nd order neuron ^{start} develop in spinal cord

∴ Tracts made up of 2nd order neuron

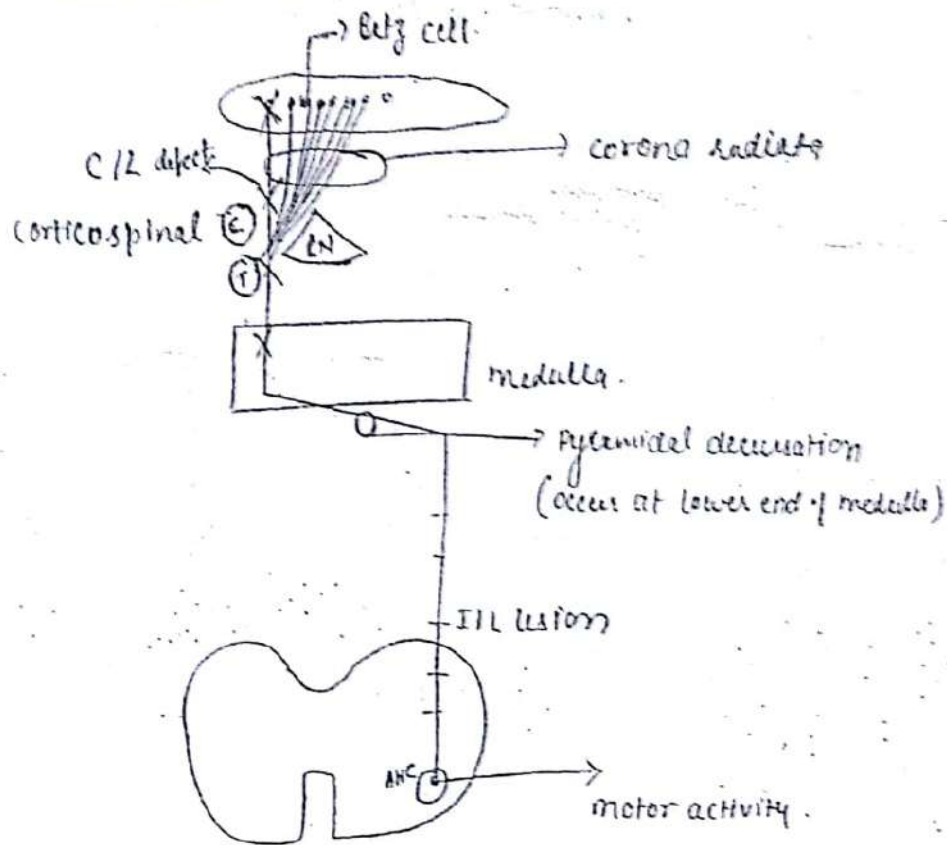
• Lesion on ST tract produces effect on opp side.

• Carry pain & temperature.



Motor's Tracts -

(97)



Corticospinal Tract

Right

Rule (4) — 48 → 477 in 480

- 1) Spinothalamic tract
- 2) Spinal nucleus of CN V
- 3) Sympathetics (from lateral RF)
- 4) Spinocerebellar tract

Cerebellum produces III lesion

Damage to ~~80~~ small (Cerebellum) →

- Low freq tremors → features of cerebellar tremor
 - coarse
 - Intentional
 - speech
- ↓
AKA terminal tremor

Ataxia

- Dysmetria → can't assess length properly.
Can be assessed clinically by past pointing
- Rebound phenomenon
- Pendular knee jerk
- Problem in alternating movement (Adysidiokinesis)
- Problem in finger nose test
- II — Heel shin knee test

98

Syndromes!—

<u>Syndrome</u>	<u>Artery</u>	<u>Features</u>
1) Lateral medullary syndrome / Wallenberg	VA > PICA	4/5 affected + 9, 10, 11 cr. N. → ext - pain -
2) Lateral pontine syndrome (Marie-Juergensen)	AICA	4/5 + 5, 7, 8 ↓ (I/L - PT) → ST. I/L - PT - face I/L - Horner's I/L - LMN facial N. palsy

* This 2 syndrome can be differentiated by cr. n. involvement only

* In both these syndrome, there is no motor involvement. (as these are not medially)

Medial syndro : → Always ML will be involved.

① Medial medullary syndrome
(Dejerine's Ant. bulbar)

ASA

ITL CN XII +
Corticospinal tract
↓
C/L Hemiparesis

② Medial pontine syndrome

(i) Millard (7)
* Gubler (C) synd

Basilar

ITL CN VI +
CST → C/L Hemiparesis
+
7th N involvement

(ii) Foville's synd-

Basilar

Millard Gubler
+
MLF

③ Mid brain:-

(i) Weber

PCA (P₁)

ITL cr. N. III +
Corticospinal
↳ C/L Hemiparesis.

(ii) Benedict synd.

PCA (P₁)

Weber's + Red nucleus
↓
C/L-tremors

(99)

Trochlear N —

- * Crosses completely to opp side
- * Thinnest
- * Longest intracranial course
- * arise posteriorly.
- * mc to involved in orbital #

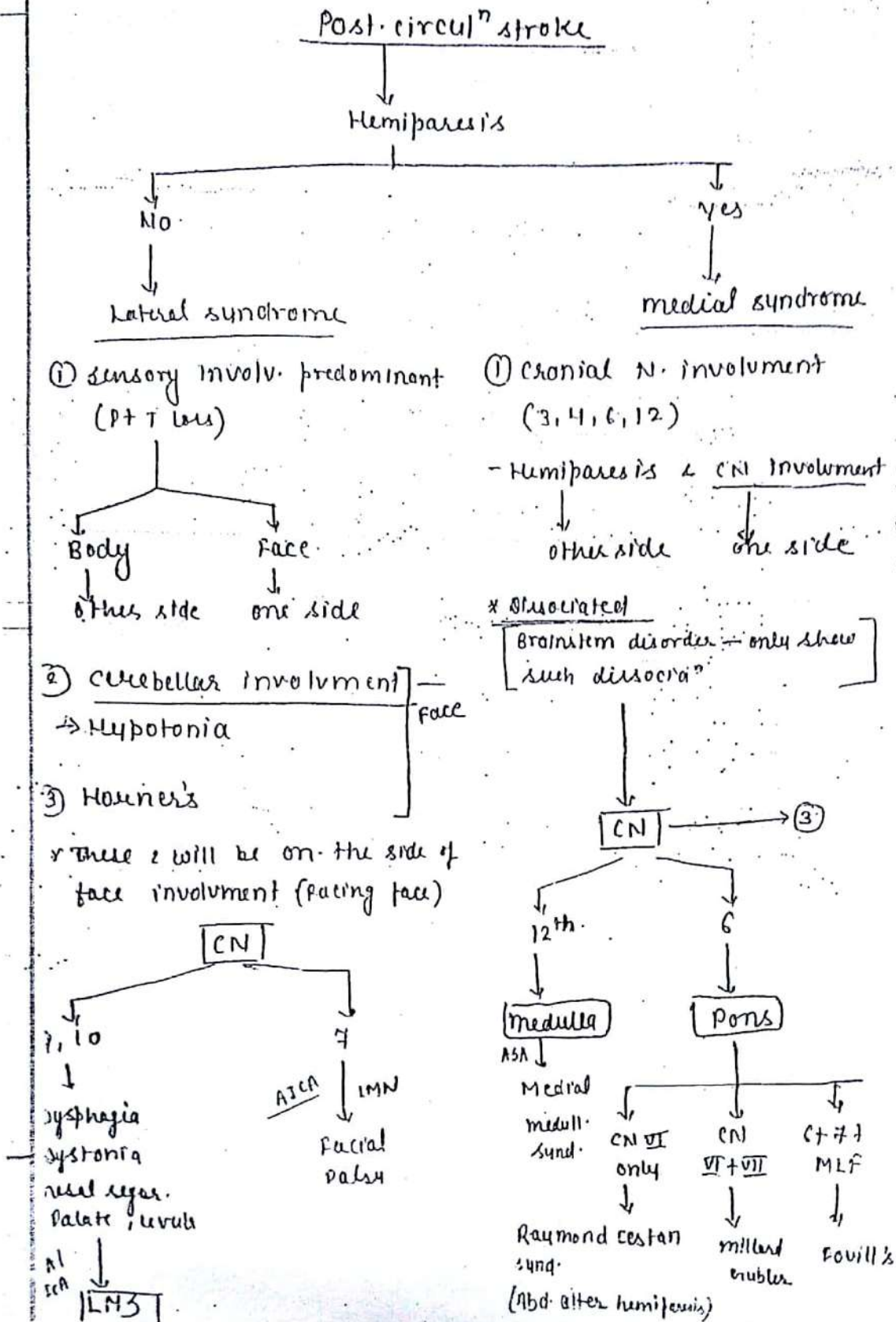
- * Longest sub arachnoid course — 6th N.

↓
So in condition when there is ↑ ICP, 6th N. is mc affected.

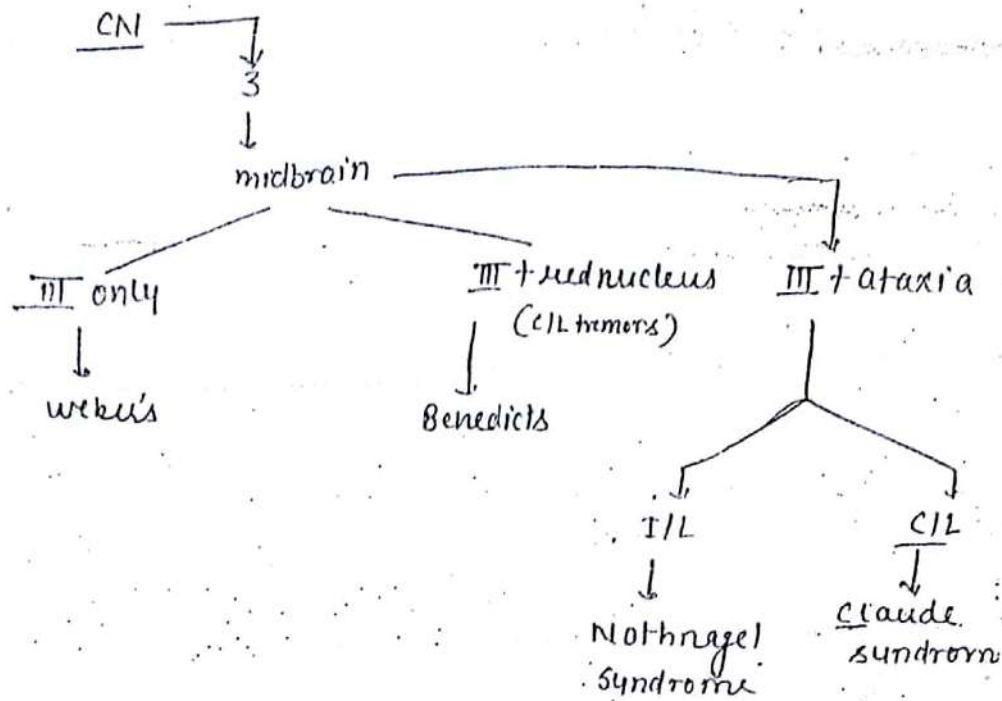
↓
So it gives false localizing sign.

↓
We think that there is problem in 6th N. but main prob. in ↑ ICP.

- * Longest intracranial course → Facial N.
- * Thickest — sciatic / Radial.
 └ Trigeminal
- Longest — vagus

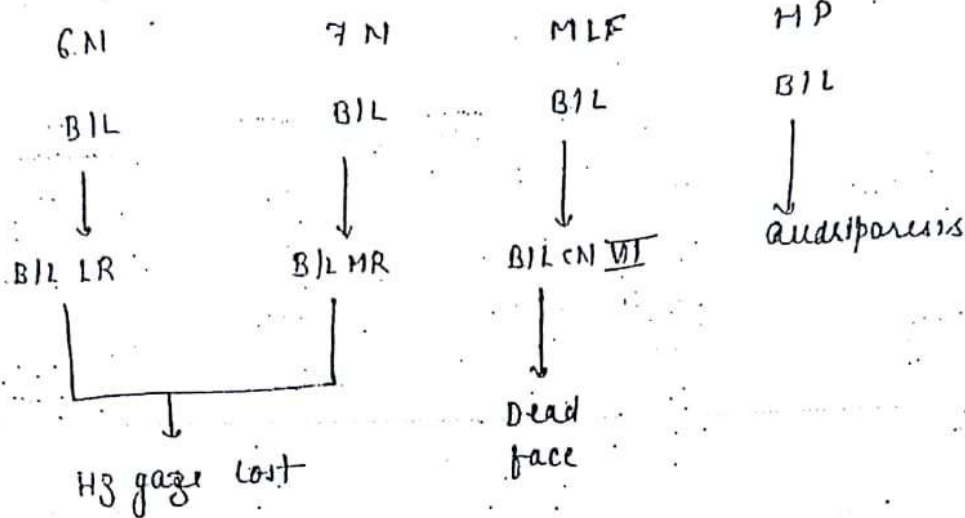


(100)



Locked in syndrome —

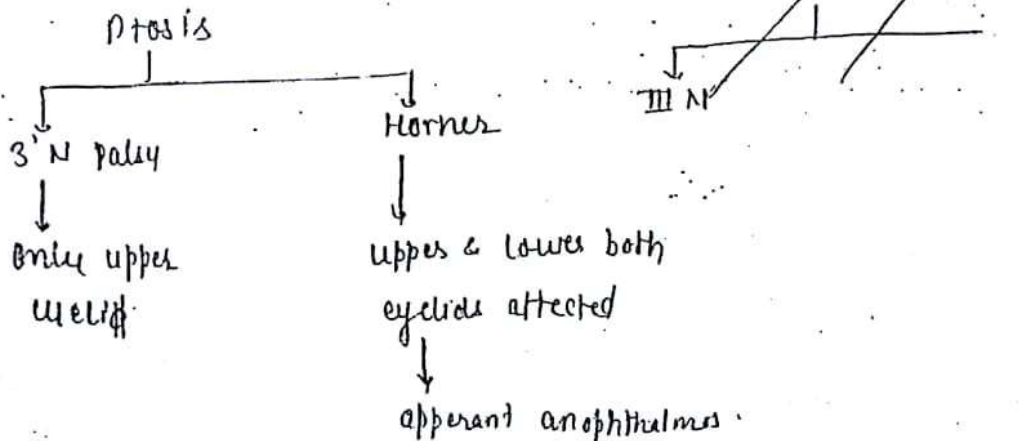
- B/L Fovill's
- GN + FN + MLF + Hemiparesis



Spared —

① 45 spared on both sides i.e., sensⁿ are intact.

② No Horner's



(10)

③ sympathetics → spared * Blinking intact.
parasympathetics →

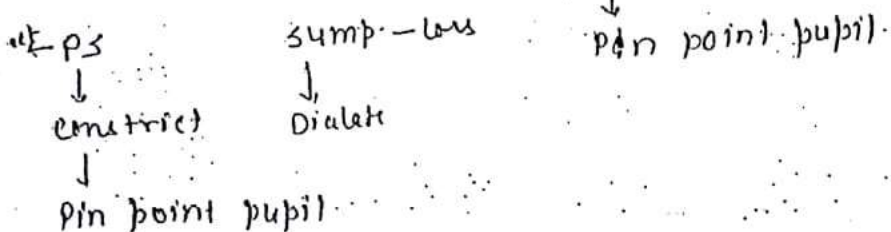
- so (N) light reflex

④ sup molecular formation (maintain consciousness & wakefulness)

⑤ vertical gaze (3^{rd} & 4^{th} N are spared)

Pontine hemorrhage — Pons totally destroyed.

- pt will be comatose (deep)
- quadriplegia
- loss of HZ ~~gaze~~ eye movements
- Hyperthermia
- loss of sympathetics → pupillary constriction

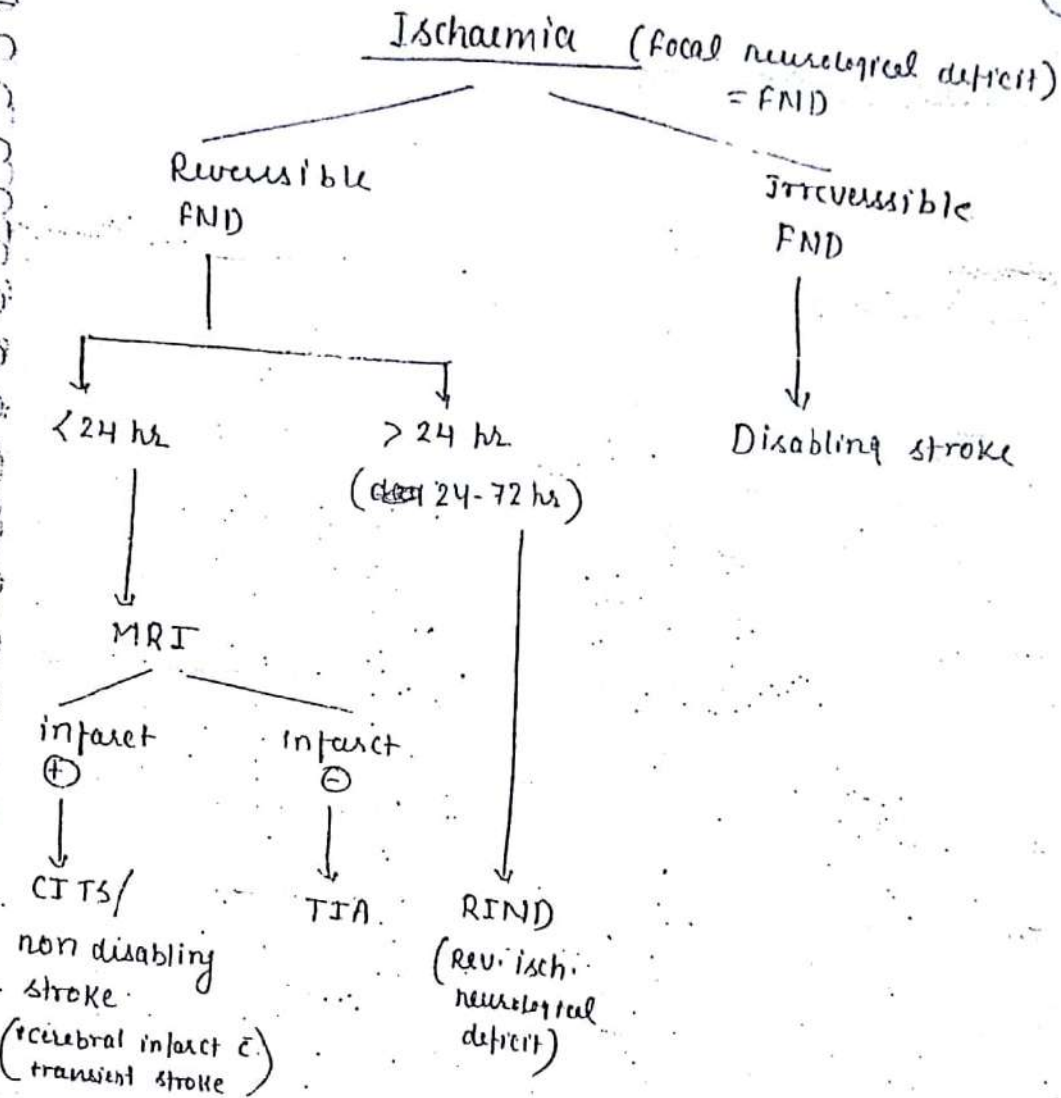


Spared — vertical eye movement (intact 3, 4 CN)

ocular bobbing — spontaneous vt. eye movement

Doll's eye reflex performed in comatose pt. for gaze

(102)



TIA

DIFF - Hypoglycemia
• syncope
• migraine

Suspected TIA

ABCD₂ score

≤ 3

low risk

elective MRI

≥ 4

High risk

urgent MRI (<24hr)

NO Infarct

TIA

Rx - Aspirin 300 mg stat
Statin (High Intensity).

carotid doppler

significant
occlusion

NASCET > 50%

ECST > 70%

↓
surgery

non significant

NASCET < 50%

ECST < 70%

↓
medical Rx

(103)

Intervention:—

- ① carotid endarterectomy
- ② carotid artery stenting.

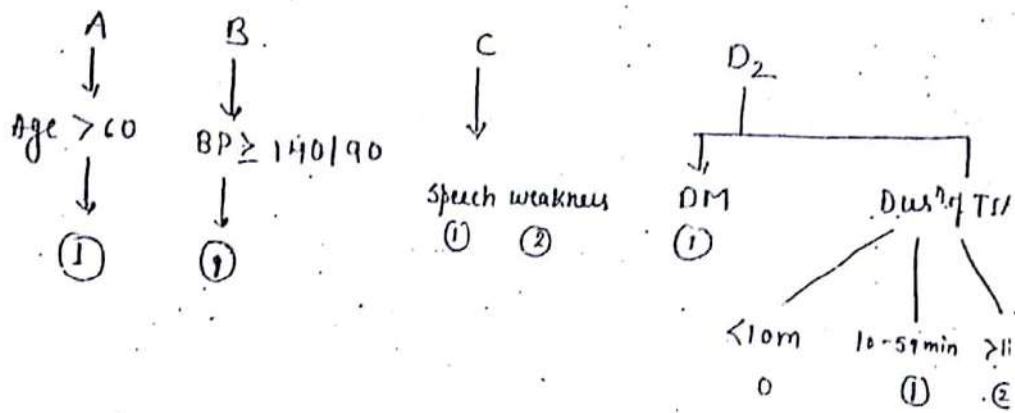


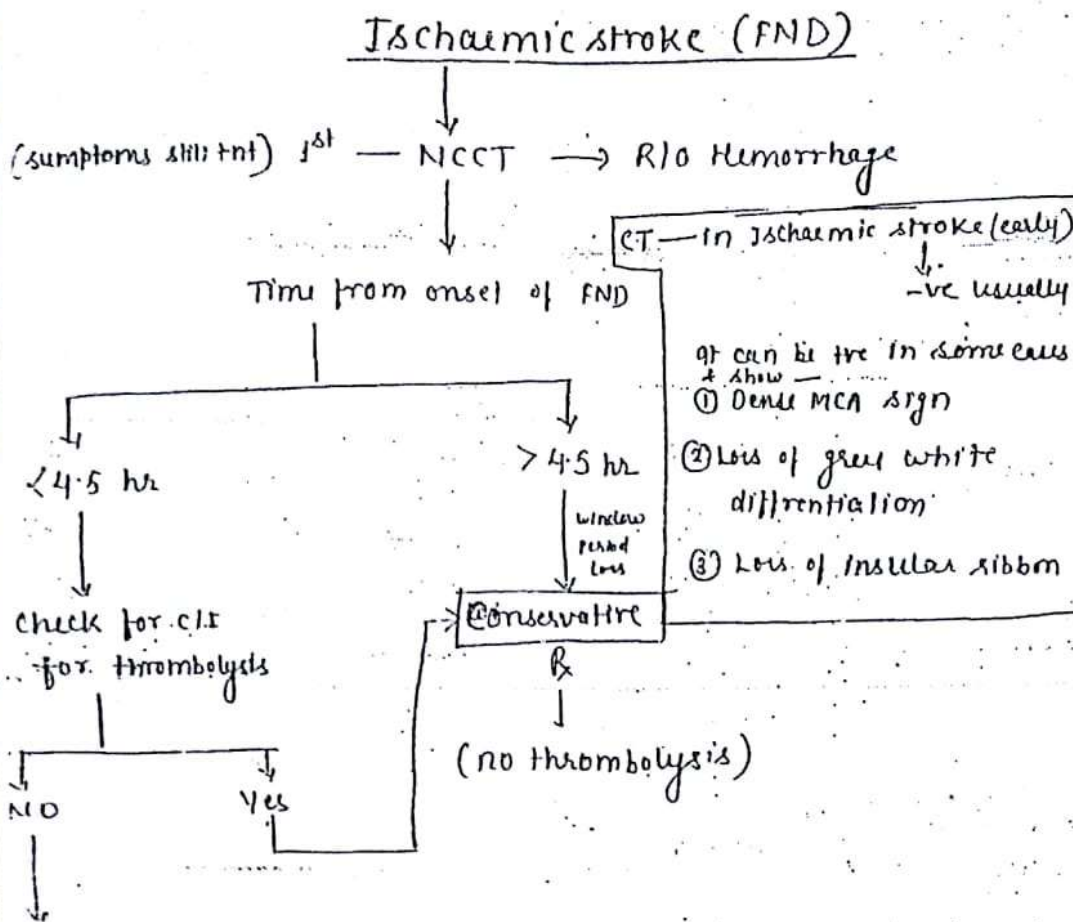
medical Rx $\Rightarrow$ Asp X 14 day



- clopidogrel (shift)
- statins (continued)

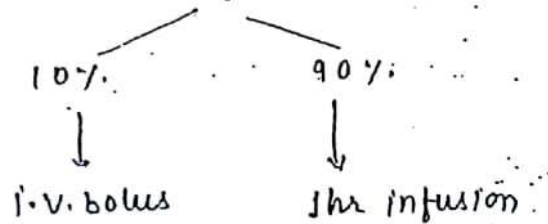
ABCD₂ score —





Thrombolysis → done to prevent ischaemic penumbra.

DOC:- Alteplase → 0.9 mg / kg (max m: 90 mg)



*



→ Thrombolysis is done to prevent extension of size of infarct.

(104)

Conservative — ① Aspirin — 1st 300 mg
• Reduces mortality.

② Statins —

already
taking

continue

not already
taking

start later
> 14 day

③ Glucose :- < 200

④ Fever → harmful → control fever immediately.

↳ as signifies ↑ cerebral metabolism rate

* Therapeutic hypothermia is very harmful → cause pneumonia.

⑤ ACE I < 24 hr

⑥ Rehab :- < 24 hr ⇒ Huminglact resolves spontaneously
(physiotherapy) (> 98%)

⑦ Dysphagia (oropharyngeal) → NG tube.

- liquid food is safe. solid food produces dysphagia.
aspiration.

*

C/I of Thrombolysis

↓
Ongoing (Active)

↓
Prior History

① BP $\geq 180/110$ (relative C/I in HT) ① H/O Hemorrhagic stroke

② Any coagulopathy

② Ischaemic stroke /
Head injury in last 3 wk

③ Thrombocytopenia (< 1 lakh)

③ GI / genitourinary bleed
in last 3 wk

④ untreated A-V malformⁿ

Brain tumor

Brain aneurysm

④ H/O head trauma 3x / major
trauma - in last 2 wk

⑤ Hypoglyc < 50 mg

⑤ H/O heparin use in
last 2 days

⑥ Hyperkalemia > 4.0

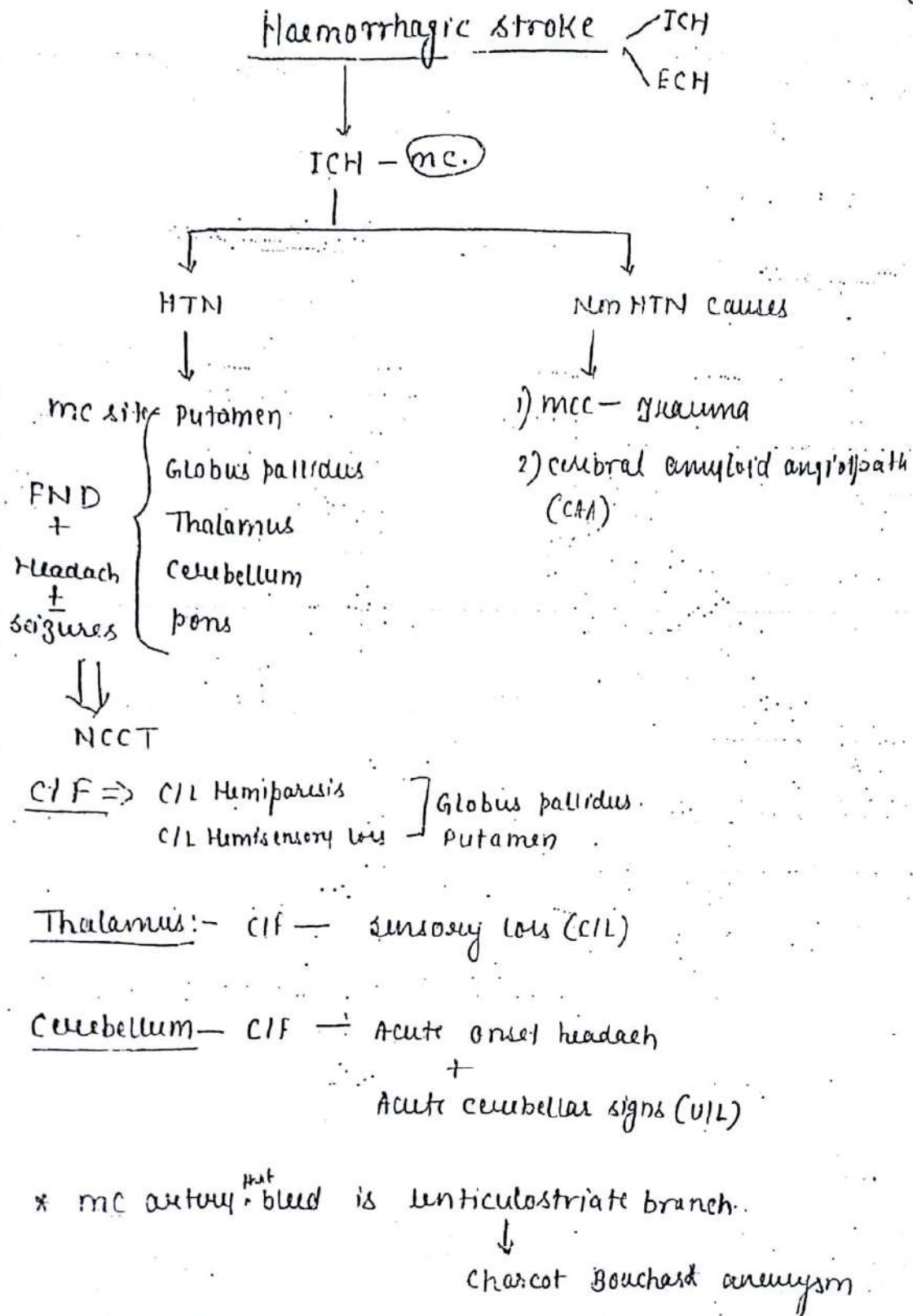
⑦ Rapidly resolving symptom

⑧ ongoing active bleed

⑨ Age < 18

⑩ on CT - edema seen
in $> 2/3$ of cerebral hemisphere

(105)



* Decompressive craniectomy $\rightarrow$ Done in all case of $\uparrow$ ICH.

* Munro Kelly Doctrin —

cranial cavity is fixed —

- If any thing comes to brain, there must be loss of some brain tissue / blood / CSF to accommodate this additional mass.

exception: — Infant

Cerebral blood flow —

white — 30 mL / 100 gm / min

grey — 75 mL / 100 gm / min

O₂ demand —

3.5 mL / 100 g / min

stores in brain lasts for 8-10s.

glucose —

5 g / 100 g / min

(N) stores is for 2 min.

Cerebral perfusion press: — Remain cons. under

(N) physiological condition $\rightarrow$ This is autoregulation

* 50-60 mm Hg of MAP $\rightarrow$ CPP can be maintained cons.

(107)

→ In HTN pressure → autoregulation threshold is
80-180 mm of Hg MAP

$$* CPP = MAP - ICP$$

if ICP ↑



Body ↓ MAP



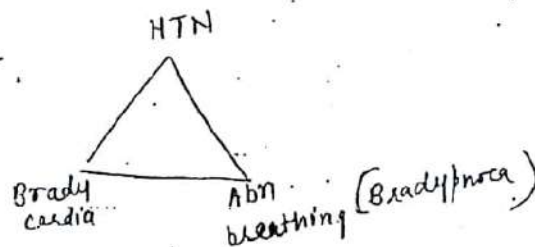
So that CPP remain cons.



So there is HTN

Cushing's triad —

In raised ICP



Waveform of ICP —

P_1 → art. pulse

P_2 — compliance (intracranial)

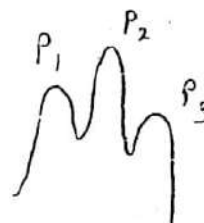
P_3 — venous



$$P_1 > P_2 > P_3$$

(N)

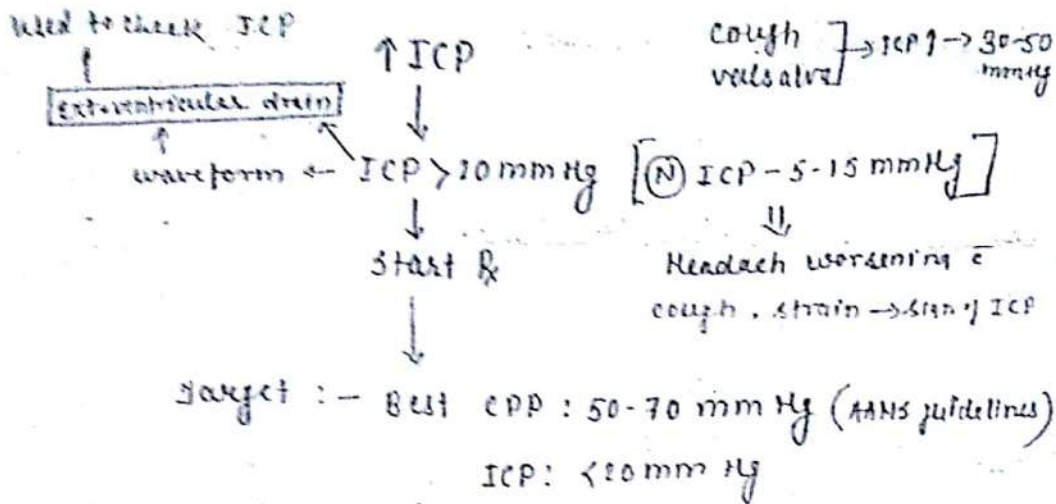
↑ mass → compliance ↓



Raised ICP

- * Lundberg A waves → slo wave ↑ ICP
- * Lundberg B waves
- * Lundberg C

Physiological



Steps -

① - CSF drainage - from Ext. and. meatus

on ↑ ICP → LP is C/I

except - meningitis → as a Δst procedure

(single intra-cranial) BIH → as a therapeutic procedure

② Sedation — Propofol

- Ramney score — midazolam

1 - hyperactive

2 - Irritable

3 - Responding to command

4 - Not responding well to command but brisk response to stimulus

5 - No response to stimulus

6 - Totally knocked out

③ Paralyze — vecuronium

④ Hyperosmolar agent — mannitol or 3% NaCl

Target - s. osmolality > 320 mOsm/kg [N - 285-295]

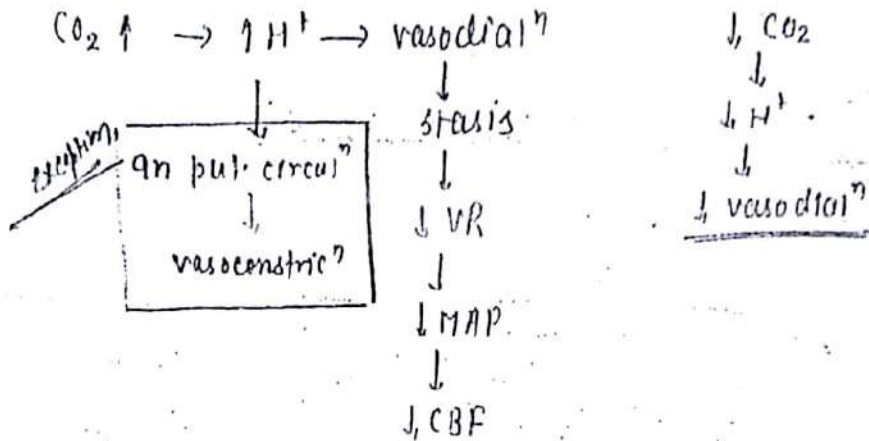
⑤ Barbiturate — Phenytoin

• Thiopentone

• Ketamine absolutely C/I.

(108)

⑥ Hyperventilation — target PaCO_2 — 30-35 mm/sec.



* SO we keep ↓ level of CO_2 . — (Therapeutic hypocapnia)

⑦ Hypothermia — (Therapeutic)

— 33-36°C — intermediate

⑧ Surgery — decompressive craniectomy.

$$V_{CA} = V_{BR} + V_{Blood} + V_{CSF}$$

If mass is there

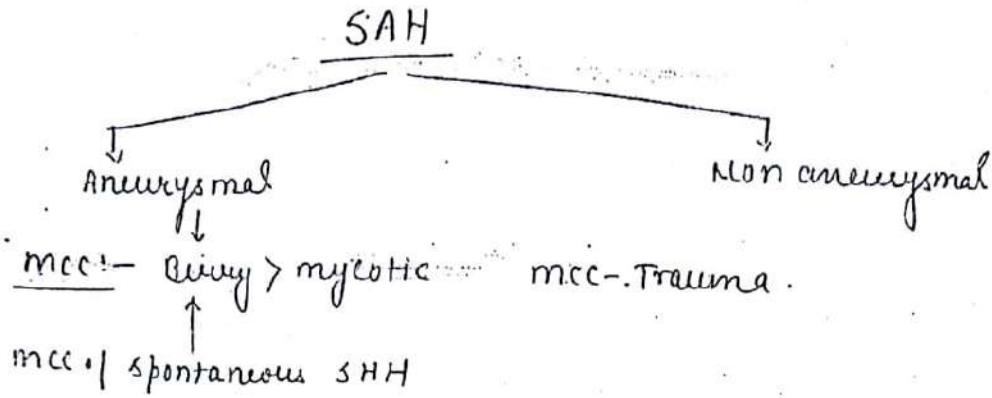
BR Blood CSF

↓ sed therapeutically.

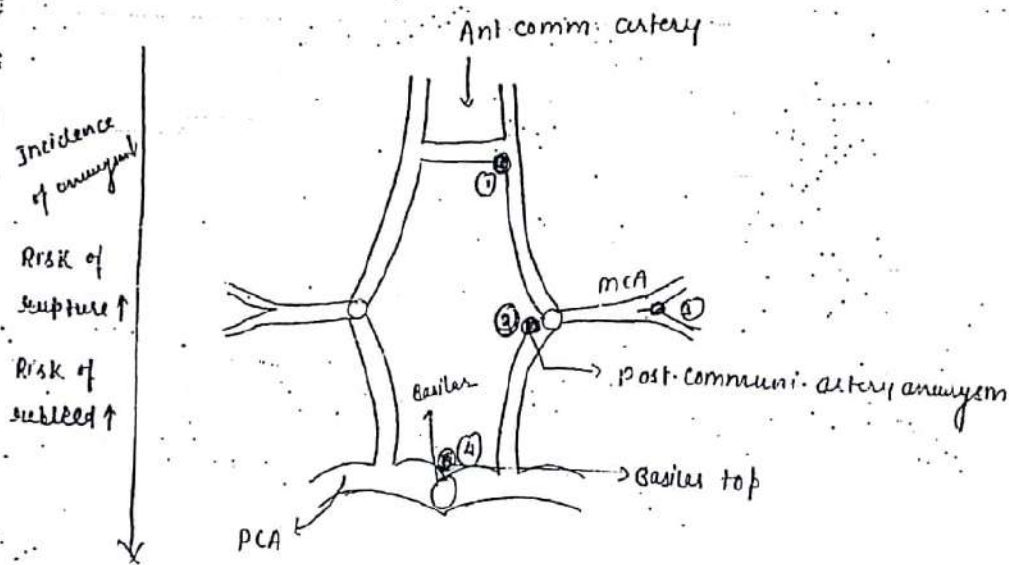
The part is implanted in abdomen

↓
When mass is gone then again
the piece is reimplanted.

(109)



Aneurysmal SAH



* incidence of aneurysm ↑ when go postures

* True aneurysm → T. media problem

Pseudoaneurysm → intima problem

CIF - ① Headache — severe (worst headache of life)
↓
Rupture "Thunder clap"
"lightning strike"

② Neck rigidity — meningeal irritation

③ FND

④ ± seizure

⇓
① IOC → NCCT

90%
+ve for blood

10%
-ve for SAH in CT

xanthochromia is produced (4-6 hr after CSF removal)

← lumbar puncture

② 3 tube testing (differentiate b/w SAH & traumatic tap)

Traumatic tap →

progressive dilution
hemostasis blood will be reduced



↑↑ RBC



↑ RBC



no RBC

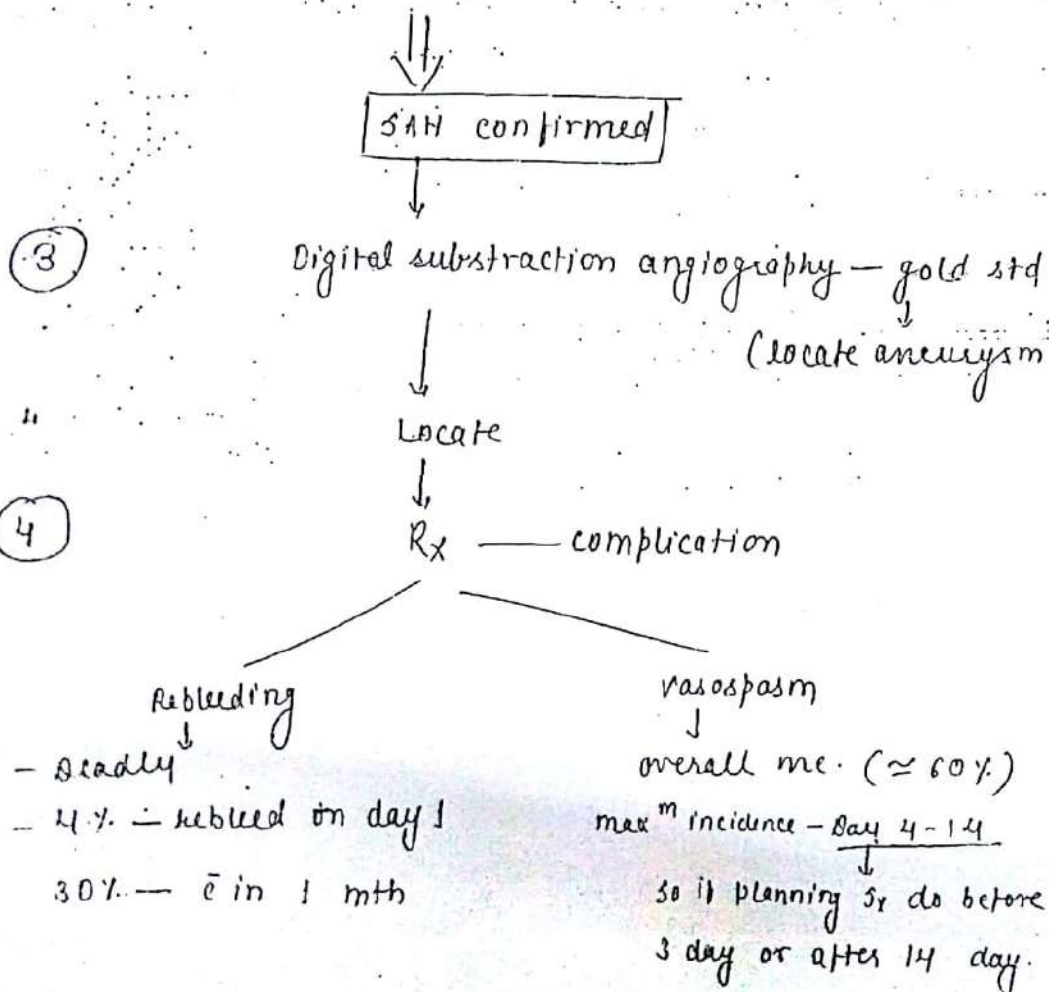
∴ No xanthochromia seen.

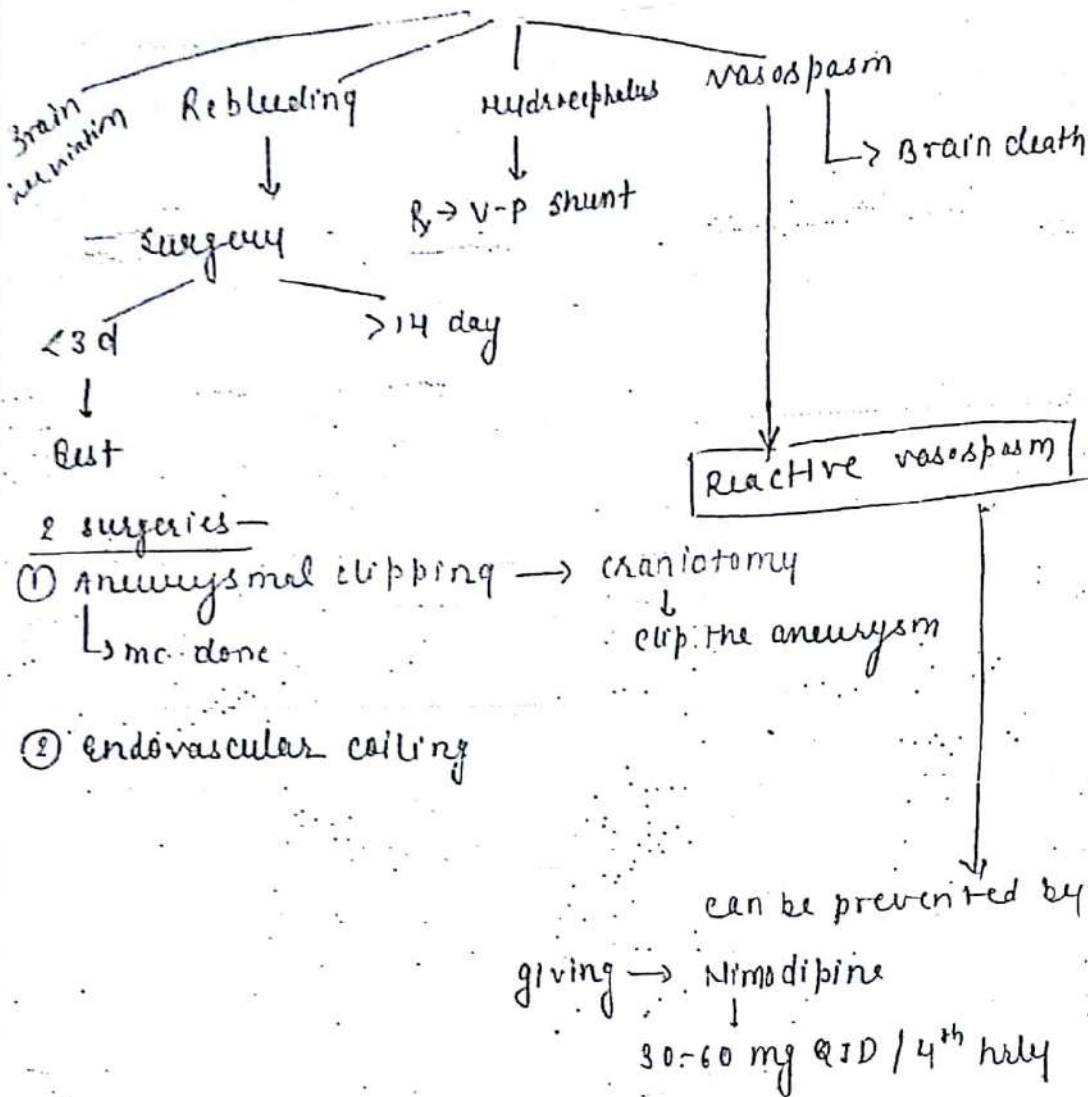
(110)

* Xanthochromia = same amt. of RBC in 3 test tube indicate SAH.

→ +ve of macrophage indicates SAH

Traumatic tap	SAH
1) Progressively ↓ red RBC in test tube	1) Same RBC
2) ⊖ Xanthochromia	2) ⊕ Xanthochromia
3) ⊖ macrophage	3) ⊕ macrophage





CAH

(iii)

Clinical scales—

(1) Hunt & Hess

(2) WFNS world federation of neurological society

CT scale - Fischer

Hunt & Hess —

	1	2	3	4	5
Headache	mild	mod-severe	—	—	→ can't be assessed
consciousness	(N)	(M) mild delirium	drowsy	stupor	coma
neck rigidity	mild	masked	✓	✓	✓
posturing	—	—	—	mild decorticate	severe decorticate
EMD	—	CM palsy only	mild hemiparesis	marked	severe
survival	70%	60%	50%	20%	10%

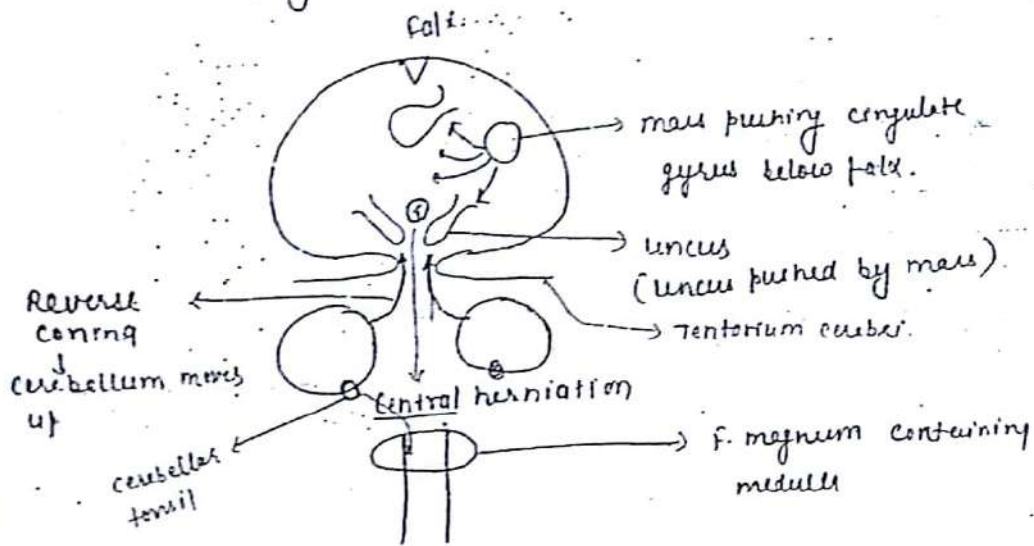
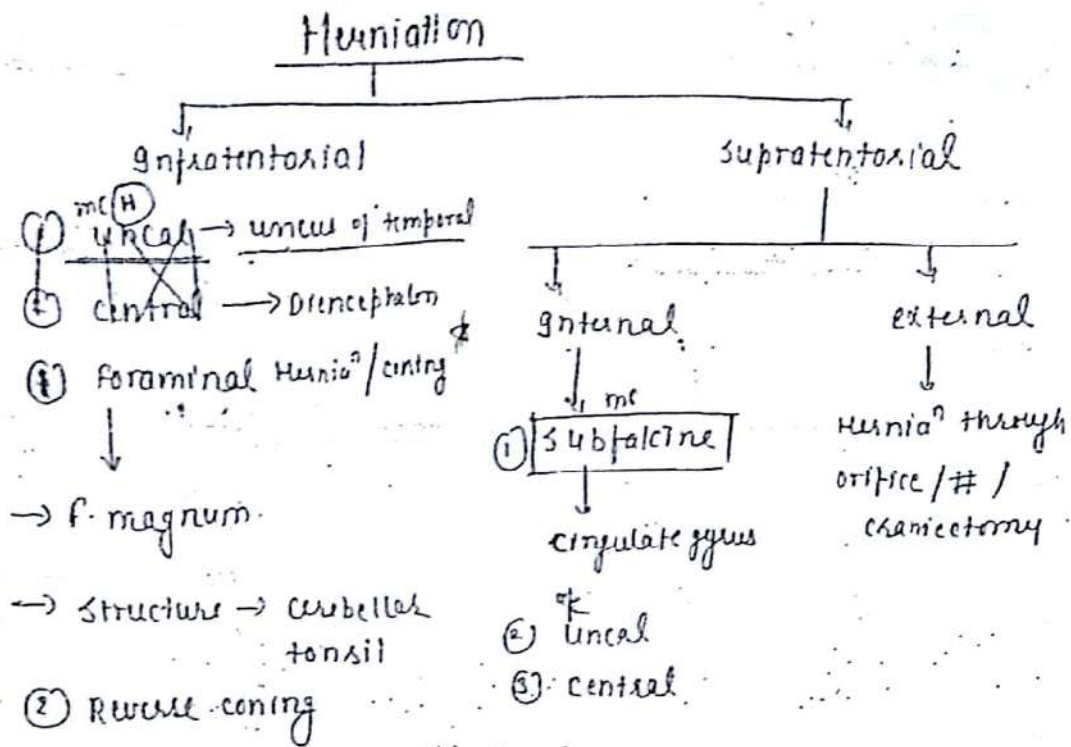
WFNS scaling —

	GCS	FND
(1)	15	—
(2)	13-14	—
(3)	13-14	(4)
(4)	8-13	+1-
(5)	≤ 7	+1-

Fischer —

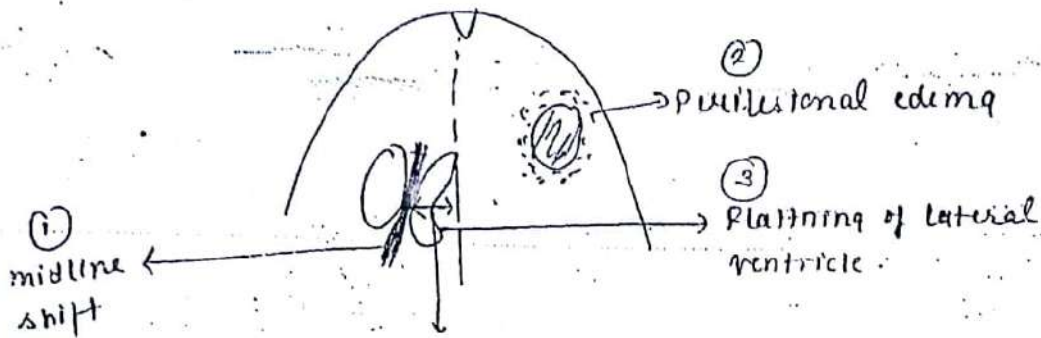
- I — NO SAH
- II — thin SAH
- III — Thick SAH + focal clots ⇒ Highest risk of vasospasm in gr-III.
- IV — Intraventricular bleed

112



midline shift — This is one of the effect of mass

shift wall b/w 2 lateral ventricle — Septum pellucidum



This dist. is measured

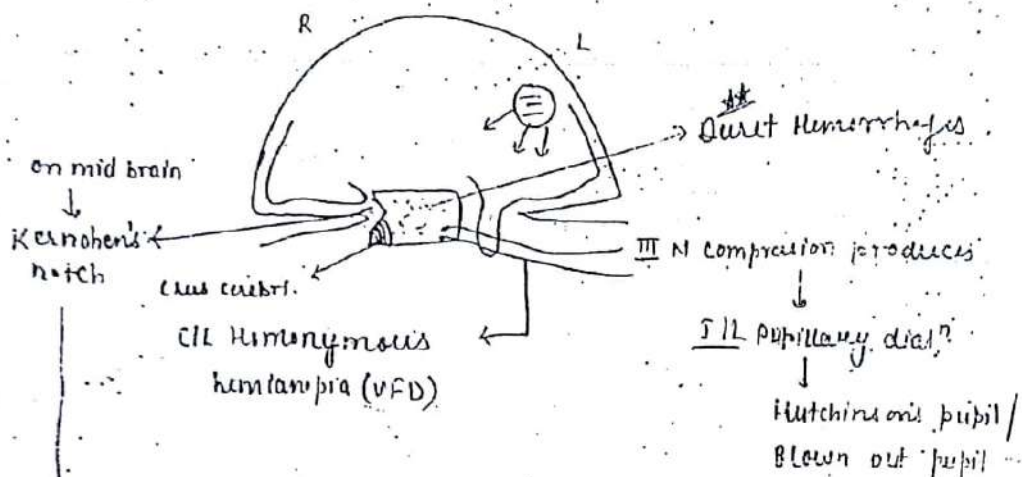
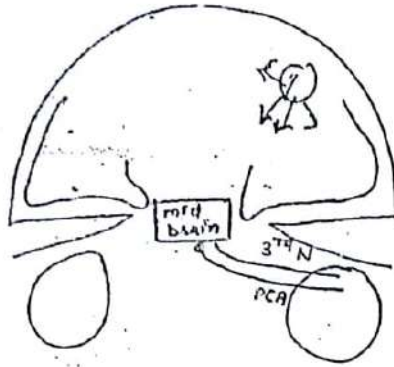
3-5 mm — mild

6-8 mm — mod.

≥ 9 mm — severe

come ←

(113)

Uncal Herniation

Kernohan Wolffman phenomenon → false localizing sign.

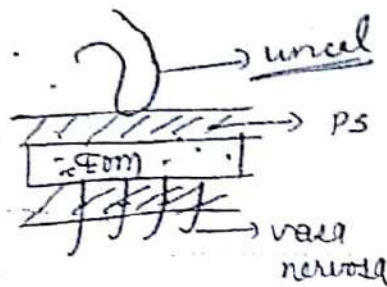
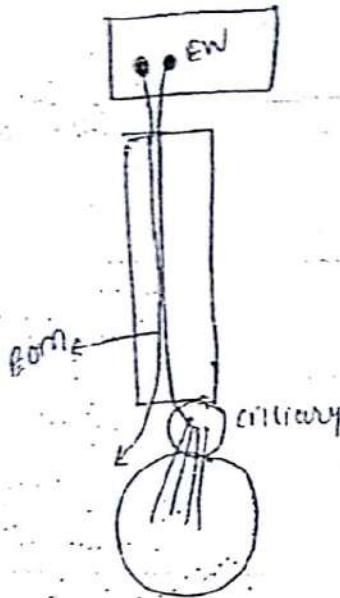
* compression of uncus cerebri. which contain corticospinal tract

It sided lesion causes problem in lt. side (Hemiparesis)

(N) In lt sided problem, lesion should be in Rt. side)

in 3rd N compression

(Post-communicating A. aneurysm & Berry aneurysm → compress 3rd N)
me.



→ in 3rd N compression parasympathetic fibres
less occur, 1st & EOM fibres remain intact
so only pupil dilated.

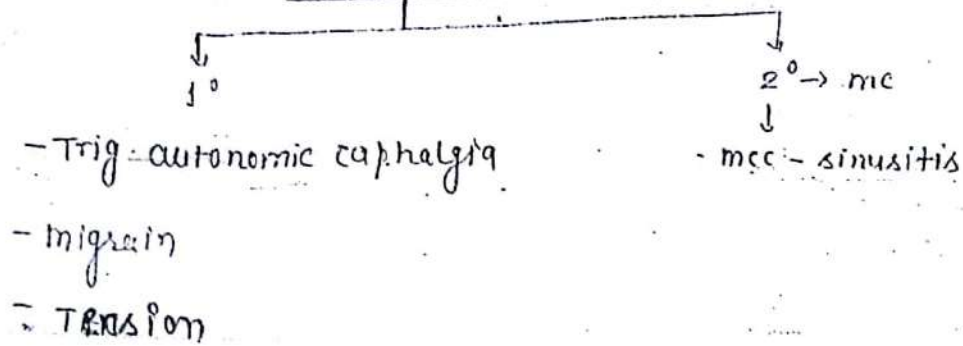
* in DM — EOM involved.
PS spared

Yhts is b/c the vasa nervorum getting compressed.

	EOM	pupil
compression	X	✓
DM	✓	X

(114)

Headache

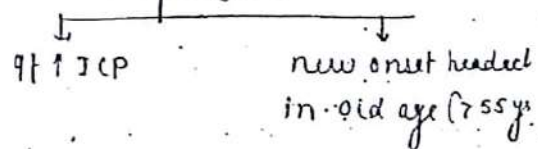


Dangerous Headach → Headach d/t ↑ ICP

Dangerous headach —

- ↑ coughing / straining
- ↑ c change in posture (lying down / bend)

Investigⁿ



migrain

- 1) P - pulsatile
- 2) O - one day
- 3) U - U/L → fronto-temp / of
- 4) N - nausea
- 5) D - disabling

Pathology - cortical
spreading depression

central molecule involved

irs. Calcitonin & related

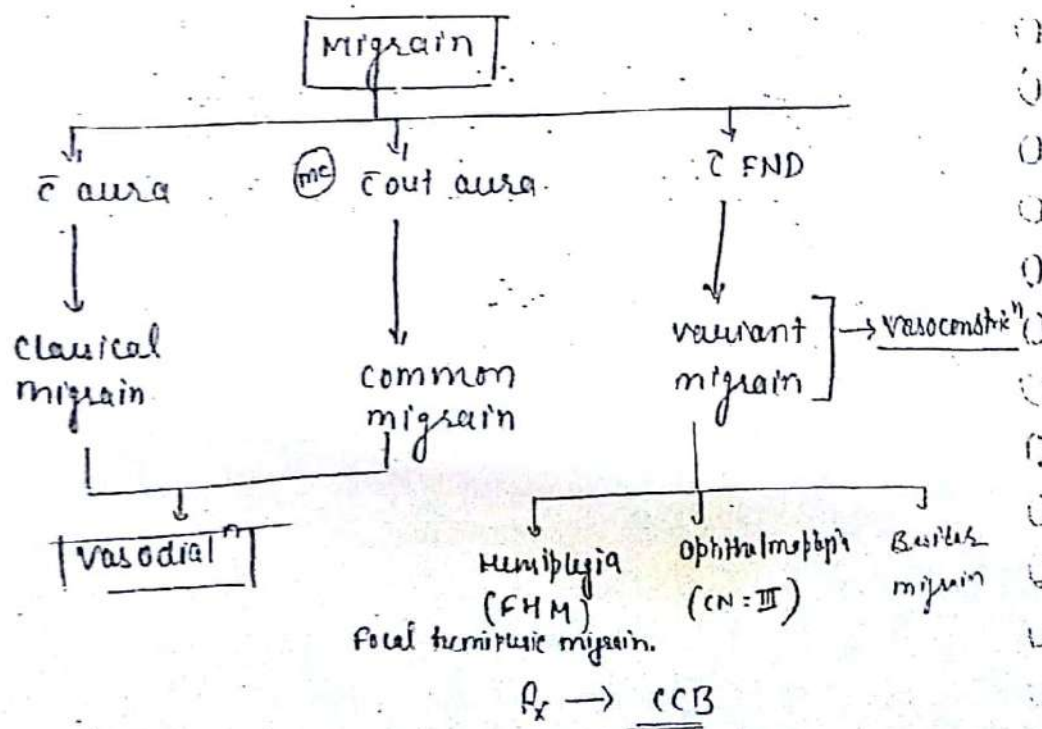
peptide (CGRP) $\uparrow$

↓
Drugs tried against CGRP
(monoclonal Ab)

Tension type headache

- ① non pulsatile
- ② variable → evening $\uparrow$
(↑ morning → frontal sinusitis)
- ③ B/L → frontal → occipital
(band)
- ④ no nausea
- ⑤ non disabling

Rx - short term analgesics



(115)

migrain having vasoconstrictor

Rx -

Acute attack — Doc — Triptans. → vasoconstrictor
→ 5HT_{1B/1D} ⊕

1st drug → NSAID

* For acute attack prefer injectable drug so that gastroperesis is avoided.

* Triptans are absolutely C/I in pregnancy.
give paracetamol only.

C/I of Triptan -

- ① ↓ flow disease (IHD, PVD)
- ② Pregnancy
- ③ H/O epilepsy.
- ④ migrain variants.

Pseudotumor Cerebri - Indicaⁿ -

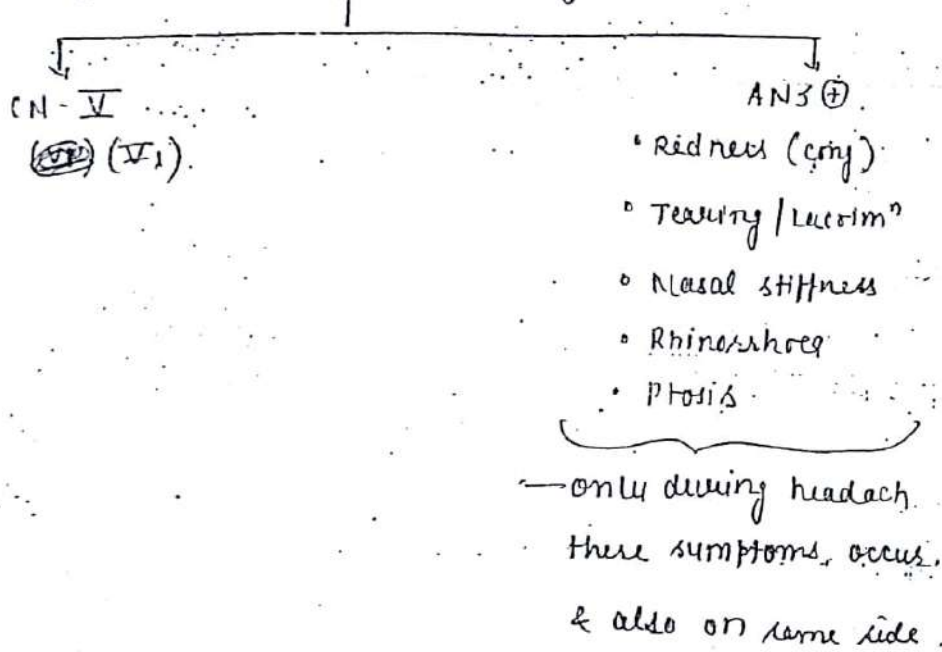
- ① ≥ 2 attack / month
- ② single attack > 2 days

DOC: - propranolol.

Aura — usually visual

- photopsia
- scintillating scotoma
- olfactory aura
- gustatory aura
- body part distortion

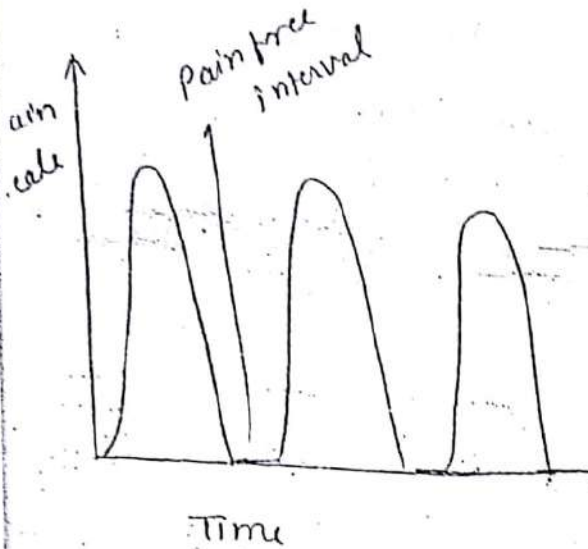
Trigeminal autonomic cephalgia —



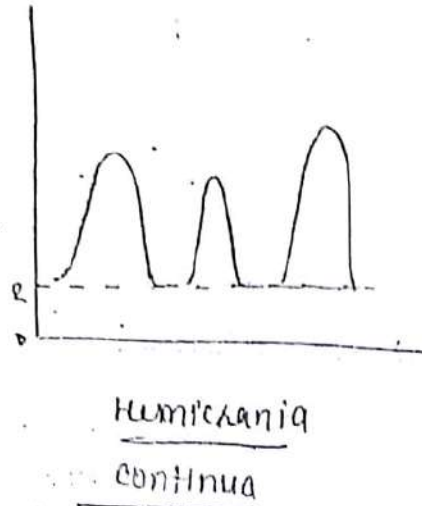
(116)

TAC

<u>Cluster</u>	Paroxysmal Hemicrania	HC	SUNCT
3 M			
→ Acute	Subacute	Chronic	Stabbing type of pain
• middle age ♂			(also produced by trigeminal neuralgia)
• middle of night	Same	Rx - TOC ↓ Indomethacin	
• middle of surge (surgeal headache)			-V]
→ Location -			
• Periorbital			
Boring type			
• ANS ⊕			
→ No. of attack -	→ multiple attack		
< 8 / day	> 8 / day		
Rx - Acute attack (min-h)	Dur ⁿ - much less than cluster headache (min/sec)		
① 500 γ-O ₂			
5-6 L/min x			
5-10 min	Rx - TOC		
↓ NA	↓		
Griptans	Indomethacin		
Prophylaxis -	Absolute response		
DOC - verapamil			
(NDHP CCB)			



cluster & Paroxysmal
Hemicrania have painless
interval



→ No painless interval

(17)

SUNCT

→ stabbing

→ $\underline{V}_1$

→ ANS (+)

→ Duration - ~~fixed~~ variable
(sec-min)

→ No touch sensitivity

→ $\sigma > \phi$

→ Difficult to treat

Trigeminal neuralgia

stabbing pain

Shock

$\underline{V}_2 / \underline{V}_3$ (facial pain)

ANS (-)

< 1 sec

→ touch sensitivity

→ $\phi > \sigma$

→ T.O.C! - CBZ

Benign intracranial HTN / Idiopathic IH / Pseudotumor cerebri

BIIH

- ♀
- OCP
- Headach
- CSF pressure ↑
- Fundus - Papilledema

⊖

→ MRI & MRV (M)

Rx → ① Removal of risk factors

② Acute: → Acetazolamide

Causes metabolic acidosis

↓
Resp. alkalosis
(Hyperventilation)

↓
CO₂
↓
ICP

3) Periodic CSF removal

Through LP

c) Lumboperitoneal shunt

d) Anterior resection

CVT (Cortical venous thrombosis)

- ♀
- OCP
- Headach
- CSF pressure ↑
- Fundus - Papilledema +/- (chronic)
- FND
- Seizure

→ MRI & MR venography

↓
Filling defect

→ Rx - Anticoagulants

(118)

LP —

q1 for Δ sis — 8-15 ml CSF can be removed

$\uparrow$ ICP $\rightarrow$ 2ml

BIH / NPH $\rightarrow$ 30-50 ml can be removed.

BIH

• Risk factor —

- obesity
- ocp
- estrogen
- hypothyroid
- DM
- acromegaly ($\uparrow$ GH)
- cushing
- steroid withdrawal
- vit-A toxicity

aPC
 $\ominus \downarrow$
Factor V
 $\downarrow$
 $\uparrow$ coagulⁿ.

CVT

• Risk factors —

① Dehydration

② Pregnancy & post partum

Post partum seizure —
- eclampsia
- CVT
- Sheehan syndrome

③ Thrombophilia

Inherited

Acquired.

$\downarrow$
mic-Factor V

$\leftarrow$ Leiden mutⁿ
(aPC resistance)

Δ sis —

CT — Delta sign

CECT — empty delta sign.

Multiple Sclerosis

- * mc demyelinating disorder.
- * temperate country
- * mc in whites
- * mc in ♀
- * it is a disease of white matter of CNS.
- So - there will be no peripheral neuropathy

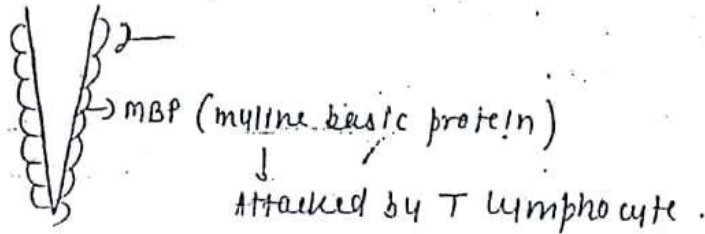
- Dementia
 - Seizures
 - Aphasia
 - no LMN type of cranial N. palsy.
 - ↳ except optic N.
- (Optic N. is a tract & covered by meninges)

 - 1) arise from diencephalon (other cr. N. from neural crest cell)
 - 2) oligodendrocyte myelinates optic N. (other N. myelinated by Schwann cell)

Oligodendrocyte can myelinate multiple axons at one time while Schwann cell myelinates single axon.

(119)

Pathophysiology — 9+ is Type IV HSR.



C/F — 1) earliest Fatigue (also mc)

2) 1st neurological manifestation — optic neuritis.

Por $\Delta \rightarrow$ VEP

3)

- Acute history
- Sudden onset
- Severely debilitated
- Loss of central vision
- Pain on extraocular movement
- Painless loss of vision

Optic neuritis

1) — Acute

2) — central vision loss

3) —

4) — Pain on extra ocular movement

5) — $\ominus$

6) — disc blurring $\rightarrow$ edema

7) — Hyperemia

8) — RAPD

2nd —

Papilledema

1) — Acute / chronic

2) — Periphal ~~trans~~

3) 1st sign $\rightarrow$ enlargement of blind spot

4) — $\ominus$

5) Headach

6) disc blurring — edema

7) $\ominus$

8) RAPD $\ominus$

(9) VEP $\rightarrow$

3) Dorsal column involved — Lhermitte's sign (Barbed chair)
Sudden flexion of neck produces electr. shock like pain.

— This sign is seen in ds. in which dorsal column involved like ① MS

② cervical spondy

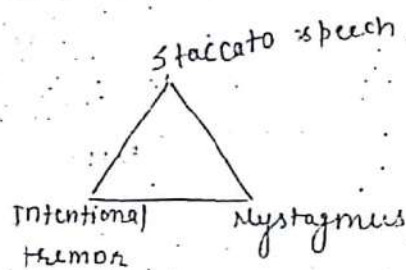
③ Tabes dorsalis

④ SAED (Bn det)

⑤ Radiaⁿ myelopathy

4) Corticospinal tract

5) Spinocerebellar tract → Chastot's triad



6) medial longitudinal fasciculus (Internuclear ophthalmoplegia)

7) Transverse myelitis (partial)

— All tract affected at same point.

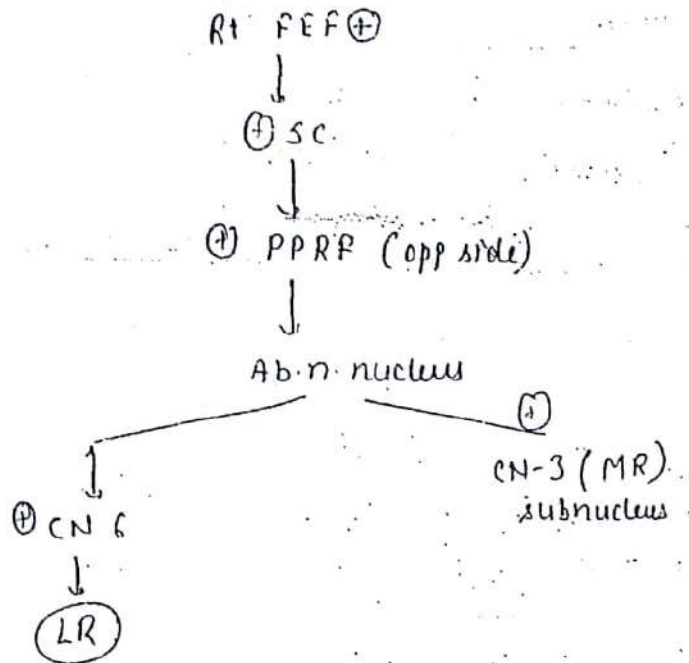


Tracts not affected →

Spinothalamic T. (b/c it is not myelinated)

So partial transverse myelitis is there.

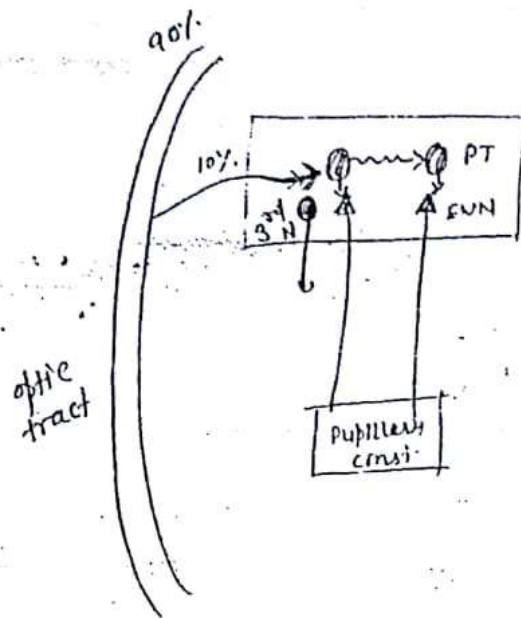
Scanned by CamScanner



* MLF lesion causes internuclear ophthalmoplegia (INO)
It is called as INO b/c it ~~connects~~ is b/w 2
nucleus.

* Pseudo INO! — (1) myasthenia gravis
(2) polymyositis (3) dermatomyositis

(121)



10% fibres from optic tract supply pretectal nucleus

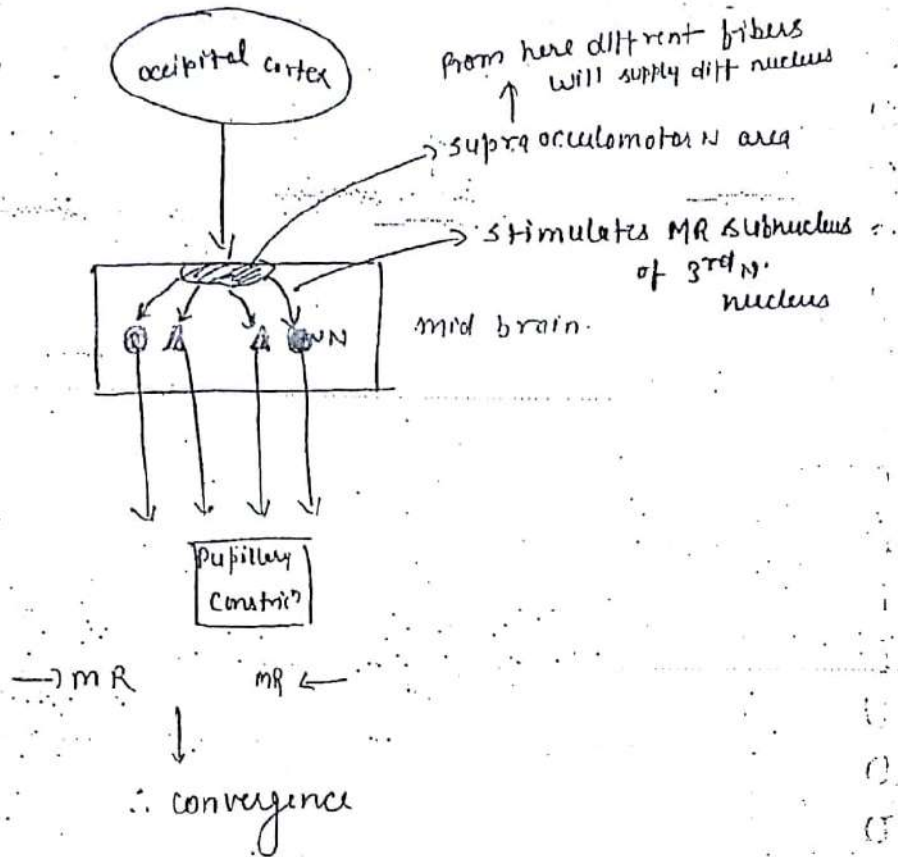
↓
From here EWN will get stimulated

↓
Pupillary constr.

∴ There is no connection b/w 3rd N nucleus & pretectal nucleus. there is no EOM movement, only pupil constriction

AEWN

oculomotor N. nucleus



⇒ In MS MLF lesion there is no loss of accommodation as the pathway is different here.

Neurosyphilis —

* 9b there is injury to pretectal nucleus

↓
pt. can't constrict pupil (no light reflex)

- But the same pt will have (N) accommodation

This is Argyan Robertson pupil (Prostitutes pupil)

This phenomenon is light near dissociation

(22)

Movements of eye—

- saccades → These are fast, jerky movements.
(slowly look at Rt./Lt. side)
↓
But this is not possible.

- smooth pursuit movement → when looking at moving object, saccades can be abolished.
→ These are always from cortex.

ex - ① voluntary saccades → voluntarily shifting gaze.

② Reflexive saccades → suddenly looking towards object of interest. No need of cortex here.

③ memory saccades → saccades moving through memory.

④ Predictive saccades → Predict the trajectory of object.
Ex - catching if something is thrown.

Vestibulo ocular reflex — No need of cortex. It requires brainstem.

- It can abolish saccadic movement.

→ VOR maintains the position of eye for ex - if head is bent to Lt, eye will be moved to right.

* It is a slow reflex & can not correct eye position very fast.

- This is the basis of nystagmus -

if we rotate head to lt side very fast



then v.o. reflex being a slow reflex can't maintain eye position & eye will move to lt side only.

→ caloric test → ⊕ Hz sec

↳ cortex perceives that head is rotating to opp side



cortex which gives fast component of caloric test

Directⁿ of nystagmus

Cold water → ^{Perceived as} Head rotates to opposite directⁿ

Hot water → ^{perceived as} Head rotate to same directⁿ

not left

(123)

① coma $\rightarrow$ cortex X $\rightarrow$ not functioning.

~~lead water~~
warm water in lt. ear.

Rt ear
 $\downarrow$

$\downarrow$
same side head movement like stimulus (lt.)

$\downarrow$
since cortex is -nt & so no fast component is there (i.e. eye will not move to lt.)

$\downarrow$
only VOR is there (so eyes move to lt. side)
lt. side

② Cold water in
lt. ear

$\downarrow$
Perceived as head is
moving to Rt side (opp)

$\downarrow$
we are moving head very
fast & so eye will move to
op. side only. Here VOR
being a slow reflex can't
able to compensate eye deviation.

③ Warm water

$\downarrow$
perceived as head is moving
to same direcⁿ

Multiple sclerosis

Inv: - ① IOC is MRI $\pm$ gadolinium enhancement.

- white matter plaques seen.



McDonald criteria is applicable

* OCB — oligoclonal bands —

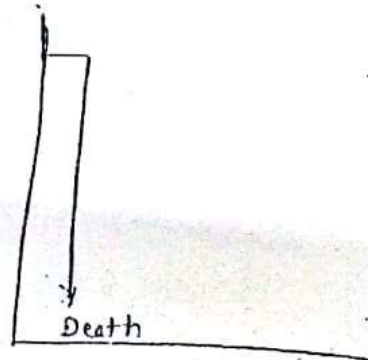
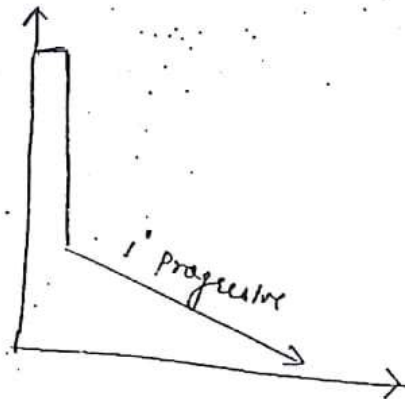
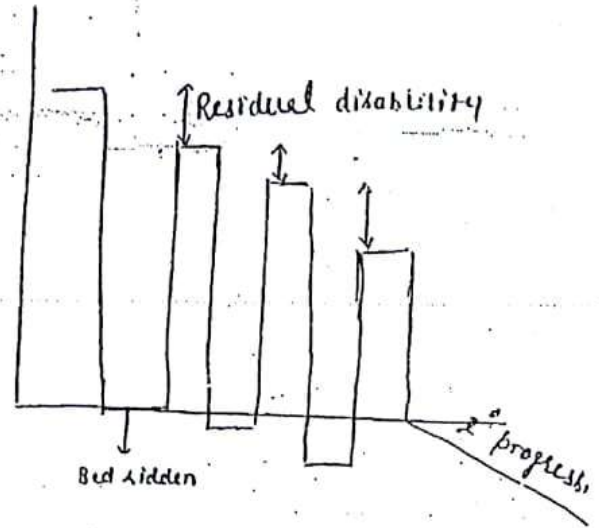
These are neither specific nor prognostic. These are seen in many conditions.

<u>OCB</u>	<u>Blood</u>	<u>CSF</u>	
	+	-	
	+	+	→ indicate CNS ds.
	-	-	
	-	+	→ most sp. for CNS disease

Rx — depends on types

(124)

1) RRMS — (Relapsing remitting)
— > 85 %



Marbury (fulminant MS)

* Acute attack —

TOC — steroids

- They shorten durⁿ of acute attack only.
- steroid don't reduce the residual disability.

* Prophylactic drug —

- Decrease the relapses.

ex- if a pt. having 5 attacks/yr ; if prophylactic drug given there will be 1 attack/yr.

- They don't work in progressive variety of MS.

* Marburg MS —

TOC — IV immunoglobulins given.

- It is an acute but fulminant drug.

Other drug —

- Mitoxantron

- Sulfasalazine

- Dimethyl fumarate

} oral

* Doc for treating fatigue in MS. → Amantadine.

Neuromyelitis optica —

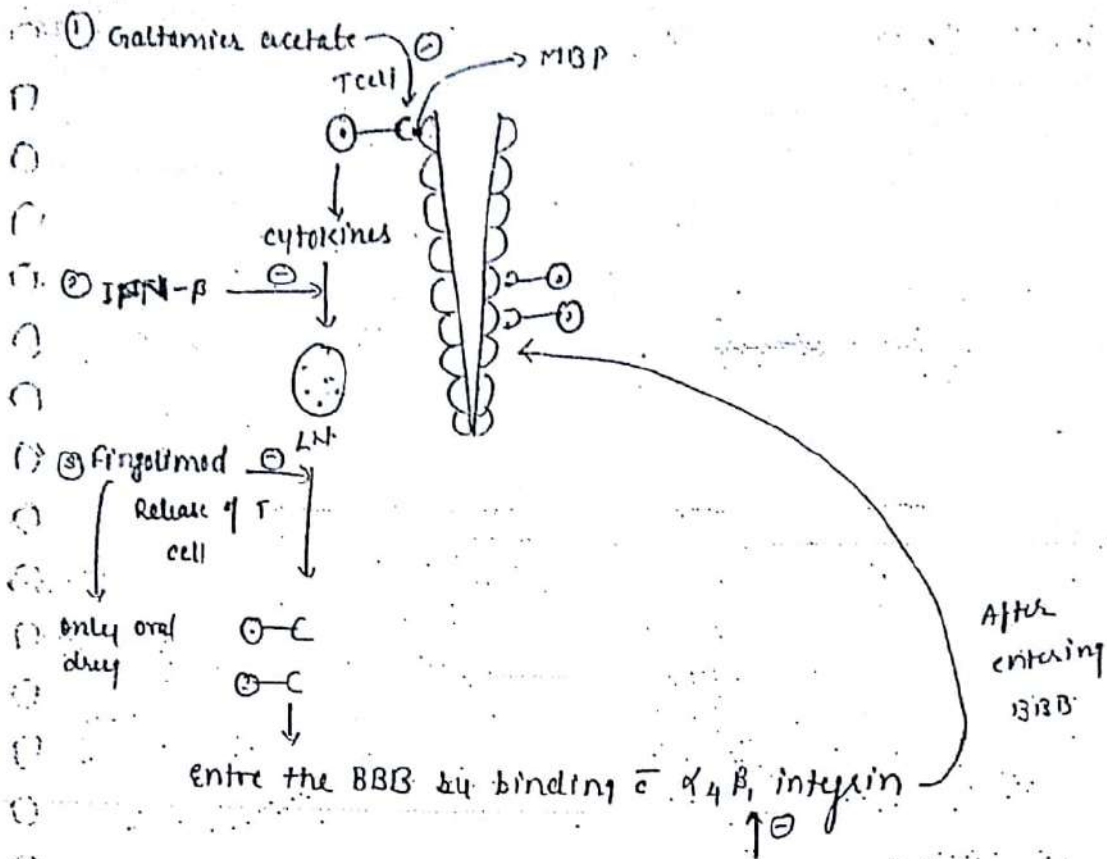
NMO (Devic's) — It is a variant of MS.

- It is more common in India than MS.

- Here > 2 segment (long segment) spinal cord demyelination occur along w/ optic neuritis (VL orbit).

Δ^{sis} — • Anti NMO IgG Ab detection (Aqua porin-4 Ab) in blood > CSF.

(125)



* Glatiramer acetate $\rightarrow$ enter the MBP & alter its structure & so no T cell dependent damage occur

$\rightarrow$ Natalizumab $\downarrow$ EDSS score max^m & it is most effective.

SIE - PML (caused by JC virus)
 $\downarrow$
(Polioma virus)

= most common in HIV pt.

(126)

- Dementia -

Reversible

Irreversible

STN - BIN

- All neurodegenerative disease

① SDH (chronic)

② Infection - except
↓
(Creutzfeldt Jacob ds)

③ Normal pressure
hydrocephalus

④ B12 deficiency

⑤ Insufficient thyroxine
(myxoedema)

⑥ some neoplasm

Cortical

- AD
- FTD
- CJD

Subcortical

- PD
- HD
- NPH

mixed

- DLB (Lewy body dementia)
- MID (vascular)
- neurosyphilis

* HIV dementia → affects glial cell > neuron
so subcortical.

Cortical

Subcortical

Mixed

Motor problem

Late

early

Aphasia

+++

—

Acaculia

++ (early)

—

Dysarthria

Late

++

Memory

↓

↓

Recall
Recognition } Lost

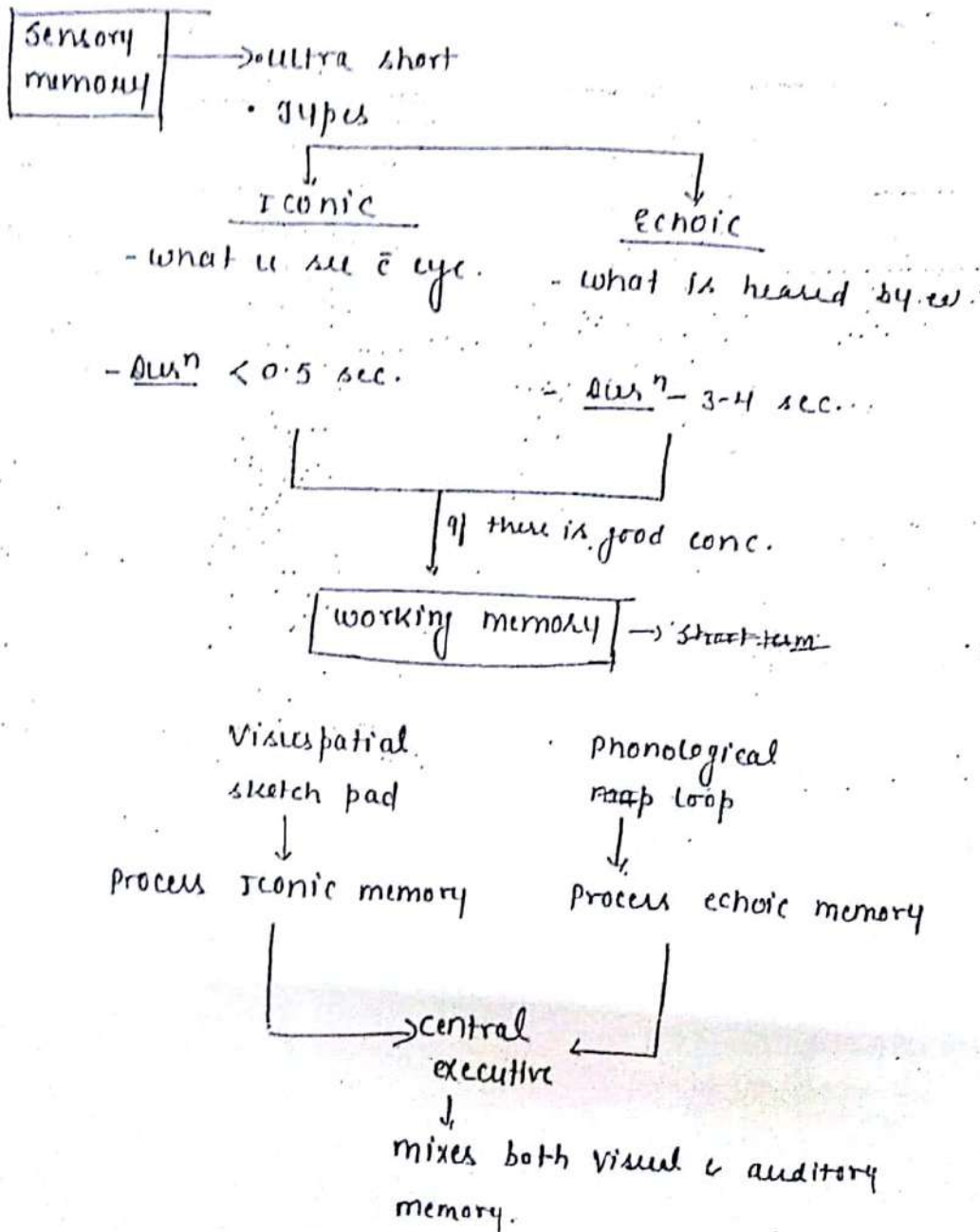
Recognition — ↓
Recall → can be improved w
clues.

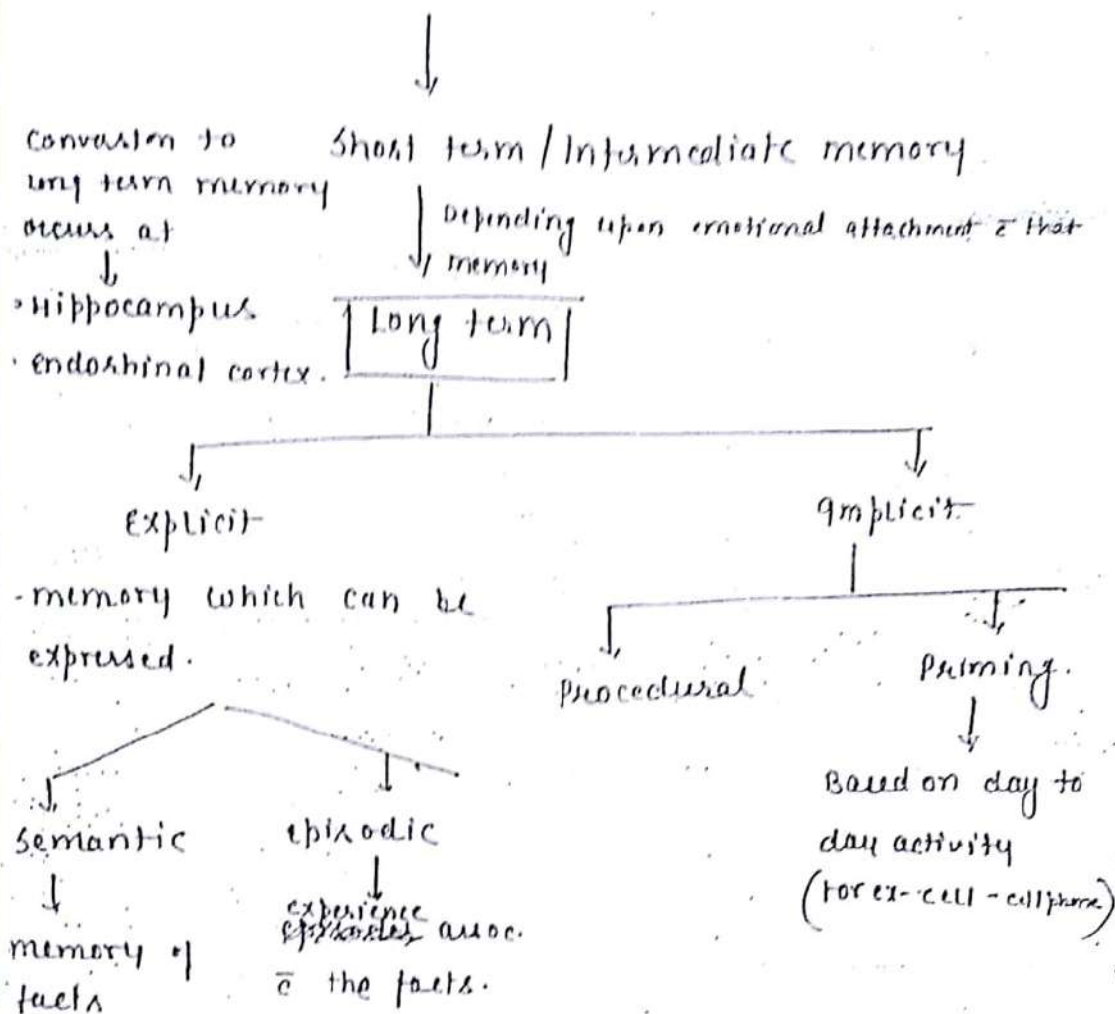
(127)

Dementia — • loss of cognition.

- memory loss may or may not occur.

Informⁿ processing model —





* Implicit memory is very resistant to dementia.

* Among explicit episodic memory is 1st to be lost.
Semantic memory loss occurs later.

(128)

— Alzheimer's ds —

* mc dementia overall & also in elderly.

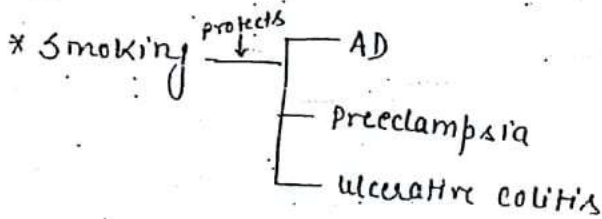
* mc dementia in young → FTD.

Risk factors — ① elderly [>90 yr → 50% have AD]

② Diabetes mellitus → 3 times ↑ risk

③ Hyperhomocysteinemia

④ Illiteracy → failure to acquire new memory.



Genetics —

Hereditary

① Presenilin-1 (chr-14) } causes
 ↓ dysregⁿ
② Presenilin-2 (chr-1) } ↑ amyloid.

③ APP gene (chr-21)

↓
9n trisomy 21 (Down's), ↑ Aβ

amyloid formed & so AD occurs at ≈ 40 yr

non herid.

↓
APO E4 mutation

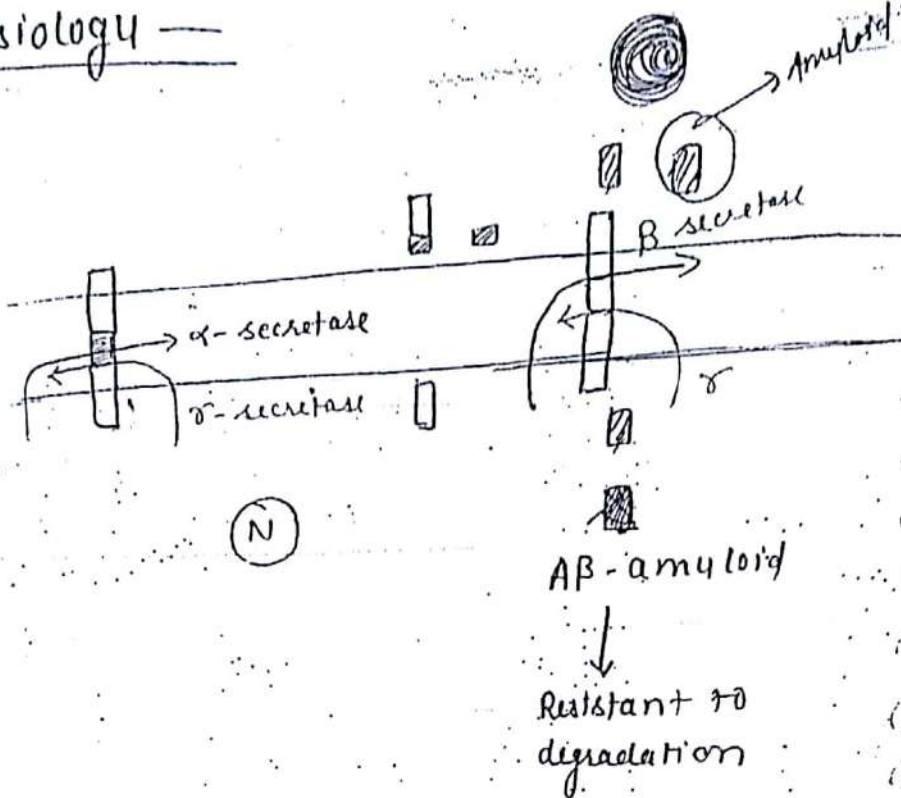
↓
→ leads to late AD.
(around 80 yr)

→ 100% will get AD.

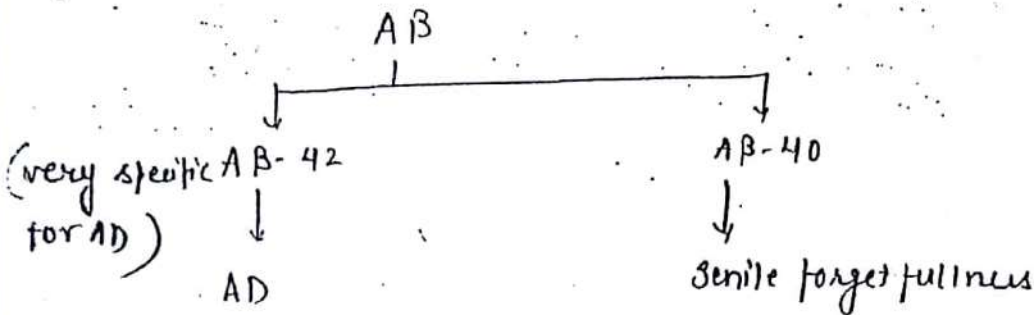
* APO E2 protective.

* early onset AD — < 60 yrs

Pathophysiology —



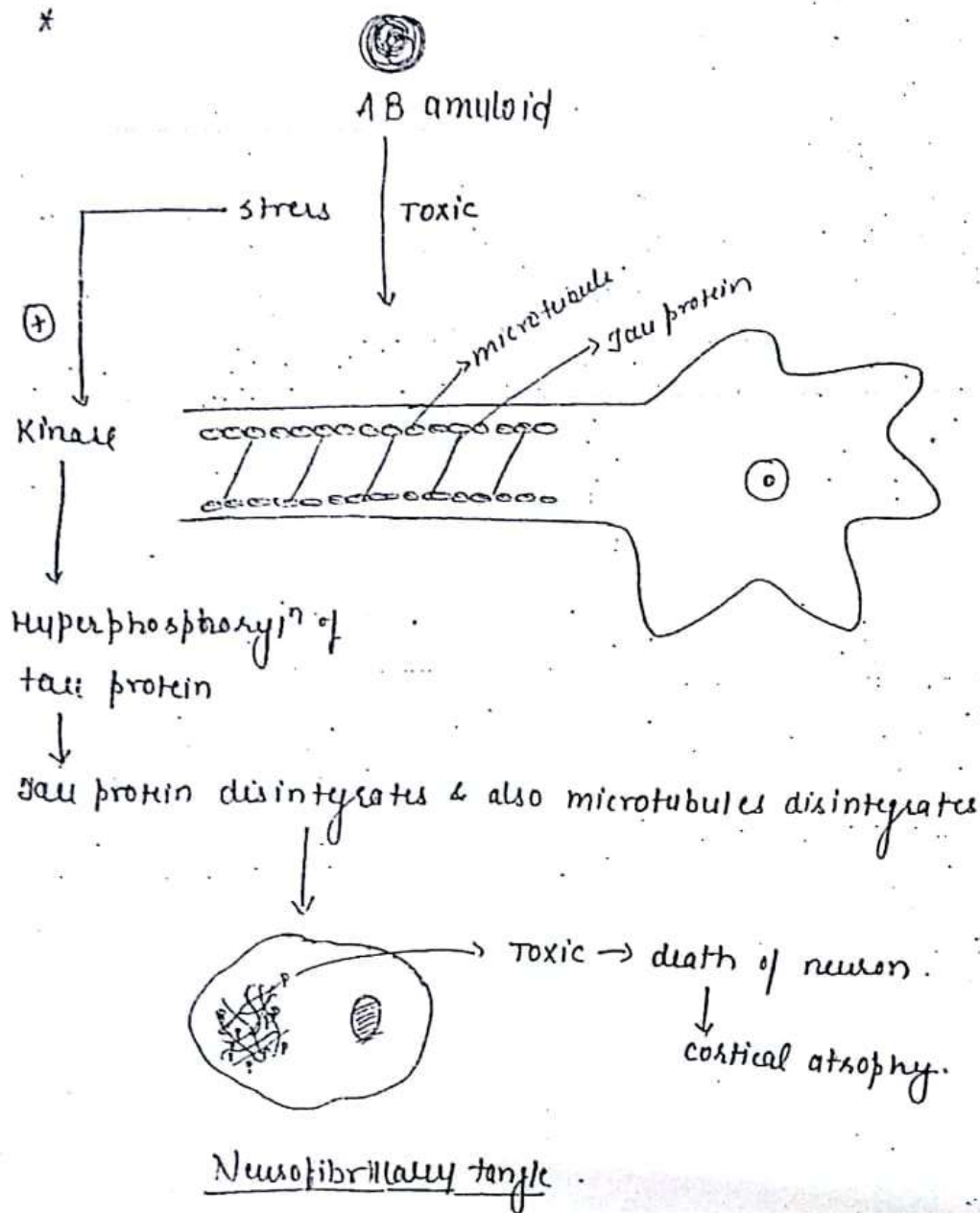
- there occur accumulⁿ of A β extracellularly.



* Both A β -42 & A β -40 can cause cerebral amyloid angiopathy. & so CAA is not specific for AD.

(129)

* Lobar hemorrhage (Intracerebral hemorrhage)
↓
occurs due to CAA.



* A β -42 is very specific for AD but it has no correlation with severity of disease.

* Tau protein —

Accumulⁿ tauopathy —

- fronto-tempo-degen.
- AD
- PD
- CJD
- CBD (corticobasal degeneration)
- PSP (progressive supranuclear palsy)

→ Neurofibrillary tangle is specific for AD.

→ Tau protein inclusion correlate with severity of AD.

* Accumulⁿ occurs in — (AP & NFT).

Endothelial cortex > Hippocampus

↓
seen in medial temporal cortex.

→ last place to accumulate → Primary areas.
so motor problems are very late in AD.

(130)

C/F — (1) Amnesia → 1st → • No new memory
• episodic lost 1st in retrograde
• Anterograde amnesia

(2) Aphasia → 1st — nominal aphasia (Anomic)
— loss of naming

(3) Apraxia →

(4) Agnosia → late feature

(5) Acalculia → • early loss • hallmark
↳ (funcⁿ of parietal lobe)

Loss in AD —

— Temporal > Parietal > Frontal > occipital
↓ ↓ ↓
- Apraxia - Behavioural problem - vision
- Acalculia - motor problem

- Nucleus basalis of Meynert — get destroyed in AD. It's funcⁿ is to produce Ach in cortical area.
So its destructⁿ leads to ↓ Ach

- ↓ GABA

Clinical phases —

A — Amnesic

B — Behavioural phase (wandering)

Phantom border → some unknown new person is there
- seen in AD.↳ Jeftoli syndrome

C — cortical

D — Decorticate (bed ridden)

↳ die of infection.

Inv — • Gold std — Brain Bx↓
NFT & AB both should be there.

- mostly it is a clinical dx

- CT/MRI → R/O Reversible cause of dementia.

- In AD → CT → ① Atrophy of medial temporal & parietal lobe.② ↑ size of ventricle → Hydrocephalus
ex vacuo

(13)

g/t — $\uparrow$ Ach.
 $\downarrow$
Central Ach E $\ominus$

∇ NMDA (R) $\ominus$
 $\downarrow$
memantine

- Donepezil
- Rivastigmin
- Galantamin

* statin $\rightarrow$ • prevent delay progression of AD.
- can't stop progression of AD once it has started.

Frontotemporal dementia

Behavioural

Semantic

Non fluent aphasia
(Pick ds.)

i) lobes affected

Frontal > Temporal

Temporal > Frontal

Frontal = temporal

ii) Inclusions —

Tau protein

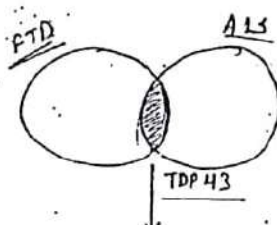
TDP 43

TDP 43

Also involve in
~~AD~~ ALS

Tau (pick bodies)
protein inclusion

↓
Intracellular
intracytoplasmic



overlapping of ALS
& ~~FTD~~ FTD

↓
Klas Guan's complex.

iii) C/F —

- Antisocial
- Incontinency

- fluent aphasia
(fluent speech & no meaning)

- difficulty in speech
- grammatical speech
- non fluent

(132)

CAT

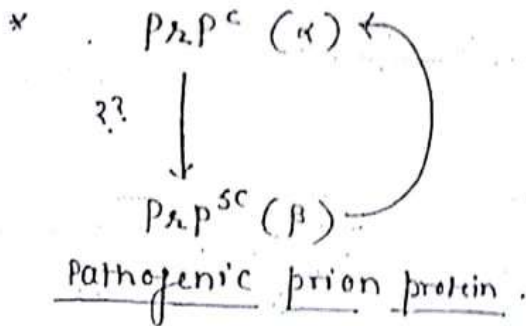
* In FTD, parietal lobe is relatively spared & so
Drawing is spared

Q11 - Rivastigmine & all other drugs of dementia.

* Edaravone is new approved drug for FTD &
ALS.

CJD (Creutzfeldt Jacob disease)

- Prion disease



Sporadic CJD

Variant CJD

1) Age - > 50 yrs

- < 30 yrs

2) CJD $\rightarrow$ rapidly progressive dementia (< 6 mth) + motor (myoclonus)

- sensory symptoms 1st + psychiatric problem

3) EEG -

- slow background $\bar{c}$ periodic sharp wave

- variable

4) MRI -

- cortical ribboning.

- Pulvinar sign

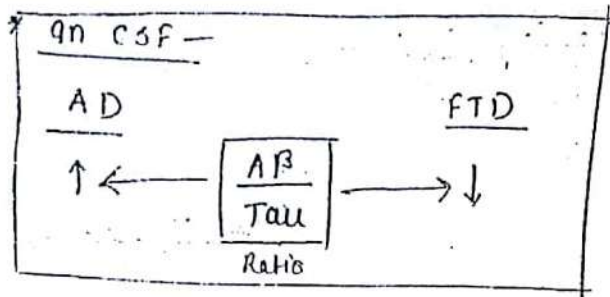
Hockey stick sign.

5) CSF - protein 14-3-3

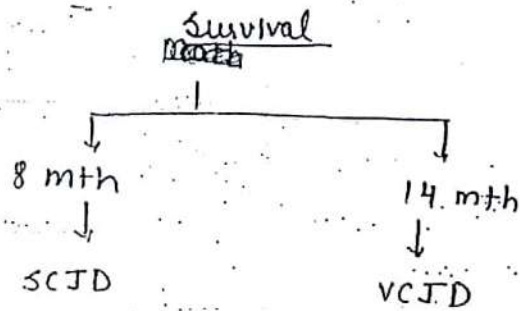
marker of neuronal injury $\downarrow$ specific

No acute causes (encephalitis) $\rightarrow$ 91 no acute causes than it is ab. for CJD.

(133)



Rx — No Rx for CJD.



Huntington disease

* Huntington gene — chr. 4

— dinucleotide repeat mutⁿ ~~AAA~~

↓
-CAG

mutⁿ

Point

Frameshift

Tri. Repeat

missense

nonsense

silent

Add / delⁿ of nucleotide
(not in multiple of 3)

aa → aa

aa → stop

aa → aa

ex- TATC added in
Fabry's disease

quality of protein

qty ↓

ex- β thalassemia

• quality of protein affected

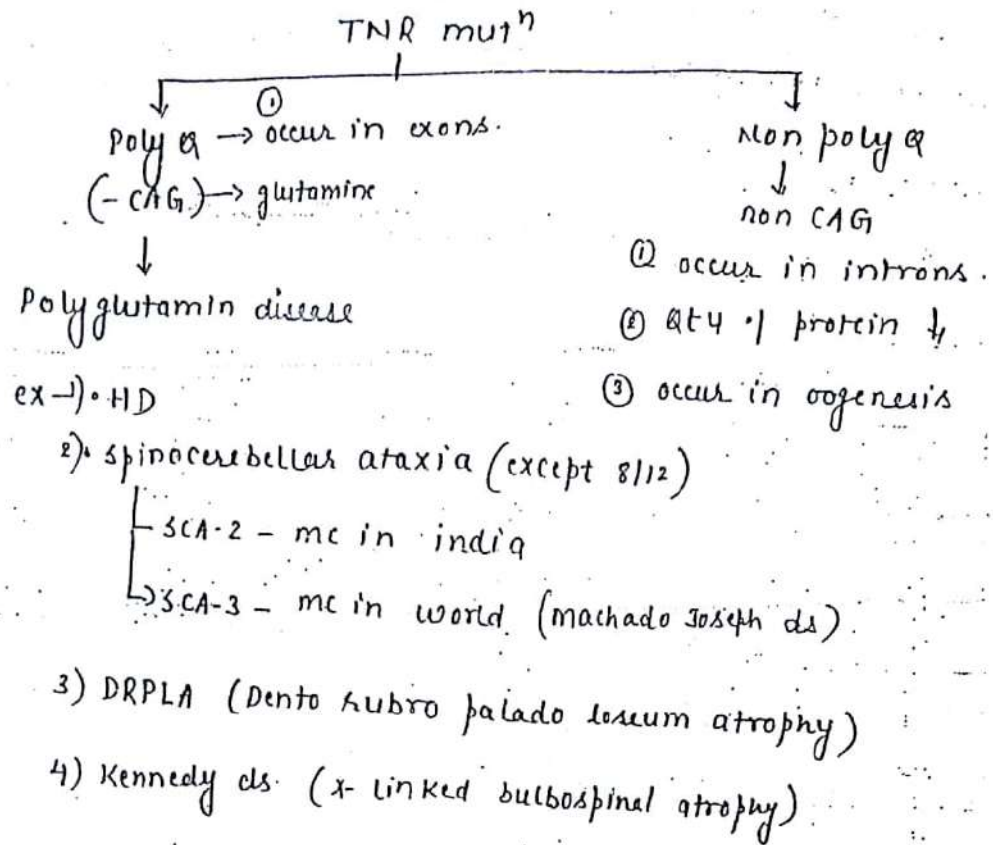
Loss of funcⁿ
(AR)

Gain of funcⁿ
(AD)

ex- sickle cell
disease

ex- Liddle syndrome

134



Non poly Q —

- * myotonic dystrophy — CTG
- * Friedrich's ataxia — ~~CTG~~ GAA
- * ~~Fragile X~~ →
- * Fragile X syndrome — CGG
- * SCA 8/12 → CTT

→ non poly Q occurs in non coding area (intron)
But there are gene regulator in this area. so involvement
of intron leads to ↓ qty of protein.

Poly Q

- occur in exon
- quality of protein ↓
- spermatogenesis - prob.

Non poly Q

- Intron
- qty ↓
- oogenesis.

Repeats - HD

- Repeats - 26-35 - mild
- 36-39 - moderate
- ≥ 40 - severe

* Normally Huntingten protein is in nucleus but when it comes to cytoplasm, it is dangerous.

- C/F - Presentation - 30-40 yrs
- Avg survival - 17 yrs

① motor problem → very early

↓
Dlt damage of
caudate + putamen
(striatum)

- chorea
- Athetosis
- myoclonus



② Dementia

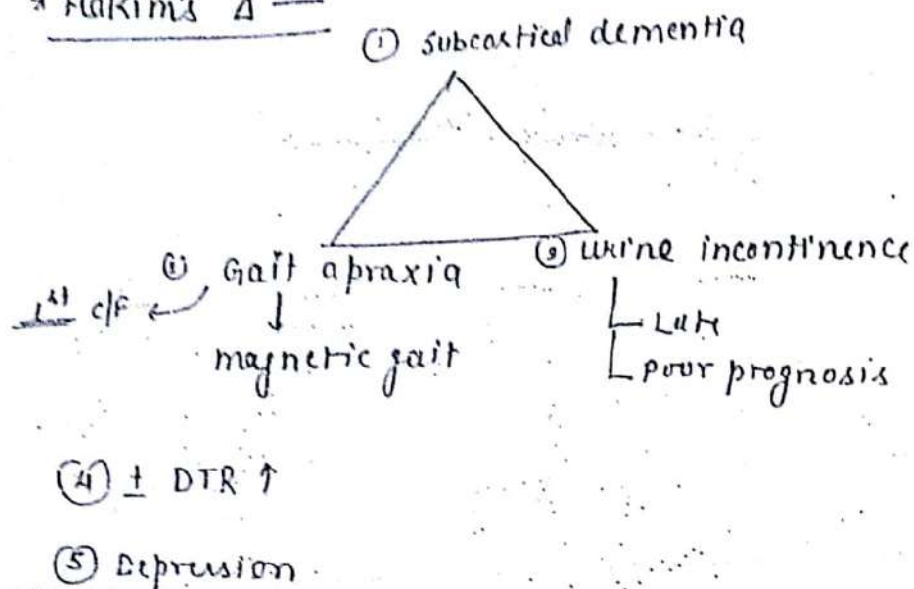
③ Psychiatric

Rx - Haloperidol

(135)

Normal pressure Hydrocephalus

* Hakim's Δ —



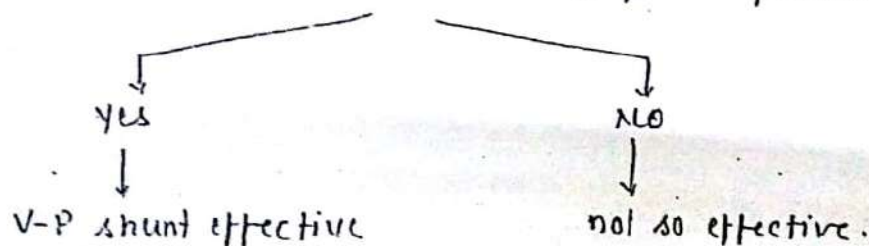
Inv — CT $\rightarrow$ Hydrocephalus

CSF pressure
Brain parenchyma] $\rightarrow$ (N)

Flt — 1) V-P shunt — miller fisher test is done

to see the efficacy of V-P shunt.

- Remove 30-50 ml CSF & see for improvement.



Dementia + Lewy body

- o Dementia (+)
- o NO amnesia
- * visual hallucination (+) → For this if we give Haloperidol
- * Parkinson's disease like features
 - ↑
 - Parkinson de. feature with ↑
 - as these pt. have ↑ sensitivity to neuroleptics

Px - Rivastigmine

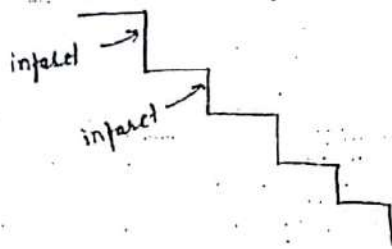
- * Lewy body is aggregⁿ of protein α -synuclein.
- It is intracellular intranuclear inclusion body.
- Lewy body →
 - Parkinson symptom
 - REM sleep disorder

(136)

multi infarct dementia (vascular dementia)

* It is due to repeated infarction.

- show step ladder pattern of deterioration.



* UMN signs -

- ① ↑ DTR
- ② Babinski sign
- ③ spasticity (clasp knife)

} ④

Rx -

Anti dementia drug
+
clopidogrel
+
statin

Parkinson's Disease (Bradykinesia)

↓
Idiopathic
PD (1°)
↓

Risk factor! - ① stroke

- ② Trauma
- ③ Mn toxicity
- ④ MPTP
- ⑤ Genetics:-

PARK-1

AD

chr. 4

PARK-2

AR

chr. 6

←
Lewy
bodies
Produced

α-synuclein

Parkinsonism

Lewy body dementia

+ REM sleep disorder

+ Behavioural disorder

Parkin

↓
No dementia

↓
Early onset PD ±

Dementia dystonia

2°
mcc: Neuroleptics

- Domperidone

- metoclopramide

- sulpirides

- Dopamin depletors
(tetrabenzene)

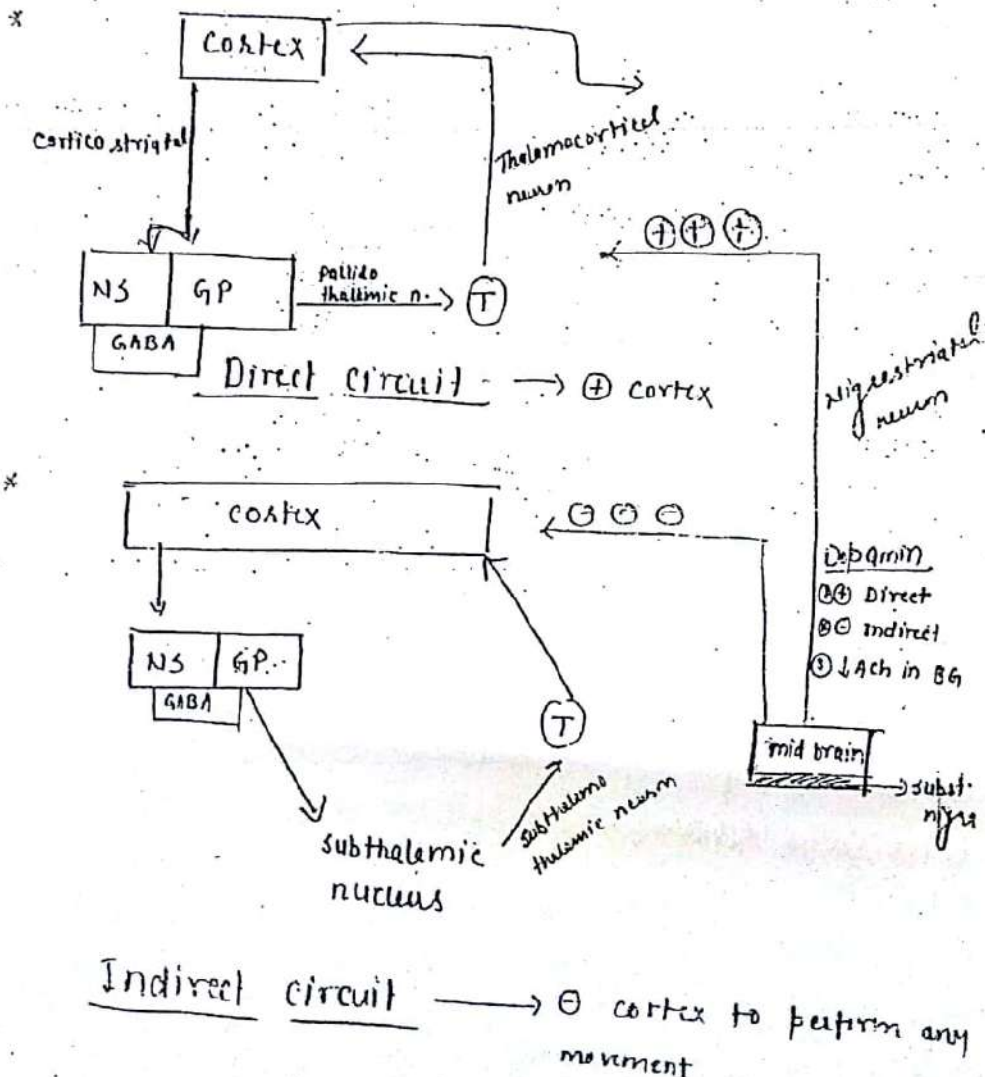
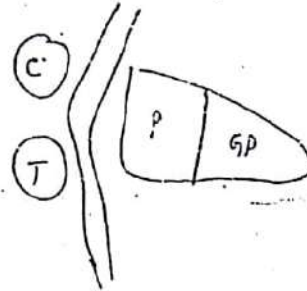
↓
guin for Hemibolism

(137)

Basal ganglia

Output of BG $\rightarrow$ through GP

Input of BG $\rightarrow$ NS



- * Basal ganglia releases GABA
- * Rest all will release glutamin (a-corticostrial, thalamo cortical)

PD :—/ Hypokinetic movement disorder :—

- * Here in mid brain there is degenerⁿ of nigrostriatal neuron leading to pallor of sub. nigra.

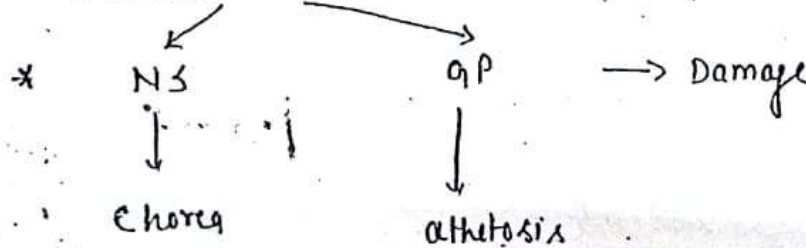
↓
there is cortical inactivⁿ leads to Bradykinesia in PD

↓
↑ Ach will cause — tremor

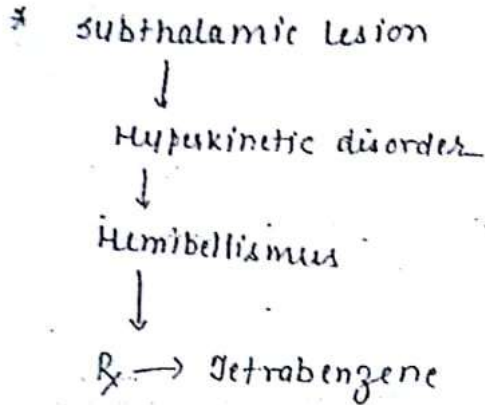
- * Lesion of B.G.

↓
↓ GABA

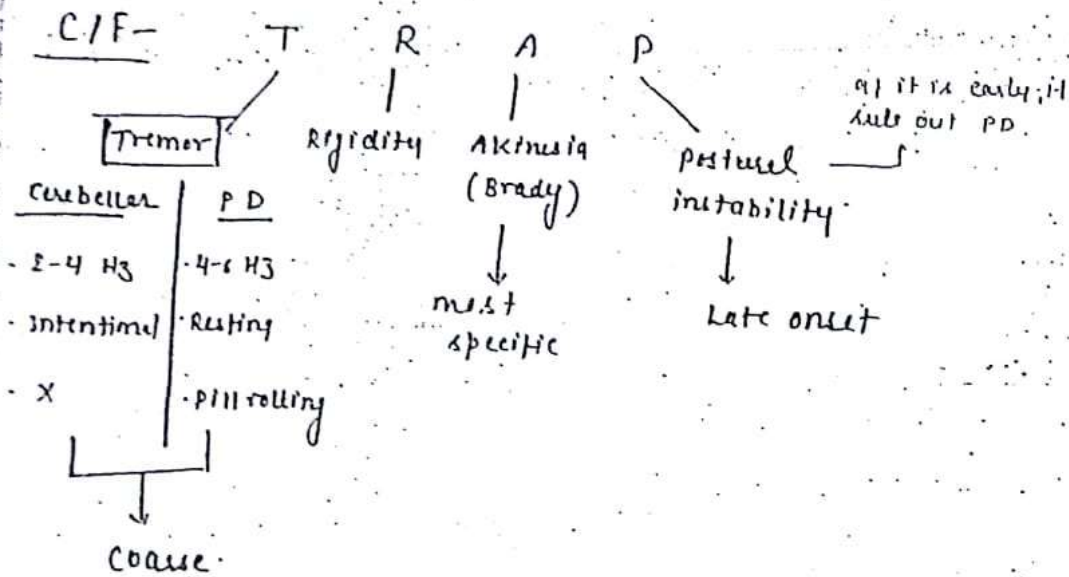
↓
It is ⊖ Neuro T. & loss of ⊖ leads to Hyperkinetic movement



(138)



Idiopathic PD



Rigidity - involve 2 group of muscle

- Cog wheel rigidity. → on slow movement there is tremor. checked in wrist.
- earliest / 1st / mc symptom of PD is tremor.

Scanned by CamScanner

(139)

Imp! - ① Dopamine scan: - Diff. b/w Parkinson's tremor & essential tremor.

Parkinson's tremor

Essential tremors

coarse
4-6 Hz

- No family H/O

- Bradykinesia

- No postural variation

- ⊖
(Jaw tremor ⊕)

- ⊖

- ⊖

- Family H/O

- -nt

- Postural variation

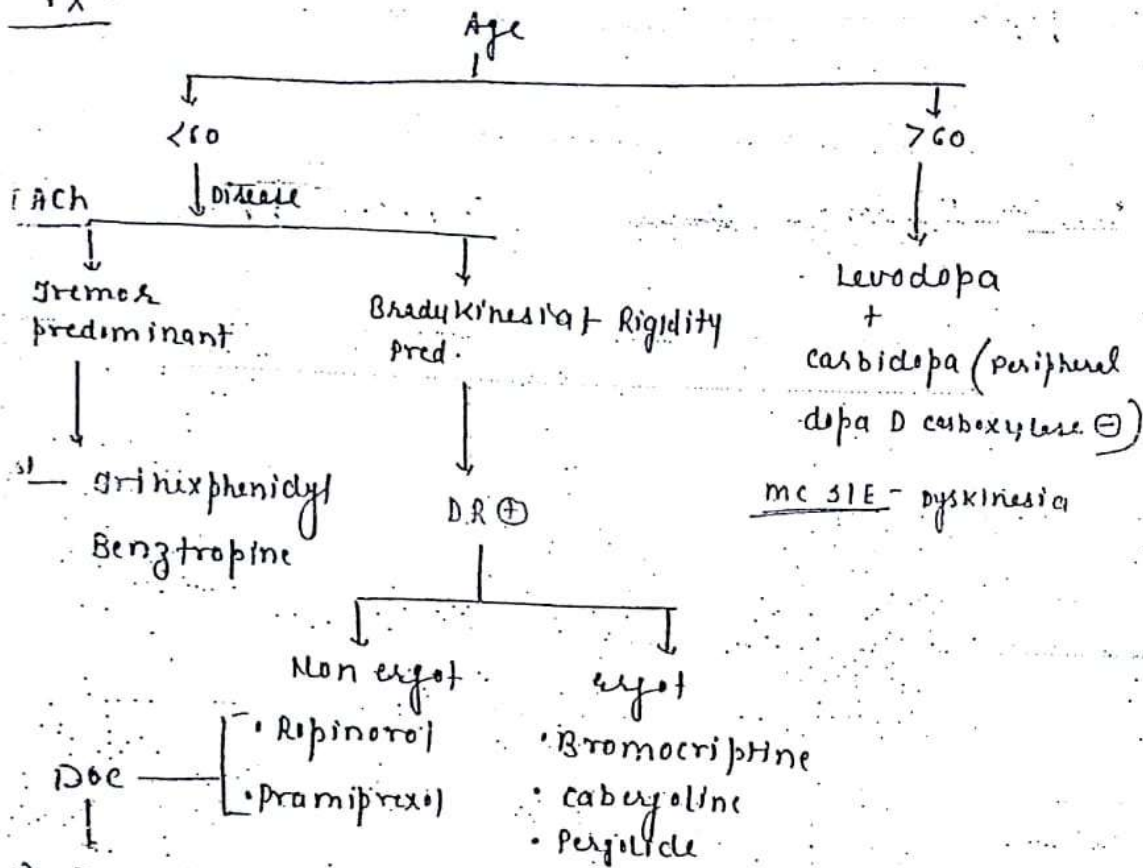
- Irritability ⊕

↓
Head movement

- Alcohol abolishes tremor

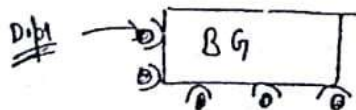
- β-blockers

Rx :-



- 1) Restless leg syndrome → causes — ① IDA
② pregnancy
③ CKD
- 2) Periodic limb movement disorder

Levodopa — S/E → ① dyskinesia



* +ve of dyskinesia is a good prognosis i.e. pt having PD.

(145)

2) Psychosis

DR ⊕ — S/E

- Dyskinesia (less)
- Psychosis (more)

COMT ⊖ — Tolcapone — enter BBB
Entacapone —

S/E :- Tolcapone → Hepatotoxicity

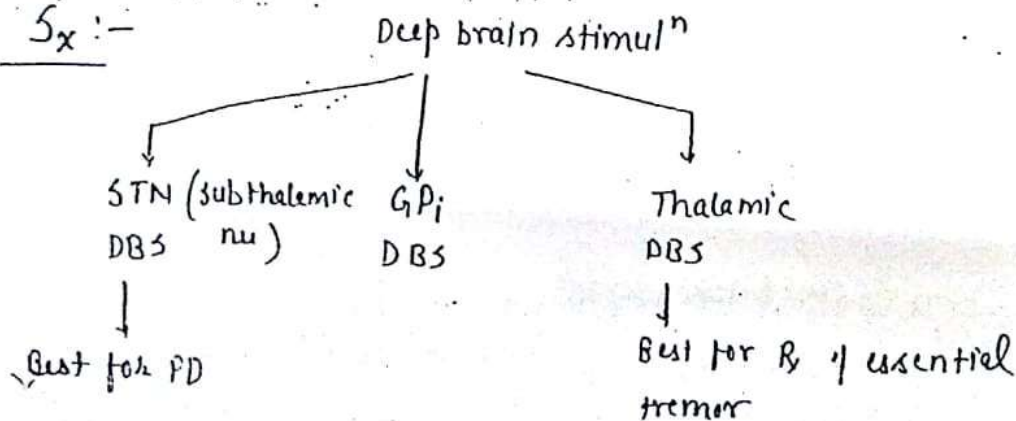
MAO ⊖ —

- Selyilline
- Rasagiline

↑ Dopa

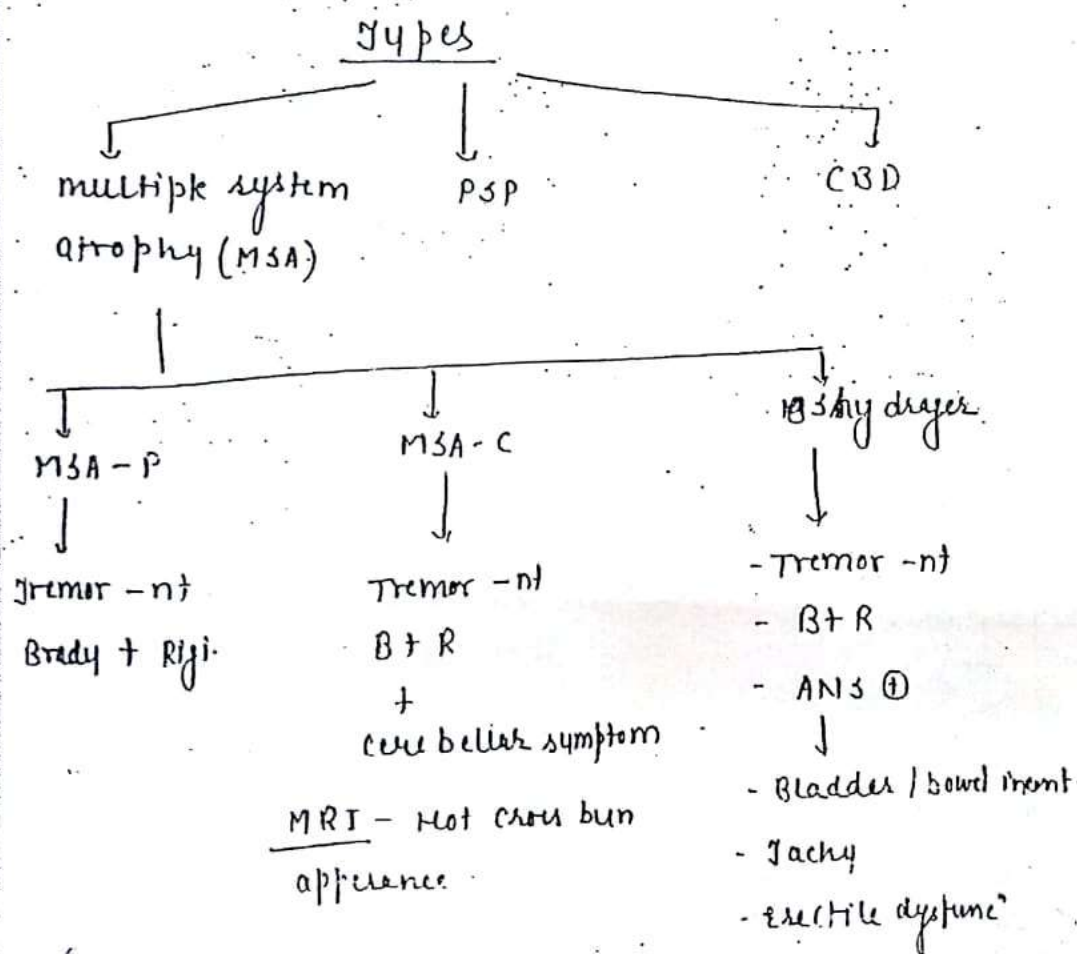
- Amantadine
- Apomorphine

Sx :-



Parkinson plus — Jlt — Levodopa

- Age > 60
- B/L symmetrical (except corticobasilar degeneration)
- Tremors (-nt) → (only Bradykinesia + rigidity)
- Poor response to L-dopa
- Poor prognosis (CBD has worst prognosis)
- (5-8 yrs median survival)



(14)

PSP / Steele Richardson syndrome /

Progressive supranuclear palsy

- Early falls / → early postural instability.
- VI. gaze palsy → down gaze 1st followed by up gaze
- slow saccades.
- square wave jerks
- surprise look (paralysis of supraorbital muscle)
- Apraxia of eyelid opening.

MRI — { Asiat - Mickey mouse ear
 Sagittal - Humming bird

CBD

* U/L — upper limb affected (non dominant)

↓
- Bradykinesia + Rigidity

- dystonia

- Alien hand phenomenon → movement of 1 limb

impairs the movement of other

* Bulbar palsy

Seizures

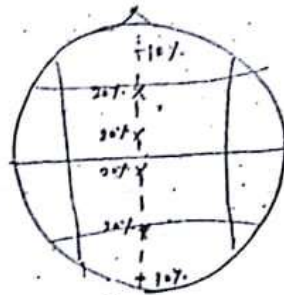
* epilepsy — min. 2 unprovoked seizure

EEG

1) International 10-20 system is used to keep leads.

2) Differential amplification

$$A - A_n \Rightarrow \sim$$



3) system : — montages — 3 types

<u>use</u>	<u>focal</u>	<u>Diffusion lesion</u>
for screening 1) Bipolar	poor	poor
2) referential	poor	good
3) laplacian most difficult	good	poor

4) In 20-30% pt. of seizure — show (N) EEG

(142)

④ Frequencies used: — DTAGT

$\delta \rightarrow 1-13 \text{ Hz}$

$\theta \rightarrow 14-20 \text{ Hz}$

$\alpha \rightarrow > 20 \text{ Hz}$

$\beta \rightarrow 4-7 \text{ Hz}$

$\gamma \rightarrow < 4 \text{ Hz}$

} Slow waves

⑤

EEG

Awake

HEMI

⑥ α Rhythm — Post-dominant rhythm (PDR)

- awake

- eye closed $\rightarrow$ open $\rightarrow$ wave

α

α

α

This is sensitivity

- Occipital lobe is involved

- Symmetric — (50% diff. b/w Rt. & Lt. side)

- Amplitude — 20-50 μV

Sleep

1) muscle artefacts will go down

2) eye movement $\downarrow$

② Lambda waves :—

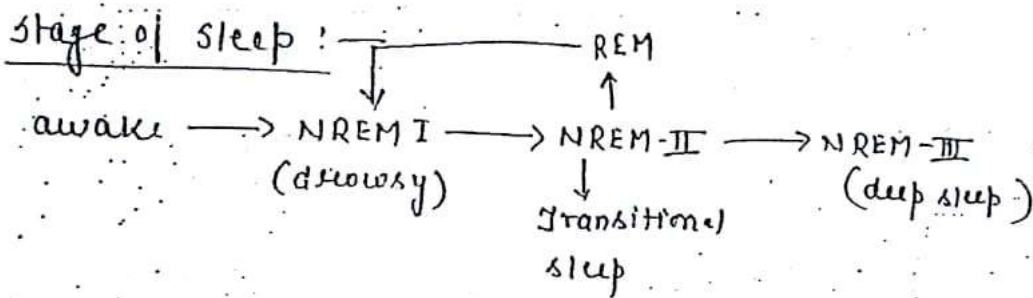
fix seen while fixⁿ / visual screening.

③ K-rhythm :—

- comes from somatosensory cortex
- it attenuates τ limb movement (even if thinking of limb movement)

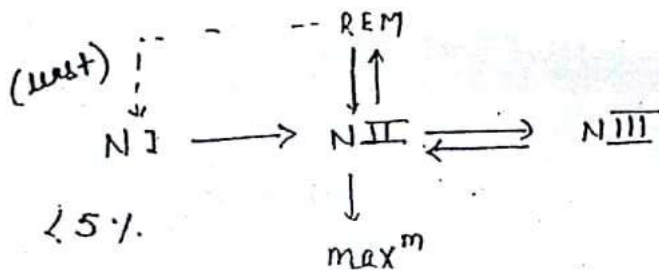
④ K-rhythm :— $\alpha + \theta$

- comes when — intense mathematical calculⁿ / planning



* N-I least — $< 5\%$ sleep

* N-II — $> 40\%$ of sleep



(143)

NREM

- CBF ↓
- Dreaming ⊕
- Hypotonic muscle
- EEG — synchro.
- ANS ⊖

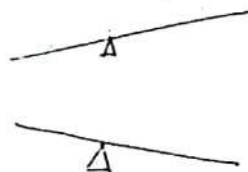
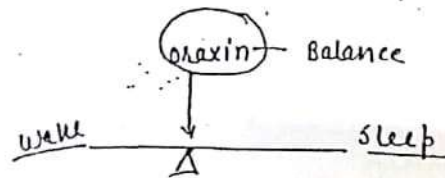
REM

- CBF ↑
- +++ vivid & active dreaming
- Atonic muscle
except → extra ocular muscle & diaphragm
- desynchro
- +++
- ↑ H.R
- erection

* usually each cycle last for 90-120 min. & avg. 5-6 cycles/day.

• early part of sleep.

• early morning sleep (later part of sleep)



Narcolepsy

↓
Low level of orexin

Narcolepsy → sleep intruding wake stage & wake intruding sleep

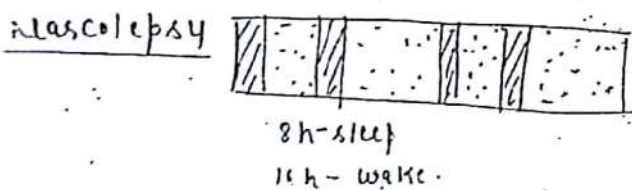
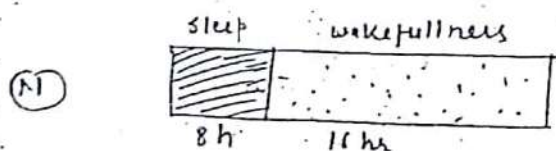
C — cataplexy — sudden total paralysis

H — hypnagogic hallucinⁿ

E — excess day time sleepiness

S — sleep paralysis

S — sleep distortion. (wakefulness intruding sleep)



Δ^{sis} — Polysomnogram + Multiple sleep latency test (MSLT)

↓
in 5 min. persons falls asleep.

R₂ — sodium oxybate (γ-hydroxy butyrate)

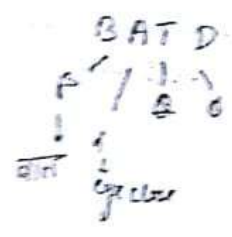
↓
Date rape drug. — (also flunitrazepam)

*modafinil — for narcolepsy

(144)

N-I-1 = 1 ↓

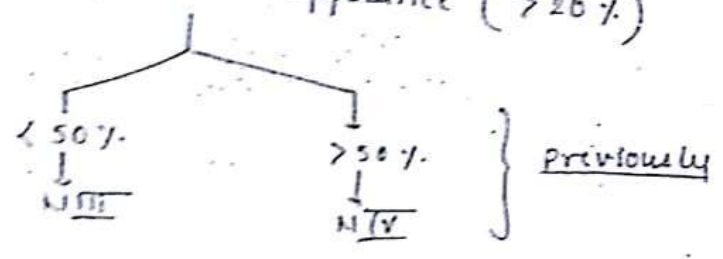
- 1) start θ wave
- 2) start slow eye movement
- 3) 'V' waves / vertex waves



N-II — 1) K complex

- 2) sleep spindles

N-III — 1) δ wave appearance (> 20 %)



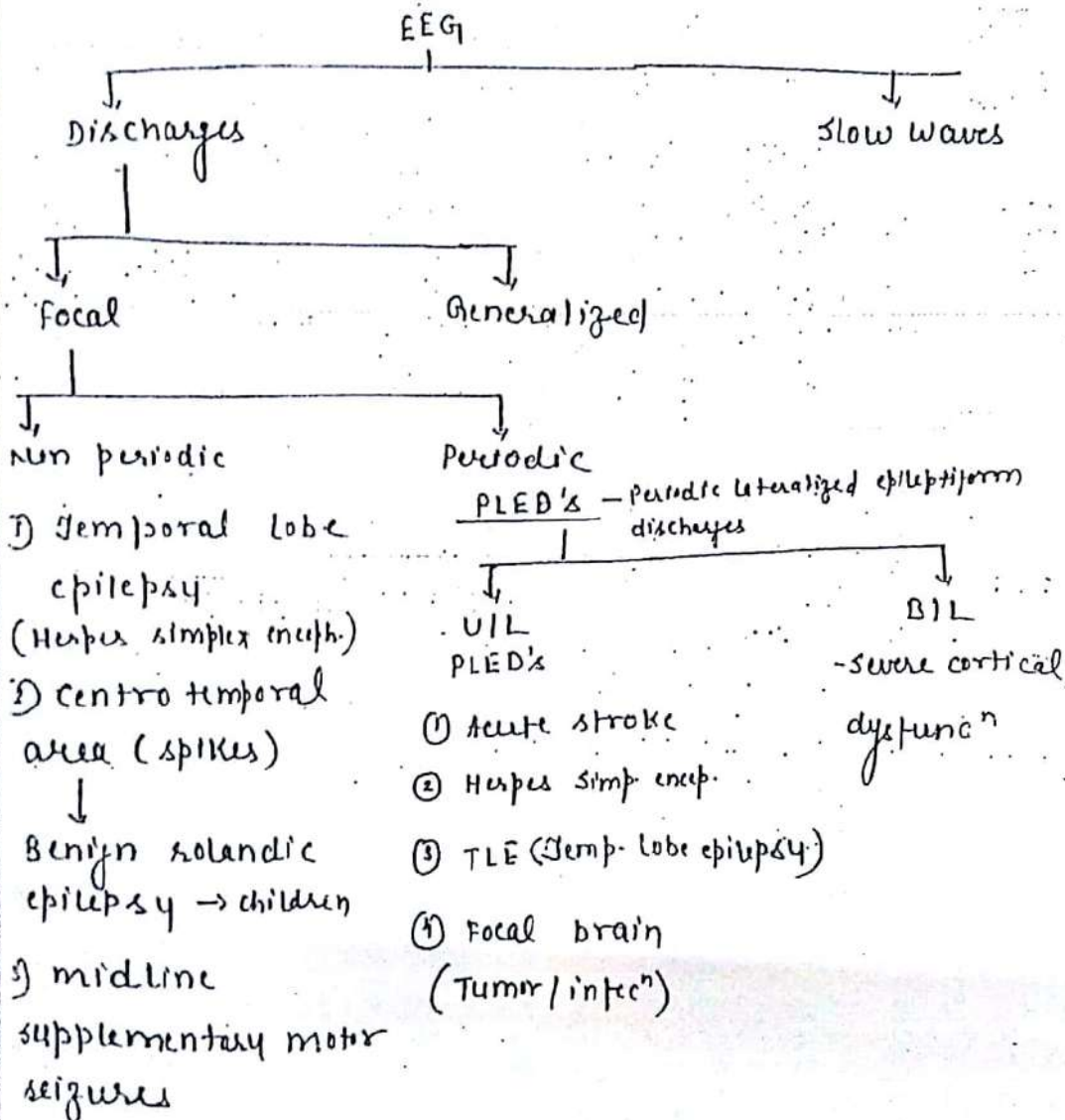
REM — eye movements → rapid / chaotic.

Atonic — zero muscle artefact

* saw tooth EEG wave.

Abn EEG

- Spike — < 70 msec.
- Sharp wave — 70-200 msec.
- Slow waves — > 200 msec.



(145)

1-3 - LGS
3 - CAE
4-5 - SME

Generalized discharges

Non periodic

① 4-6 Hz → Juv. myoclonic epilepsy
spike wave

② 3 Hz → CAE
spike & wave

③ < 3 Hz - Lennox Gastaut syndrome

- Hypsarrhythmia -

- Inf. tremor syndrome / west syndrome

- Chaotic EEG

- Infant

- Diffuse cortical damage

⊕

- a/c ^{tubercles} multiple sclerosis

Periodic

① Triphasic waves -

↓
metabolic encephalopathy

└ Hepatic

└ Leukaemic

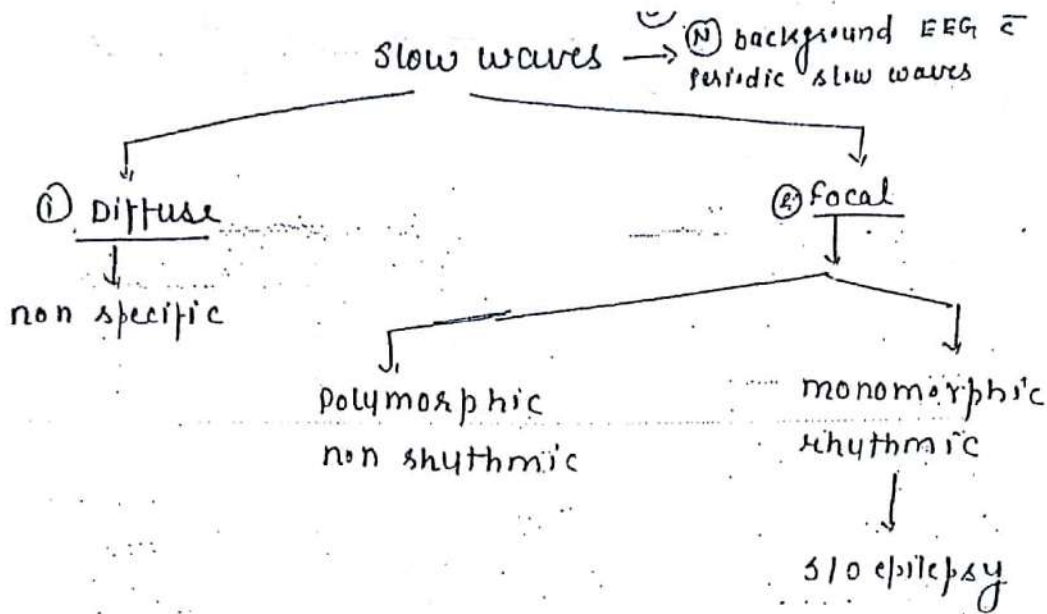
② slow background & periodic sharp wave -

SCJD (sporadic crutzfeldt Jacob's ds)

③ Burst suppression -

- Severe hypoxic encephalopathy

- It shows bad prog. in post cardiac arrest pt.



* These slow wave & (N) background are characteristic of SSPE.

There are 4 types of Rademecker complex.

R of SSPE → Inosiplex

(146)

LGJ5

- * Juvald —
- ① multiple types of seizures
 - ② EEG showing < 3 Hz spike & wave pattern
 - ③ cognition dysfunction

Rx — valproate

(No ch Θ) Rufinamide — exclusive for LGJ5

Benign Rolandic epilepsy

* Avg. age — 5 yr.

- During sleep there will be twitching on face & lip.

* EEG — Centro temporal spikes

Rx — supportive

Juv. myoclonic epilepsy

Childhood Absence epi.

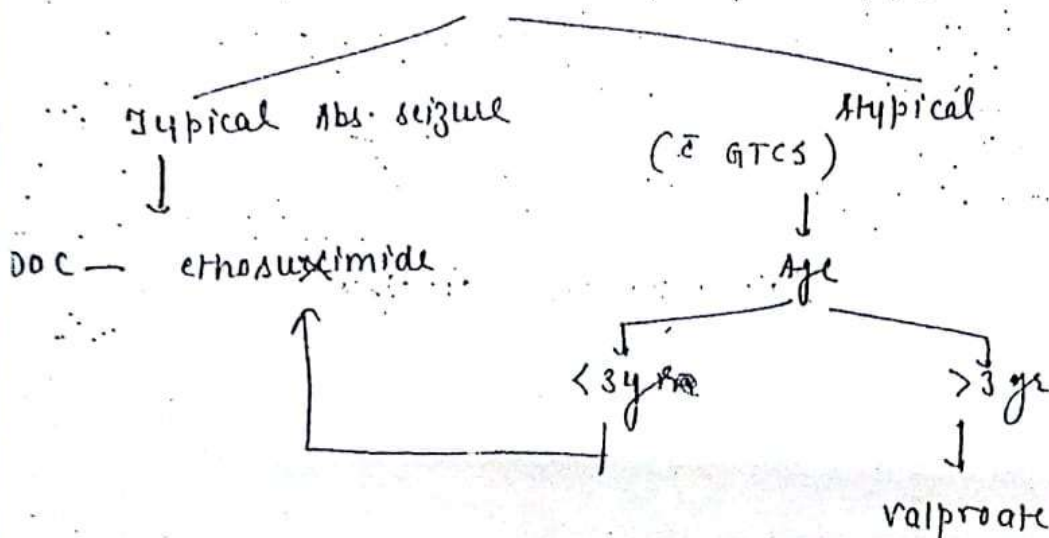
- < 10 yrs
- ♀
- stare for few sec & forget the event
- No loss of postural tone
- inc trigger → hyperventilⁿ
- EEG: — < 3 Hz spike & wave
- Low risk of GTCS

Rx — TAC — ethosuccimide
(exclusive for -nce seizure)

JUV. myoclonic epi

- 10-30 yrs
- ♂
- myoclonus (jerks)
↳ early morning
- ↑ risk of GTCS
- Need long term tit b/c they relapse & also remission will take more time.

Rx — valproate



(147)

* Toc for partial seizure → carbamazepine

* Doc for GTCS → valproate

Inf. tremor syndrome

↓
vigabatrin

↓
ACTH/stuoid

* Pregnancy → Not a single drug is safe in preg.

Highest teratogenicity → valproate

↓
* If pt. is on valproate → change drug → if not possible
↑
Continue valproate

- Any other drug → no need to change the drug.

* Pt. on valproate & carbamazepine.

↓
to reduce neural tube defect, give folic acid 4 mg/day.

* valproate -- can cause PCOS

* Topiramate & zonisamide → wt. loss

* Phenytoin → purple glove syndrome - dit
severe thrombophlebitis.
Pseudolymphoma.
osteomalacia.

Status epilepticus

Old:- • seizures > 30 min

• 2 consecutive seizures w/out recovery in b/w

New:- Any seizure not controlling $\bar{c}$ in 5 min

Rx - < 10 min

1st → i.v. line

yes

- i.v. lorazepam

↓ NA

↳ repeat X 1 time

i.v. Diazepam — (can't repeat)

NO

- Retal diazepam

10 - 30 min

Pt. on phenytoin

yes

→ take blood for phenytoin level.

→ use alt. drug like
levetiracetam.
i.v. valproate

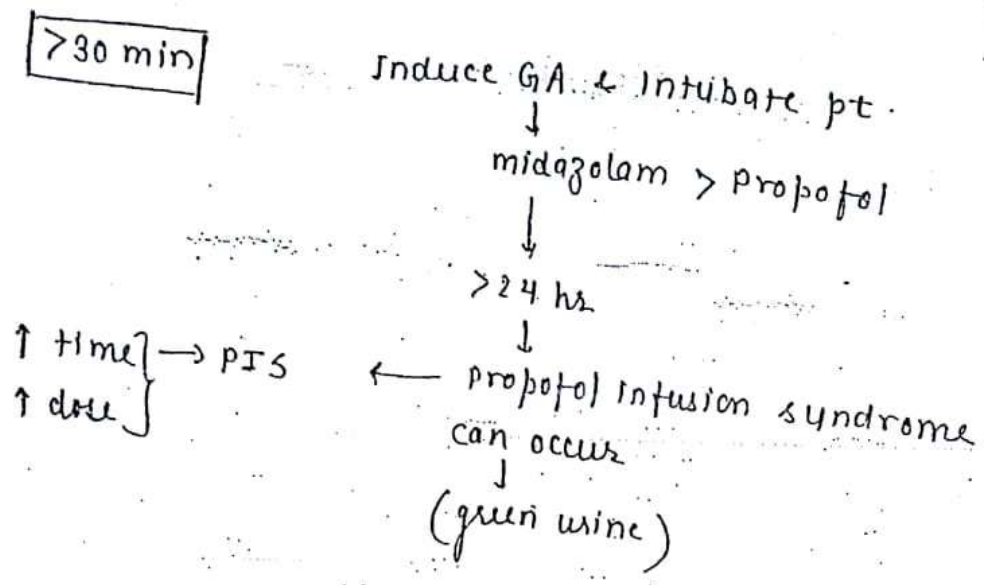
NO

- Phenytoin

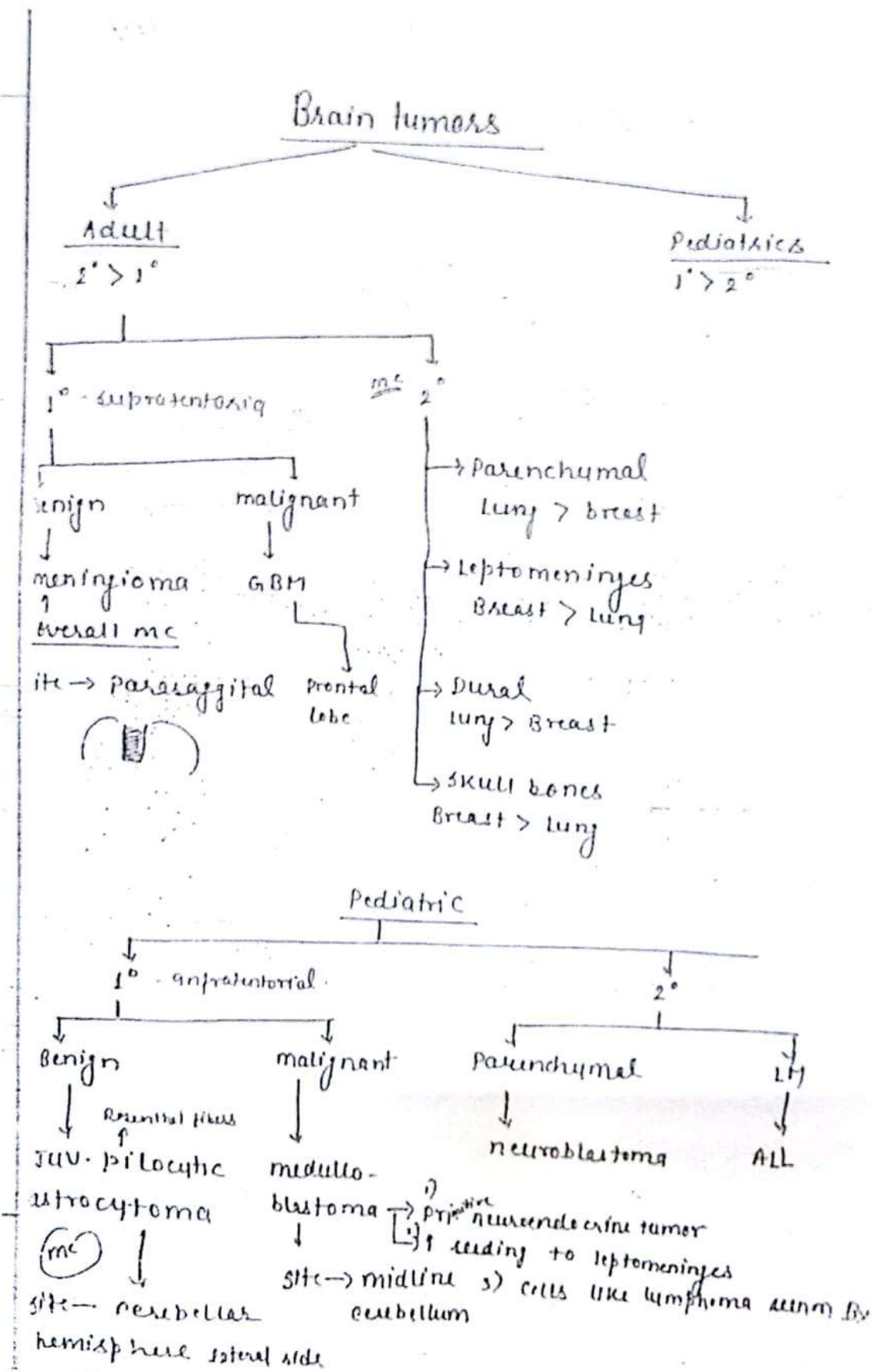
- Fosphenytoin

- Alt. drug.

148

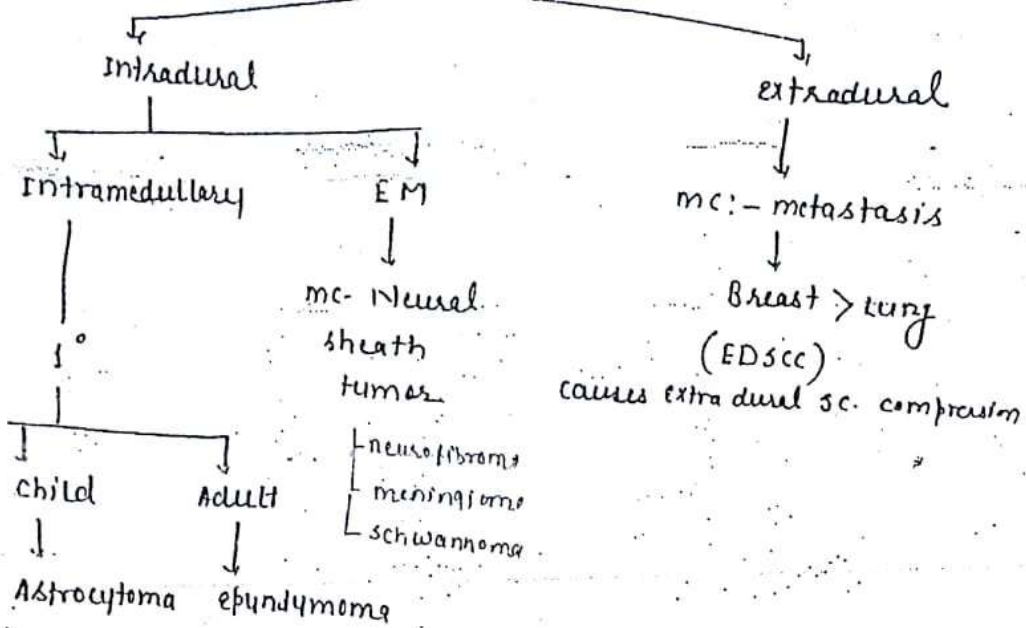


- ↓↓
- Fails
- ↓
- Sevoflurane
 - Isoflurane
 - N₂O



(149)

spinal cord tumors

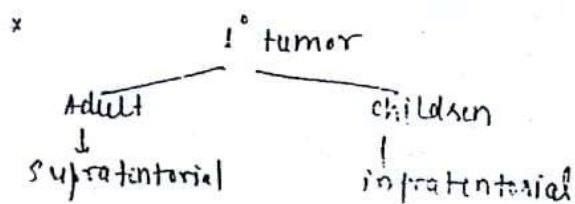


* mc tumor in HIV / AIDS → 1° CNS lymphoma

↓
mc-DLBCL
↓
mc-immunoblastic variety

* mc tumor of CP angle — vestibular schwannoma > meningioma

* mc extra axial tumor in adult — meningioma
children — craniopharyngioma



* supratentorial tumor in children — mc. craniopharyngioma

* precocious puberty is mc caused by

↓
Hypothalamic hamartoma

↓
Also causes gelastic seizure → excessive emotional burst

* mc brain tumor of pineal region → Germ cell tumor

↓
germinoma — mc.

* mc intraventricular tumor in adult → central neurocytoma.

* slow growing tumor assoc. w higher incidence of seizure.

* Dysembryoplastic neuroectodermal tumor (D-NET)

↓
100% incidence of seizure.

(150)

Meningioma! — • ♀ mc involved

• NF-2 gene deletion (chr. 22)

• mc presentⁿ → Asymptomatic (incidental finding)

• ♂ present & symptom → seizure is mc.

* mc location Parasagittal > cerebral convexity

* Foster Kennedy syndrome! —

IL optic atrophy + c/L papilledema



olfactory groove meningioma

→ This tumor is progesterone dependent & grew in size during pregnancy

Inv! — MRI

Dural tail } sign of any extraaxial tumor
CSF cleft }

R_x — excision

• Radiotherapy

— ♂ meningioma is at base of skull — incomplete excision

* Pseudomoma body ⊕

GBM

- tumor of old age (250 yrs)
- It is a diffuse type & so poor prognosis.
- mc site — frontal lobe.
- MRI — central necrosis
- Butterfly tumor (spread to white matter)

Bx — Pseudopalisading & central necrosis

Rx — 1) RT

2) Temozolamide → only drug that crosses BBB
• Alkylating agent

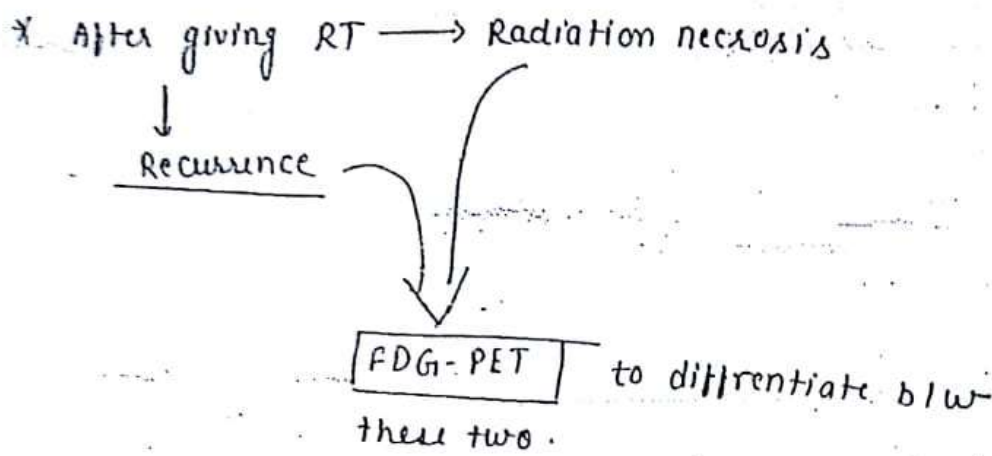
3) Intrathecal methotrexate → Refractory cases

IPN

* Rosenthal fibers

- small round blue cells seen.

(15)



MetS :- Indication of resection of mets —

- single mets
- Surgically accessible

Indication of whole brain RT (Prophylactic) —

- ① Small cell lung cancer
- ② Acute lymphoblastic leukemia
- ③ medulloblastoma → ↑ Incid. of leptomeningeal seeding

Neurocutaneous syndrome / Phakomatosis

① NF-1 → • chr. 17

↳ All are AD except
sturge weber

• Von Recklinghausen

② * min 2 neurofibroma

③ * min 2 mm axillary freckle

④ * 2 Lisch nodule

⑤ * café au lait macule — Pre puberty > 5 cm
After puberty > 15 mm

⑥ * Family H/O NF-1 (1° relative)

⑦ * optic n. glioma

⑧ Bone abnormality (mc - scoliosis > sphenoid dysplasia >
osteous dysplasia of long bone)

For Δ sis → 2/7

Assoc. feature — ① Low IQ

② ADHD

McAune albright

③ HTN (renal A stenosis)

④ Pheochromocytoma

⑤ Learning disability

⑥ Precocious puberty

152

② **NF-II** → ① Bil. acoustic neuroma

② 1° relative to NF-2

+

Any 1 — A → unilat. acoustic neuroma

B → meningioma

C → schwannoma

D → neurofibroma

E → post. subcapsular opacity

③ **Tuberous sclerosis**

Gene — TSC-1



Hamartin

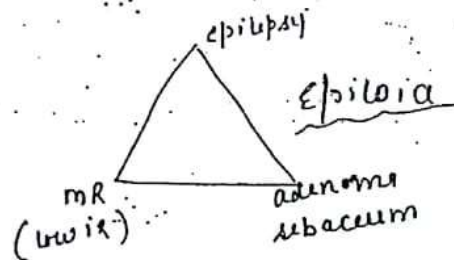
TSC-2



Tuberinc

Vogt triad —

Also seen



Vogt's Δ — Post cong glaucoma

glaucomphaken
+
atrophy of iris
+
pupil constriction

* cortical tumor } → candle wax dripping sign
seen in TS

* S-SEGA

A — Angiomyolipoma

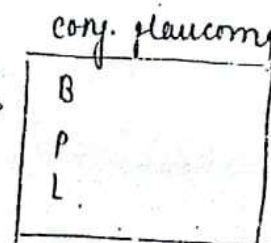
A — Angiofibroma

R — Rhabdomyoma

S — subependymoma

↳ 9; bleed, Wunderlich syndrome

Vogt's Δ →



- Forehead — encephalomas
- Adenoma sebaceum
- Retinal hemangioma
- café au lait macule seen but size criteria not met
- Rhabdomyoma in heart
- Lung → Lymphangioleiomyomatosis
- Kidney → Angiomyolipoma
- Skin & appendages —
 - 1) Ash leaf macule
 - 2) Shagreen patches
 - 3) Periungual fibroma → Koenen tumor

④ VHL syndrome

- VHL gene on chr. 3
- It is tumor suppressor

C/F —

1) CNS & retinal hemangioblastoma (cerebellar)

* Brightly enhancing mural nodule
↓
cystic tumor should be removed



(153)

④ Angiodysplasia of GIT $\left\{ \begin{array}{l} \text{upper} \\ \text{lower} \end{array} \right\} \rightarrow \text{GI bleed}$

⑤ mc vascular cause of lower GI bleed $\rightarrow$ Angiodysplasia
mc $\longrightarrow$ " $\longrightarrow$ Diverticulosis

④ Clear cell RCC assoc $\bar{c}$ VHL

⑤ can produce cystadenoma in pancreas & Broad ligament.
(serous cystadenoma)
(fibrous cystadenoma)

④ Pheochromocytoma

⑤ Sturge Weber syndrome - sporadic

• Birth mark (port wine stain)

$\downarrow$
mc in ophthalmic st. region

• on same side of this $\rightarrow$ dural AV malformⁿ

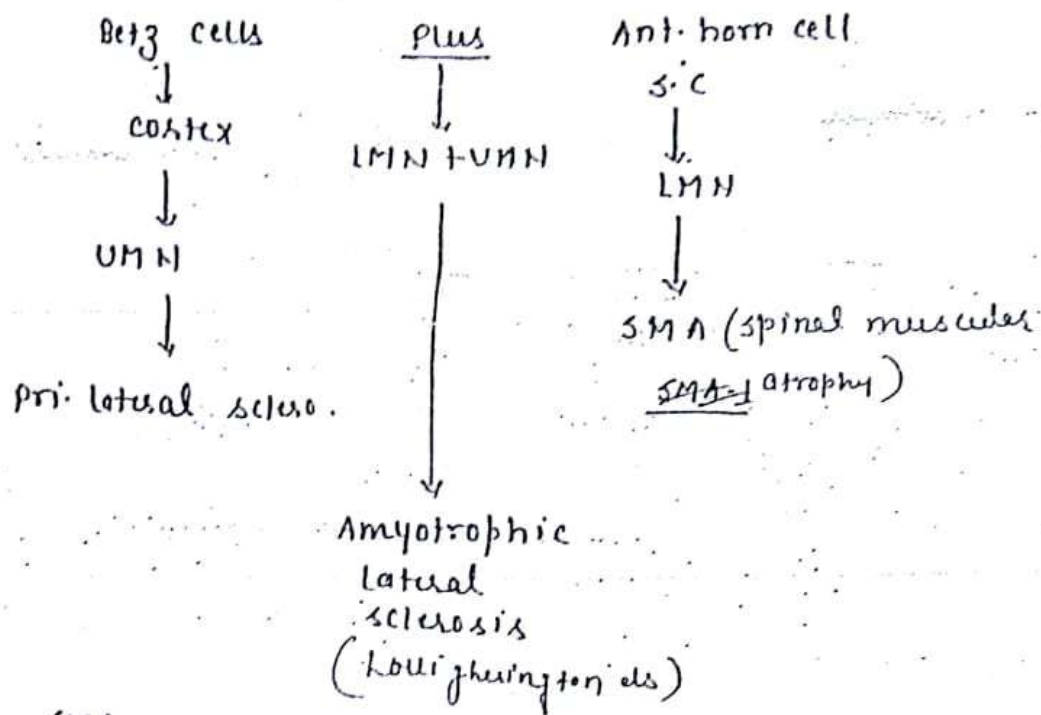
$\downarrow$
on CT $\rightarrow$ Tram track app^r

• cortical atrophy
(Ole steel phenomenon)

• mental retardⁿ

• seizure — on cll side of port wine stain.

Motor neuron disease



SMA

SMA-1 - infant — Werdnig Hoffman

SMA-2 — child — Dubowitz

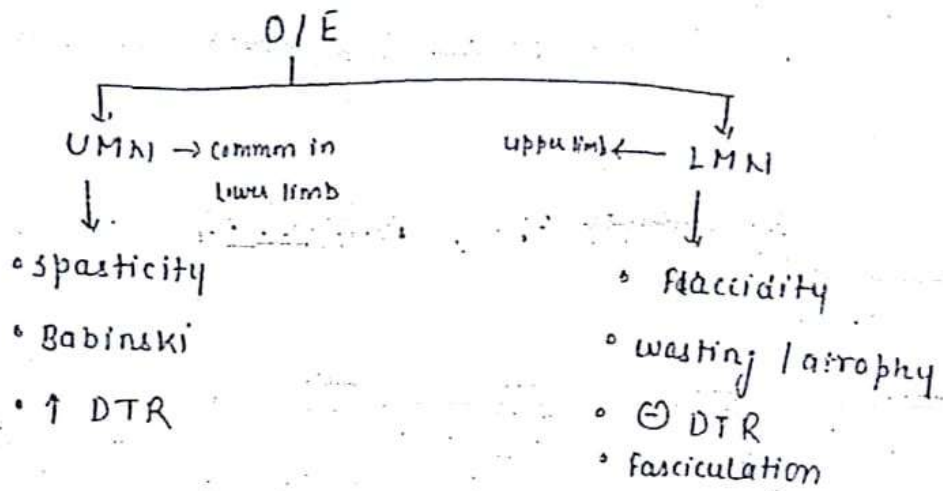
SMA-3 — Juvenile ~~Kugelberg~~ Kugelberg

SMA-4 — Adult

ALS

c/f — muscle cramping.

(154)



* Both these feature can be seen in same limb also.

DD — 1) cervical spondylosis — compress brachial plexus
2) Friedreich ataxia. 3) Ataxia telangiectasia — Both UMN & LMN

No's in MND —

- ① No sensory symptom.
- ② No Bowel & bladder (Onn) nucleus is not affected
- ③ No IQ problem. (No dementia, rarely may occur)
- ④ No extra ocular muscle involvement.

Inv! — clinical Δ's

— No 2/0 other causes — MRI
EMG/NCS

Rx — ① NMDA ⊖ → Riluzole → survival rate ↑ by 3 mth
↳ causes hepatotoxicity.

② Edaravone ③ But t/t → ↑ survival → nocturnal NIV (BiPAP)

Cause of MND —

- Polio

Peripheral neuropathy

Nerves —

1) A α fiber $\rightarrow$ α motor neuron
• motor to skeletal muscle

myelination ↓
Diameter ↓

2) A β fiber $\rightarrow$
→ Ia — afferent from muscle spindle
→ Ib — afferent from Golgi tendon

3) A δ fiber — II $\rightarrow$ sensory afferent from skin

4) A γ fiber — γ motor neuron
• motor to muscle spindle

5) A δ fiber — sensory afferent from skin. (fast pain)

6) B fiber — preganglionic autonomic

7) C fiber — postganglionic autonomic

olfaction

slow pain.

* muscle spindle should also contract at same time
so that we can know upto how much extent the
muscle is contracted. so they also contract $\bar{e}$
EF fiber. & for this we have γ motor neuron.

- CST.



α & γ motor neuron.



q1 there is inj. to CST $\rightarrow$ Loss of $\ominus$ will occur

* Golgi tendon organ — when stress exceed

↓
GTO stimulate

↓
 $\ominus$ α motor neuron.

↓
No stretch.
muscle relax

... Inverse stretch reflex

↓
This is the basis of clasp
knife spasticity.

(156)

Demyelinating disorder — motor system affected

muscle power loss

Areflexia.

Axonal → mcs. Diabetes

① small fiber (less myelinated)

② Sensory symptom

Pain & (spinothalamic tract) length dependent
Temp → as these are less myelinated fiber

③ Loss

- so glove & stocking type sensory loss

③ motor symp.

↓
less

↓
confined to area of sensory loss

④ ANS fibers affected
(as these are small)

• Bladder / bowel invol.

→ mcs GBS
Demyelinating → multifocal

① Large fiber

② motor > sensory symp.

↓
global symptom

↓
global weakness (w. of L)

↓
global areflexia (w. of I₂)

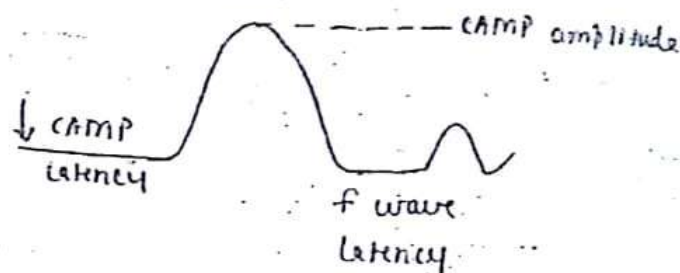
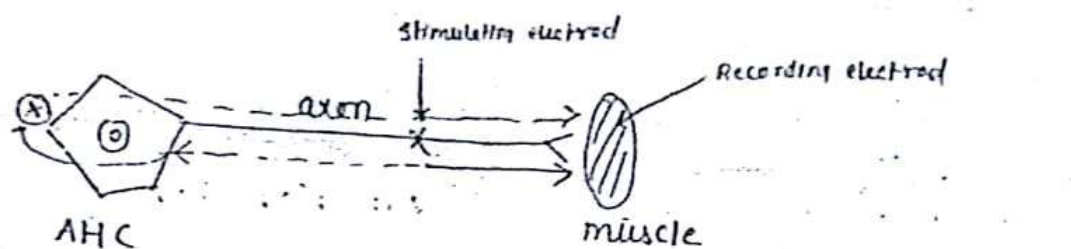
③ sensory symptoms

• Loss of post. column

sensation. (A_α fiber).

④ ANS is spared
(as these are non myelinated)

Nerve conduction study



gt stimulate muscle
after a lat. period

↓
after stimulating
muscle it produces
CMAP.

→ Ht. of CMAP → i.e. CMAP amplitude → Depends upon
no. of axon

→ CMAP latency → time from

↓
Depends on vel. of conducⁿ

velocity of myelination status

↑ myeline $\Rightarrow$ less latency

→ f wave → not a routine wave.

(157)

Axonal

Demyelinating

(1) CMAP amplitude — ↓

(1) — (N)

(2) Latency — (N)

(2) ↑

(3) velocity of conducⁿ — (N)

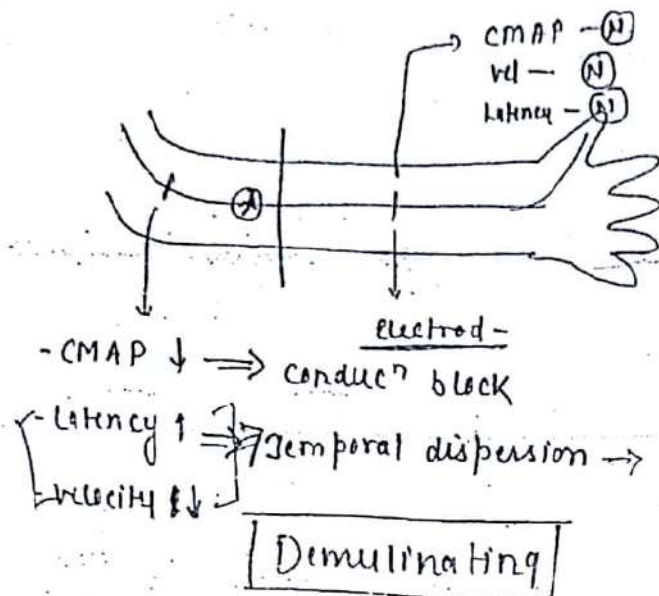
(3) ↓

(4) conducⁿ block

(5) temporal dispersion

(6) f. wave latency — (N)

(7) f. wave latency — ↑



- * Carpal tunnel synd → it is demyelinating disord.
- * compression causes demyelination.

H-reflex - electrical equivalent to ankle jerk.

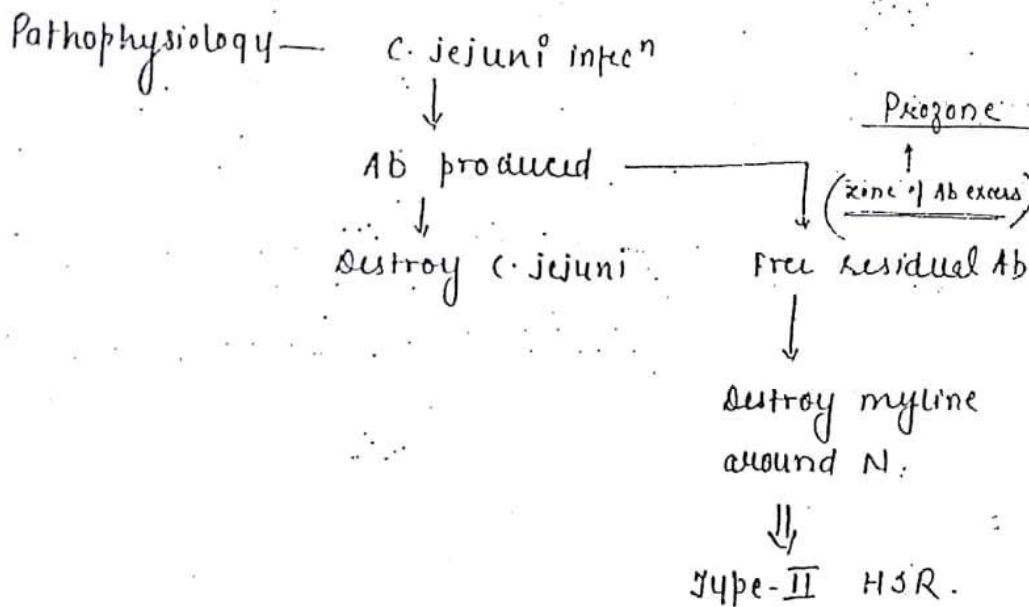
- used to diagnose S₁ neuropathy / tibial neuropathy.

(158)

GBS

- Prototype demyelination neuropathy
- Acute ~~dem~~ inflamm. demyelinating neuropathy (AIDP)
- Acute ascending areflexic flaccid quadripareisis.
↓
(< 8 wk)
↓
if > 8 wk $\rightarrow$ it is CIDP

D/D — ① Hypokalemia (m. imp.)



* Pt. give H1O — URI

* H1O — diarrhoea $\rightarrow$ poor prognosis

* mc. cranial N. affected is — 8th N.

* mc. affected EOM is — lateral rectus

Inv! —

1) Nerve conducⁿ study → demyelinating pattern

2) CSF → Albumino cytological dissociation.

Protein ↑ cells (N)

• Reverse is seen in — Multiple sclerosis
(cells ↑, Protein ↓) cells → 5-50

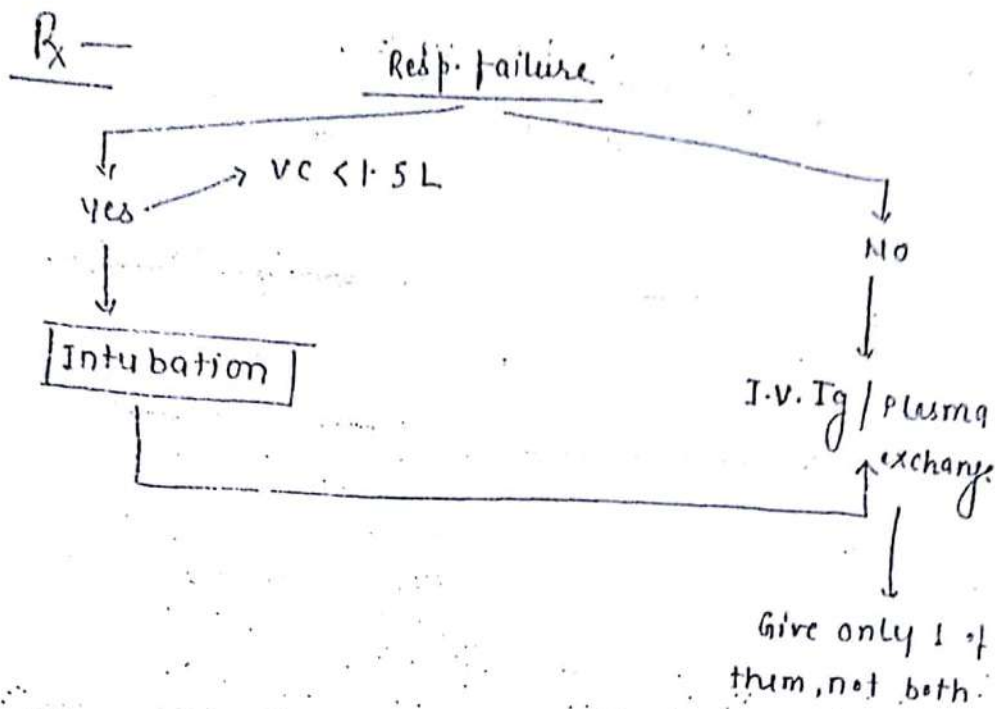
• cells ↑, Protein ↑ → Infectⁿ

→ All these will occur after 1 wk

↓
Give tilt irrespective of this investigⁿ

↓
• Excellent prognosis

Box: GM1 antibody seen. — GBS
GQ1b Ab seen in — Miller Fisher syndrome

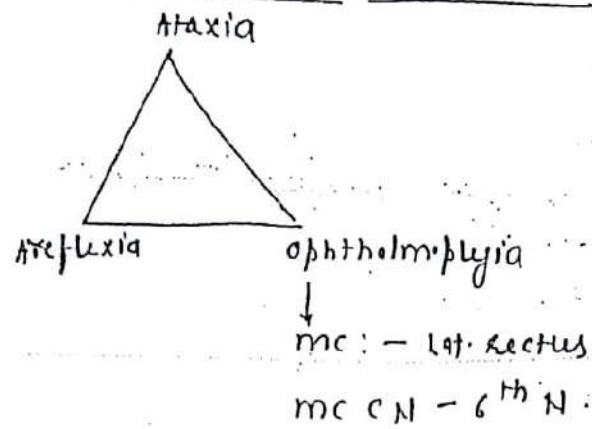


* steroids are not effective in GBS

↓
∴ already Ab are formed.

* on CIDP → steroids can be given as they decrease the ongoing Ab production.

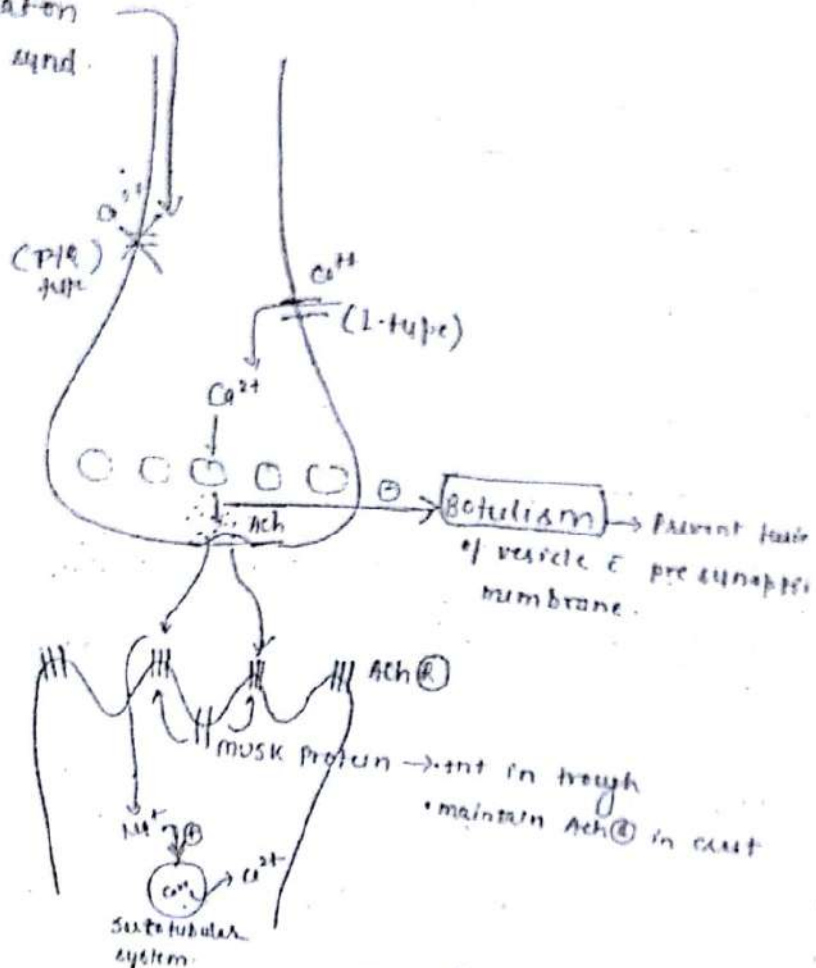
Miller fisher syndrome



Rx — same as GBS.

Myasthenia Gravis

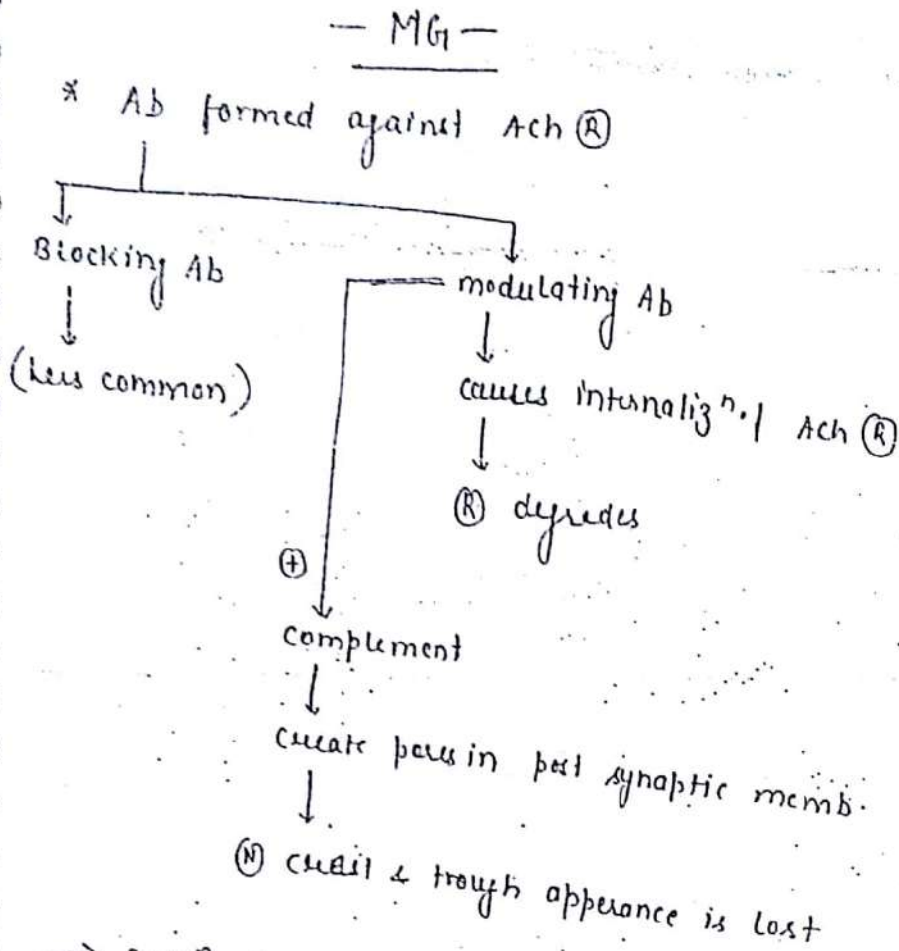
Lambert Eaton
myasthenic synd.



* ACh bind to (R)
↓
Na⁺ ch. open
↓
Na⁺ move in
↓
Sarcotubular syst
↓
Release of Ca^{2+}
↓
muscle contracⁿ



(16)



→ funcⁿ of crest — ↓ the dist. b/w Ach & AchR so that Ach esterase will not act immediately on released Ach.

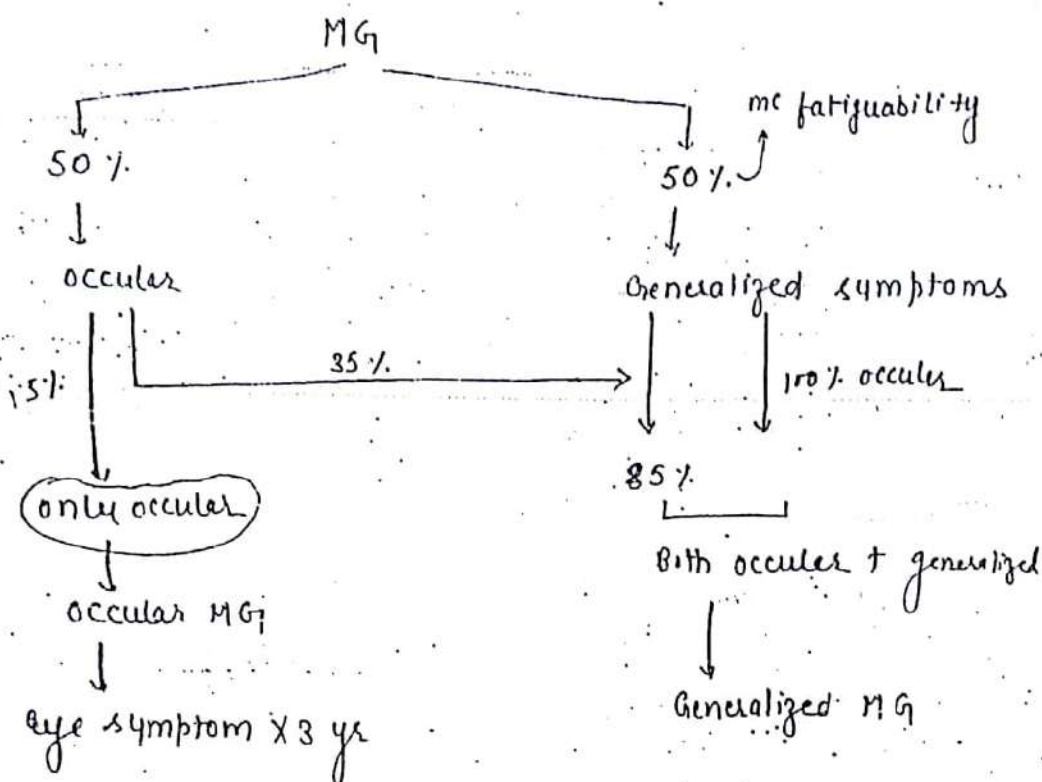


Anti musk Ab — ↓ no. of AchR in post synaptic memb
Regulate conc. of AchR in post synaptic termin. Features like MG

C/F — ① Fatigability

② mc presentation — ocular sign

mc sign — Ptosis ($> 50\%$)



D/E — ① Proximal weakness

(All muscle disorder causes prox. weakness except myotonic dystrophy → it causes distal weakness)

② Diurnal variation (evening $>$ morning) of weakness
fatigability.

(162)

- ③ (N) DTR
④ (N) Tone
⑤ (N) bulk } Rule in MG

- ⑥ Ocular sign! — i) ptosis
ii) ophthalmoplegia (complex)

↓
No particular pattern. Any Extraocular muscle can be affected

Test!:-

- 1) Simpson test → inability to maintain upward gaze.

* Blinking is never affected in MG — as it is b/c of Muller muscle which is supplied by parasympathetic.

- 2) Ice pack test — very accurate. (>90% specificity)
If +ve → MG confirmed.

Keep ice pack on the eye having ptosis
↓
ptosis improves

- 3) Goswami test — when examiner try to open the eye having ptosis → the other eye will develop ptosis

④ Cogan lid twitch sign →

↑ upward gaze
↓
when see down lid also comes down & eye ball but d/t weakness it droops down
↓
Then the lid goes to (N) position, seen as twitch

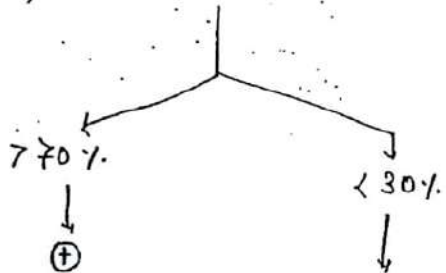
INV:-

1) - Single fiber EMG → shows jitter

↓
must sn.

↓
delayed NM transmission

2) - ACh (R) Ab → must specific



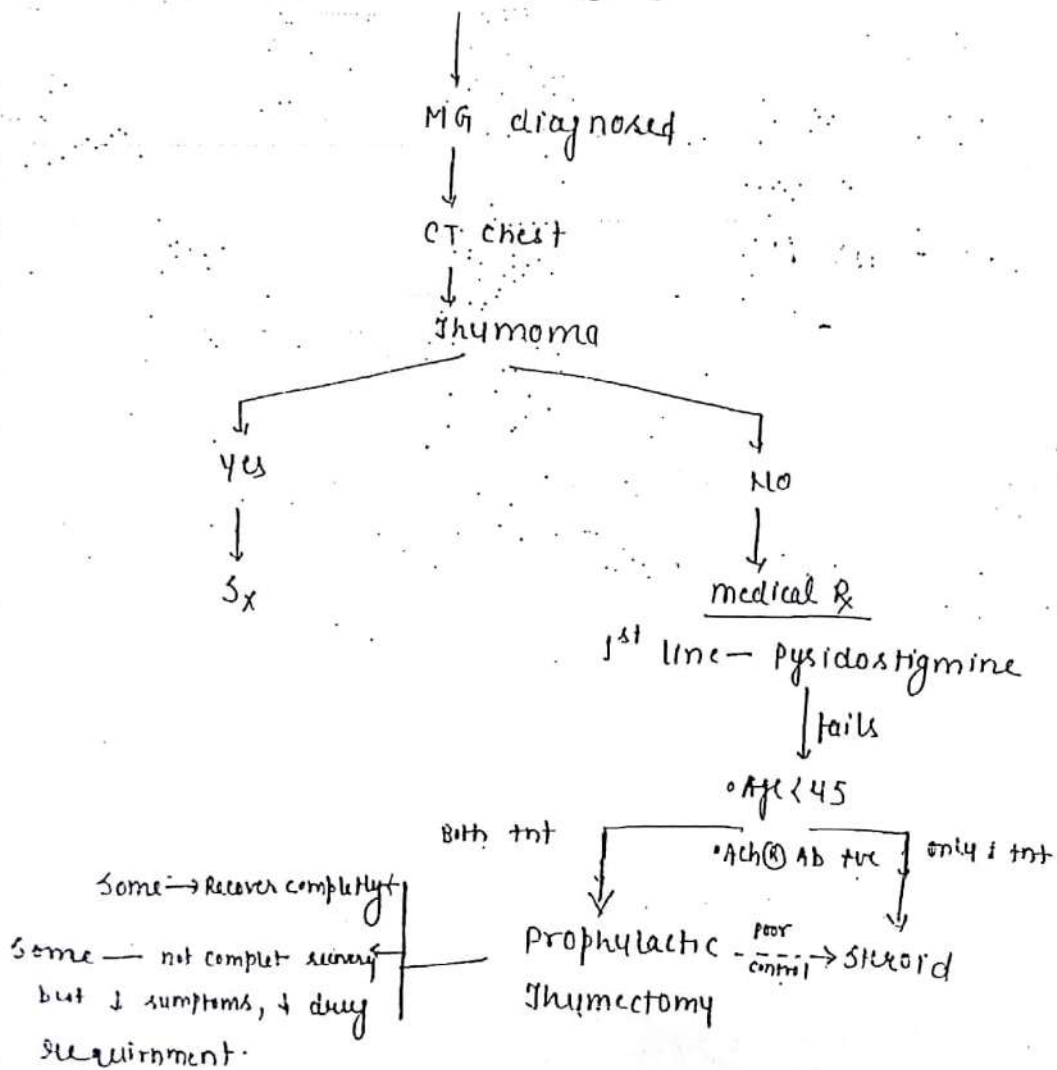
* Anti MUSK Ab ⊕ only if ach Ab is -nt.

(163)

3) Edrophonium test — neither sp., nor sensitive.

- Done only for ocular MG but there also it is not ~~sp~~ or specific.
- When edrophonium given, it improves one muscle but other muscle may get deteriorate.

Preferred Invi- EMG + AChR Ab



Other Drugs —

Cic / Tacrolimus

mycophenolate mofetil

Azathioprine

* Rituximab → used for ocular MG

→ steroid causes → Paradoxical initial worsening

* Post op. there are also ↑ chances of myasthenic crisis

Anti musk. Ab —

• AchR Ab — ve

• Bulbar weakness & atrophy

• ↓ ocular symptoms

Drugs exacerbating MG —

A — Ab → Aminoglycosides

B — β -blocker

C — chloroquin

D — D-penicillamine

E — extra —
→ MgSO₄
→ interferon
→ Botulinum toxin

(169)

* Depolarizing type of muscle relaxant are given
in MA pt. for Sx, as the recovery will be fast
w them.

MG

1) - post synaptic

2) - Ach (R) Ab.

3) - Proximal weakness
+
ocular weakness
(Rare)

4) Deep tendon reflex (N)

5) ANS X

6) PNS → detrimental response

7) ^{Muscle power} ↓ c. exercise

8) PNS — ≈ 15% cases

↓
mc tumor

Ant. mediastinal thymoma

mass is thymoma until prove otherwise.

9) Pyridostigmine ± steroid

LEMS

1) - Pre synaptic

2) - Anti P/Q Ca^{2+} channels
(Anti VGCC) not good Ca^{++} ch.

3) - Proximal weakness
+
Girdle weakness (Hip abduction)

4) ↓ ↓

5) ANS ✓

6) repeated N. stimuli?

↓
Incremental response

7) ↑ c. exercise

8) PNS ≈ 90% cases

↓
mc - SCLC

9) 1/2 - 1/3 of cancer +

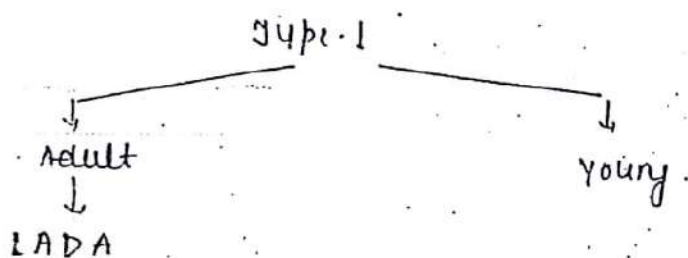
2/3 Diaminopyridine

Diabetes

① Type-1

② Type-2

③ MODY → monogenic diabetes (single gene) → AD



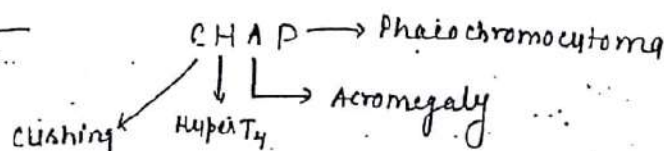
④ 2° Diabetes — Diet • chronic pancreatitis

• Fibrocalculous pancreatitis

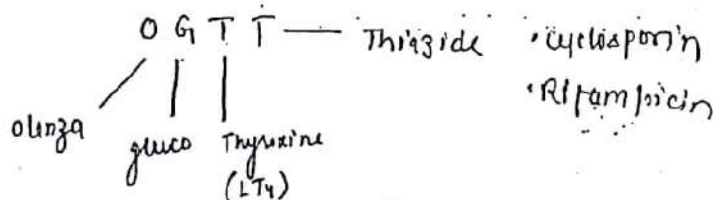
• cystic fibrosis

Infect → • CMV

⑤ Endocrine —



⑥ Drugs —



⑦ Genetic — Klinefelter

• Turner's

• Prader willi

• Friedreich ataxia

• myotonic dystrophy

⑧ Chromium deficiency

Ans:- ① OGTT $\rightarrow$ 75 gm OGTT is gold std. (166)

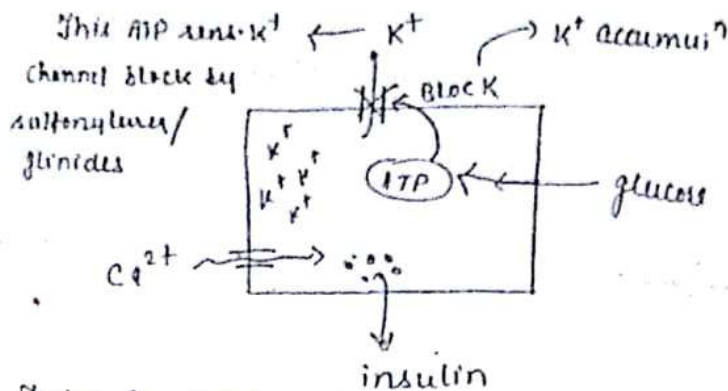
FBS	PPBS	Inference
<100	<140	(N)
100-126	<140	impaired fasting glucose
<100	140-199	IGT
100-126	140-199	IFG + IGT
≥ 126 (or)	≥ 200	DM
		- if both $\oplus \rightarrow$ DM
		- if 1 $\oplus \rightarrow$ ^{times} 2 test to be done

DM:-

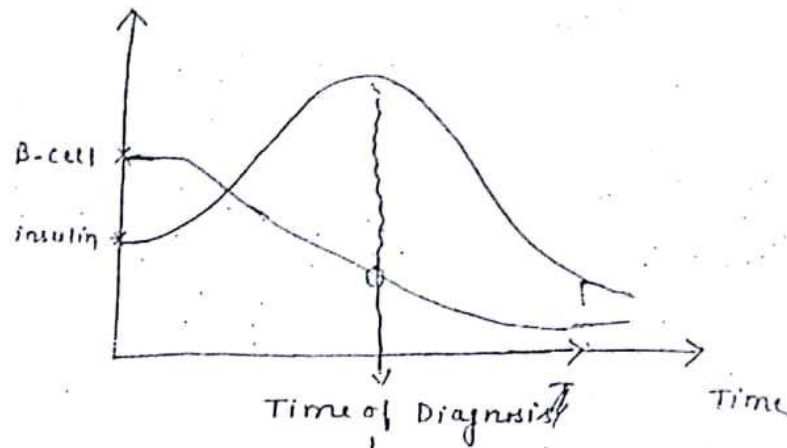
- ① FBS ≥ 126
 - ② PPBS ≥ 200
 - ③ HbA1c $\geq 6.5\%$
 - ④ RBS ≥ 200 + classical symp. (PU/PD/~~etc~~ wt loss)
- 1/4 - enough

Type-1	2	MODY	MODY LADA
Age- <25	>25	<25	>25
Absolute insulin deficiency	Insulin resist.	Insulin release	
Family H10			
⊖	+/- one generation	+++ [≥ 2 gen]	⊖
Weight - under wt	over wt.	(N) wt.	under wt
Insulin - ↓↓	↑ (N) / ↓	(N)	↓↓
β-cell mass - ↓↓	↓	(N)	↓↓
Metabolic synd. X	✓	X	X
Auto Ab ++	-	-	++
Insulin auto Ab			m. specific Ab is GAD65 Ab.
ICA			
IA - IA			
GAD65			
DKA prone - ++	-		++
OHA response ⊖	++	variable MODY-3 → well responsive	initially responsive ⊖ in 12 mth ↓ insulin.
Insulin	OHA ↓ >12 mth insuline	OHA or Insulin	OHA ↓ <12 mth insulin

(167)



Type-2 Diab. mellitus —



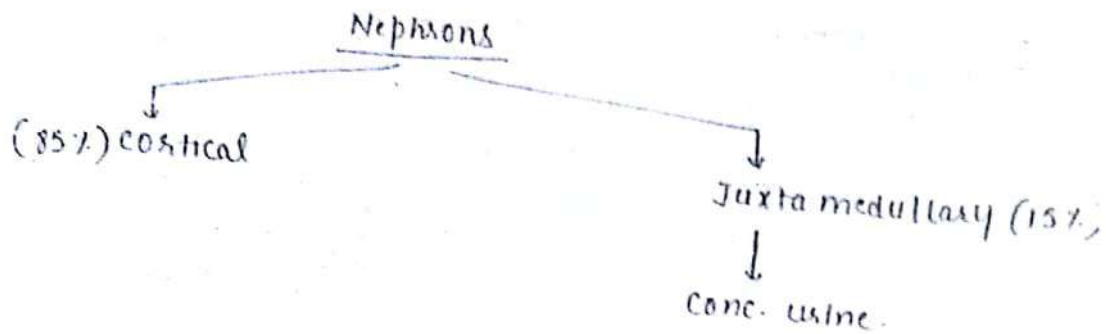
↑ lipogenesis → insulin ↑
 It is trophic → B-cell mass ↓ 30-50%
 hormone & ↑ everything in body
 • ↑ skin tags
 • Acanthosis nigricans

MEDICINE
DILIP KUMAR (P2)
2017
PG-NOTES

(2)

Nephrology

* Total nephrons = 2 million



Clearance

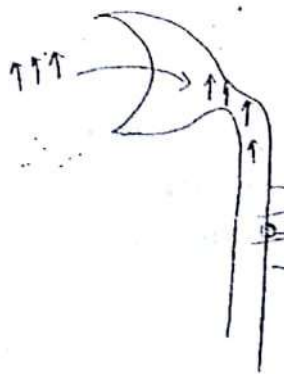
Amt of subs. $\uparrow$ int in GFR

out of this how much is there in urine

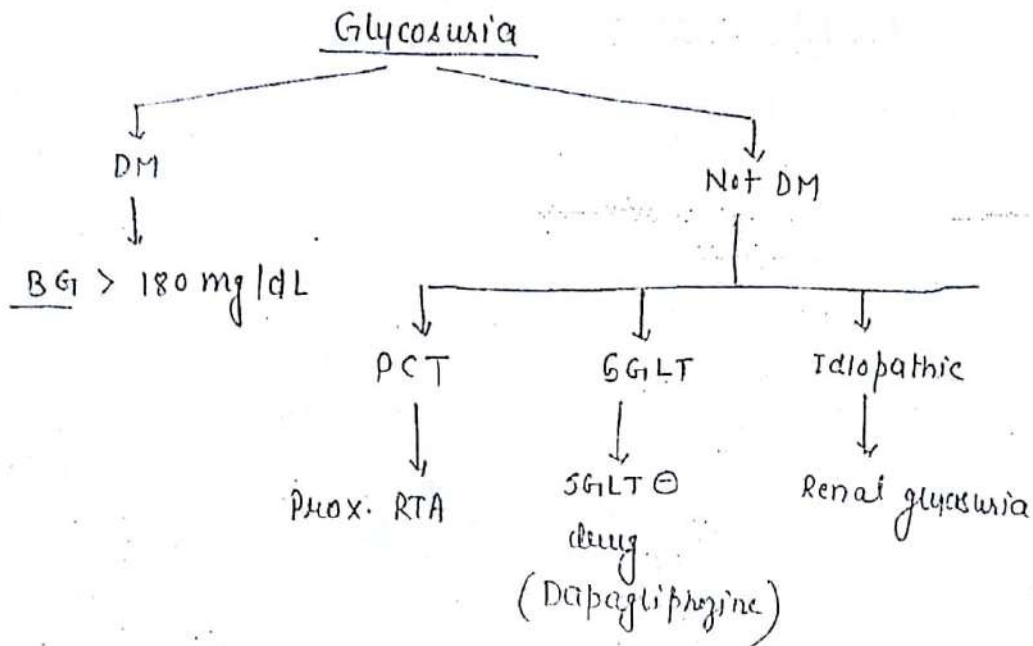
CL of glucose = 0 i.e. it completely reabsorbs.

- 9% glucose $\uparrow$ int in urine $\rightarrow$ glycosuria

$\downarrow$
Blood glucose > 180 mg/dL



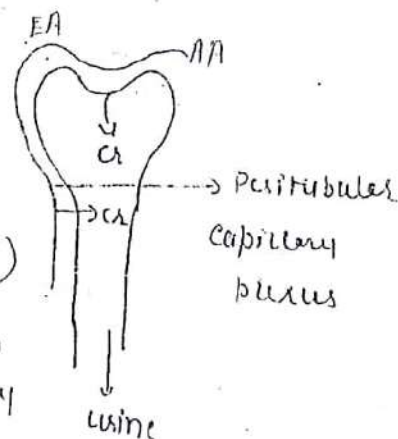
Transporter $\rightarrow$ Beyond certain point
they can't absorb &
subs. will release in urine



<u>Subs.</u>	<u>clearance</u>
① glucose	0
② urea	40-60 — Partially reabsorbed
③ Inulin	125 — neither reabsorbed / nor secreted
④ creatinine	100-140 =
⑤ Para amino Hippuric acid (PAH)	625 → completely secreted

→ CL of PAH $\approx$ blood flowing through kidney (total secⁿ)

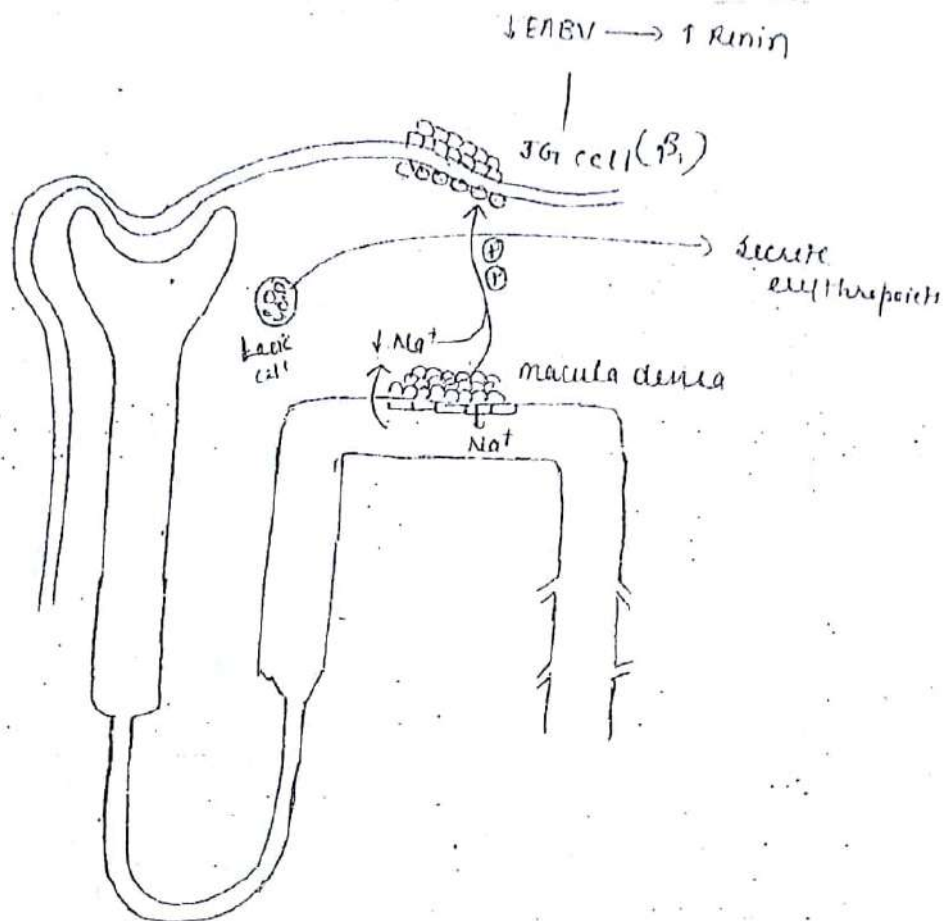
~~Antic/ab~~ $\approx$ Blood flow through peritubular capillary

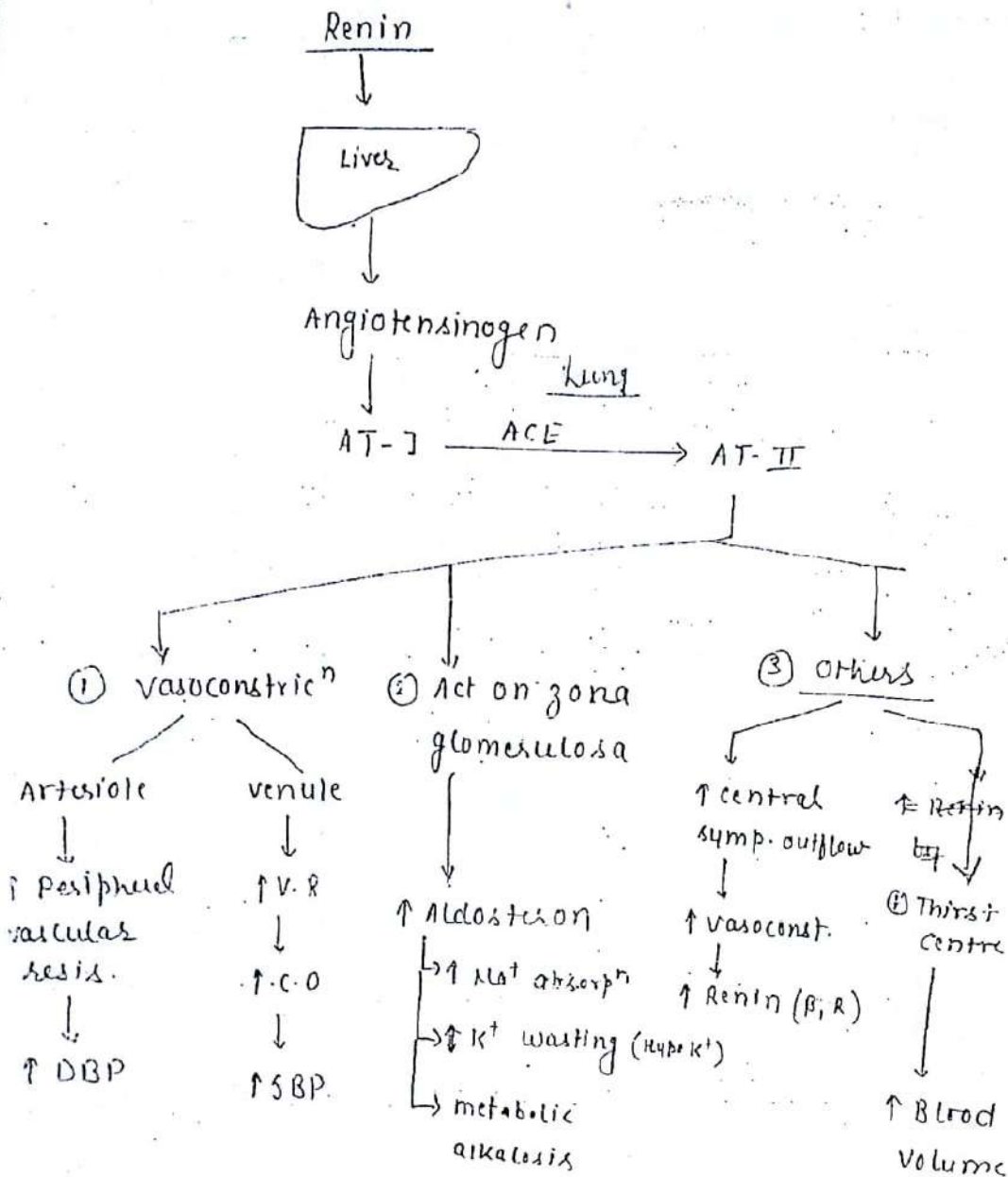


(3)

* PAH is best for measuring renal plasma flow

(3) → extraglomerular mesangial cell (Lacis)





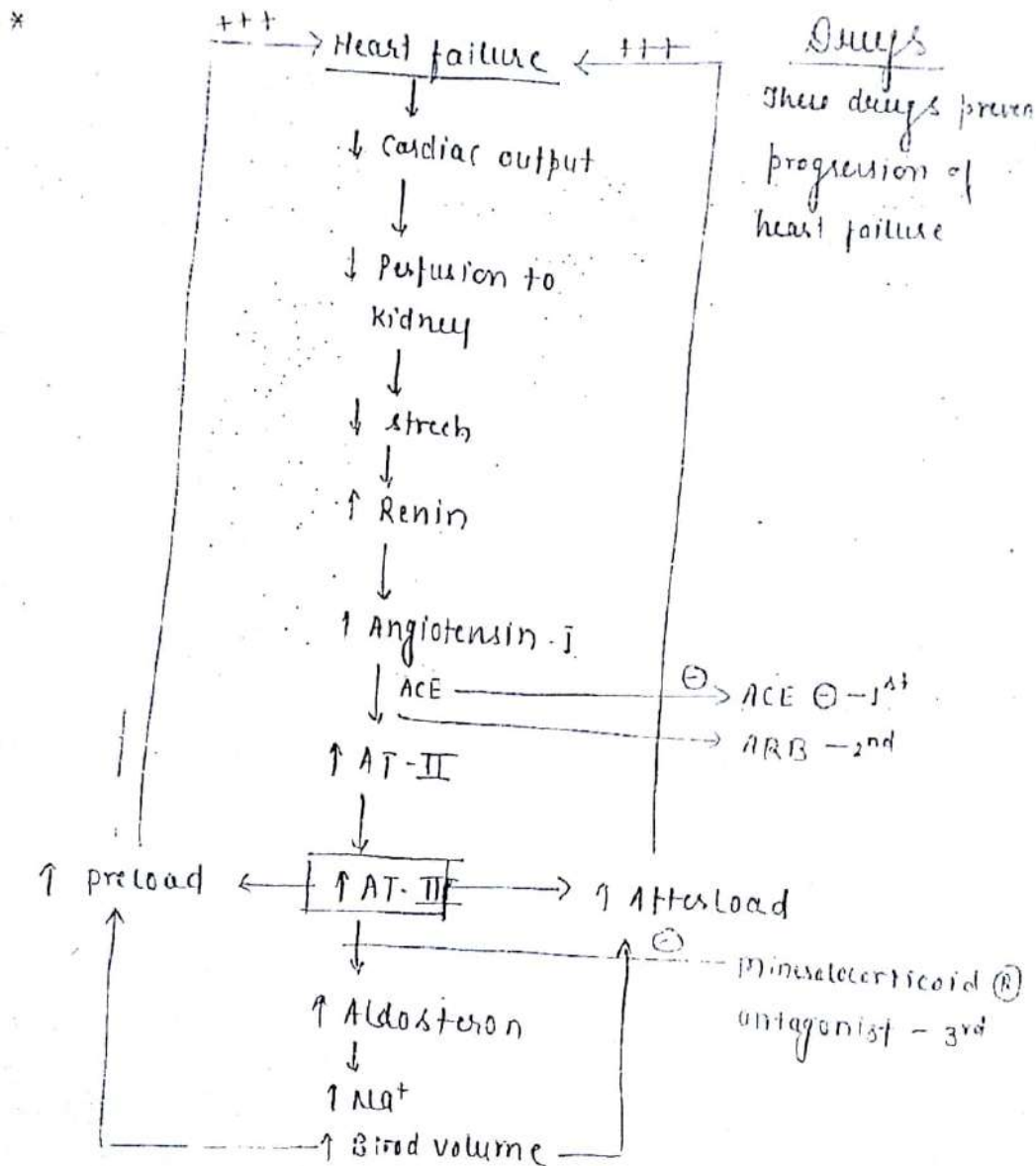
(4)

* Physiological +ve feed back loop

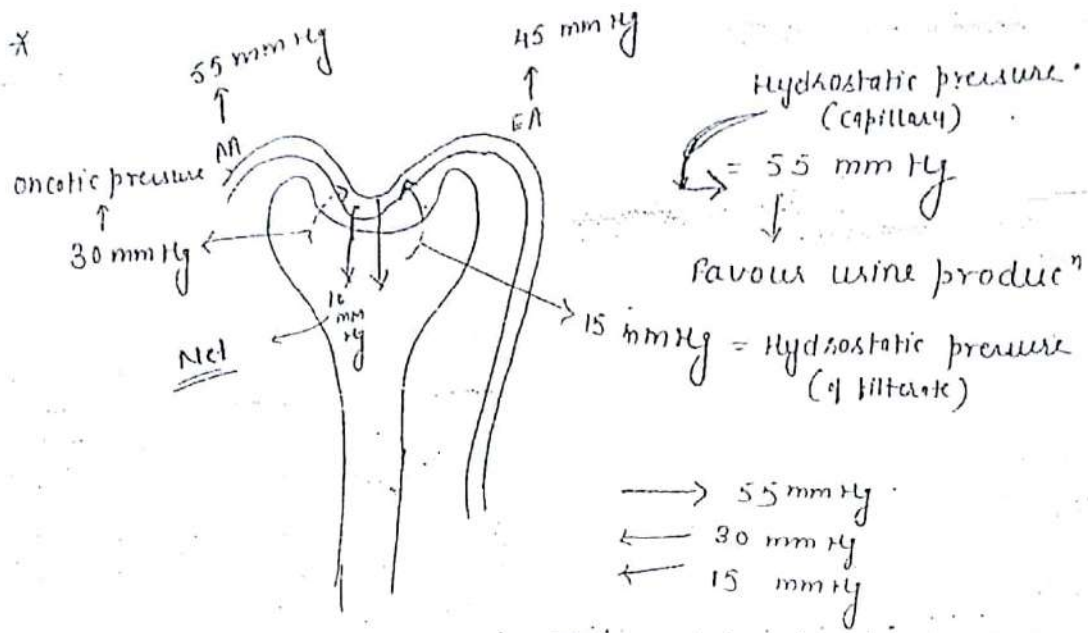
- Breast feeding (lactation)
- child to breath after birth

→ But all are -ve feed back loop.

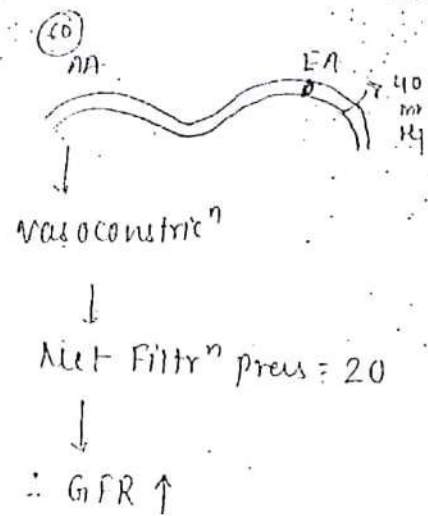
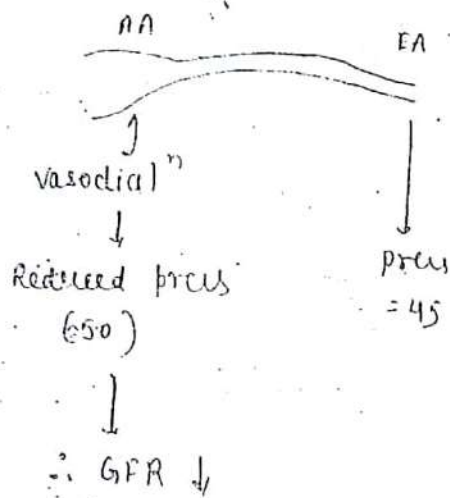
→ Pathological +ve feedback loop —



(5)



Net filterⁿ pressure ≈ 10 mm Hg



Afferent arteriole —

Diam — $\uparrow \Rightarrow GFR \downarrow$
 $\downarrow$

efferent arteriole

Diam — $\downarrow \rightarrow GFR \uparrow$
 $\uparrow \rightarrow GFR \downarrow$

* width & diameter of AA is under control of prostaglandin

$PGI_2 \rightarrow \rightarrow AT-II$

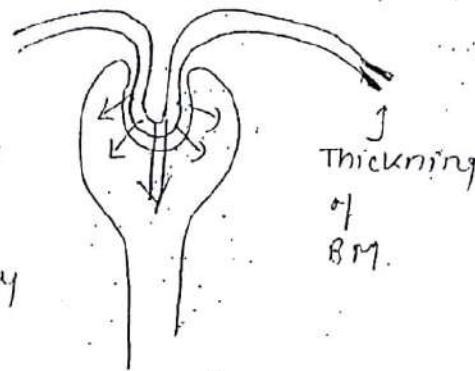
$PDA \rightarrow$ dilate afferent

$ACE \rightarrow AT-II$ constricts efferent

* efferent arteriole — AT-II

ex. Diabetic nephropathy

$\rightarrow$ $\downarrow$ Diam. of EA
 $\downarrow$
 $\uparrow GFR$ — early stage
 $\downarrow$
Hyperfiltration injury

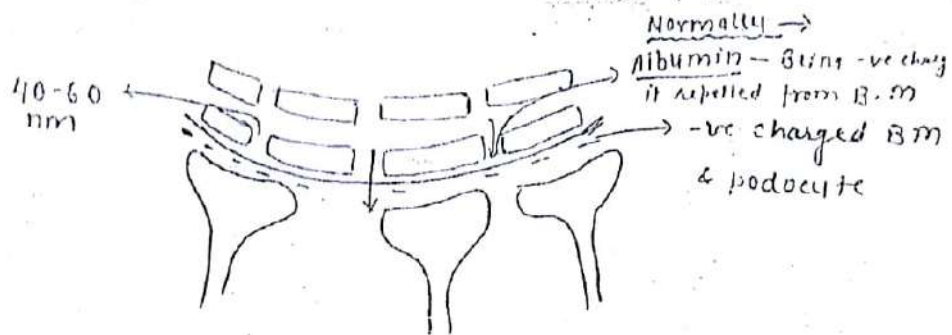


$\rightarrow$ Damage to filter slit
 $\downarrow$
High m.wt. molecule will also filter
 $\downarrow$
 $\therefore$ Proteinuria

$\rightarrow \downarrow$ diam. of AA

(6)

filtration slit —



In DM → Glycosylation of B.M protein

↓
it loses -ve charge

↓
so albumin can come through the
filtration slit

↓
Albuminuria

∴ This hyperfiltration causes further damage

ACE I
↓
↓ GFR

↓
To prevent this give ACE I

↓
It reduces AT-II

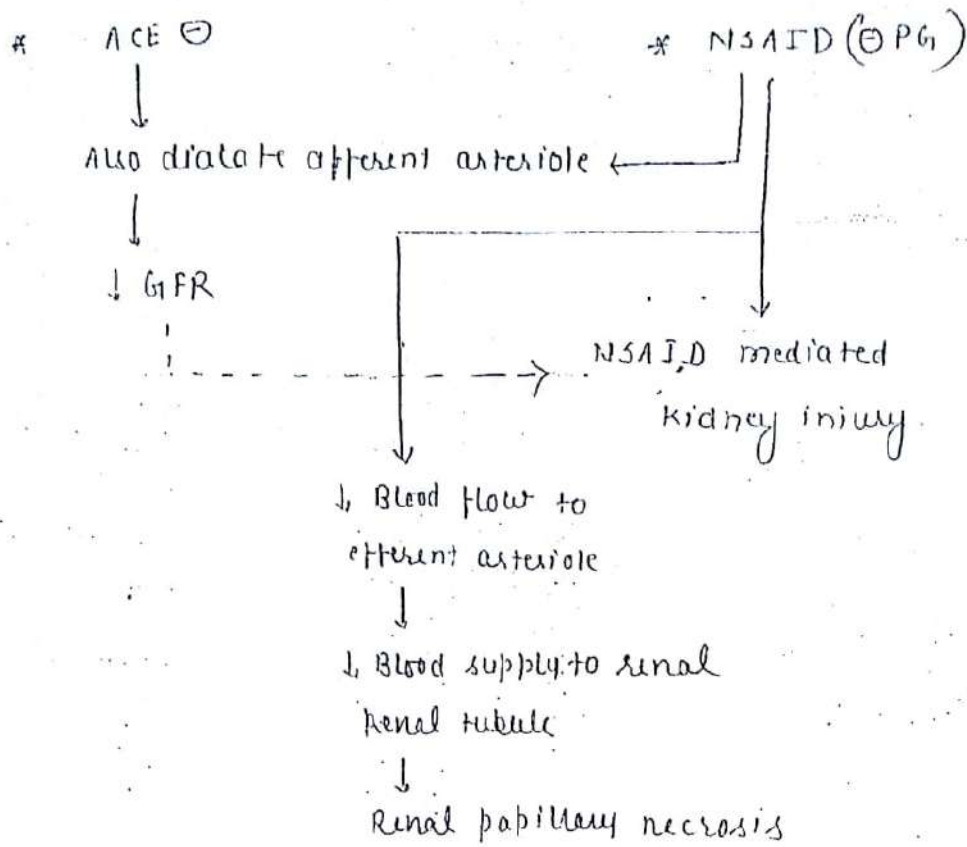
↓
Vasodilation of EA

↓
↓ Filtration pressure

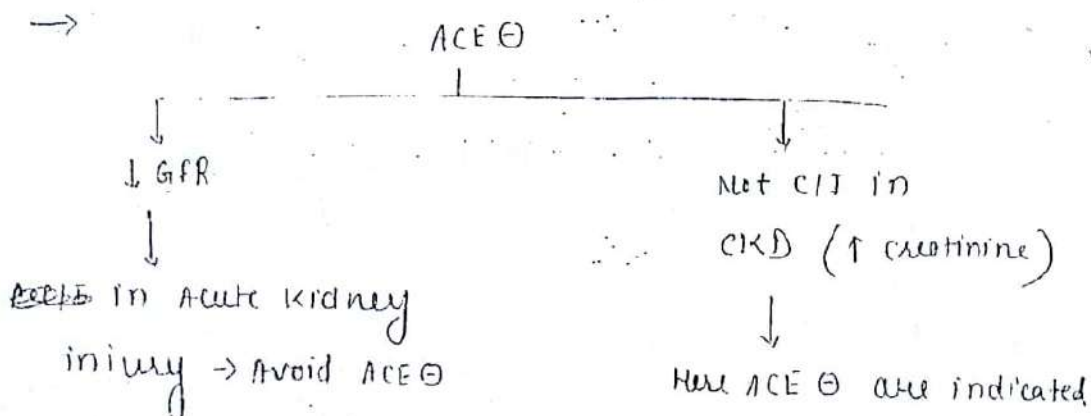
↓
↓ Proteinuria

ACE I
↓
Doc for any
proteinuria

FP ≈ Proteinuria



ACE Inhibitors in DOC for any proteinuria



IN CKD-

* Up to 30% ↓ in GFR
 up to 25% ↑ in s. creatinine

Acceptable
↓
Beyond this

(7)

* ACE $\ominus$



↓ AT-II



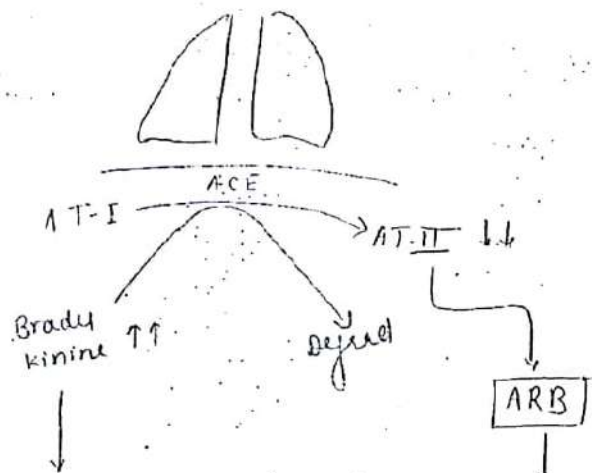
↓ Aldosterone



Hyperkalemia

→ so ACE $\ominus$ are C/I if s. $K^+ > 5$.

*



(1) cough (~20%)
dry

(2) Rhinorrhoea / nasal
congestion.

(3) Angioedema.

→ ↓ cough as compare to
ACE, & it is b/c of some
unknown mechanism.

$$* \boxed{GF = K_f \times NFP}$$

→ depend on ^{surface area} ~~area~~ of nephron → depend on no. of nephron

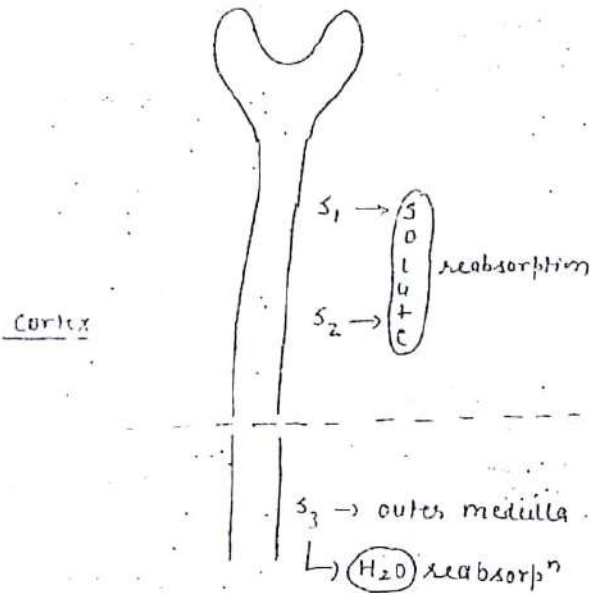
- In CKD → ↓↓ no. of nephron

↓
↓ K_f
↓
↓ GF

(8)

Tubular function

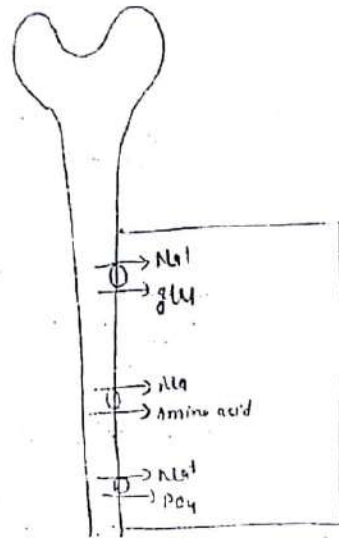
- ① PCT :—
- ① solute & water reabsorption
 - ② HCO_3^- Reclamation
 - ③ NH_3 genesis
 - ④ vit-D synthesis $\rightarrow$ Dlt 1 α hydroxylase



S₁, S₂ has highest mitochondrial content bcz they actively reabsorb solute

x S₁, S₂ segment

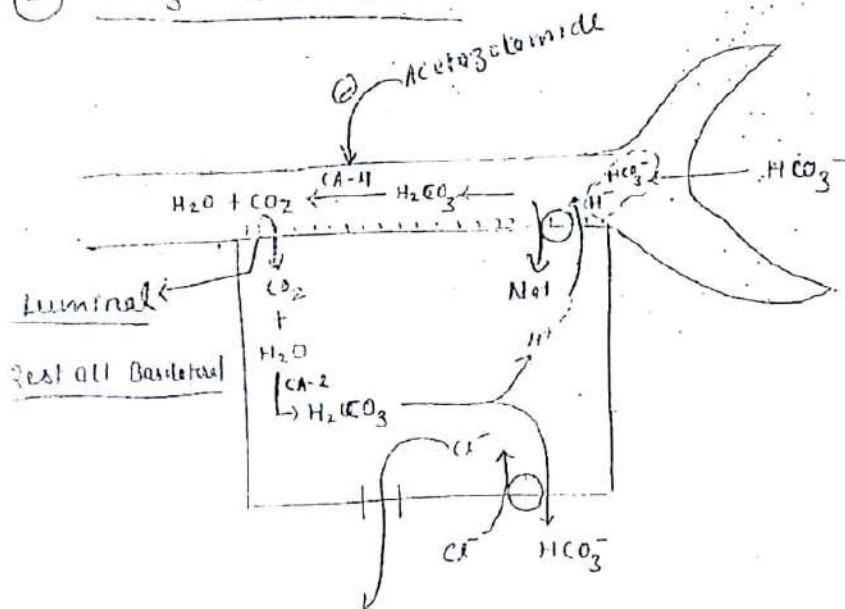
1) *



> 65% absorption of solute occurs in PCT (also H_2O)
except - $\text{Mg} \rightarrow$ its max^m absorption occurs in DCT

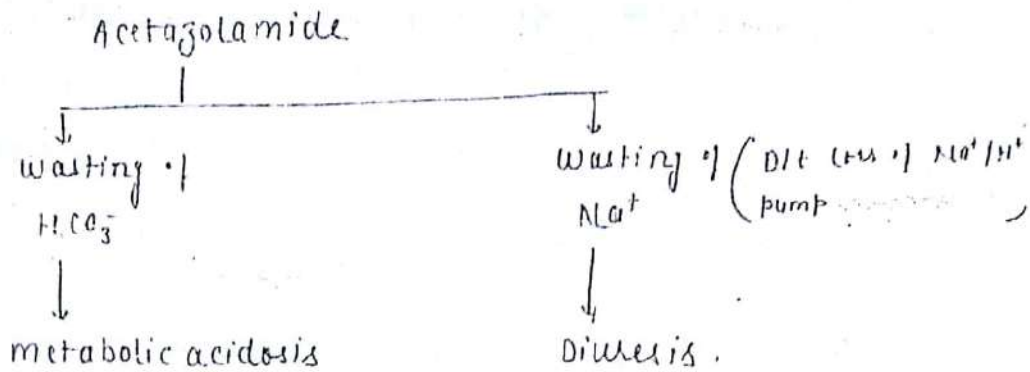
(25%) top of Henle $\rightarrow \text{Na}^+ - \text{K}^+ - 2\text{Cl}^-$
(23%) DCT $\rightarrow \text{Na}^+ - \text{Cl}^-$ pump
(27%) CD $\rightarrow \text{ENaC}$

2) HCO_3^- Reclamation —



- HCO_3^- is not directly getting absorbed, it is absorbed indirectly & so it is Reclamation.

⑨



→ The diuretic effect is poor b/c when Na^+/H^+ pump fails, other pump get activated to prevent loss of Na^+ , there are

- 1) Na^+/glu
- 2) Na^+/aa
- 3) Na^+/PO_4
- 4) Na^+/K^+ ATPase

uses - ① ICP

- ① mountain sickness
- ② HAPE (High altitude pulmonary edema)
- ③ Angle closure glaucoma

→ ↑ ICP → met. acidosis → ↓ HCO_3^-

↓ CO_2
↓
vasodilation
↓
↑ Blood to brain
↓
↑ ICP.

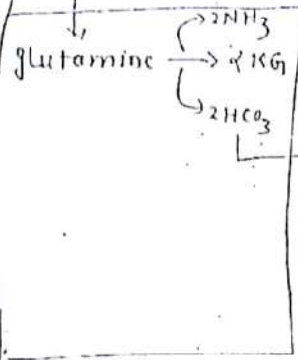
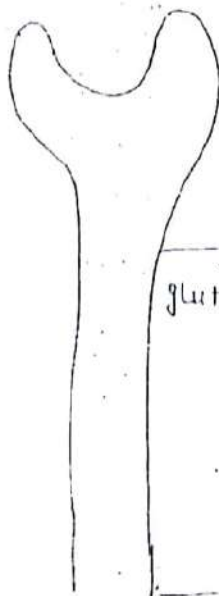
(3) NH₃ genesis — Trigger → acidosis



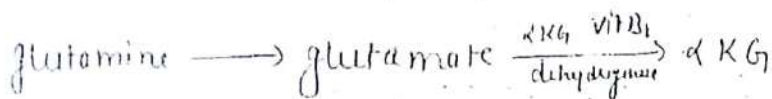
Trigger liver



secretes glutamine



→ main reason for combating acidosis



* In alcoholic



def. of vit B₁



accumulⁿ of glutamate $\longrightarrow$ ↑ glutamin



excitotoxicity



toxic to neuron

Wernicke Encephalopathy

(10)

Causes of Wernicke's encephalopathy

- (1) Alcohol
- (2) malnutrition (cancer)
- (3) Hyperemesis gravidarum

C/F - COAT RACK

C - Confusion

O - ophthalmoplegia

A - Ataxia

T - Thiamine



Completely reversible

R - Retrograde } amnesia

A - Antegrade }

C - Confabulation

K - Korsakoff



Partially reversible

T/T - Thiamine



250 mg Bolus



100 mg OD/BD

→ Following T/T → Wernicke's encephalopathy will be completely reversed but there will be unmasking of feature of Korsakoff.

* 1st to recover → ophthalmoplegia

* 1st cranial N. affected → 3rd N

* Recovery — ophthalmoplegia > ataxia > confusion > Amnesia.

Inv:- 1) IOC — MRI

→ mammillary body necrosis — Wernicke

→ mammillary body atrophy — Korsakoff.

→ Dorsal thalamic nucleus necrosis & atrophy.

↓
Diencephalon is affected.

→ Tells about severity of disease.

* Hippocampus is very rarely affected (not affected).

* RBC transketolase

* Never give glucose before giving Thiamine bcz glucose metabolism will utilize thiamine.

* If there is hypoglycemia & wernicke's

↓
give glucose 1st then thiamine. bcz we need to improve hypoglycemia first.

(11)

Diameter

GFR

EA

EA

AA

AA

AA + EA

↓

↓

AA + EA

↑

↓↓

ACEI

PGI

↑

GFR

EA ↓

AA ↑

NSAID

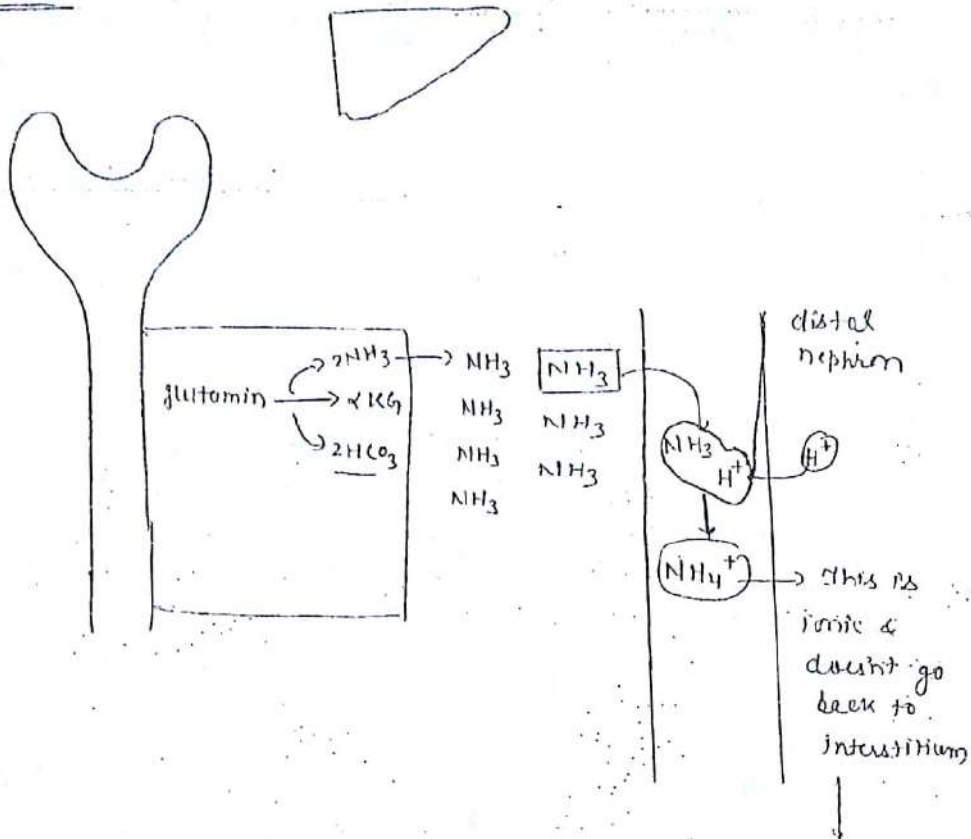
↓ GFR

EA ↑

AA ↓

EA	AA	GFR
↓	N	↑
↑	N	↓
N	↓	↓
N	↑	↑
↓	↓	↓
ACEI ↑	↑	↓
PGI ↓	↑	↑
NSAID ↑	↓	↓

Acidosis



This NH_4^+ formⁿ

is mechanism to low extra

H^+ from body during acidosis.

Mechanism to combat Acidosis.

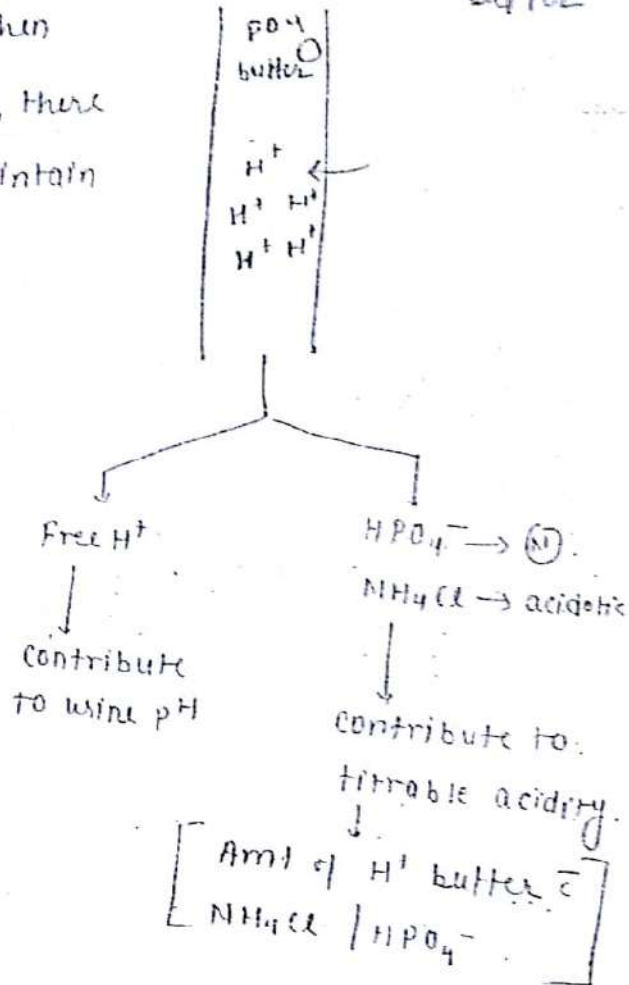
- * 2 extra HCO_3^- produced - help in combating metabolic acidosis
- * NH_4^+ formⁿ also takes $\frac{1}{2}$ extra H^+ out of body
- Also there is 1 release of glutamine during acidosis.

(12)

* when there is no NH_3 — PO_4 Buffer < Acetate buffer

- in ~~still~~ (N) person (when there is no acidosis), there is PO_4 buffer to maintain H^+ conc.

↓
- PO_4 combine $\bar{\text{c}}$ H^+ which comes out through urine.
- Also some free H^+ comes out.



* if there is hindrance $\bar{\text{c}}$ NH_3 product

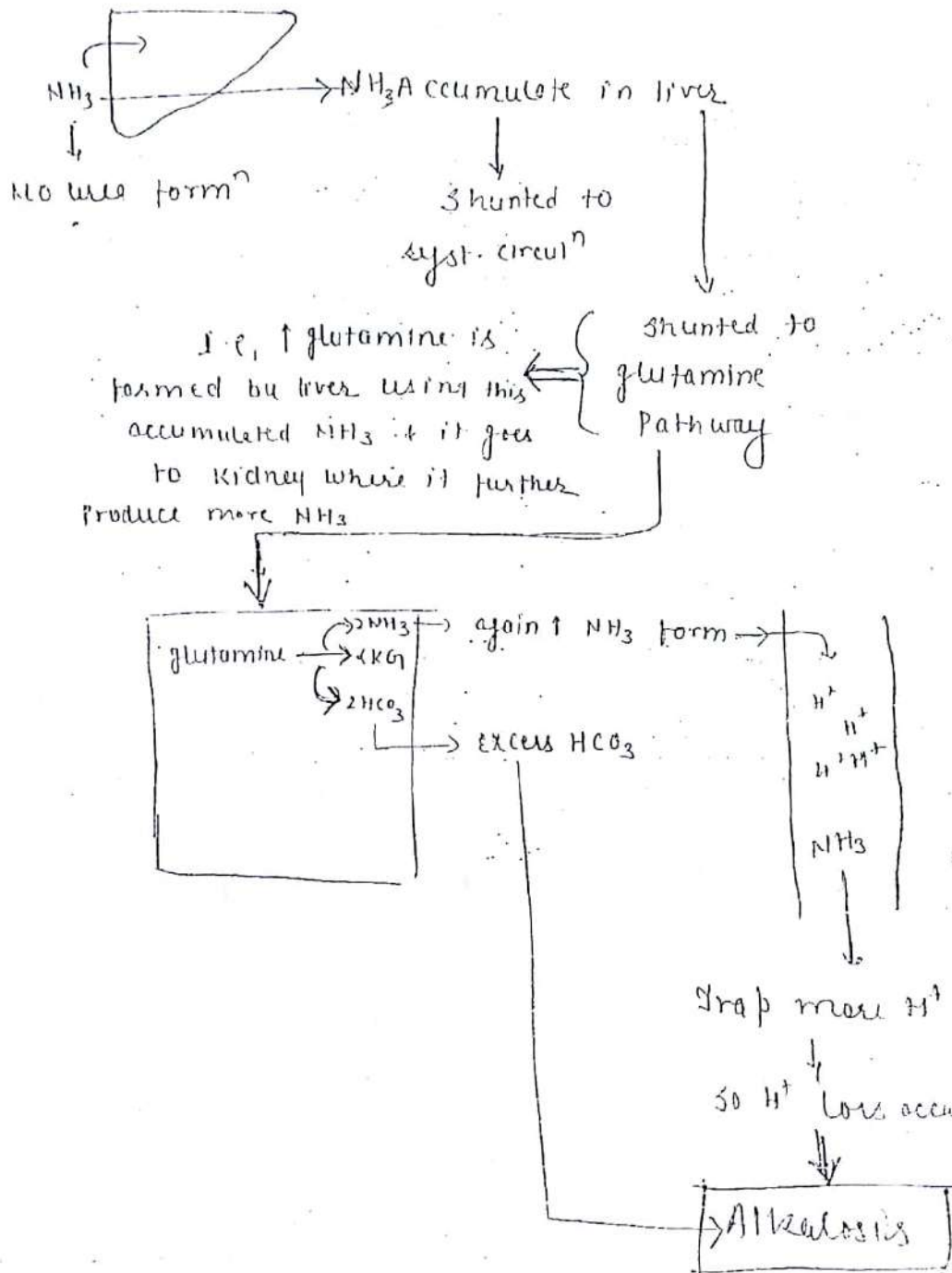
↓
acidosis will not be compensated by

NO HCO_3^- produced

H^+ can't be excreted
 $\bar{\text{c}}$ NH_3 as NH_4^+

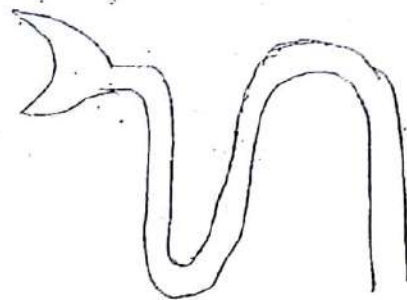
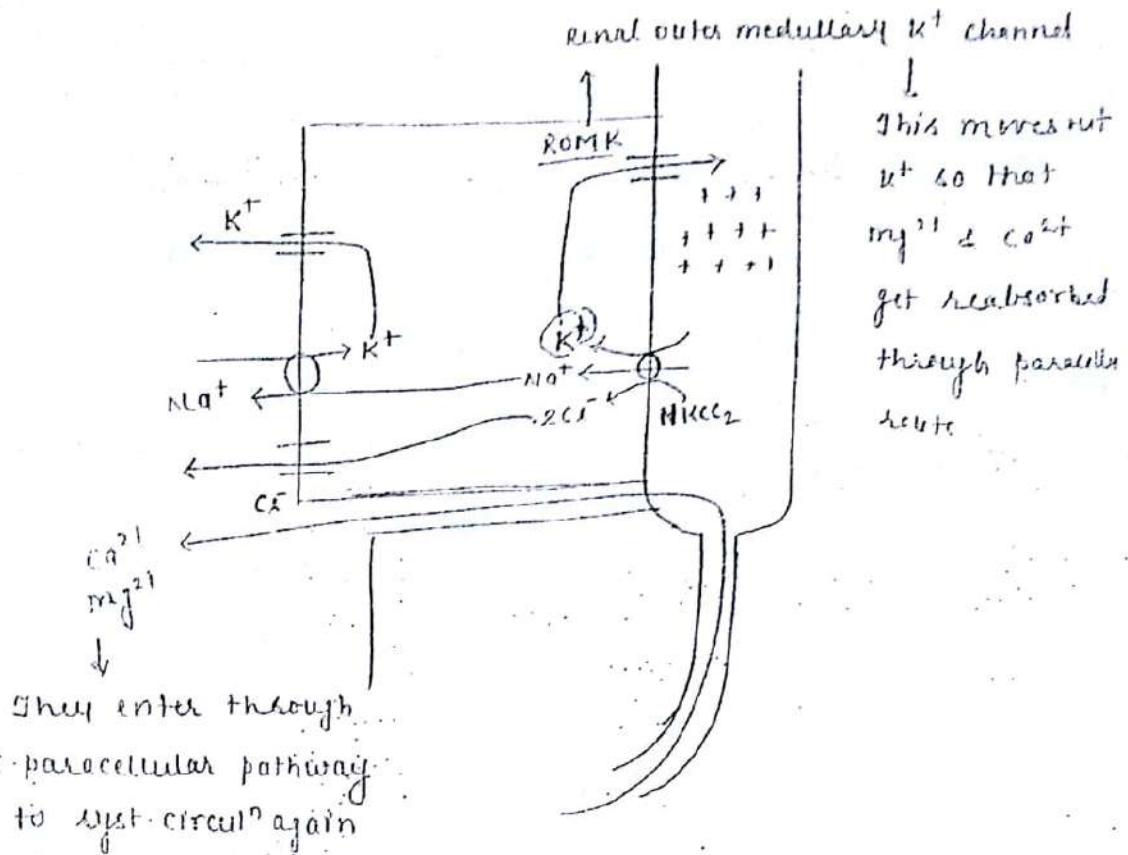
* This acidosis will be seen in chronic kidney disease.

Liver failure —



(13)

(2) Loop of Henle Thick ascending limb

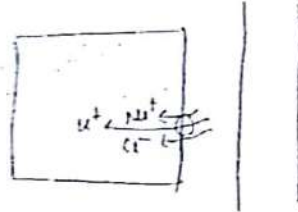


Free water — water which move $\bar{c}$ out solute

* $\boxed{\text{func}^n \text{ of } \text{Na}^+ / \text{K}^+ / \text{Cl}^- \text{ ATPase}}$

→ The segment in which this channel is located is impermeable to H_2O .

So through this channel only $\text{Na}^+ \text{Cl}^-$ will move in & no H_2O will enter cell leads to dilution of urine

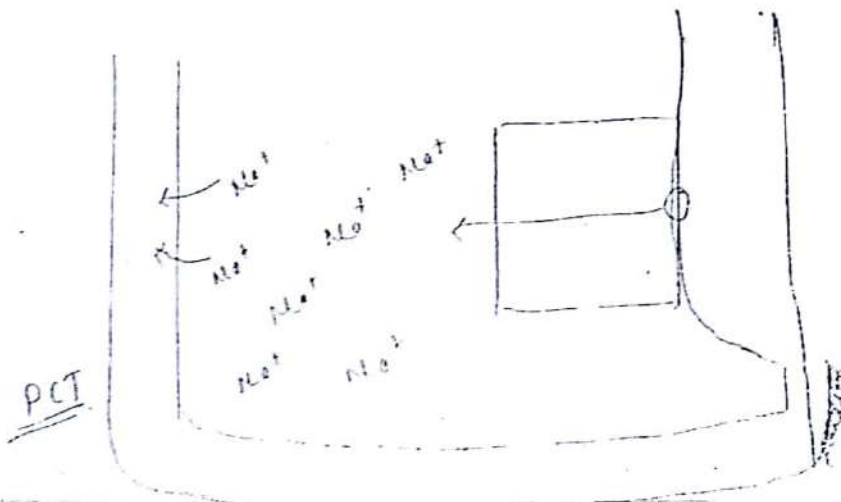


* medullary interstitial ^{osmolarity} gradient → Abolished by isotonic

↓
Responsible for H_2O reabsorption by

PCT

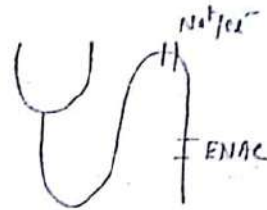
↓
∴ 15% Na^+ & H_2O is absorbed in PCT.



(14)

Na⁺ reabsorption —

- * $\text{Na}^+ / \text{K}^+ / 2 \text{Cl}^- \rightarrow 20-25\%$
- * $\text{Na}^+ - \text{Cl}^-$ channel $\rightarrow 5-7\%$
- * ENAC channel $\rightarrow 1-2\%$



Loop diuretic —

- * Abolish medullary int. hyperosmol.
↓
Leads to — Dilution of urine
— Hyponatremia.

$$* S. \text{Na}^+ = \frac{\text{Body } \text{Na}^+}{\text{Total body water}}$$

① Diarrhoea — $\uparrow S. \text{Na}^+$

↳ Bcz water loss is more than Na^+ loss.

$$\textcircled{2} \text{CKD} \rightarrow \downarrow S. \text{Na}^+ = \frac{\text{TB } \text{Na}^+ \uparrow \uparrow \uparrow}{\text{T. B. water } \uparrow \uparrow \uparrow}$$

- * ADH causes absorpⁿ of free H_2O .

(3) SIADH $\rightarrow$ $\uparrow$ ADH

$\downarrow$

$\uparrow$ water absorpⁿ

$\downarrow$

Total body H_2O $\uparrow$

$$\therefore \downarrow S. Na^+ = \frac{T. Body Na^+ (N)}{T. B. H_2O \uparrow \uparrow \uparrow \uparrow}$$

$\Downarrow$

Euvolemic Hypo Na^+

(4) Psychogenic Polydipsia $\rightarrow$

- Diluⁿ Hyponatremia
- Euvolemic

$$\downarrow \downarrow S. Na^+ = \frac{TB Na^+ (N)}{TB H_2O \uparrow \uparrow \uparrow}$$

* T. body Na^+ determine the volumic status of person.

$\downarrow$

q1 total body Na^+ (N)

$\downarrow$

Euvolemic

(5) Loop diuretic--

$$\frac{S \cdot Na^+}{T \cdot B \cdot H_2O} = \frac{T \cdot B \cdot Na^+ \downarrow \downarrow}{T \cdot B \cdot H_2O \downarrow \downarrow}$$

Here
water loss $\approx$ Na^+ loss
proportional to

I) mild hyponatremia $\rightarrow$ 125-130

Na^+ (M) $\rightarrow$ 135-145

II)

Hyponatremia

$\downarrow$ ①

RAAS

$\downarrow$

$\uparrow$ Aldosterone

$\downarrow$

- Hypokalemia

- met. alkalosis

III) Hypocalcemia

IV) Hypomagnesaemia

$\therefore$ Natriuresis + Kalemia + Hypercalcaemia

$\downarrow$
Renal stone.

V)

vestibulotoxic

{ Gentamycin
streptomycin

ototoxic $\begin{matrix} \swarrow K \\ \swarrow A \\ \swarrow N \end{matrix}$

$Na^+ - K^+ - 2Cl^-$

Also int in cochlea in scala media

Ototoxicity $\rightarrow$ it is reversible

Barrier syndrome

• cong def of $Na^+ - K^+ - 2Cl^-$

Types -

Type - I	—	NKCC2	} defective
Type - II	—	ROMK	
Type - III	—	Cl ⁻	

Type - II

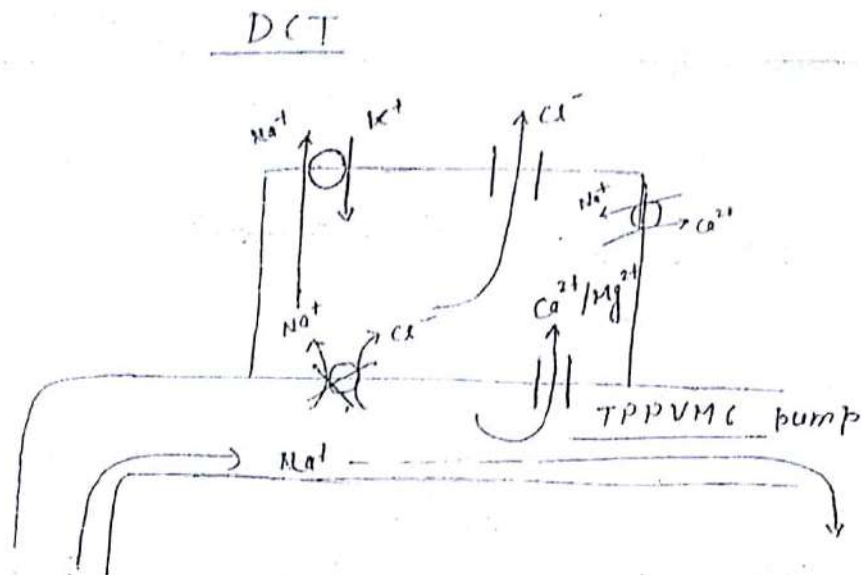
K⁺ accumulⁿ in cell

Type - III

Cl⁻ accumulⁿ in cell

Failure of NKCC2 pump

(16)



* TPPVMC — o Absorbs $\text{Ca}^{2+}/\text{Mg}^{2+}$

• only 1 ion absorbed at one time.
which depend on the selective preference of pump.
for ex. under influence of PTH
↓
↑ Ca^{2+} absorpⁿ

* Thiazide diuretics block Na^+/Cl^- channel

↓
 Na^+ will be pass through DCT & not get absorbed. Also this part has no contribution to
↓ medullary hyperosmotic gradient.
But this part is impermeable to H_2O & so
no H_2O loss occur → so no diluted urine &

There is profound Na^+ loss (even more than loop diuretic)

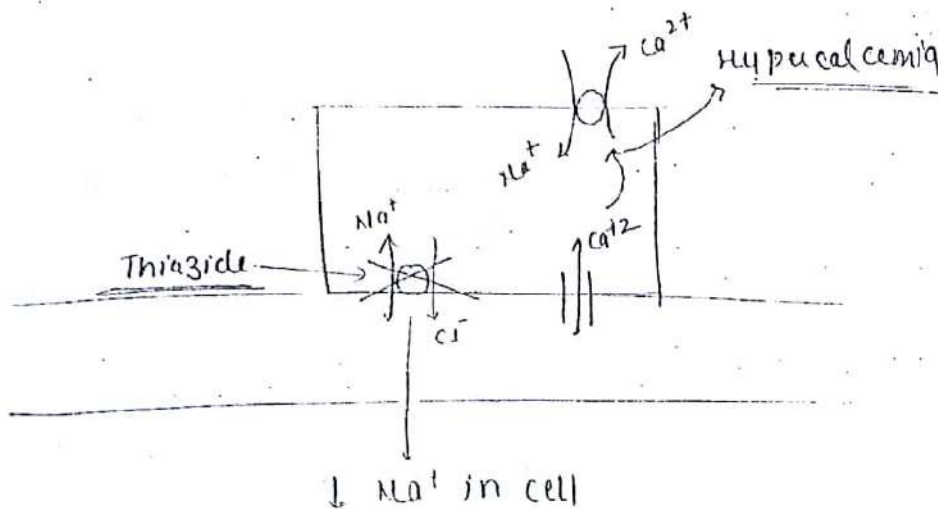
↓
So best for t/t of 'HTN also'.

↓
profound ↓ in B.P.

x Thiazide also causes

Hyperglycemia
Hyperlipidemia
Hyperuricemia

x Thiazide causes Hyper Ca^{2+}



↓ Na^+ in cell

↓
So compensate this another channel
get activated ($\text{Na}^+-\text{Ca}^{2+}$ channel)

↓
For functioning of this pump Ca^{2+}

should be there in cell which occurs

However for Thiazide pump

(17)

↓
∴ Hypercalcaemia & Hypocalcaemia

Summary —

- 1) Urine — conc. — (dil not low) $\xrightarrow{+}$ RAAS
- 2) Hypo K^+ ↓
↑ Ald
- 3) met. alk
- 4) Hyper Ca^{++}
- 5) Hypocalcaemia
- 6) Urine Mg^{++} ↑
- 7) Hypo Mg^{++} ↓

Uses of thiazide —

- (1) Syst. HTN
- (2) DI (rare)
- (3) Recurrent urinary stone (Ca^{++} stone)

* Gitelman syndrome —

• Congenital def. of Na^+ - Cl^- channel.

CIF — same as Thiazide diuretic except for Ca^{++} .

→ Here Ca^{++} is (M) / ↓.

↓
* This hypocalcemia is alt loss of intestinal
absorption of Ca^{++} (Ca^{++} may be $\approx 1/4$)

→ Hypomagnesemia is very profound bcz there
is neither absorpⁿ of Mg^{++} in intestine nor
in nephron.

(18)

Distal part of nephron

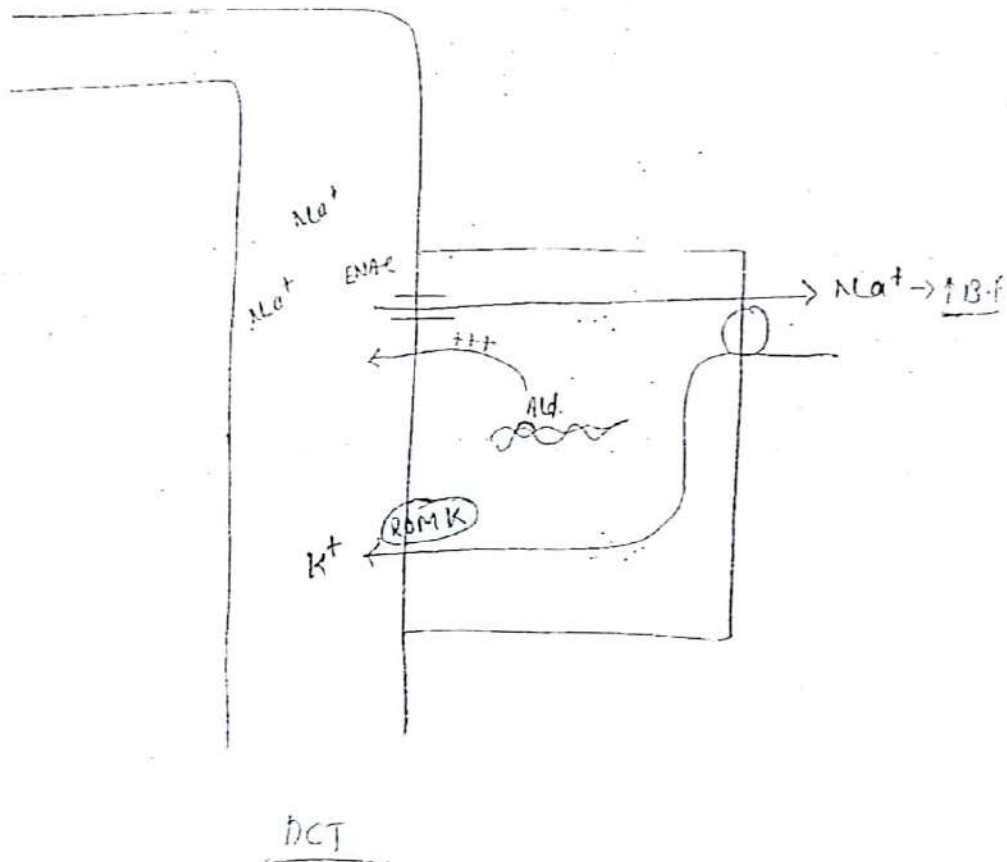
Distal → 2 type of cell

P cell (principle cell)

Intercalated cell

↓
site of action of aldosterone

- Aldosterone is steroid hormone



more Na^+ in DCT



whole this Na^+ can't be absorbed b/c
it is beyond the mechanism of ENaC



But while trying this Na^+ reabsorpⁿ they
paradoxically secrete more K^+ in DCT



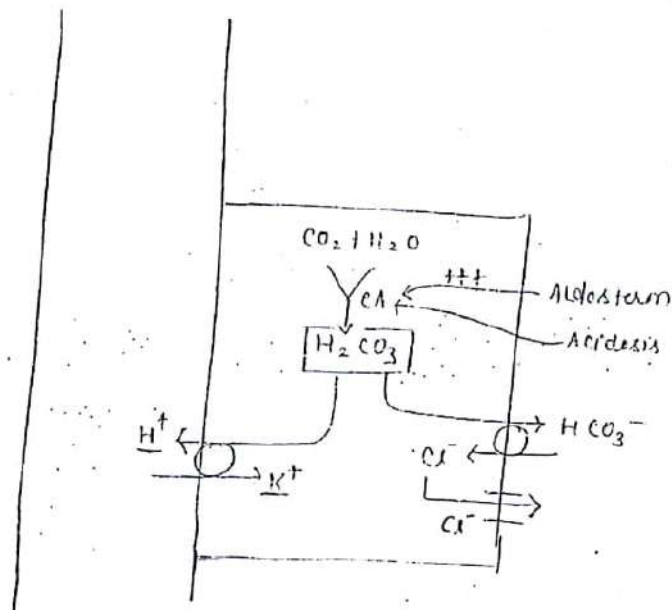
so profound hypokalemia



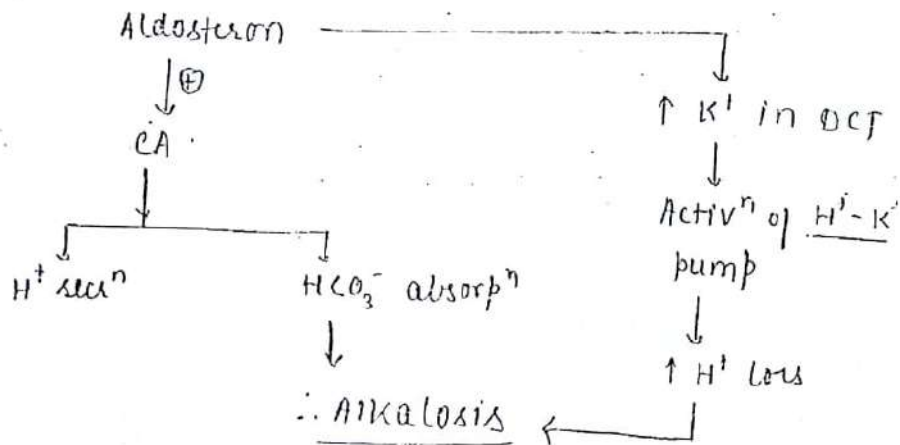
By this mech. Thiazide induced K^+ loss is
aggravated.

(19)

→ d intercalated cell pump in combating - Acidosis
↳ produces ^{new} HCO_3^-

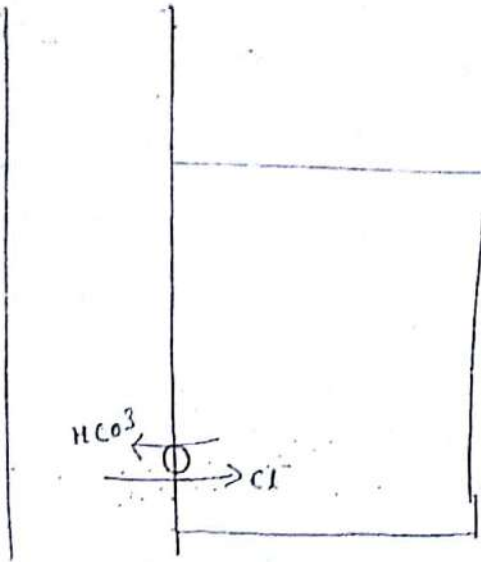


DCT



* Hypokalemia maintain met. alkalosis.

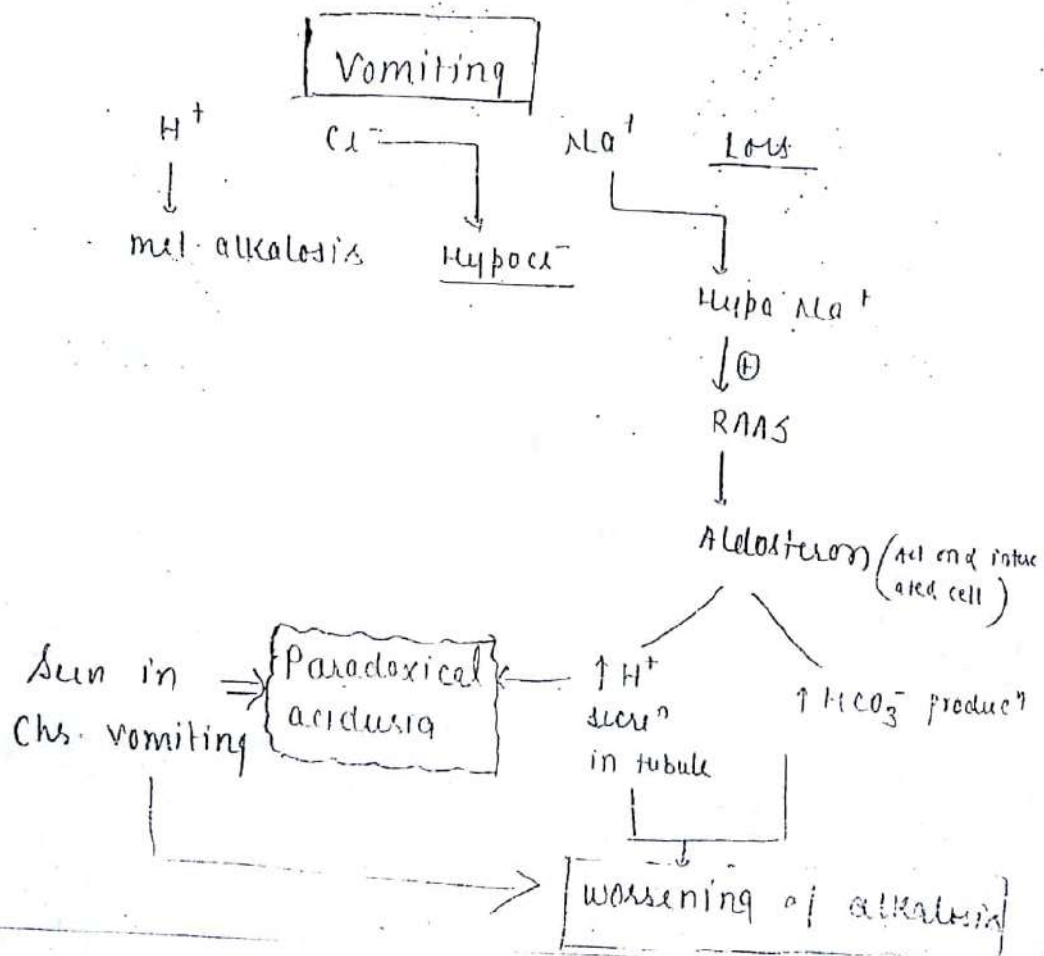
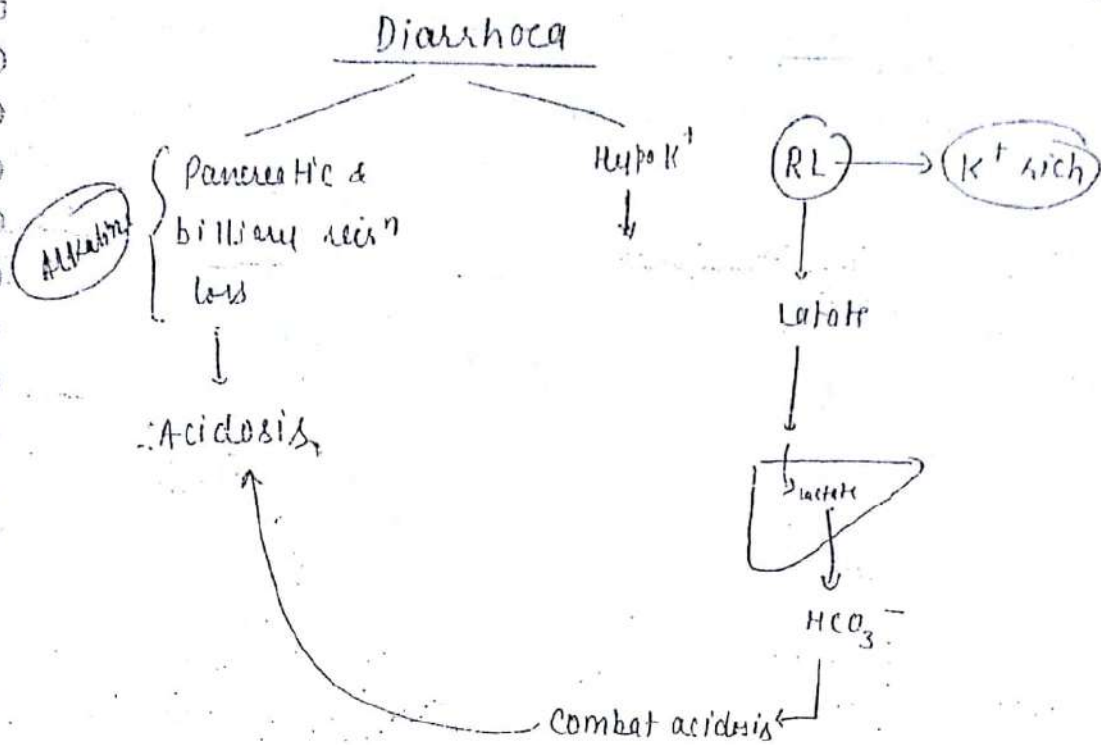
β -intercalated cell — combat alkalosis
↳ secrete HCO_3^-



DCT

↳ Hypo K^+ maintain alkalosis

(20)



* on case of vomiting

↓
1st we need to correct Hypo Cl^-

↓
once Cl^- become adequate

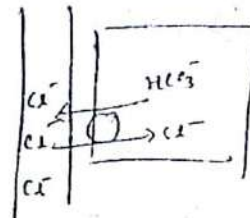
↓
then only there will be

↑ Cl^- in tubule

↓
⊕ $\text{HCO}_3^- - \text{Cl}^-$ pump

↓
∴ HCO_3^- will be excreted

↓
Cl- responsive Alkalosis



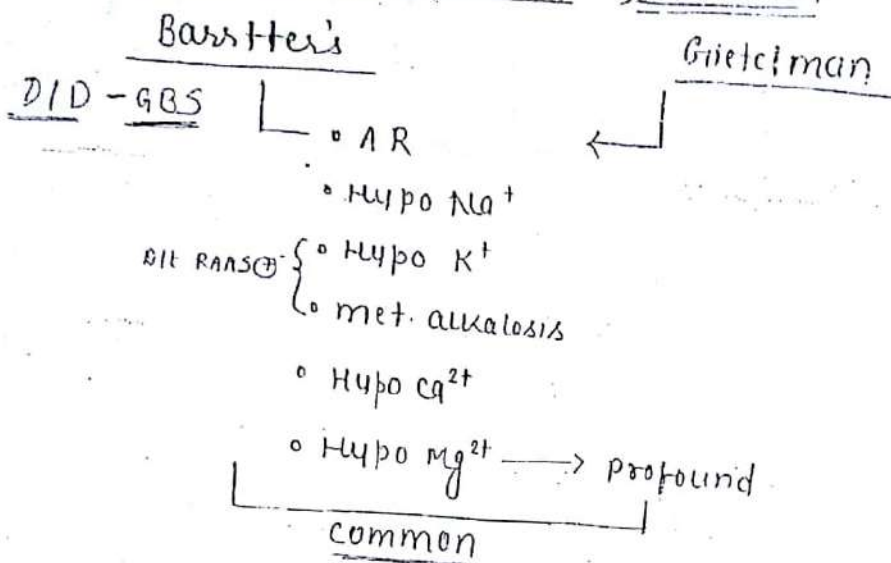
β -intercalated

cell

* Hypochloremic met alkalosis & paradoxical aciduria

(21)

Tubular disorder — 1) Inherited



① urine $\text{Ca}^{12} \uparrow$

C/FT child

- Poor scholastic ($\downarrow \text{IQ}$)
- Short stature
- Nephrocalcinosis
- Deafness (type-1)

① urine $\text{Ca}^{2+} \downarrow$

Adult

Asymptomatic

* if symptomatic —

• Fatigue > Tetany
(all Hypo Mg^{2+})

Inv:- Renin $\uparrow$

Aldosterone $\uparrow$

urine $\text{Ca}^{2+} \uparrow$

$\uparrow$

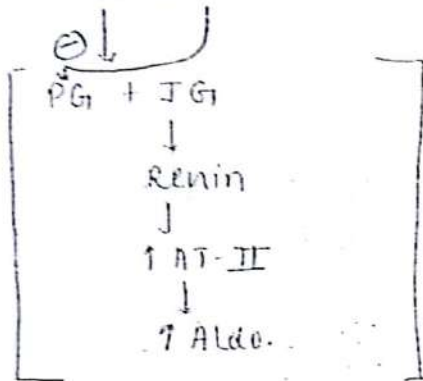
$\uparrow$

urine $\text{Ca}^{2+} \downarrow$

Rx — Barstar

- K^+ supplement
- K^+ sparing diuretic

• Indomethacin



Gitelman

- Mg^{2+}
- spironolactone

* In Heart failure → salt restrictⁿ ??
HTN

↓
Salt is given in moderate amt.

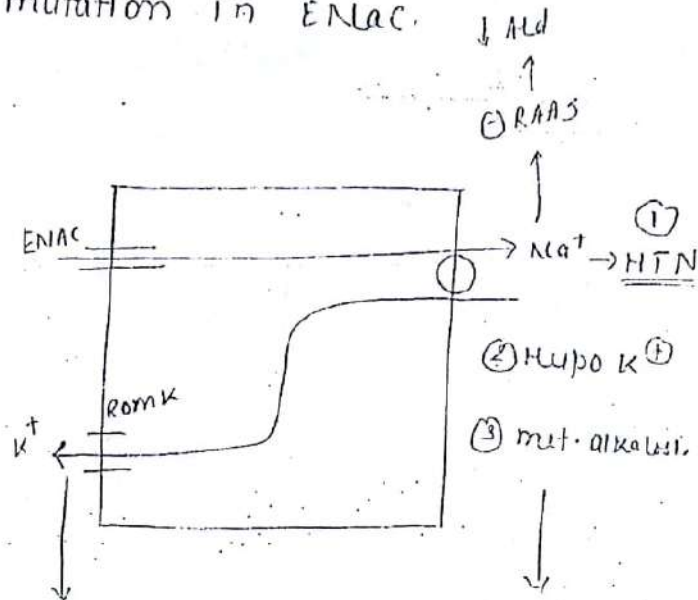
↓
↓ salt (No!)
↓
more activⁿ of RAAS

(22)

Liddle syndrome

* AD

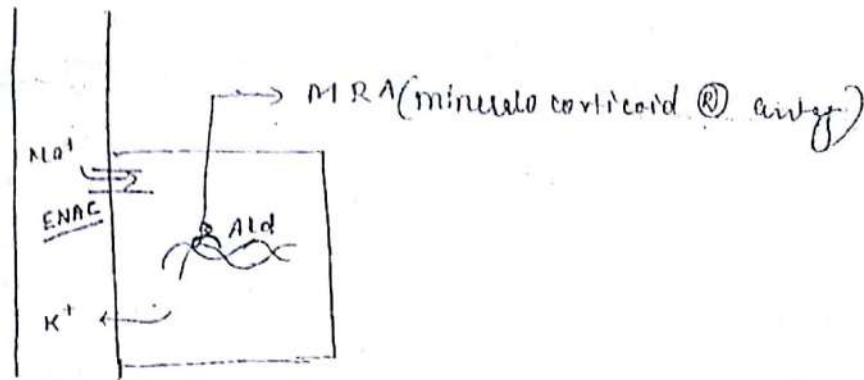
* Gain of funcⁿ mutation in ENaC.



R_x — Amiloride

* Spironolactone are of no use

DCLD → Disabling chronic liver disease



In DCLD pt continuous diuresis is needed

K⁺ sparing diuretics

⊖ ENaC



- Amiloride
- Triamterene

MR^A



- spironolone
- Eplerone

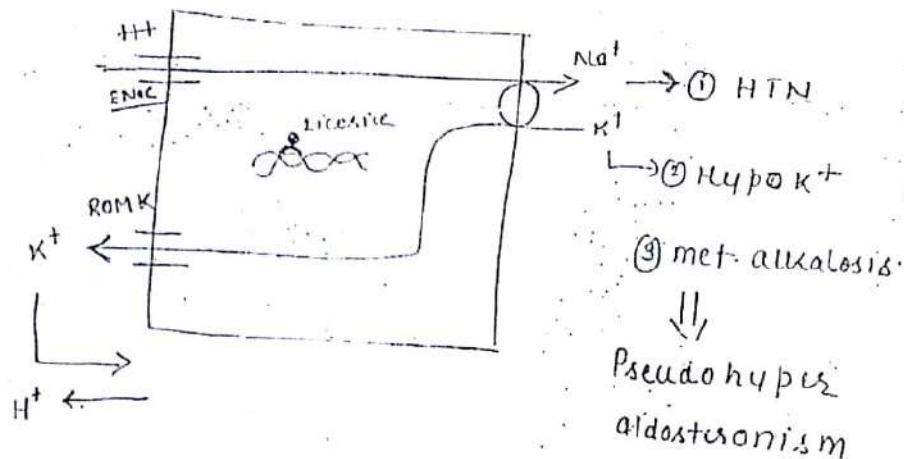
(23)

Licorice — Resembles Liddle's.

- It is acquired disorder.
- Licorice is structurally similar to aldosterone.

↓
But it stimulate aldosterone (R)

↓
④ ENaC



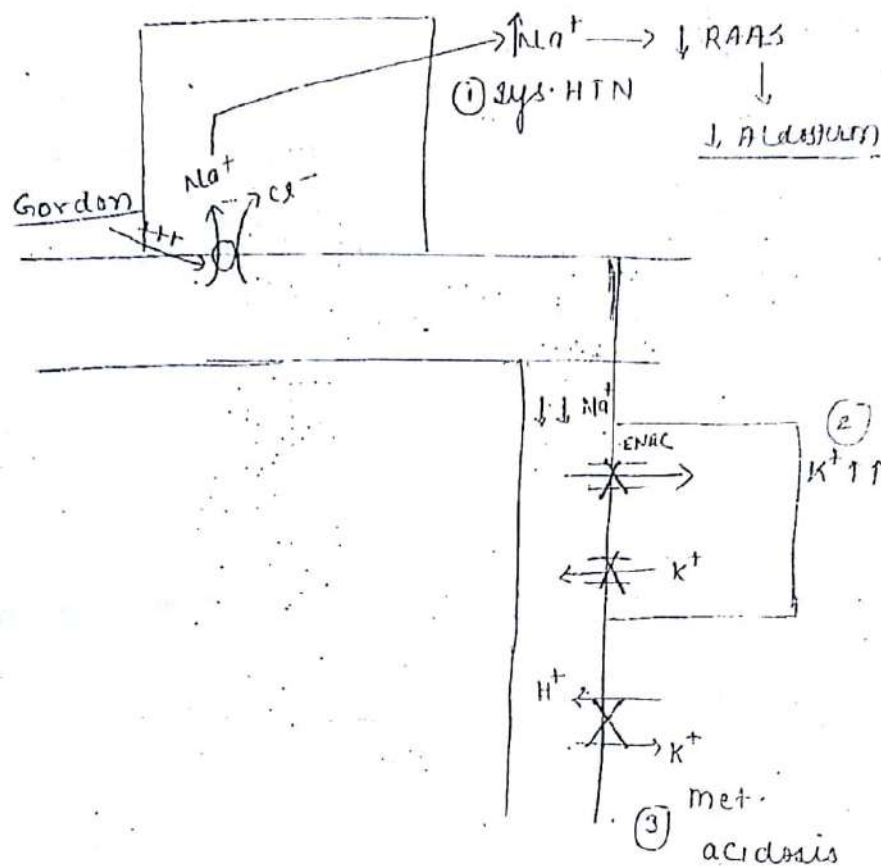
R_x — Give spironolactone + K⁺ supplement

↓
It binds to (R) & so that Licorice will not be able to bind

Gordon syndrome

* AD

* Gain of funcⁿ mutⁿ in $\text{Na}^+ - \text{Cl}^-$



C/F - Pseudohypoaldosteronism

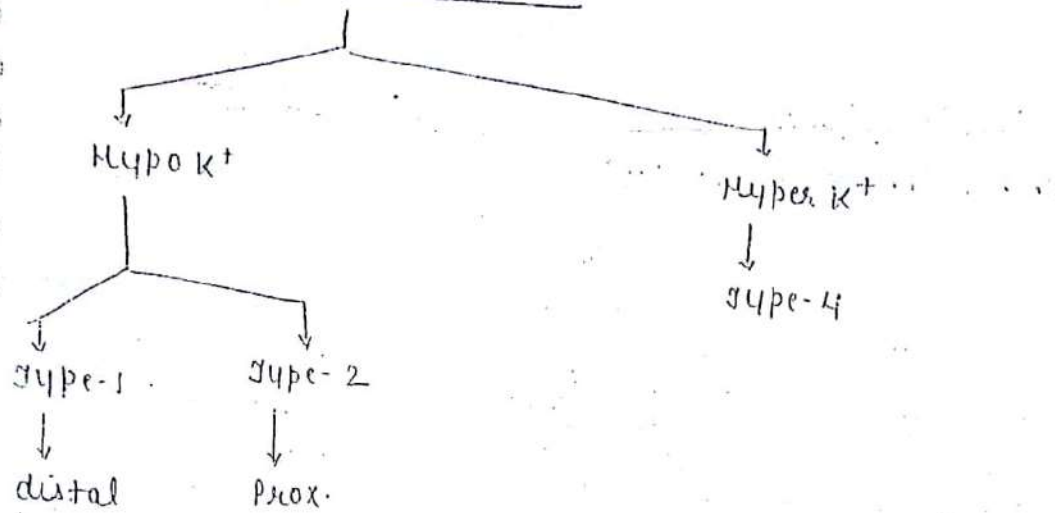
→ But here B.P will be $\uparrow$

Rx - Thiazide diuretics → Doc.

(24)

Acquired tubular disorders

Renal tubular Acidosis —

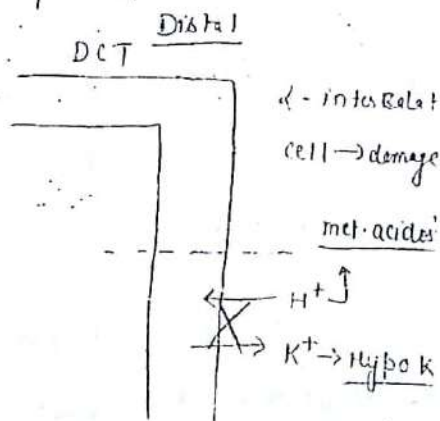
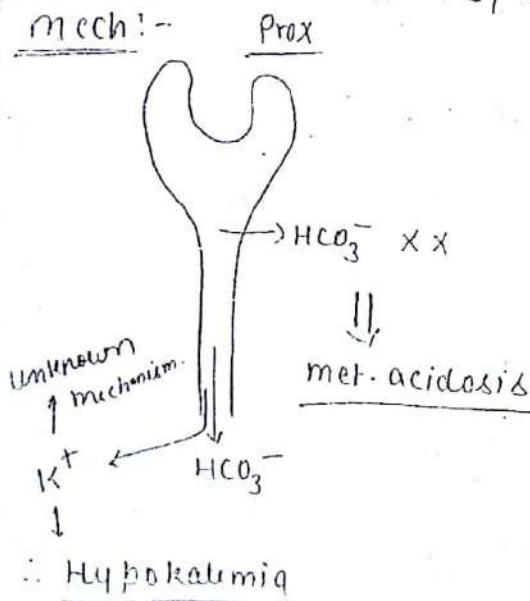


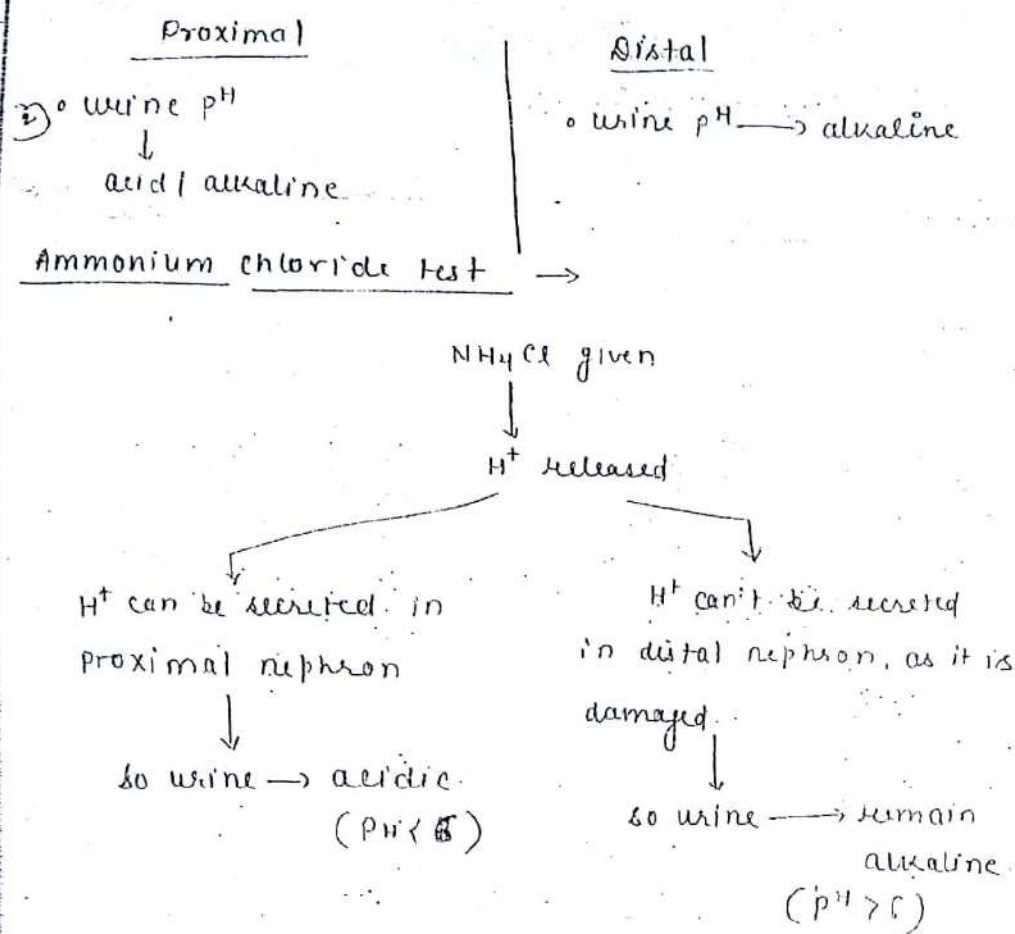
Proximal (Type-2)

- 1) Hypo K⁺
- 2) met. acidosis
- 3) (N) anion gap
- 4) (N) BPG/s. creatinine/s. urea

Distal (Type-1)

mech:-





* Acidosis is more severe in distal type b/c it is the distal nephron which is responsible for acid-base balance.

* Also K^+ handling is a funcⁿ of distal nephron so in distal variety severe Hypokalemia is there.

* If acidosis occur in proximal variety → it can be compensated by distal while in distal, there will be severe acidosis.

(25)

Prox

Distal

(3) mild-mod. acidosis

(3) severe acidosis

(1) $S.HCO_3^- > 15$

$S.HCO_3^- < 15$

(4) urine $HCO_3^- \uparrow$

(4) $U.HCO_3^- \uparrow / \downarrow$

(5) HCO_3^- replacement —
 $< 5.5 \text{ mEq/kg/day}$

(5) HCO_3^- replacement —
 $> 5.5 \text{ mEq/kg/day}$

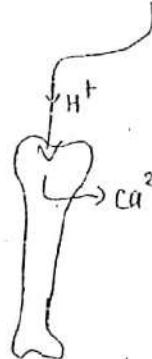
(6) citrate can't be absorbed as PCT is affected

(6) urine $Ca^{2+} \uparrow \uparrow$

↓

5) severe acidosis is int
 $H^+ H^+ H^+$

↑ citrate in urine



↓
so no free Ca^{2+} as it will go c citrate

$Ca^{2+} \rightarrow$ Hypercalcaemia

↓
so no nephrocalcinosis

Bone buffer

II) Acidosis $\rightarrow$ triggers PCT

↓
so cause reabsorp of citrate

↓
so urine citrate ↓

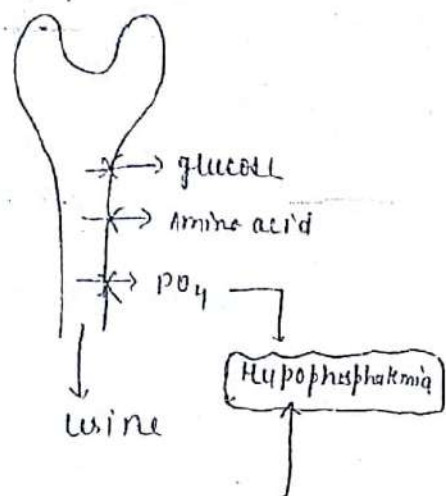
↓
free Ca^{2+} will not bind to citrate

Hallmarks of Distal RTA

Nephrocalcinosis

↑ Ca^{2+} pass in urine

1) X



→ ALSO ↓ vit-D synthesis

II

Bone problems predominant

5) ^{Any} Connective tissue disorders
↳ RA / SLE / Scleroderma

causes — (4 Any fancy condition)

- (1) Fanconiⁱ
- (2) Wilson
- (3) cystinosis
- (4) Drugs: — 1) Acetazolamide

- (5) Drugs → • Lithium
• AMPB
• Demeclocycline

** II) Genotoxic (nephrotoxic)

1) Rx → Treat the cause

2) Treat the cause

7) NO bone problems

causes —

↑ $3 \cdot Ca^{2+}$ → toxic to distal nephron

- (1) vit D toxicity
- (2) Hyper PTH
- (3) multiple myeloma
- (4) sarcoidosis

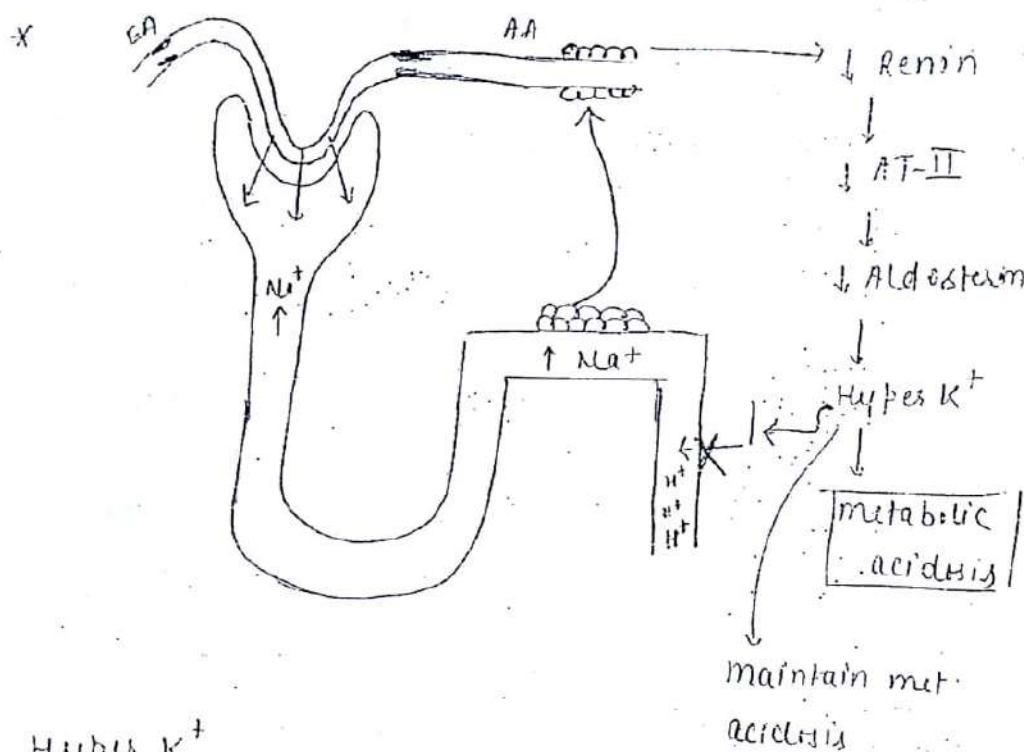
(26)

Type-4 RTA

Pathology — $\downarrow$ Aldosterone / Aldosterone Resistance.

Cause —

- ACE $\ominus$
- DM
- NSAIDs



Hypok K^+



$\downarrow$ NH_3 production



No H^+ will come to tubule to bind NH_3



$\therefore$ Acidosis maintained

ClF — (M) anion gap.

(27)

Arterial Blood Gas

* Preferred site — Radial A.

↓
B/c here good collateral supply is
+ve through ulnar A.

→ we here want to poke Radial A, so we check
patency of ulnar A. this by modified Allen's test.

* Anticoagulant → Heparin is used
for { ABG
OFT

- heparin is coated over syringe only & rest of
the heparin is drained

Values :-

PO_2 — 75-100 mm Hg

PCO_2 — 35-45 mm

pH — 7.35-7.45

Hq^+ — 135-145

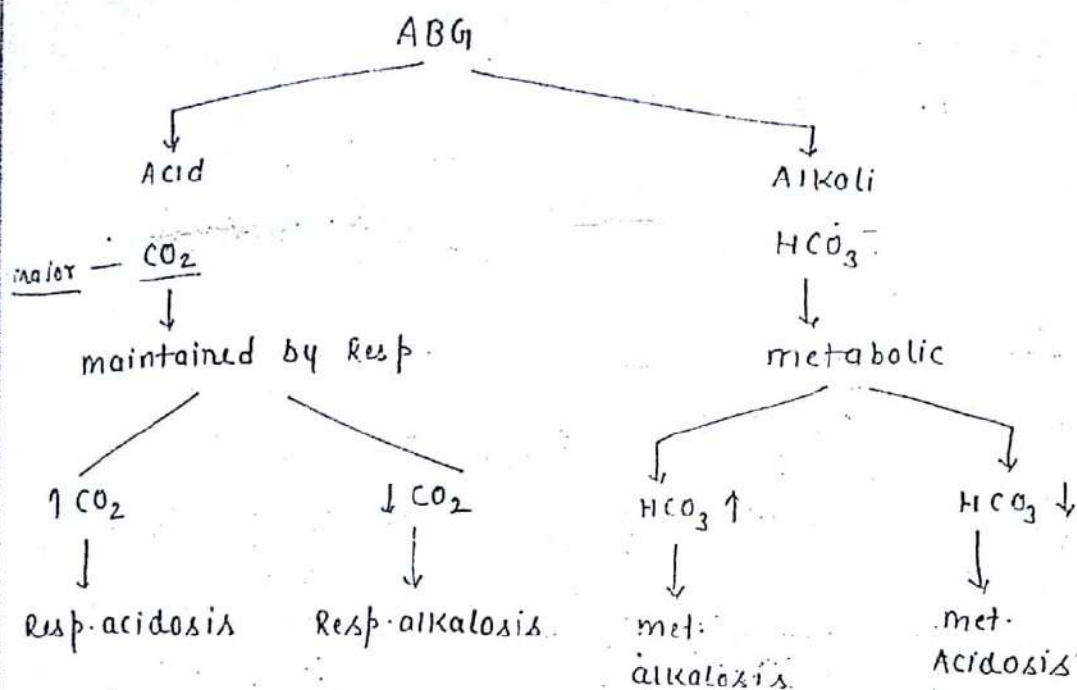
K^+ — 3.5-5.5

Cl^- — 95-105

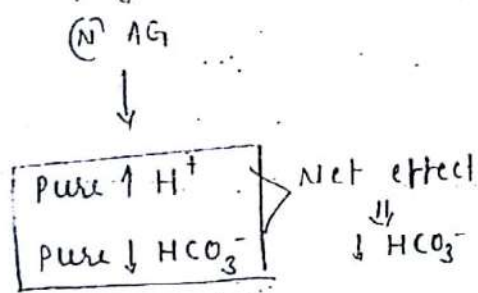
HCO_3^- — 24-27

AG — 8-11 meq/L

$$[AG^+] = [Cl^- + HCO_3^-]$$



AG → (cation - anion)



Causes — U-RAD

- 1) uretic diversion
- 2) RTA
- 3) Addison's disease
- 4) Diarrhoea

It is impure → organic acid

↓

Here any extra anion is there.

(28)

$$\text{Anion gap} = \frac{\text{Na}^+ - (\text{HCO}_3^- + \text{Cl}^-)}{1000}$$

$$\text{Na}^+ - (\text{HCO}_3^- + \text{Cl}^-)$$

$$\text{ex- } 140 - (15 + 115)$$

$$= 10 \Rightarrow \text{N ABG}$$

If loss of more HCO_3^-

↓

Body try to conserve
-ve ion, by conserving
 Cl^- .

↓

∴ Anion gap is **(N)**

→ This is also K/a as
Hyper

Causes - GOLD MARK

G - glycol (ethylene glycol)

O - Oxoproline (Acetaminophen toxicity)

L - L-lactic

D - D-lactate

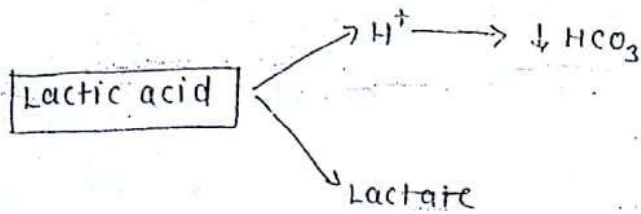
M - methanol

A - Aspirin

R - Renal failure

K - Ketoacidosis

Why the extra organic acid is impurity?



$$\text{Na}^+ - (\text{HCO}_3^- + \text{Cl}^-)$$

$$140 - (15 + 100)$$

$$140 - (115)$$

$$\boxed{\text{AG} = 25}$$

$\downarrow$
 $\uparrow \text{AG}$

There is no need to absorb more Cl^- b/c for every HCO_3^- loss there is lactate anion to maintain -ve charge.

* $\uparrow \text{AG}$ is measure of unmeasured anions.
(Here lactate is not measured)

(29)

	(girls) <u>HCO₃</u>	(Boys) <u>PCO₂</u>
Resp. acidosis	↑ (compens.)	↑ (I')
Resp. alkalosis	↓ (c)	↓
metabolic acidosis	↓	↓ (c)
meta. alkalosis	↑	↑ (c)

* compensatory events occurring to maintain pH not to correct disease.

for ex - In DKA (meta. acidosis)

↓
↓ PCO₂ to correct pH

* → There is never overcompensation i.e., once pH is normalized, compensatory mechanism will stop.

Rule-

① $\downarrow / \uparrow \rightarrow$ qf arrows are in opp. direcⁿ, it is
100% mixed problem.

② qn a metabolic event (1^o metabolic event)

$\downarrow$
qf CO_2 levels are (N)

$\downarrow$
100% it is mixed disorder

$\rightarrow$ This is bcz resp. compensation should occur
immediately in case of metabolic event.

③ For 1^o Resp. event

$\downarrow$
 HCO_3^- level (N)

$\downarrow$
It is an acute event

- Bcz metabolic compensⁿ will take time & HCO_3^-
levels if (N) it indicate that there is acute presentⁿ
& till now compensⁿ has not occurred

* HCO_3^- level $\downarrow / \uparrow \rightarrow$ chronic

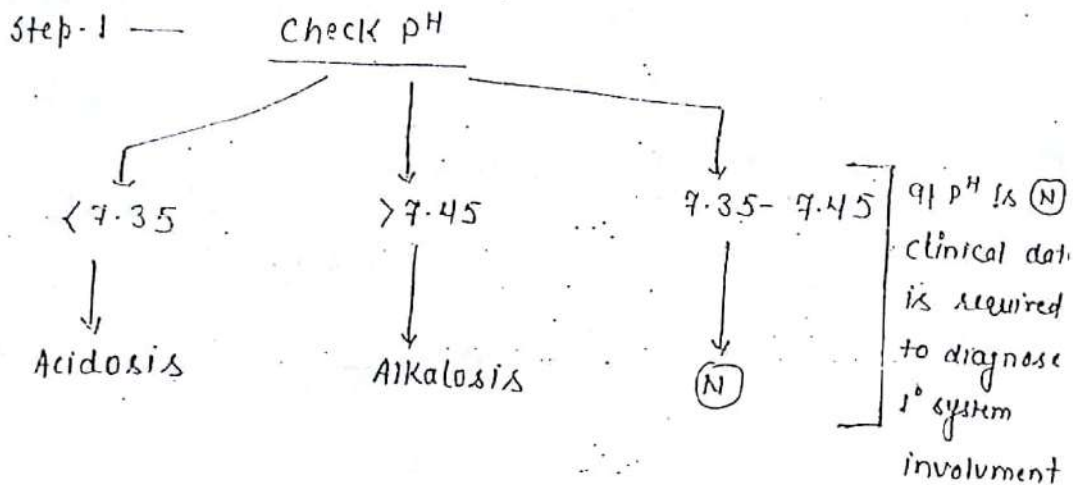
(30)

④ In acute Resp. event $\rightarrow \text{HCO}_3^- \downarrow / \uparrow$
 $\downarrow$
 mixed event

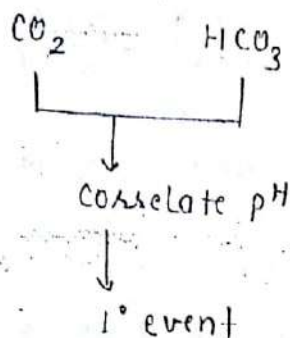
(metab. compensⁿ takes time but here in acute presentⁿ HCO_3^- is changed, so it is mixed event)

⑤ Chs. Resp. event $\rightarrow \text{HCO}_3^- \text{ (N)}$
 $\downarrow$
 It is mixed disorder

⑥ Both arrow in same direcⁿ —



Step-2.



ex - $p^H = 7.1 (\downarrow)$

$HCO_3^- = 10 \downarrow$
$PCO_2 = 22 \downarrow$

→ correlate p^H so it is 1° event

↓
this is compensatory

ex - $p^H = 7.2 (\downarrow)$

$HCO_3^- = 34 \uparrow$
$PCO_2 = 98 \uparrow$

→ this is compensatory

→ correlate $\bar{c}$ acidosis (p^H)

↓
it is 1° event

- $p^H = 7.4 (N)$

$HCO_3^- = 10 (\downarrow)$
$PCO_2 = 15 (\downarrow)$

Acc. to clinical data

(31)

Step-3 - Appropriate compensation -

(i) met. acidosis - $\downarrow \text{HCO}_3^- (1^\circ)$ $\downarrow \text{PCO}_2$ (comp.)

$$\boxed{\Delta \text{PCO}_2 = 1.2 \times \Delta \text{HCO}_3^-}$$

ex- $\text{pH} = 7.1$

$\text{HCO}_3^- = 10 \downarrow \Rightarrow$ correlate $\bar{c}$ $\text{pH} = 1^\circ$ event

$\text{PCO}_2 = 20 \downarrow \rightarrow$ comp.

$$\begin{aligned} \Delta \text{PCO}_2 &= 1.2 \times (25 - 10) \\ &= 18 \end{aligned}$$

So PCO_2 should fall 18 for this change in HCO_3^- .

$$(N) \text{PCO}_2 \approx 40$$

$$= 40 - 18 = 22 \pm 3$$

$$\boxed{\text{PCO}_2 = 19 - 25}$$



On this range we can assume that compensation occurs is proper: as the $\text{PCO}_2 \approx 20$ which fall in this range.

So here problem is met. acidosis, & Resp. sys.

is (N)

ex-2. if $PCO_2 = 30$

then pH ~~will~~ it is out of range of 7.35 - 7.45

it signifies there is resp. acidosis also along w/ pathology.

ex-3. if $PCO_2 = 7$

it is out of range = 7.35 - 7.45

→ it signifies that pt. has resp. alkalosis (bic ↓ PCO_2) also along w/ metabolic acidosis

(2) met. alkalosis — here problem is $\uparrow HCO_3^-$ (1°)
compensⁿ = $\uparrow PCO_2$

$$\boxed{\uparrow \Delta PCO_2 = 0.7 \times \Delta HCO_3^-}$$

(3) Resp. acidosis — $\uparrow PCO_2$ (1°)
 $\uparrow HCO_3^-$ (compensⁿ)

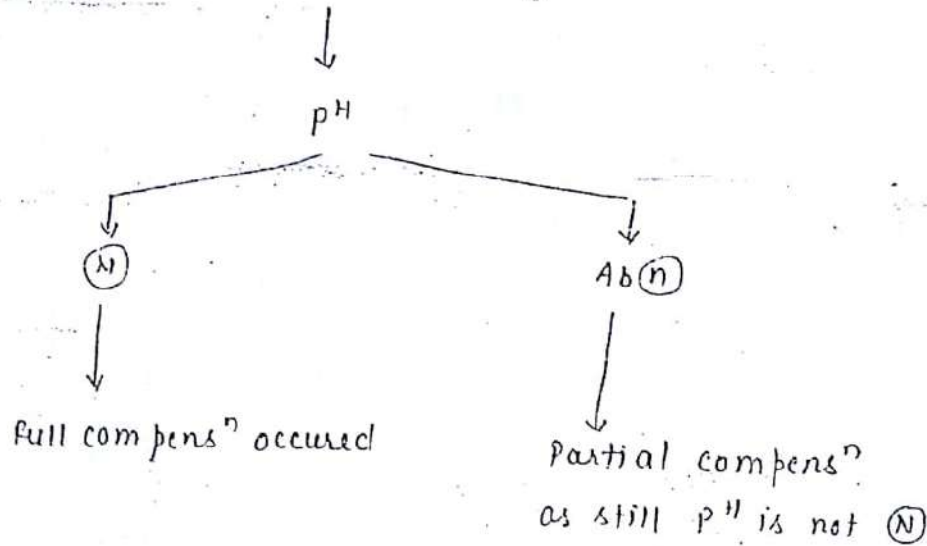
$$\boxed{\uparrow \Delta HCO_3^- = 0.4 \times \Delta PCO_2}$$

(4) Resp. alkalosis — $\downarrow PCO_2$ (1°) $\downarrow HCO_3^-$ (comp.)

$$\boxed{\downarrow \Delta HCO_3^- = 0.5 \times \Delta PCO_2}$$

(32)

Step-4 — Applicable for single event



Step-5 — mandatory — Anion gap measurement

→ As it can be the only evidence of met. acidosis/alkalosis which is going on.

Q. $pH = 7.21$ ($\downarrow$)
 $HCO_3^- = 35$ ($\uparrow$)
 $PCO_2 = 12$ ($\uparrow$) — 1^o event = Resp acidosis

$$\uparrow HCO_3^- = 0.4 \times PCO_2$$

$$\approx 0.4 \times 70$$

$$\approx 28$$

$$28 \neq$$

$$\textcircled{N} HCO_3^- = 25$$

$$= 2.5 + 28 = 53 \pm 3$$

$$\text{expected } HCO_3^- = 50 - 56$$

Here HCO_3^- is $\downarrow$ than expected

$\Rightarrow \therefore$ it is metabolic acidosis mixed to

Resp acidosis.

(23)

Q. $pH = 7.1$ ($\downarrow$) Acidosis

$HCO_3^- = 10$ ($\downarrow$) $\rightarrow$ metabolic acidosis (1°)

$PCO_2 = 21$ ($\downarrow$) $\rightarrow$ comp. $\downarrow PCO_2$

$$\downarrow \Delta PCO_2 = 1.2 \times 15$$

$$= 18$$

For this $\downarrow 10 HCO_3^-$, $18 PCO_2$ should be decreased.

$$\therefore 40 - 18 = \underline{22}$$

$$\therefore 22 \pm 3 = 19 - 25$$

Here PCO_2 fall in this range so it is not a mixed event, it is single metabolic acidosis with partial compensation.

Q. $p^H = 7.51 \uparrow$ — alkalosis

$HCO_3^- = 25$ (N)

$PCO_2 = 18 \downarrow \rightarrow$ Resp. alkalosis

$\rightarrow$ Here HCO_3^- is (N) in a resp. event

$\downarrow$

$\therefore$ it is acute resp. alkalosis

Q. a pt. chronic ds. $\rightarrow$ shows mixed ds.

1° — Resp. alkalosis ($PCO_2 \downarrow$)

$\downarrow$

So HCO_3^- should also fall

$\downarrow$

But HCO_3^- here is (N)

$\downarrow$

So here pt. has metabolic alkalosis

Q. $p^H = 7.46 \uparrow$ (alkalosis)

$HCO_3^- = \uparrow$

$PCO_2 = \downarrow$

mixed — Resp. alkalosis + met. alkalosis
($\downarrow PCO_2$) ($\uparrow HCO_3^-$)

(31)

Q. $p^H = 7.24$ ($\downarrow$) acidosis

$PCO_2 = 7$ ($\downarrow$)

$HCO_3^- = 12$ ($\downarrow$) — metabolic acidosis is 1st event

$$\begin{aligned}\Delta pCO_2 &= 1.2 \times \Delta HCO_3 \\ &= 1.2 \times 13 \quad (25 - 12) \\ &= 15.6 \\ &= \underline{15}\end{aligned}$$

$$4.0 - 15 = \underline{25} \pm 3$$

But 7 not in range, it is more $\downarrow$, ^{wt}

$\therefore$ it is Resp. alk.

Q. $p^H = 7.56$ ($\uparrow$ alk).

$HCO_3^- = 41$ ($\uparrow$) — 1st metabolic alkalosis

$PCO_2 = 42$ (N) But CO_2 is (N), it should ideally $\uparrow$.

so it is Resp. alkalosis & metabolic alkalosis.

Infusion rate

$$\begin{array}{c} \mu\text{g/kg/min} \\ \downarrow \\ \text{ml/hr} \end{array} = \frac{\text{Dose}(\mu\text{g}) \times \text{wt}(\text{kg}) \times 60 \times \text{vol.}}{1000 \times \text{amount}(\text{mg})}$$

ex. Dopamin at rate of 10 $\mu\text{g/kg/min}$ → multiply by 60 to get in hr

2 vial of dopamin each contain 200 mg dopamin

NS = 500 ml

wt of pt = 80 kg

Infusion rate = ?

$$= \frac{10 \times 80 \times 60 \times 500}{1000 \times 400}$$

$$= \frac{8 \times 3 \times 5}{2} = 60 \text{ ml/hr} \times \frac{DF}{60}$$

* Adult - Drip factor = 15

15 drop contribute to 1 ml

* Pediatric - DF = 60

* Blood drip set - DF = 4

(35)

$$60 \text{ ml/hr} \times \frac{15}{60} = 15 \text{ min}$$

Q. Dobutamin = $10 \mu\text{g/kg/min}$

wt = 80

calculate drip rate

1 vial of dobutamin containing 250 mg dry

vol = 250 ml NS

$$\begin{aligned} \text{I.R.} &= \frac{10 \times 80 \times 60 \times 250}{1000 \times 250} \times \frac{\text{D.R.}}{60} \\ &= 48 \times \frac{15}{60} = 12 \end{aligned}$$

$\therefore 12 \text{ drops/min}$

I.R. = 48 ml/hr

Q. NTG = 50 μ g / min

wt = 80 kg

1 vial of NTG containing 25 mg in 5 ml.

Vol = 45 ml NS

Infusion rate = ?

$$I.R = \frac{\text{Dose}(\mu\text{g}) \times \text{wt} \times 60 \times \text{vol}}{1000 \times \text{amt}(\text{mg})}$$

$$= \frac{50 \times 80 \times 60 \times (45+5)}{1000 \times 25}$$

$$= \frac{50 \times 60 \times 50}{1000 \times 25} = \frac{60}{10} = 6$$

$$\boxed{IR: 6 \text{ ml/hr}}$$

(26)

Q. NA — 20 $\mu\text{g/hr}$

wt = 80 kg

1 vial of NA containing 4 mg in 2 ml.

NS = 48 mL

J.R = ?

$$J.R = \frac{\text{Dose}(\mu\text{g}) \times \text{wt} \times 60 \times \text{vol}}{1000 \times \text{amt}(\text{mg})}$$

$$= \frac{20 \times 80 \times 50}{1000 \times 4} = \frac{10}{40} = 0.25$$

$$J.R = 0.25 \text{ ml/hr}$$

Q. Dose = 10 mg/hr

4 vial = 20 mg

vol = 500 ml NS

wt = 80 kg

$$J.R = \frac{\text{Dose} \times \text{wt} \times 60 \times \text{vol}}{1000 \times \text{amt}(\text{mg})} \times \frac{DF}{60}$$

$$= \frac{10 \times 500}{20} = 250 \times \frac{15}{60} = 12$$

$\approx 15 \text{ drops/min.}$

Q. 1 mg / min

Dose = 300 mg (1 vial)
↓
in 2 mL of am

NS = 48 mL

wt = 80 kg

$$IR = \frac{\text{Dose} \times \text{wt} \times 60 \times \text{vol}}{1000 \times \text{amt}}$$

$$= \frac{1 \times 80 \times 50}{300} = 10$$

$$\boxed{IR = 10 \text{ mL/hr}}$$

(37)

$$\begin{aligned} \text{Q. } Na^+ &= 130 & S. Cl^- &= 103 \\ K^+ &= 5 & BUN &= 20 \\ Cl^- &= 96 \\ PCO_2 &= 24 \\ PO_2 &= 89 \\ HCO_3^- &= 14 \end{aligned}$$

$$\Rightarrow pH = 7.39 \downarrow$$

$$HCO_3^- = 14 \downarrow \text{ — 1' met. acidosis}$$

$$PCO_2 = 24 \downarrow$$

$$\begin{aligned} \Delta PCO_2 &= 1.2 \times \Delta HCO_3^- \\ &= 1.2 \times 11 = \underline{\underline{13.2}} \end{aligned}$$

$$40 - 13 = \cancel{27} \quad 27 \pm 3$$

$$= 24 - 30$$

$$\underline{PCO_2} = \bar{c} \text{ in range}$$

$$\text{Anion gap} = \cancel{130} - (\cancel{96} + \cancel{14}) \quad 130 - (96 + 14)$$

$$AG = 20$$

* ~~Partially compensated~~

* Full compensation

Q. → elderly, fever, UTI, DM/HT

$$Na^+ - 140$$

$$pH = 7.39$$

$$K^+ - 4$$

$$HCO_3^-$$

$$Cl^- - 106$$

$$PCO_2 = 24$$

$$HCO_3^- - 14$$

1° metabolic acidosis

↓
Based on history

$$AG = 140 - (106 + 14)$$

$$= 20$$

⇒ ↑ Anion gap & full compensation

Q. ♀, productive cough

$$Na^+ = 140$$

$$K^+ = 4$$

$$Cl^- = 102$$

$$pH = 7.30 \text{ (↓)}$$

$$PCO_2 = 38 \text{ (N)}$$

$$HCO_3^- = 18 \text{ (↓)}$$

} mixed

1° → metabolic acidosis

PCO_2 should be ↓ but it is (N)

↓
Resp. acidosis

Ans 1° metabolic acidosis mixed & Resp. acidosis

(38)

Q. 75 ♂, Diff. of breathing,

$$Na^+ = 140$$

$$K^+ = 4$$

$$Cl^- = 91$$

$$pH = 7.55 (\uparrow)$$

$$PCO_2 = 38 (N)$$

$$HCO_3^- = 33 (\uparrow)$$

metabolic alkalosis

⇒ PCO_2 should $\downarrow$ but it is not $\downarrow$

∴ Resp. alkalosis is assoc. w/ metabolic alkalosis

Q. 60 ♂, smoker, impending doom, SI

$$LVF \quad EF = 32 \%$$

$$Na^+ = 142$$

$$K^+ = 3.4$$

$$Cl^- = 88$$

$$HCO_3^- = 42 (\uparrow)$$

$$PCO_2 = 67 (\uparrow)$$

$$pH = 7.42 (N)$$

PCO_2 is $\uparrow$ ⇒ Resp. acidosis = 1^o event.

∵ HCO_3^- is also changed it shows problem is chronic resp. acidosis.

$$\begin{aligned}\uparrow \Delta \text{HCO}_3^- &= 0.4 \times \Delta \text{PCO}_2 \\ &= 0.4 \times (67 - 40) \\ &= \frac{0.4}{10} \times 25 = \underline{10}\end{aligned}$$

$$\begin{aligned}27 + 10 &= 38 \pm 3 \\ &= 35 - 41\end{aligned}$$

HCO₃⁻ $\bar{c}$ in (N) range

↓
∴ Resp. acidosis $\bar{c}$ full compensation.

Q. 60 ♀, known case of CKD, persistent vomiting

Na⁺ = 142

S. Cr = 4.0

K⁺ = 3.0

S. urea = 200

Cl⁻ = 95

pH = 7.42 (N)

PCO₂ = 40 (N)

HCO₃⁻ = 25 (N)

$$\begin{aligned}\text{Anion gap} &= 142 - (95 + 25) \\ &= 22\end{aligned}$$

↑ Anion gap ⇒ ↑ Anion gap met. acidosis

(39)

Solⁿ: Before vomiting - HCO_3^- must be $\downarrow$
 pH also $\downarrow$

$\Downarrow$

In vomiting there is loss of H^+ , Cl^- $\downarrow$

$\uparrow$ of HCO_3^- to (N)

level

$\downarrow$

This is b/c of vomiting (alkalosis),
once vomiting settle down, HCO_3^- will
again go down.

* This is actually a double mixed event i.e.,
metabolic acidosis & metabolic alkalosis,

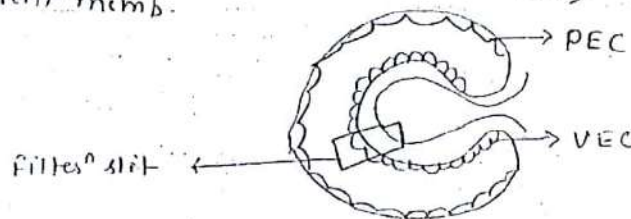
Glomerular Pathology

Nephritic

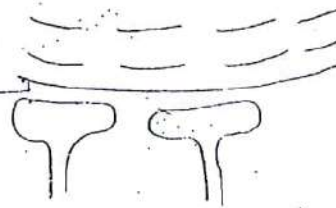
Nephrotic

1) Pathology → Endothelium & ~~epithelium~~ Basement memb.

1) Path — VEC (visceral epi- cells)



type 4 collagen
B.M
collagenases
non collagen.
Antigenic



2) CIF → ...

Hematuria = 4+

(> 3 RBC/HPF)

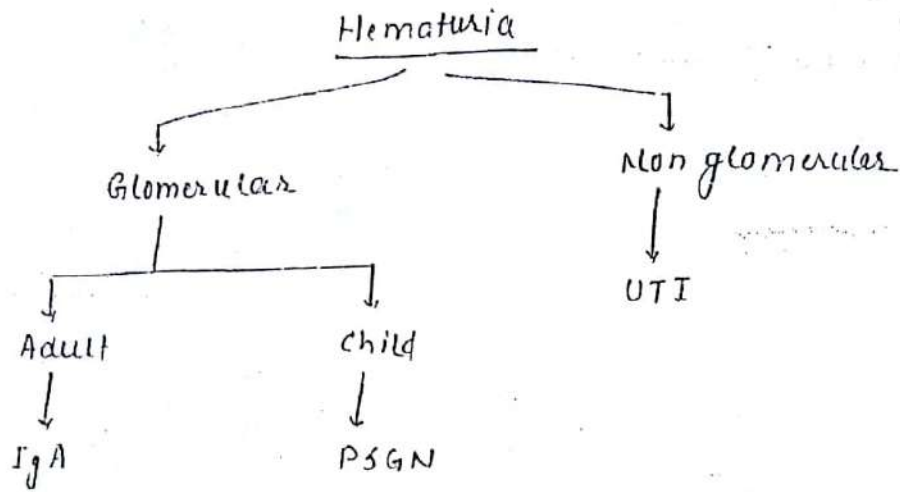
↓
microscopic Hematuria

Hematuria = 1+/-

* mce of Hematuria → UTI

* mce of glomerular Hematuria →

(40)



* Dysmorphic RBCs are sign of glomerular disease

* In non-glomerular causes RBCs are isomorphic

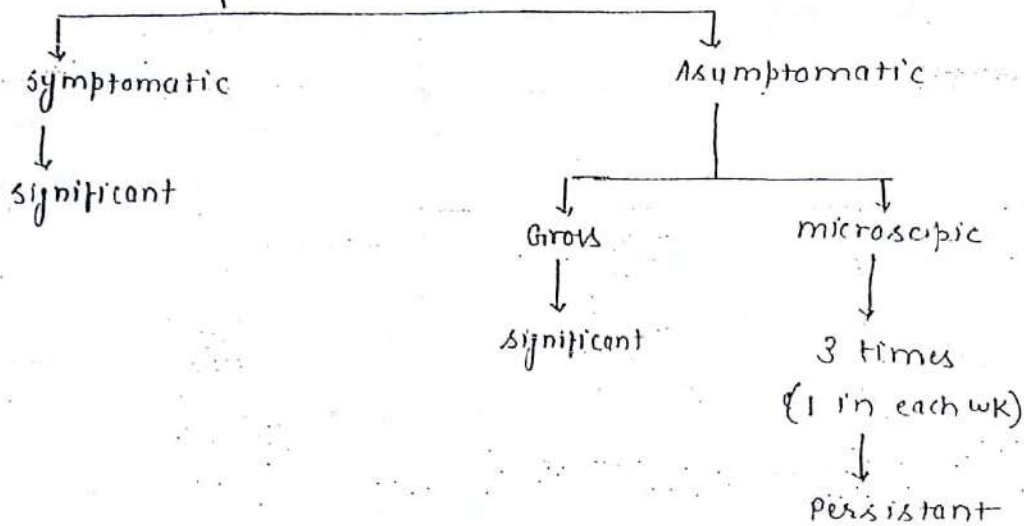
Glomerular :-
 • Dysmorphic RBC
 • RBC cast

Dangerous sign of Hematuria —

- 1) * Painless Hematuria in elderly
- 2) * chronic smoker
- 3) H/O occupⁿ in dye / rubber industry
- 4) Pelvic irradiation
- 5) cyclophosphamide exposure

Significant Hematuria

(+) Gross Hematuria



* Proteinuria → $< 150 \text{ mg/day}$ (N) passed in urine
Jamm Horsfall protein (tubular)

Albuminuria — $\uparrow$ cause Sys. HTN > D.M

microalbuminuria

$30 - 300 \text{ mg/day}$



— assoc $\bar{e}$ $\uparrow$ risk of
CVD & stroke.

overt
~~micro~~albuminuria

$> 300 \text{ mg/day}$

* TCC — ACE $\ominus$

Nephritic

- 1) Path
- 2) • Hematuria - +++
- 3) • Proteinuria - ++
($< 2.5 \text{ gm/dL}$)
- 4) • AKI - ++++
- 5) BP - $\uparrow\uparrow\uparrow$

Cause of edema -

- $\downarrow$ oncotic pressure
- $\uparrow$ hydrostatic pressure

overflow hypothesis

Nephrotic

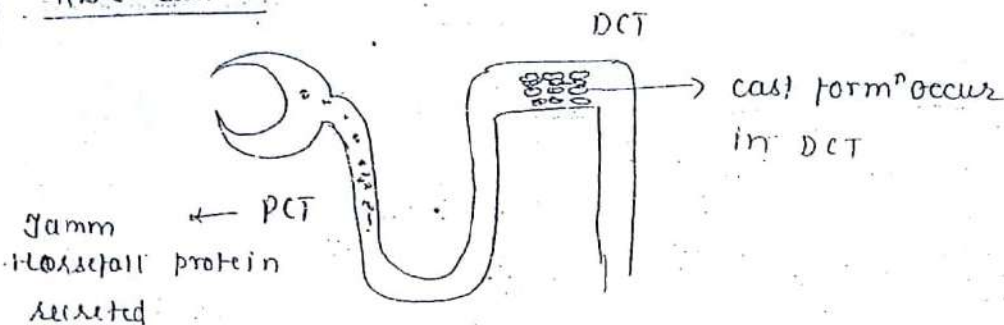
- +/-
- ++++
($> 3.5 \text{ gm/dL}$)
- AKI - +/-
- 5) $\uparrow\uparrow$
- 6) edema
- 7) hyperlipidemia
- 8) lipiduria
- 9) Thrombotic tendency:
mc: Renal v thrombosis

underfill hypothesis

Gamm Horse tail protein

→ They are formed by PCT & help in formⁿ of cast.

RBC cast



Types of cast

Cellular

- 1) RBC cast — glomerulonephritis (specific)
- 2) WBC cast — • pyelonephritis
• Acute interstitial nephritis
- 3) Epi. cast — • ATN

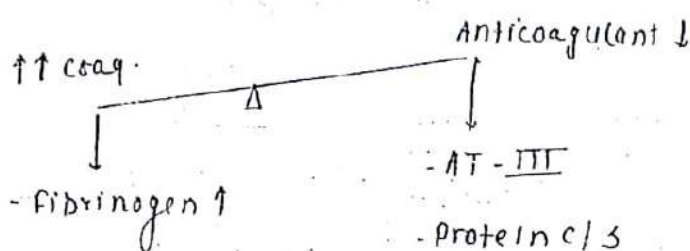
Acellular

- very specific
- 1) Broad waxy cast — • CKD
 - 2) muddy brown — ATN
 - 3) Hyaline cast — nm sp.
 - 4) Fatty cast — Lipiduria
↓
Maltese cross

(42)

Thrombosis in Nephrotic syndrome :-

Antic Δ coag



	<u>Viscosity</u>	<u>Aml (%)</u>	
* Globulin — 42 %		38% ✓	Both of these contribute more to viscosity
* Albumin — 36 %		55%	
* Fibrinogen = 22 %		5-7% ✓	
↓	max ^m contribution to viscosity.		

→ so if Albumin is ↓ ^{sign} the other protein will
- which contribute more to viscosity
↑ & there will be hyperviscosity. → so ↑ risk
of thrombosis.

→ if Fibrinogen ↓ → Viscosity ↓ → ↓ Thrombosis

* In disabling chronic liver disease & liver failure
↓
↓ tendency of coagulⁿ

* main contributor for thrombosis in Nephrotic is ↓ Albumin & ↑ Fibrinogen.

Nephritic

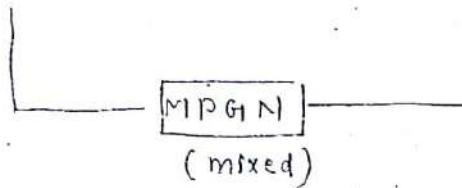
- ① RPGN (100%)
- ② PSGN (>95%)
- ③ IgA nephro. (>60%)

* In nephritic, pathology is proliferative (↑ cells)

Nephrotic

- ① MCD (100%)
- ② FSGS (>95%)
- ③ MGN (>80%)

- Non proliferative pathology



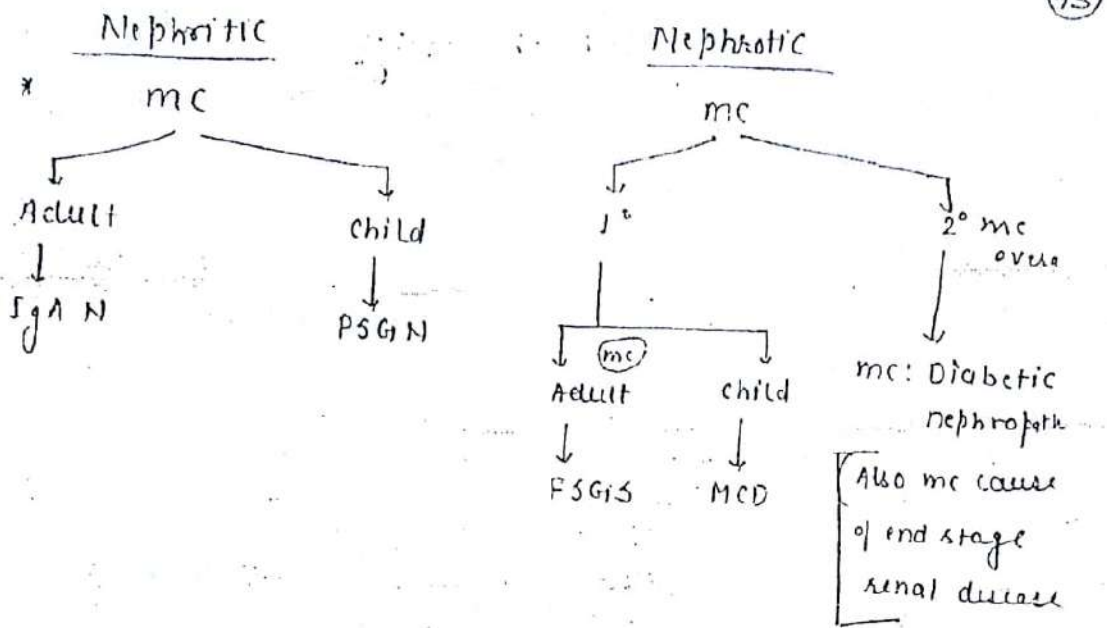
2° causes —

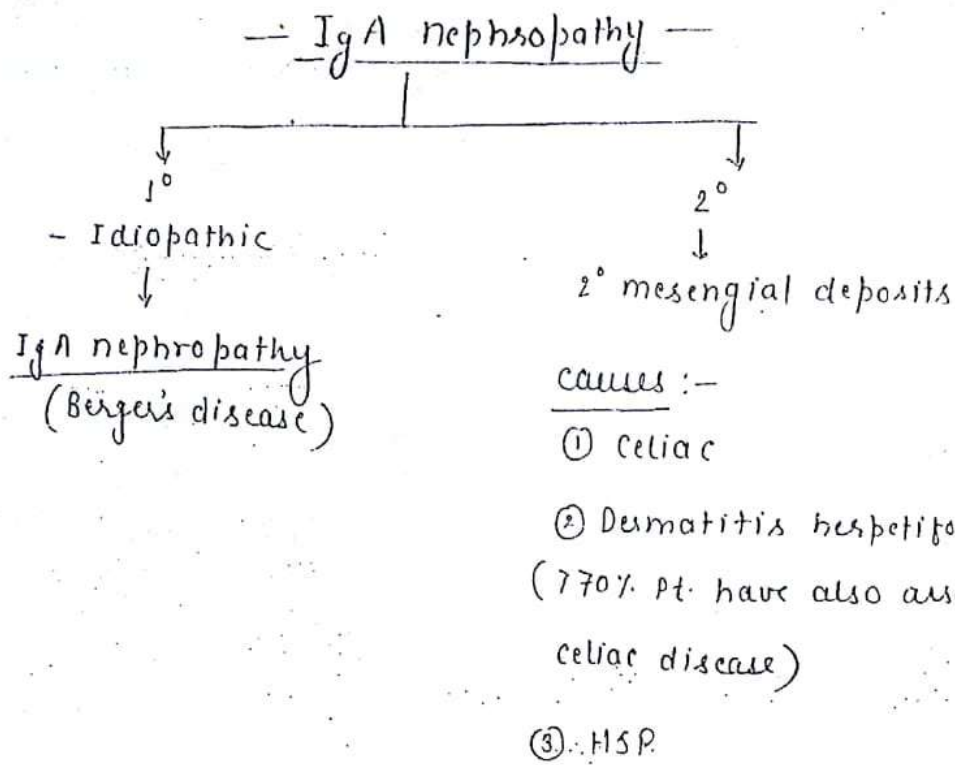
Lupus nephritis

→ They don't presents like other. They have own features.

- ④ • Diabetic nephropathy
- ⑤ • Amyloid

(4/3)





Celiac disease :- Gluten hypersens.

- TTG Ab. → gliadin (Tissue transgluten Ab)
- Food :- BROW (Barley, rye, oat, wheat)
↓
contain

DH :- H10 diarrhoea (± celiac disease)

- Blistering (very itching)
- B/c of itching blistering may not be seen.
- Seen on elbow (extensor aspect)

(44)

Inv: Bx - Immunofluorescence

TTG deposition ← at dermal papilla → IgA formed against TTG

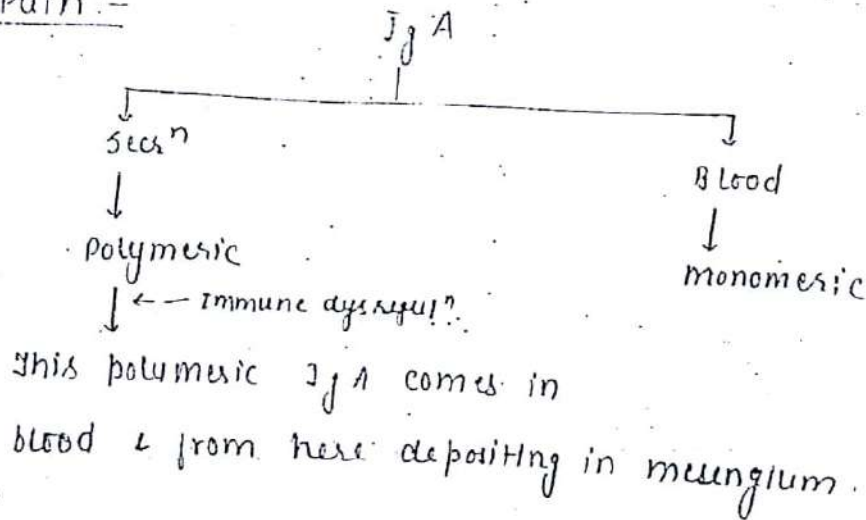


- It is the disease of dermoepidermal junction.

IgA nephropathy -

H/O URT → Hematuria (gross)
← 1 wk

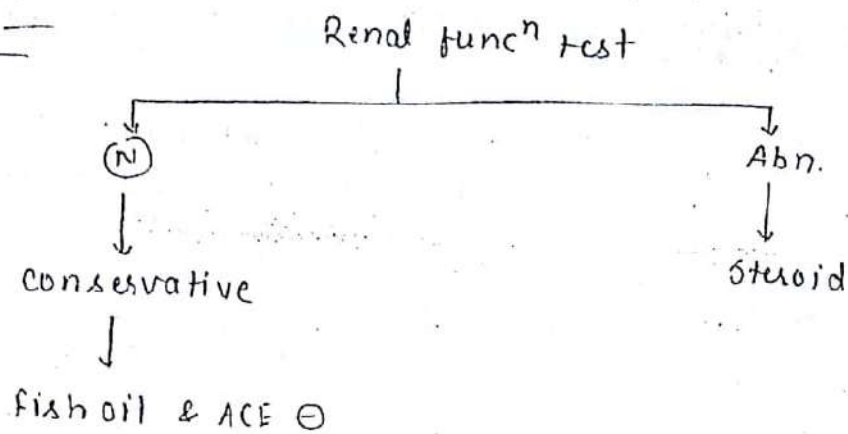
Path:-



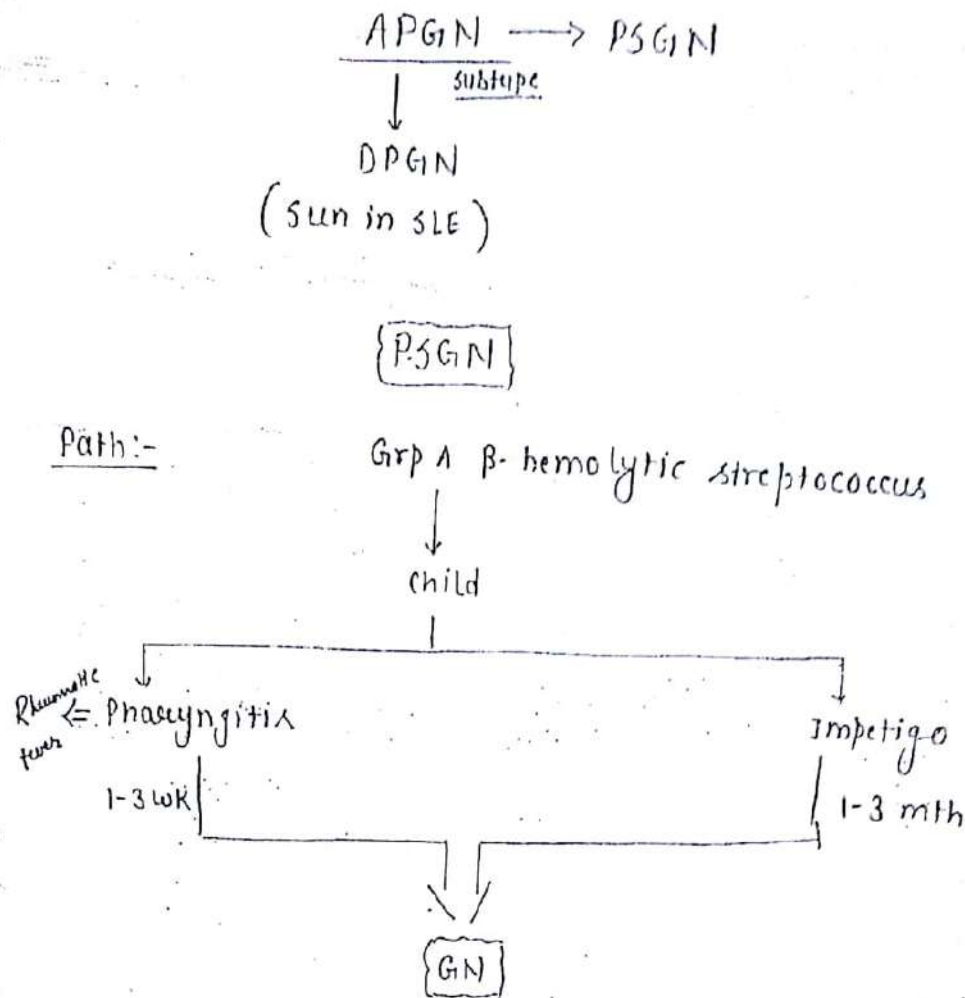
* IgA₁ is pathogenic (nephritogenic Ig)

* on Bx → light micro:-

Rx —



(15)



C/F- Asymptomatic hematuria (gross)

Bx- show proliferⁿ $\rightarrow$ APGN

↓

entire glomerulus proliferate (glomerular hypercellularity)

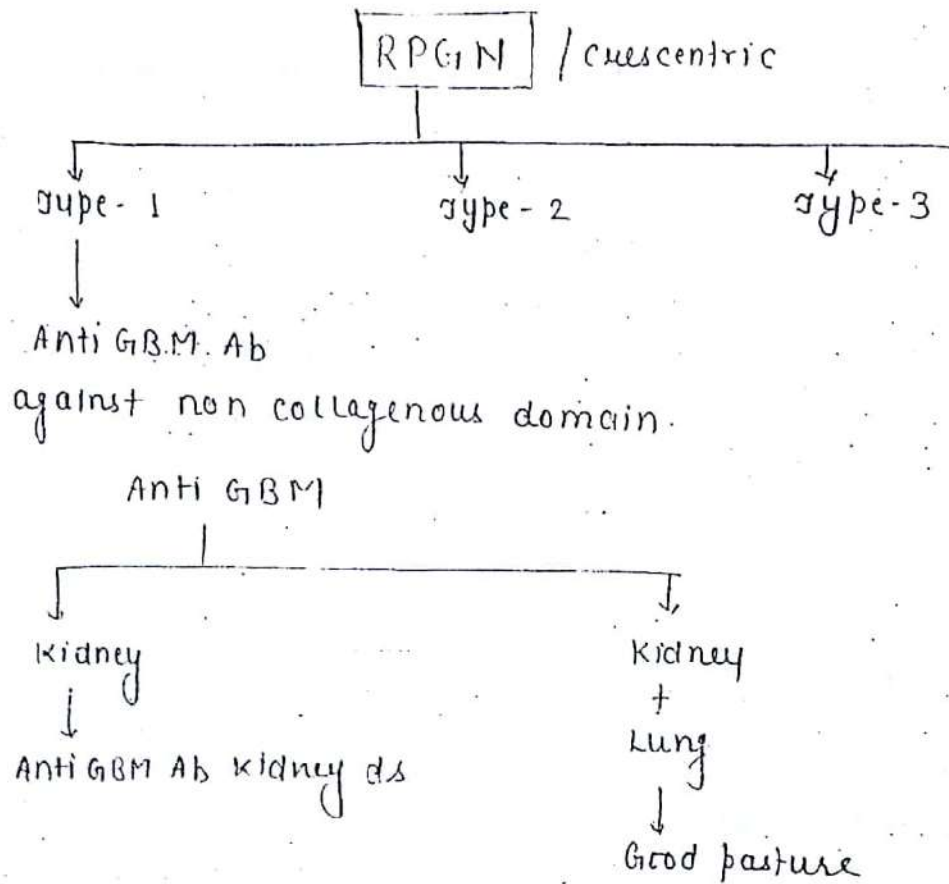
↓

>100 nucleus / glomerulus

* Also mesangial hypercellularity is there but it is not a specific feature.

R_x — • supportive R_x

- great infecⁿ
- ACE ⊖
- edema — Diuretics



Type-2 - Immune complex deposits

ex- SLE, PSGN, IE

(46)

Type-3-

Pauci immune

↓
ANCA associated

↓
c-vasculitis

↓
2° RPGN

↓
CANCA > P

↓
c-ovl vasculitis

↓
1° RPGN

↓
PANCA > C

C/F- Nephritic presentⁿ

Bx - light micro! — crescents seen

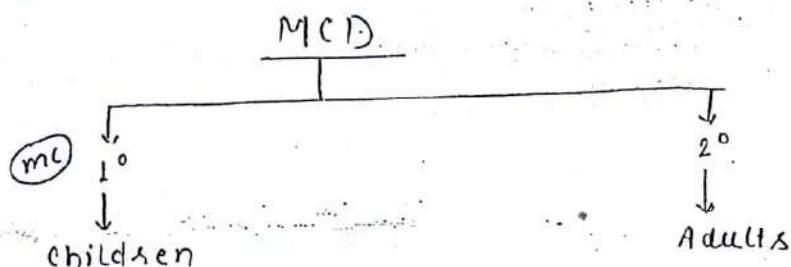
↓
clump of epithelial
cell (parietal epi. cell)

↓
it is an emergency to save kidney

↓
together c fibrin.



Rx - immediate cyclophosphamide.



causes - ① NSAID
② lymphoma/
Leukemia.

* Analgesic nephropathy → mc. it is MCD

Clf - o Asymptomatic edema. (subacute)
o BP. (N) (2° MCD may have HTN)

urine analysis - Proteinuria (4+)
↓
24 hr urine collectⁿ done for proteinuria: highly selective i.e. predominantly albumin is lost

Bx - Light microscopy → normal

EM - effacement of foot process of podocyte.
(seen in all cases of nephrotic synd.)
But in MCD, it is the only finding.

Rx - o steroid

Bx:- 1) tip variant → Best prognosis

2) cellular

3) Peritubular

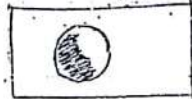
OK

4) collapsing → worst prognosis

FSGS

F - Focal - $< 50\%$ glomeruli involved
($> 50\%$ → diffuse involvement)

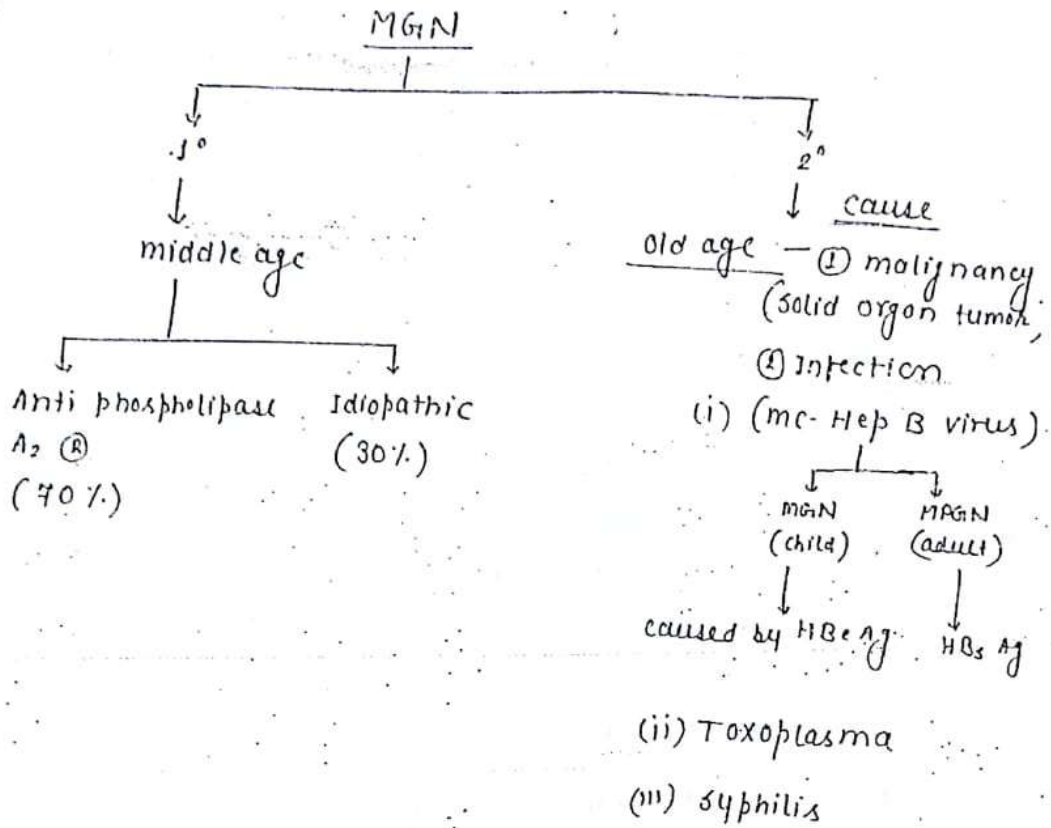
S - Segmental -



S - sclerosis - Deposition of Hyaline

R - Do not respond

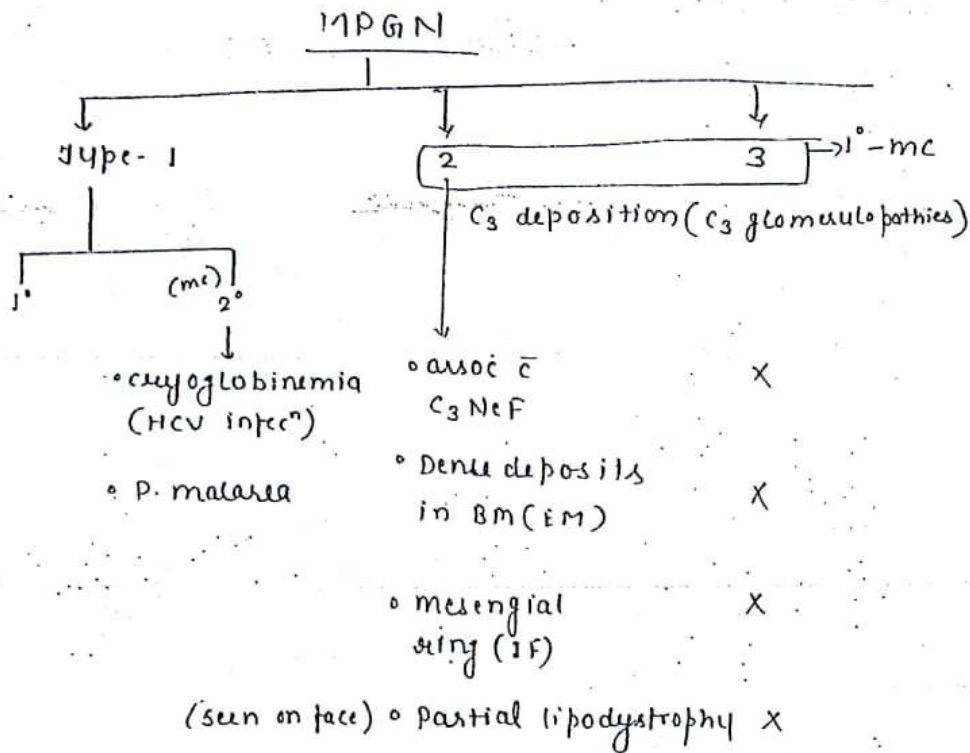
(48)



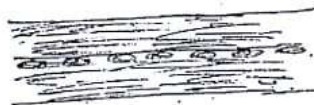
B_X → LM → severe thickening of BM (Duplication)

R_x — for 1° → steroid
immunosupp

2° — treat cause



Bx - BM thickening
+ cell proliferation



Gram track appearance

Rx - 1° ← steroid
immunosuppressant

2° - Great cause

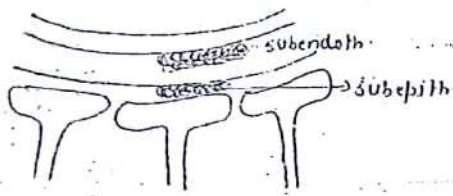
leprosy me causes — Amyloidosis

(49)

Electron microscopy

① IgA nephropathy — mesangial deposits

② PSGN — initially — subendothelial deposition of immune complex



↓
Later — subepithelial

↓
Classic site of deposition in MPGN

* The deposition is not in any specific manner. They are hump like (lumpy) deposit. Also the deposition is haphazard.

③ MPGN —

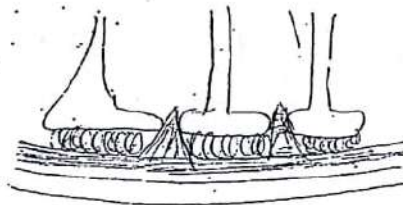
Epimembranous spike

& dome appearance

subepithelial deposit

+

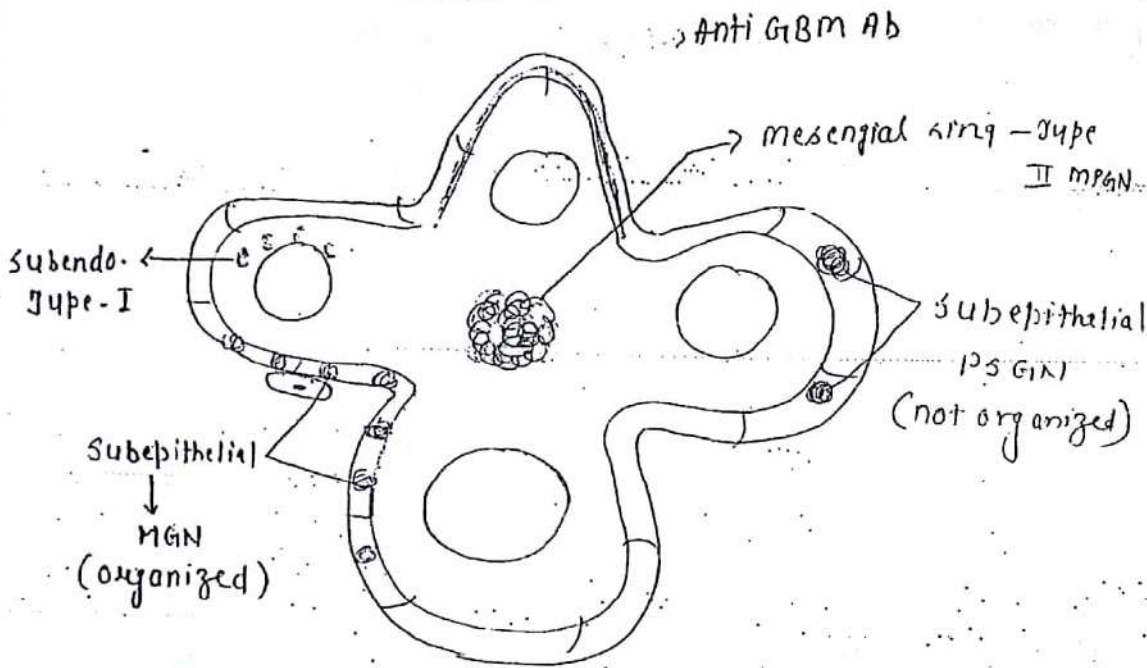
proliferation of BM



④ MPGN — I → subendothelial deposits

II → intramembranous → dense deposit (IDD)

Immunofluorescence



① PSGN → starry sky appearance
subepi



② MGN → • Subepithelial
• Irregular



③ Anti GBM Ab — Regular smooth deposition



(50)

(4) Type 1 MPGN —

(5) Type 2 MPGN — mesangial ring

(6) IgA nephropathy — mesangial deposition

* All deposits are

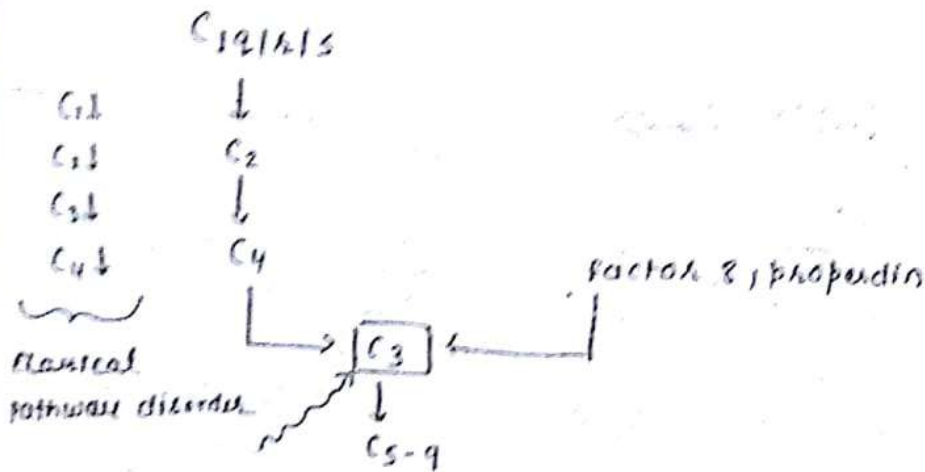
(i) granular except Anti GBM Ab

(ii) IgG ± C₃ — except IgA nephro.
Here IgA deposits

(iii) -ve IF — (i) MC

(ii) FSGS

(iii) Pauci immune (T-3 RPGN)



Classical + Alt

- SLE
- MPGN-I

Alt

- RPGN
- MPGN-II

(N) Complement seen in —

- (1) MCD.
- (2) FSGS.
- (3) RPGN — except type II
- (4) 1° MPGN (2° MPGN — ↓ complement)
 - ↳ ex HBV
 - ↳ SLE
- (5) IgA nephropathy

↓ complements —

(51)

① cryoglobulinemia

② IE

③ shunt nephritis

④ cholesterol emboli

Notes:

For pregnant ♀ $>3 \text{ gm/dL}$ is nephrotic range
proteinuria.

AKI

① $\uparrow$ s.c.r. by $\geq 0.3 \text{ mg/dL}$ in 48 h from baseline

② s.c.r. $\uparrow$ by 1.5 times of baseline

③ $\downarrow$ urine output [$<0.5 \text{ mL/kg/hr}$] $\times 6 \text{ hr}$

$\Rightarrow$ Any 1/3

Markers -

- * cystatin C tells about renal status better than creat.
- * NGAL
- * Kidney injury molecule 1 (KIM-1)
- * L-FABP
- * osteopontin
- * clustarin
- * Alanine amino peptidase
- * ALK. phosphatase
- * IL-18

(52)

Pre renal	Intrinsic renal	Post-renal (USG)
↓ Any condition causing hypoperfusion → severe/perist	→ Acute tubular necrosis ex @ post op hypotension ② Aortic rupture ③ - clamping renal A ⇓ All these are severe hypoperfusion condition. → ATN	↓ • obstructive uropathy • Retroperitoneal fibrosis (causes B/L Hydro-nephrosis) AKA Armond's ds
- Diarrhoea ↓ if not treated		
* Here kidney (N) but only GFR ↓ (DIE ↓ perfusion)	Here kidneys are damaged	
- Tubular funcⁿ (N) → • solute reabsorpⁿ → • urine concentrⁿ	- Tubular funcⁿ lost } lost	

	<u>Prerenal</u>	<u>Intrinsic renal</u>
1) Specific gravity	low RBF ⊕ RAAS ↓ more H ₂ O absorp ⁿ so conc urine is passed > 1.020	< 1.010
2) urine osmolality	> 500	< 500
3) urine Na ⁺	U _{Na} ⁺ < 10	> 20
4) FE _{Na} (fractional excretion of Na ⁺) or Renal failure index (RFI)	< 1	> 1
5) FE _{urea}	< 35	> 35
6) $\frac{\text{BUN}}{\text{creatinine}}$ $\text{BUN} \approx \frac{\text{urea}}{2}$	↑↑↑ (DIT ↑ reabsorp ⁿ) = ↑ mild ↑ > 15	↑↑↑ (DIT poor reabsorp ⁿ) ↑↑ < 15
7)	hyaline cast (non specific)	epithelial cast (nm sp)

(32)

8) causes

1) septic shock

if not treated

→ ATN

↓
Pooling of blood in
pulmonary1) contrast induced
nephropathy

↓

↓ V-R

2) cholesterol emboli

↓

↓ CO

↓
Hypoperfusion

② Hepatorenal syndr.

* consider septic shock when pt. not responding
to resuscitation & fluid.

→ pt. is sepsis + Hypotension

↓
1st — Fluid resuscitation.↓
Inotropes (NA)HRS → liver causing renal failure.

→ If pt. is on diuretics → stop

→ Give albumin & replace volume.

→ Remove any nephrotoxic drug.

still pt. having
renal failure↓
[AKI - HRS]

* rule of renal failure in hepatic failure — sepsis

- HRS is very rare.

R_x — Deslipressin + albumin
↓
causes splanchnic vasoconstriction & ↑ res-
-perfusion.

Sp. causes of ATN —

CIN

- ① • H₂O contrast exposure & contrast is the main problem specially ionic/osmolar contrast.
- ② CIF — ↑ S.Cr
- ③ Timing — < 2 days (12 hr)
- ④ Asymptomatic
- ⑤ Inv → qf is benign.
— NO Bx
- ⑥ complement (N)

Cholest. emboli

- ① catheter is the problem
- ② ↑ serum creatinine
- ③ > 2 day [5-7 day]
- ④ Non specific symptoms —
• Arthralgia
• Fever / malaise.
Specific —
• cyanosis of toes
• Hollenhorst plaque
- ⑤ Bx done → shows
thrombi/emboli in capillary
complement ↓

(54)

⑦ Prevention —

- IV fluid (NS)

- N-acetyl cysteine (continuous)

⑧ Avoid femoral route

⑨ B_x — supportive⑩ B_x — same as AKI

No Hemodialysis

B/c if pt. has ↑ s-cr. he
will never come back to

⑪ level. but if pt. has

⑫ cr → there is no problem
they will come to ⑪ level

↑ s-cr.

⑬ s-cr.

2.1

0.6

↓

↓

3.2

1.2

↓

↓

2.5

1.2

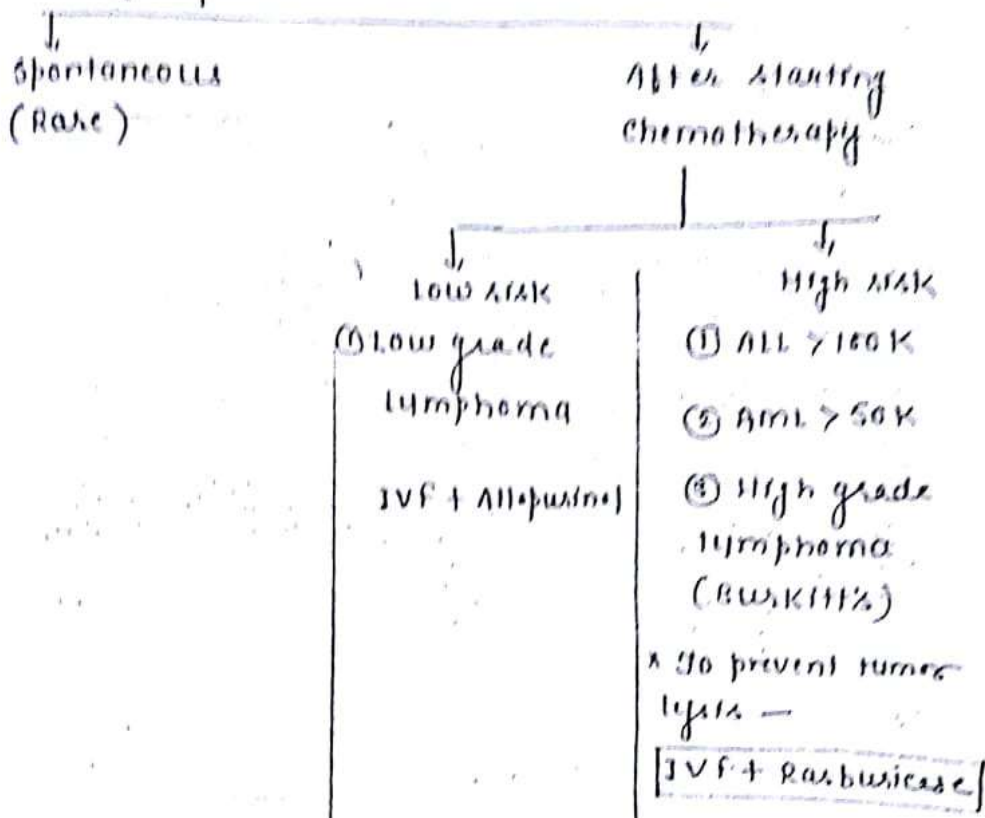
↓

↓

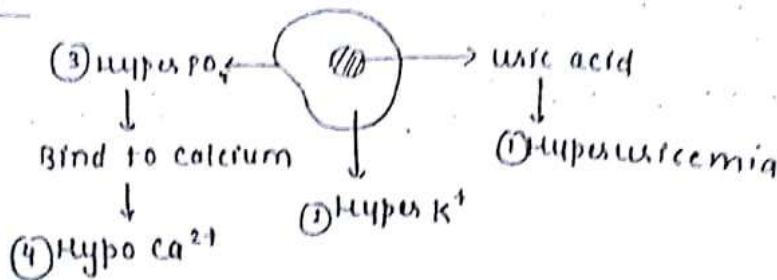
2.1

0.6

Tumor lysis syndrome:-



CIF -



Caixob Bishop criteria

(55)

R_x — ① For prevention → 1. urinary pH (>7)

- But once tumor lysis starts, urinary alkalinⁿ should be stopped.
- Give Rasburicase
- Hemodialysis

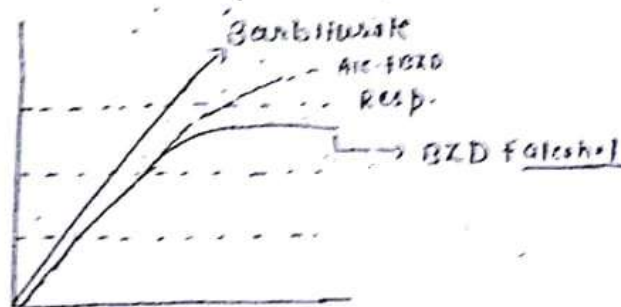
Rhabdomyolysis —

Risk factors :- ① Crush injury

② Prolonged Ischemia (compartment syndrome)

③ Snake bite

④ Prolonged Immobilization
(alcohol intoxication, BZD)

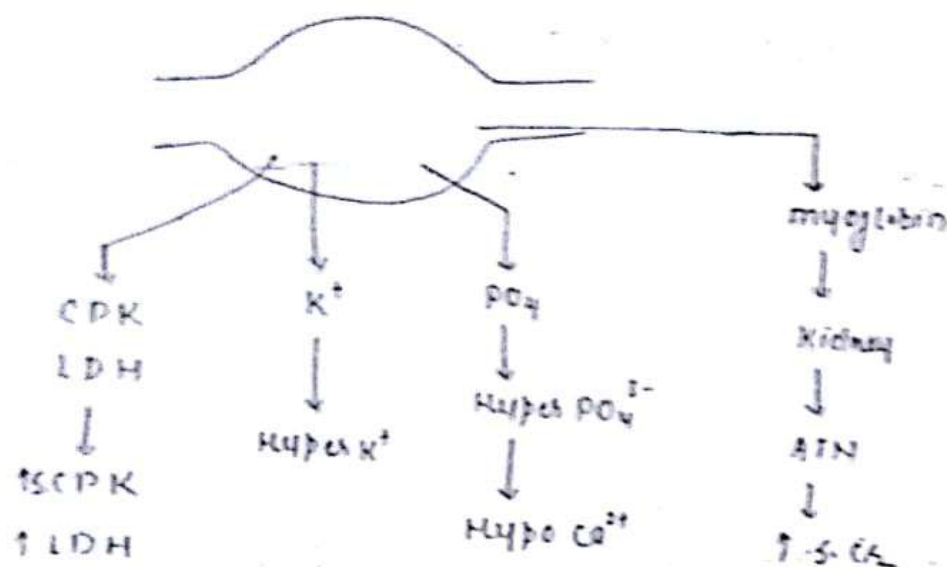


⑤ Drugs :- statins

- fibrates
- Sch

⑥ status epilepticus

⑦ High K⁺ → triggers muscle for K⁺ release
↓
Rhabdomyolysis



Inv -

For Δ sis — ① ↑S-CPK

② urine myoglobin ++

Indirect method to detect myoglobin

Dipstick — +++ Blood

microscopy — - RBC

Rx -

- Hemodialysis
 - Urine alkalization
 - mannitol
-] controversial

Aminoglycoside induced ATN is non oligemic

Stages of ATNI

Initiation

① urine output ↓

② S-Cr ↑

Oliguria — urine

output < 400 ml

- This is applicable
for person & 2 kidney

Maintenance

① urine output ↓↓↓
(Anuria)

Anuria —

• For ① person

↓
urine < 100 ml

• For CKD - 2-3

↓
urine < 50 ml

• For CKD 3-4

↓
no urine output

② S-creatinine ↑↑↑
(Peak)

③ Uremic features
(gastroenteritis, vomiting,
Hiccups)

④ Electrolyte — K^+ ↑
↑ Anion gap
metabolic acidosis

⑤ Volume overload

P_r — fluid restriction
- Hemodialysis

Resolving

- Same pt go for
resolving phase

① urine output ↑↑
(Paradoxical
polyuria)

② S-creatinine ↓

↓
③ Stop getting
uremic symptom

④ If loss of electrolyte
in polyuric phase

↓
Hypo K^+
Hypo Na^+

↓
Dehydrⁿ

⑤ - ↑ fluid given

- HD X

Indicⁿ of HD — in AKI —

- ① Hyper K^+ ≥ 6.5
- ② Refractory vol. overload $\rightarrow$ Pul. edema not responding to diuretic

Relative —

- ① met. acidosis ($P^H < 7.3$)
- ② severe hyperthermia
- ③ uremic symptoms —
 - i) uremic encephalopathy
 - ii) ur. pericarditis
 - $\downarrow$
 - can transform to hemorrhagic pericarditis
 - $\downarrow$
 - causing tamponade
 - $\downarrow$
 - $\therefore$ absolutely HD is required
 - iii) uremic platelet dysfunction

④ Dialysable drugs: —

- B — Barbiturate
- L — Lithium
- I — Isoniazide
- S — Salicylates
- T — Theophylline / Aminophylline
- E — ethylene glycol / methanol
- R — carbamazepine

(57)

CKD

* Any str. or functional problem in kidney for
> 3 mth.

Evidence of CKD

- 1) Contracted kidney in USG (< 7 cm in its max^m dimension)
- 2) corticomedullary differentiation (CMD) lost

Any pt. w new raised $\uparrow$ creatinine should be treated as AKI b/c in AKI we extensively treat pt. to reverse the condition.

Stages — • MDRD formula

• CKD EBT formula

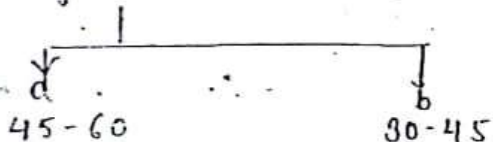
Based on GFR

Stage-1 - $\text{eGFR} > 90$

- No functional prob.

Stage-2 - $\text{GFR} = 60 - 90$

Stage 3 - $\text{GFR} = 30 - 60$



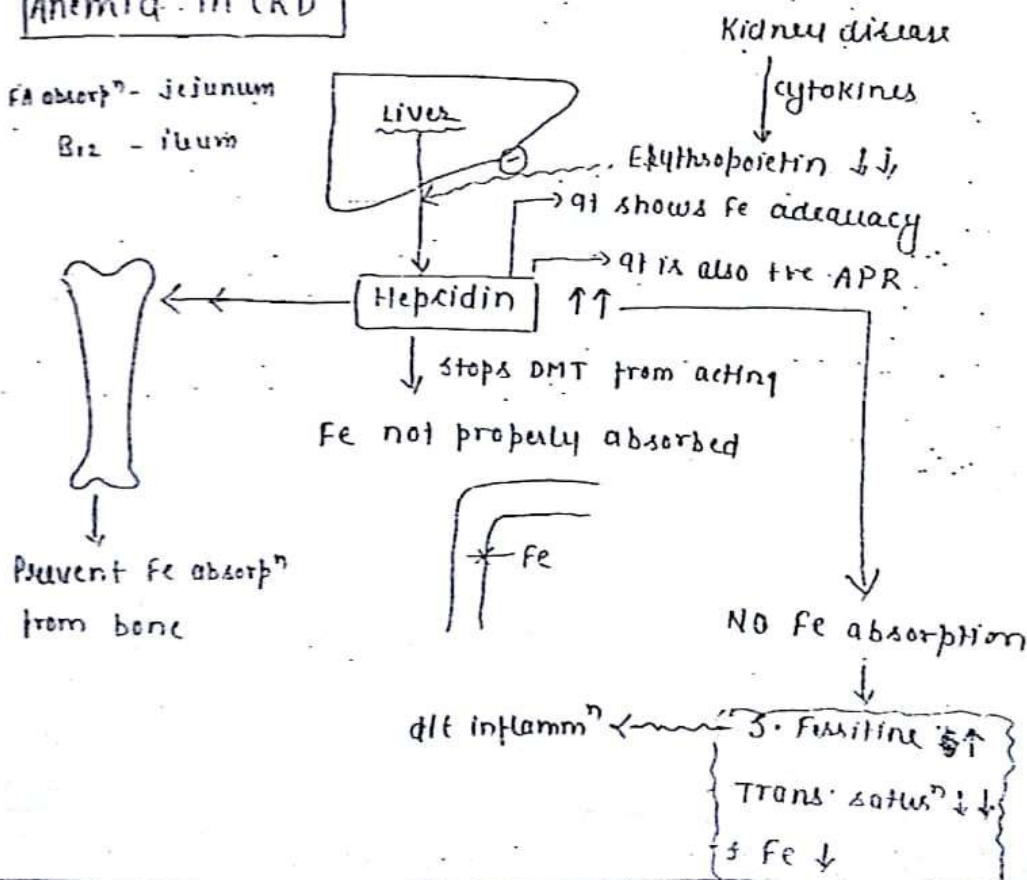
Stage 4 = $\text{GFR} = 15 - 30$

Stage 5 = $\text{GFR} = < 15$

- Problems -
- Hyper K^+
 - $\uparrow$ Anion gap met. acidosis
 - Dilutional hyponatremia
 - Na^+ overload
 - Hypocalcemia
 - Hyper PO_4^{2-}
 - Anemia (Iron deficiency anemia)

↓
occurs dlt hrs of blood in dialysis circuit

Anemia in CKD



(58)

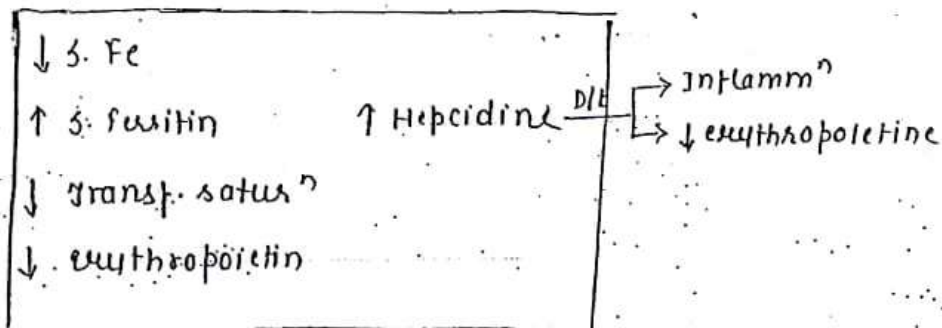
Erythropoiesis will not takes place

↓ bc3

↓ erythropoietin

↑↑ Fe in bone

↓
this marrow iron ↓
erythropoiesis.

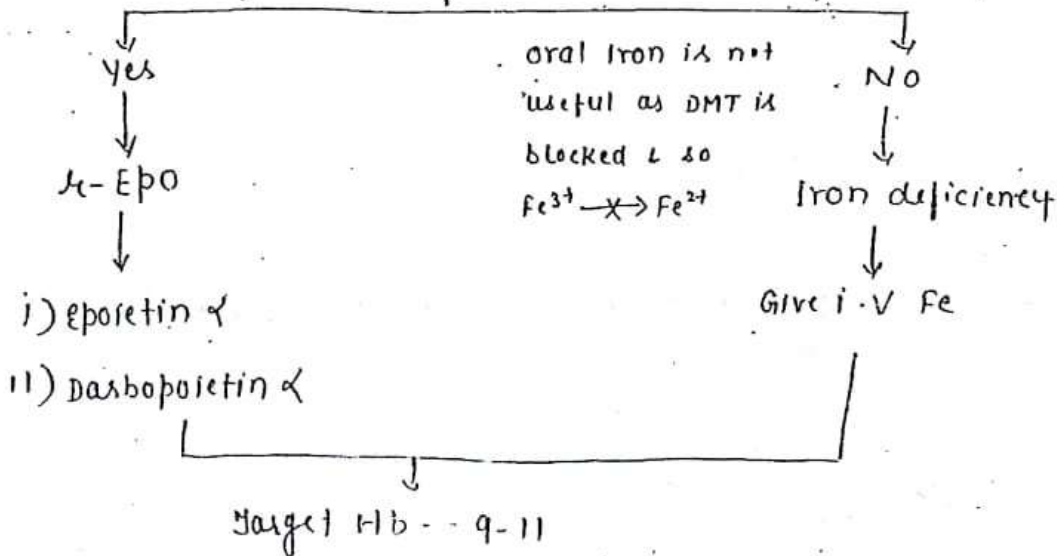


Anemia in chronic kidney dis.

R_x —

Anemia + CKD

↓
S. ferritin > 200 (> 100 — U.S guideline)
TSAT > 20 % (N) ferritin — 20 - 200

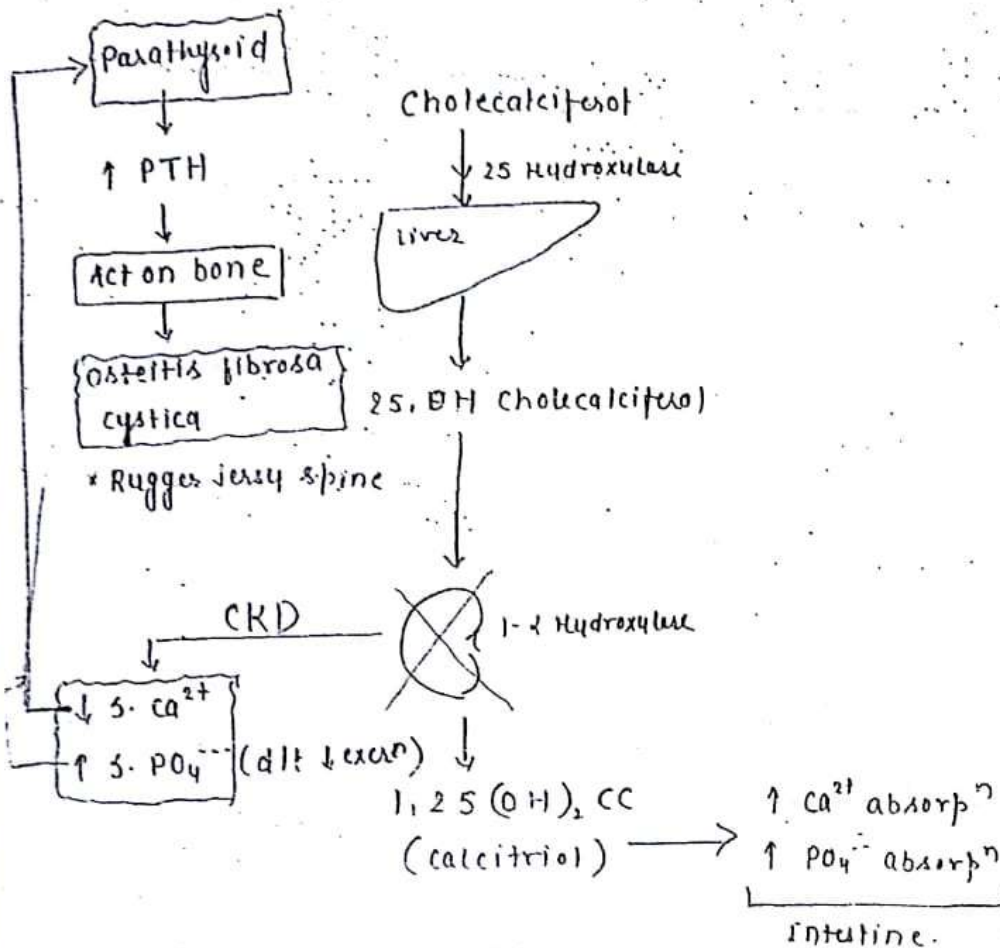


S/E of erythropoietin — HTN

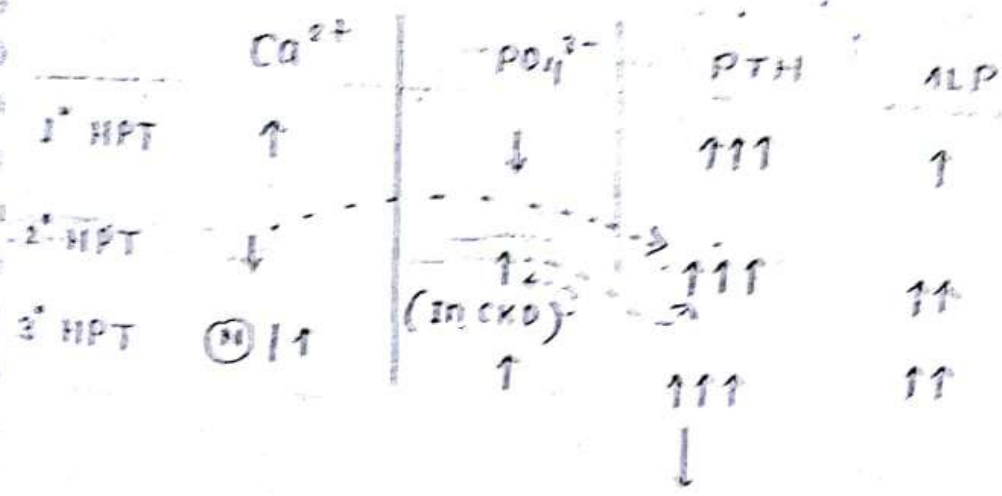
gtt — ↑ dose of ^{anti} HTN drug. No need to stop erythropoietin.

* mce of death in CKD pt → Cardiovascular

CKD-MBD mineral bone disease



(59)



beg of continuous stimulus
from Ca^{2+} , PTH become
↑↑ & become autonomous
↓

After few hours the stimulus is
lost i.e. Ca^{2+} become ⊕ / (normal)
1) but still PTH is not
coming down, as it is autonomous

2° HPT -

- ① Ca. supplements + vit-D
- ② Phosphate binder $\begin{cases} CaCl_2 \\ Sevelamer \end{cases}$

3° HPT - + surgery (removal of parathyroid)

Overall Rx in CKD

- ① modify risk factor —
- quit smoking
 - Na⁺ restricted diet (<4g/d)

• protein

↓
Not on dialysis

↓ restrict

<0.8g/kg/day

↓
Dialysis

= 1.5g/kg/day

- ② Rx comorbidities —

DM — HbA_{1c} < 7%

HTN — JNCB :- 140/90

U-albumin

↓
<30 mg/d

↓
140/90

↓
>30 mg/d

↓
130/80

- ③ Rx CV risk —

- Aspirin
- Statin
- β -blockers

- ④ special problem —

(60)

⑤ Routine problem R-

- i) Hyper K^+ $\rightarrow$ conservative by giving K^+ binders
(unless it is life threatening)
 $\xrightarrow{\text{fail}}$ Dialysis
- ii) met. acidosis $\rightarrow$ soda bicarb (controv. as it may $\uparrow H_2O$)
- iii) edema $\rightarrow$
 - salt restriction
 - fluid restriction
 - loop diuretic

Diabetes in CKD -

- Best $\rightarrow$ insulin (But requirement $\downarrow$ due to metabolism)
- metformin is C/I as it $\uparrow$ acidosis (lactic acidosis)

Safe drug - (Renosafe)

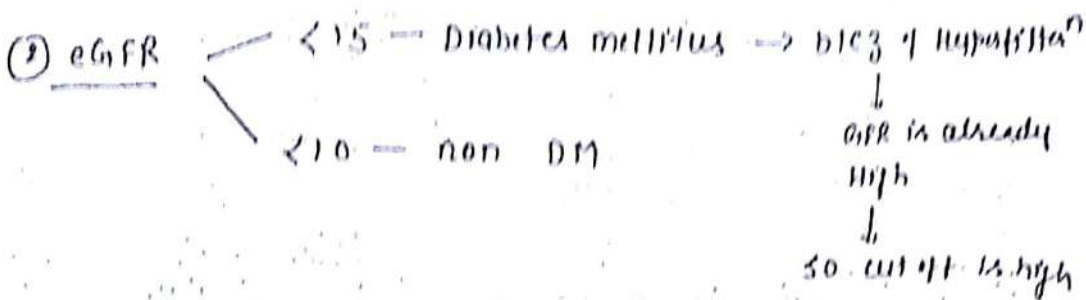
- ① Glipizide ($\approx 2.5 \text{ mg/dL}$) $\rightarrow$ s.c.
- ② Linagliptin $\rightarrow$ most safe gliptin, as excreted by liver.
can be given upto s.c. $\approx 4 \text{ mg/dL}$
- ③ Pioglitazone $\rightarrow$ s.c. $= 4 \text{ mg/dL}$
 $\rightarrow$ Absolutely C/I in volume overload, as it $\uparrow$ vol. overload

Indicⁿ of routine maintenance dialysis in CKD —

① Refractory symptoms

Chyne stroke — low O_2 related breath $\rightarrow$ they want more O_2 so expires for longer time.

Kussmaul — Rapid & shallow breathing



* Best ill for ESRD is transplant. Hemodialysis is only a bridge.

Well respond to Dialysis $\rightarrow$ Polycystic kidney dis.

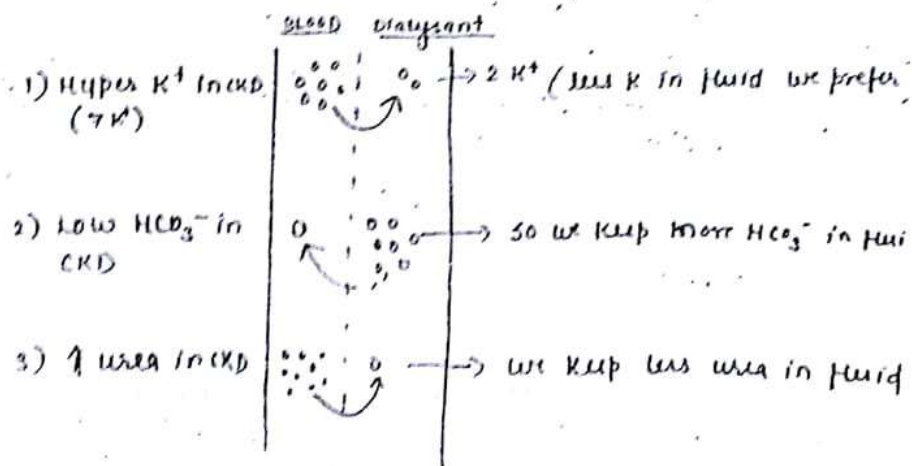
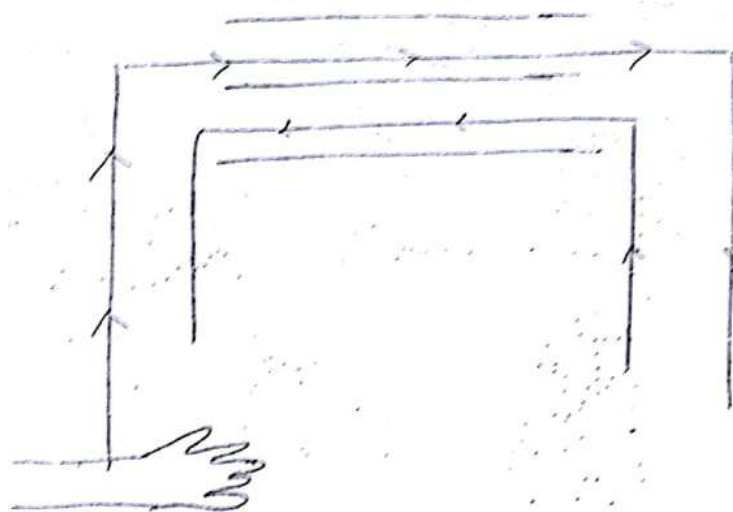
Poor response — Diabetic

(61)

- Dialysis -

Hemodialysis — 2 component — Dialysis
Filtration

* Dialysis works through osmosis.



* Once the level of ion become equal on both side, movement stops.

• Creatinine is not effectively corrected by dialysis.

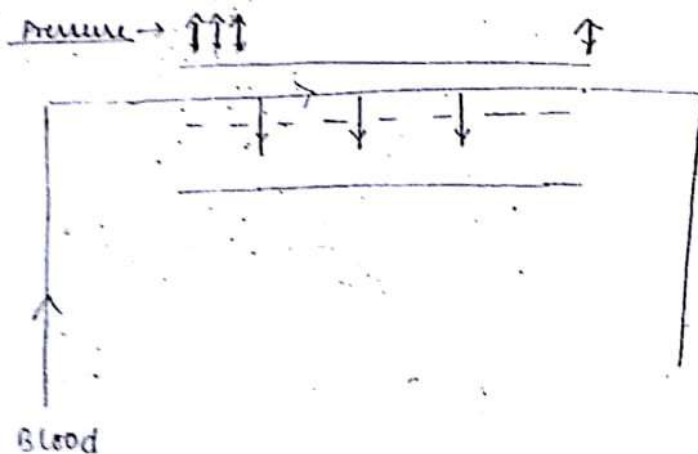
Well corrected — • urea
• K^+
• Acidosis

→ creatinine is marker of injury & is not corrected by dialysis.

→ H_2O movement doesn't occur in dialysis.

→ middle & large molecule can't move through dialysis (i.e. toxins)

Hemofilter — • works like kidney.



• Based on filtration pressure → ultrafiltrate formed

→ Here we try to create pres. difference, same like kidney. ultrafiltrate formed which pass through pores.

(62)

Adv:- we can remove middle molecule also. bcz we can change pore size.

* Nowadays Hemodiafilterⁿ is done combinely.

Dose:-

10 hr/wk $\rightarrow$ Dose of dialysis

Divide in 3 session of 3 hr

Adequacy of dialysis / session -

1) if $\frac{KT}{V} > 1.2$ / session

2) urea reducⁿ ratio $> 65\%$

Site -

• Rt. int. jugular vein $\rightarrow$ in AKI
mc site for initiation

* Flow rate - 300-800 ml/min required
- Dialysant flow - 400-600 ml/min

• For continuous ttt -

↓
we create fistula

- Tunneling is done & used for 1-3 mth, & till that time fistula get mature.

Cimino Brescia fistula —

* Cimino Brescia fistula → mcc of fistula

(Sialogenic)

↓
site — Radio cephalic site



Brachio cephalic

Adv:- ① Anast. i artery



High flow rate



so risk of closure of fistula is very less.

② High flow rate can be maintained for adeny

③ easy & ↓ risk of infecⁿ

④ easy accessibility

Complicⁿ — ① Hypotension — Intra dialytic ~~Hypotension~~ Hypotension
(mc.)



SBP fall > 20 mm Hg

MBP fall > 10 mm Hg

Rx — • Stop dialysis

• push 250 ml NS bolus

UFR = < 0.6 ml/kg/hr → we keep
ultra filtrⁿ rate

(63)

② Dialysis disequilibrium syndrome →

- urea > 150 → this syndrome can occur.

- Neurological symptom during/after dialysis

③ malnutrition — Along c UF, imp protein will be lost

④ Dialysis related amyloidosis — β_2 microglobulin
↓
not effectively filtered

⑤ calciphylaxis → it is meta. calcifren. dlt PO_4
 Ca^{2+} deposition in blood vessel, skin, soft tissue

↓
Area will undergo necrosis**

↓
Rapid intxn

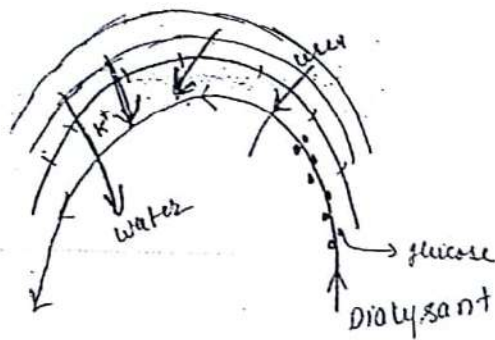
↓
sepsis

↓
Death

* mcc of death → cardiovascular > withdrawal of dialysis

Peritoneal Dialysis —

We use peritoneum as SPM.



- we add lots of glucose to dialysant
↓
this creates osmotic drive to bring water
in dialysant fluid.

* This is less efficient method.

→ ~~CIS~~ — Hypotens

→ Adv! —

- (1) Bed ridden.
- (2) CIS of Hemodialysis
- (3) No proper vascular access for HD.
- (4) Pt. not willing to come Hosp.

(64)

* Aquaporin-1 is found in peritoneum

↓
Help in H₂O movement

→ middle molecules are not removed properly.

Prerequisite - some residual kidney funcⁿ should be there.

q) there is complete renal shut down peritoneal D not done.

Peritonitis -

Gm +ve → S. aureus > CONS

1st sign → cloudy peritoneal fluid.

TOC → Intraperitoneal Antibiotics

Hyperglycemia → Another imp. complication

* Rest all complications are same.

Transplant

DONOR

Recipient

1) ABO matching

2) HLA matching — MHC

II → DR → m. int
I → B

— Selective Renal angiography → To check anatomy.

Types of Donors —

	Cadaveric	Live
1 yr	90%	95%
10 yr	50%	70%
expectancy	14 yr	20 yr

But

Types of Cadaveric —

- I — Brought dead → not used
- II — death after unsuccessful resuscitation
- III — awaiting cardiac arrest
- IV — CA after brain dead ⇒ Best donor
- V — In-hospital cardiac arrest

(65)

- * Left Kidney → Placed on Rt. iliac fossa
↳ Bigger renal A.

Heterotopic transplant

Ortho — Take transplant & keep it on same place. For ex- Esophagus, Liver

- * In Kidney Trans — we don't take out native kidney.

Anast — At ext. iliac vessel

RA ↔ ext. iliac A

RV ↔ ext. iliac V.

- * Anastomosis is not done to int. iliac vessel
bcz it may cause sexual dysfunction bcz kidney is highly perfused organ & it steal blood

- * Cerebral patch → not in cadaveric kidney.

Bladder Tx — submucosal tunnel is created



Lead Beaker Politano technique

* mce complicⁿ of renal Tx — Post op ileus

Immunosuppression —

MHC-I → [CH2-C] ← MHC-II

• HLA A, B, C

+nt in nucleated cell

- These molecules are for endogenous Ag
ex- virus

• HLA - DP, DQ, DR

- +nt in APC

- For exogenous Ag
ex- Bacteria

* nef → suppress expression of MHC-I

66

MHC-I

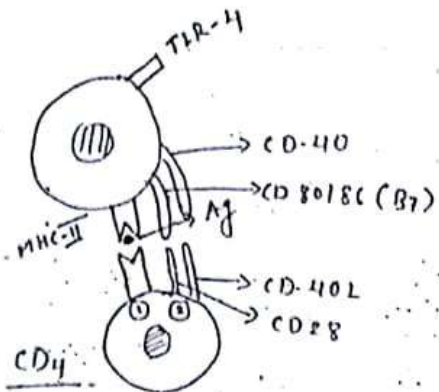
α_3
 $\alpha_2 \rightarrow \beta_2$ microglobulin
 α_1

CD8

MHC-II

$\alpha_1 - \beta_1$
 $\alpha_2 - \beta_2$

CD4



1 + 2 $\Rightarrow$ activⁿ

1 — anergy

↓
("Impotent T cell")

Once anergy occur
the T cell never ever again
interact w/ APC.

TLR-4 recognizes (on APC)
↓
Pathogen associated
molecular pattern (PAMPs)
↓

(Come from Antigen/bacteria)

This recognition leads to activⁿ of co stimulatory
molecule.

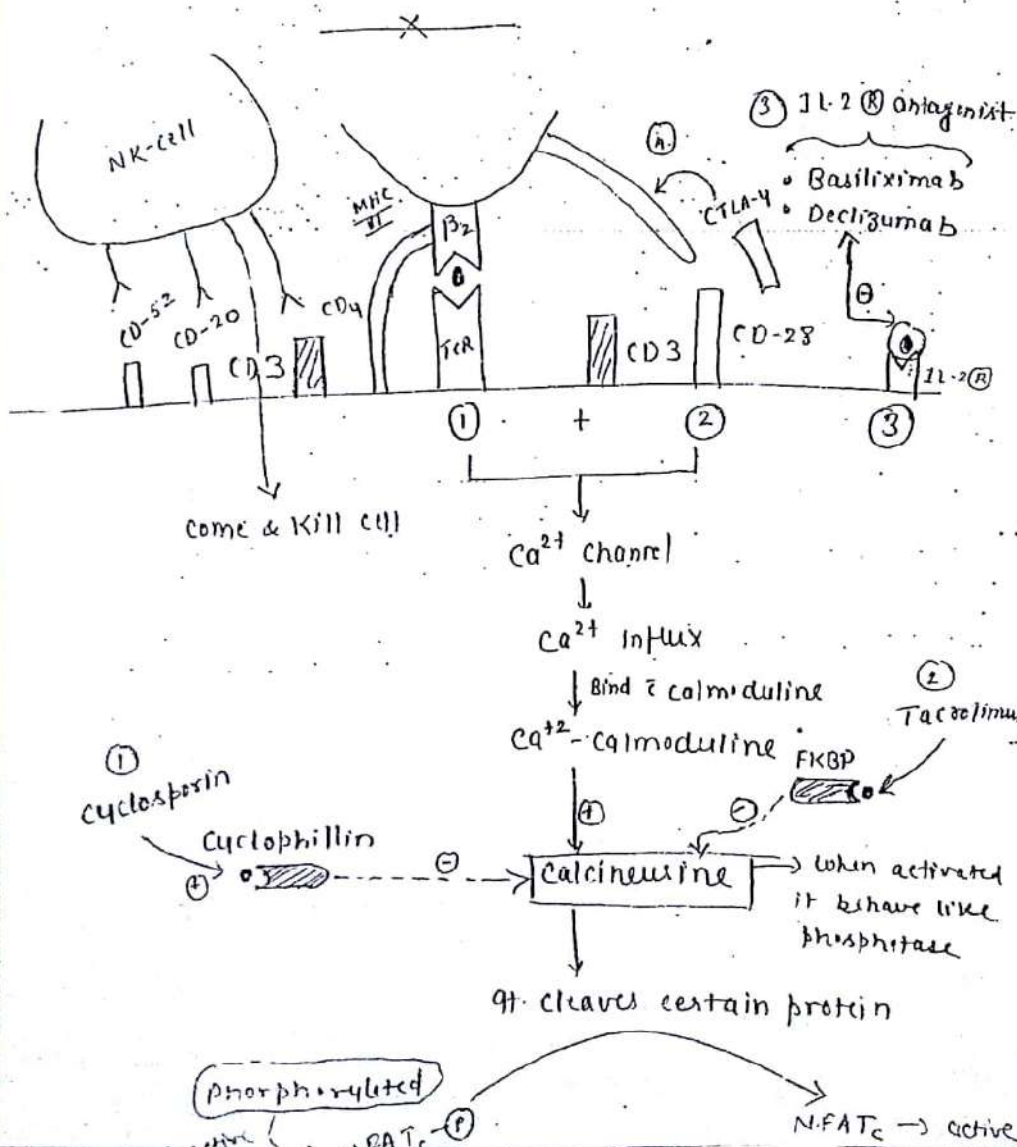
* If APC is presenting Ag w/ co-stimulatory
molecule $\rightarrow$ it shows that the Ag is not
exogenous & it is self Ag

↓
So in this case we need to suppress the T-cell

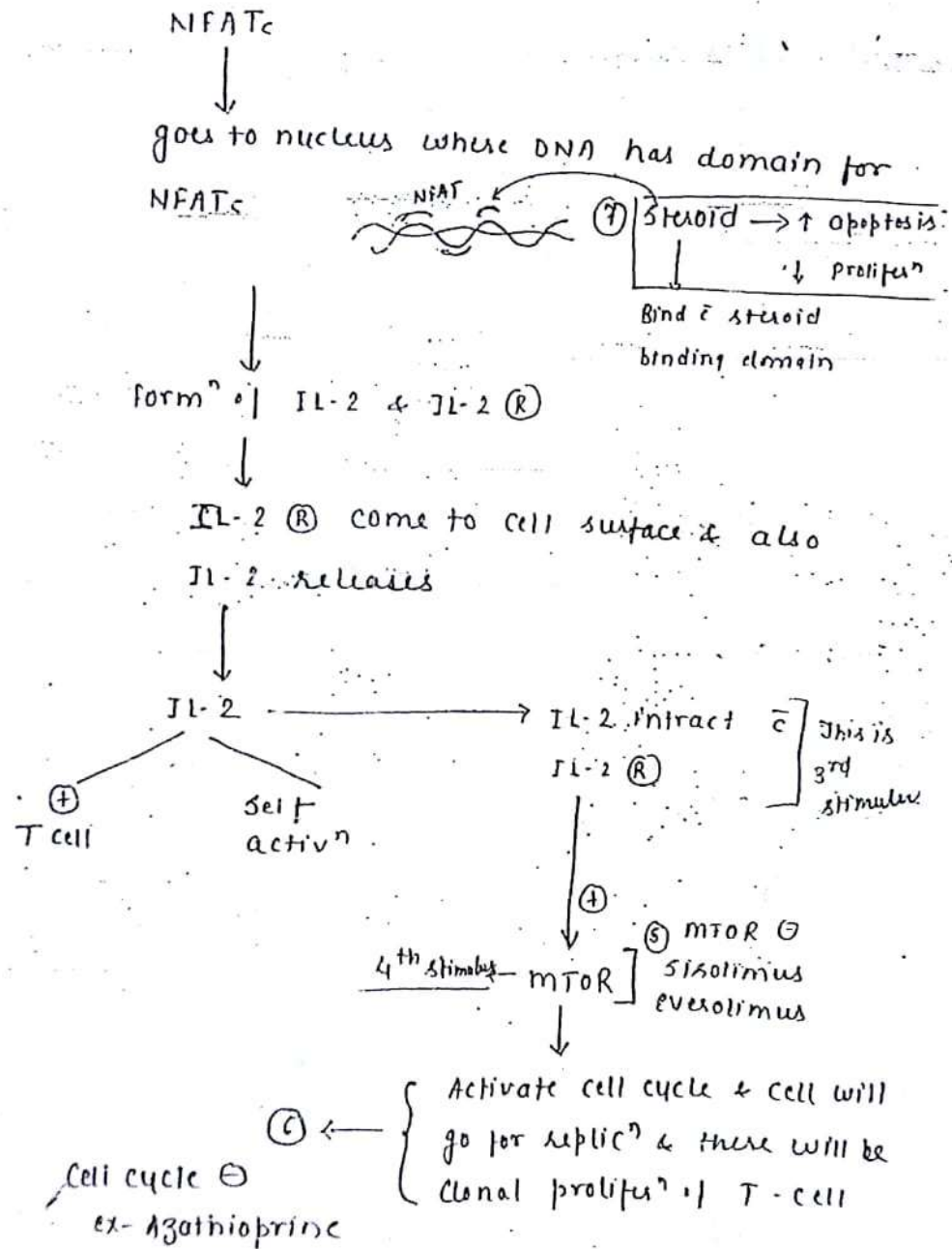
otherwise T cell will kill self A.g

so energy occur to prevent intracⁿ of T cell
i auto antigen

so energy is protective mechanism.



(67)



(4) CTLA-4 — they combine $\bar{e}$ CD28/153 & Huv @ its
fusion $\bar{e}$ CD28

— we are forming CTLA-4 fusion protein



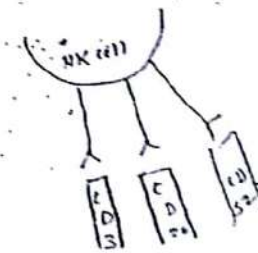
— Abatacept

— Belatacept

(8) Anti CD₃ — OKT-3
muromona b

(9) Anti CD₂₀ — Rituximab
ocrelizumab

(10) Anti CD52 — Alemtuzumab



NK cell will
come through
FcγR (R) & kill
the cell.

(68)

Side effect —

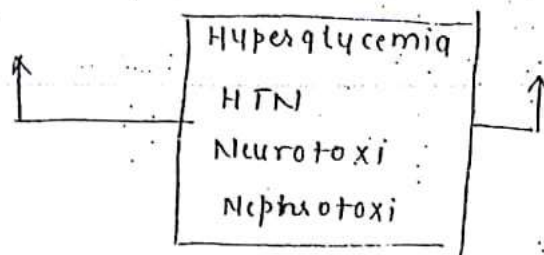
H ₂ O ₂	Neurotoxicity	}
HTN	Nephrotoxicity	

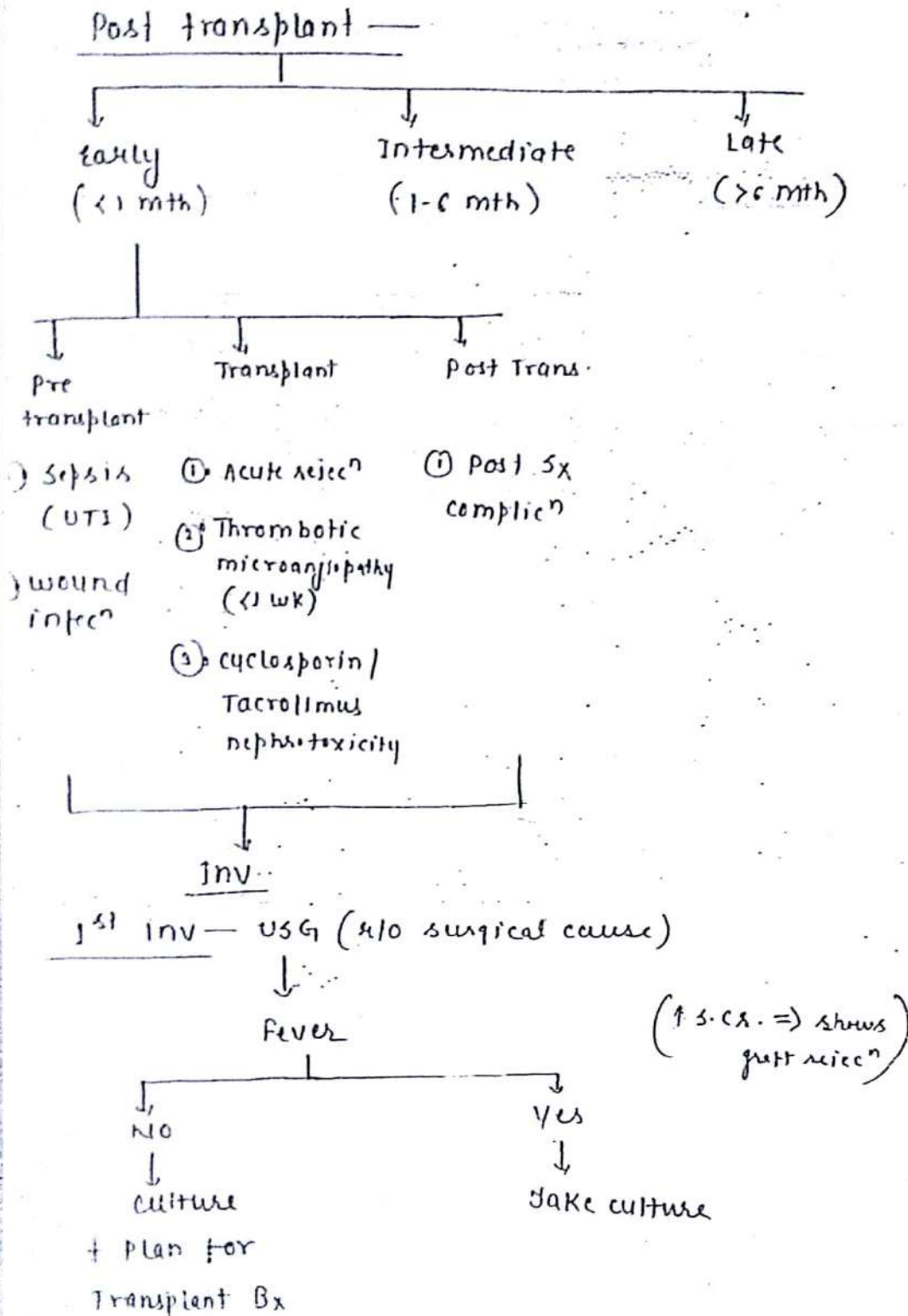
cyclosporin

Hirsutism
Hyperlipidemia
Gum Hyperplasia
Hyperuricemia

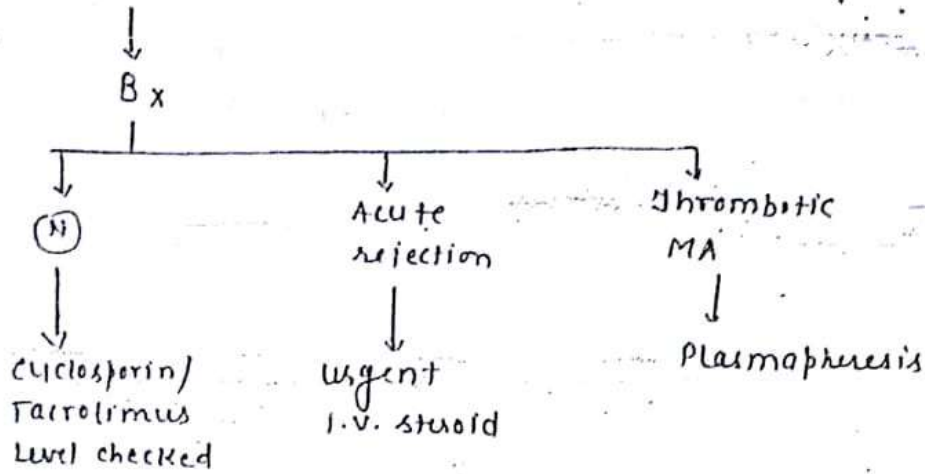
Tacrolimus

↑ Hyperglyc.
↑ neurotoxicity





(69)



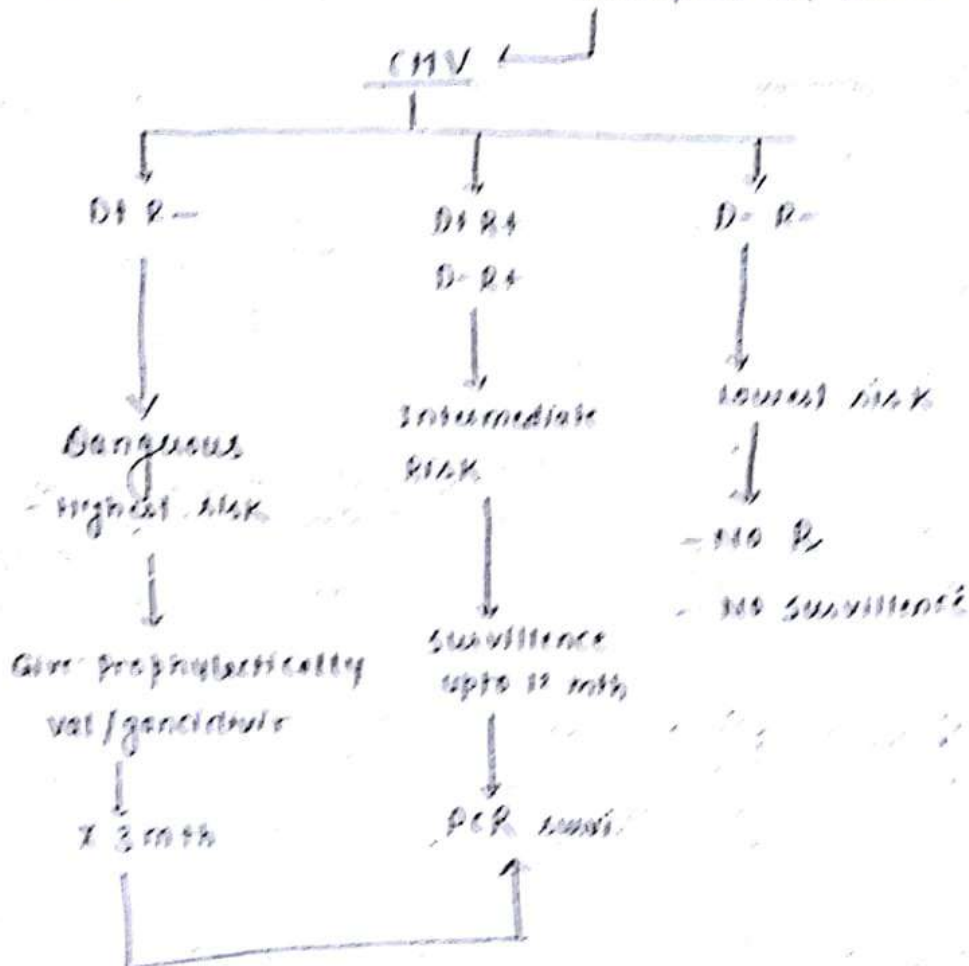
Acute rejecⁿ — modified Banff classificⁿ — Grading of Ac. rejecⁿ
↓
Peritubular capillaritis shows acute rejection.

Intermediate complicⁿ —

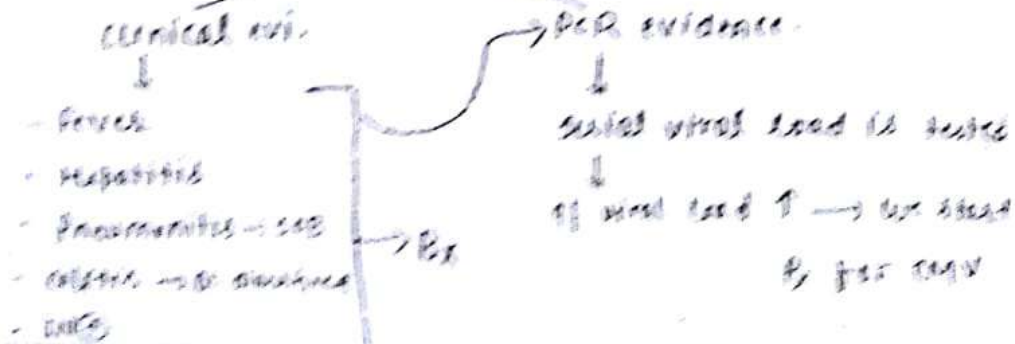
1) Opportunistic Infectⁿ — most common

- CMV infectⁿ
- Dissem. Herpes simplex
- Legionella
- Pneumocystis carini

[CMV] → Pre transplant work up in both donor & recipient
serological by ELISA



Evidence of CMV Infection



(70)

Bx — Inclusion body (owl's eye)

↓
Basophilic

* If all these PCR & Bx finding is +ve

↓
Give val/ganciclovir

Late complication

BK virus nephropathy — Grad
(Polyoma) • Renal failure

• Late onset ureteral stricture

• Decey cell in urine.

Δ^{sis} — • Decey cell in urine

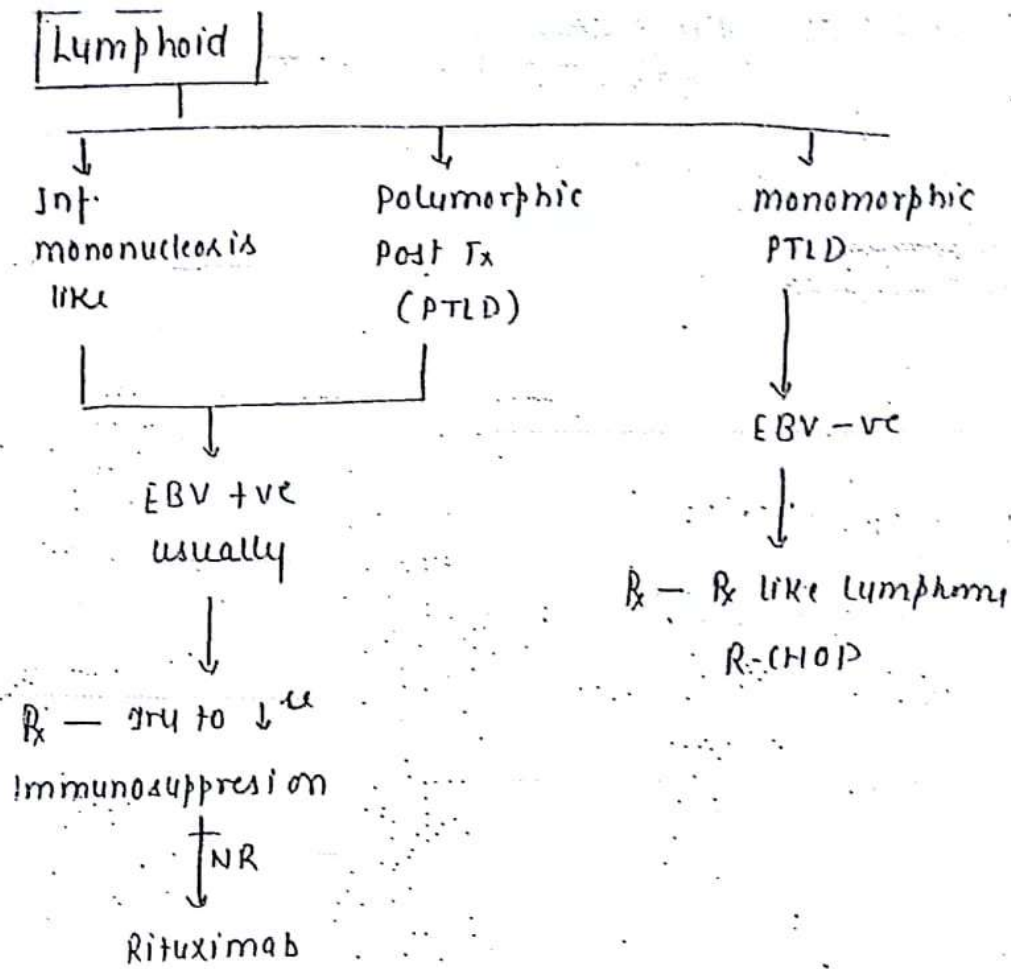
• BKV PCR +ve

• BKV IHC +ve.

Rx — ↓ Dose of immunosuppressant

±

cidofovir



(71)

Cancer — (1) mc skin cancer

- sqcc > BCC > Kaposi. > mal. melanoma

Cystic Kidney diseases

Polycystic Kidney disease



* PKD gene have very high penetrance
i.e., family H10

Penetrance → whether ds. expressing or not.

Expressivity → How much ds. is expressed

C/F — (1) Renal angle mass (abd. mass)

(2) Nephropathy

(3) Cysts → (1) MC site — Kidney

(2) MC extra renal site — Liver

* Liver cyst are harmless in ADPKD but in ARPKD

it is a problem. * They causes fibrosis in liver

(3) Spleen

(4) Pancreas

(72)

(5) Brain → Berry aneurysm → Presents as SAH

(1) Lungs < 2 %

Complicⁿ -

→ mc complicⁿ → sys. HTN → 1 RAAS

↓
accelerates ESRD

Rx → TOC is ACE ⊖

→ mcc of death → cardiovascular disease

Inv:-

* 10C — USA abdomen → 100% sn & sp.

↓
Also Best for screening

Rewine's criteria we use for screening —

<30 — 2

30-60 — 4

>60 — 8

Age cyst

* Genetic testing of PKD gene is done if the person is potential donor for his father. bcz we can't leave pt. w/ 1 kidney which is also not functioning.

Rx - ACE $\ominus$

• Dialysis

↓ N.R.

Transplant

- After Tx they don't get disease [PKD
Alport] No ds. after Tx

→ Recurrent ds. - after Transplant

↓
Highest c Diab. nephropathy

→ MPGN-II → mc 1° disease to recur after Tx

→ HUS D- > FSGS → High risk of graft loss following Tx

* Urine stones are very rare in these pt.

↓
If get these are uric acid stone.

(73)

Alport

* X-LD, also all other form of inheritance.

X-LD

F - Fragile X-

A - Alport

I - Incontinentia pigmenti

R - Retts syndrome

vit-D^Ricketspathology - Def. of B.M protein

Def. of COL-4 & 5 gene

Triad of Alport

① family H/O nephropathy

+

Nephropathy — Hematuria

↓
ESRD

② SNHL

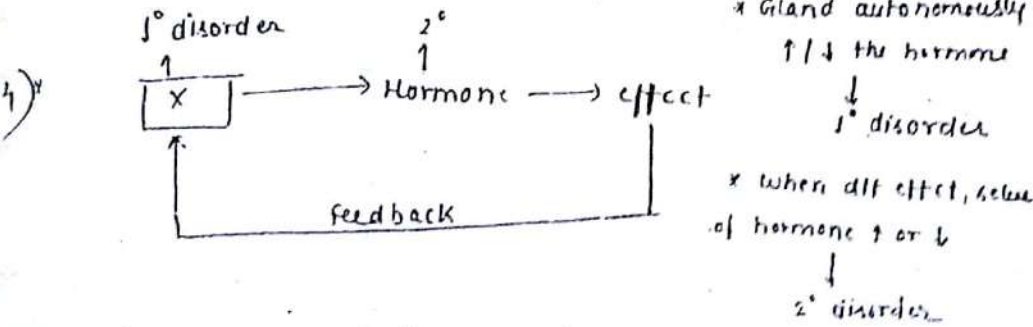
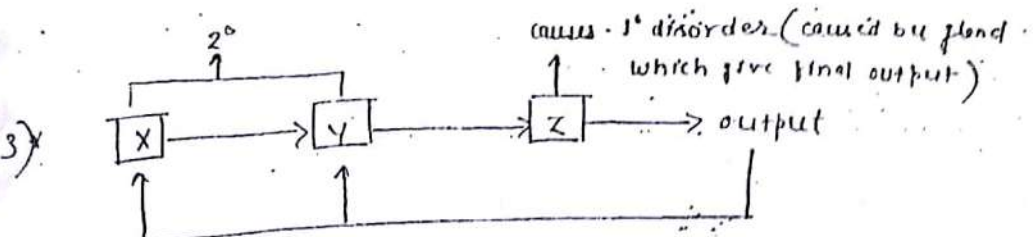
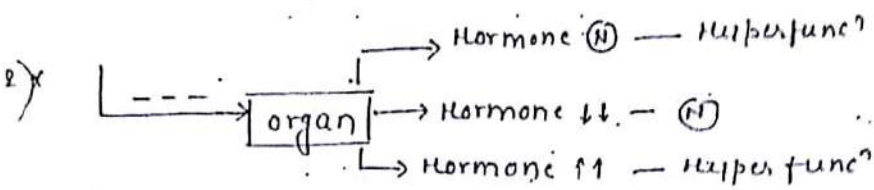
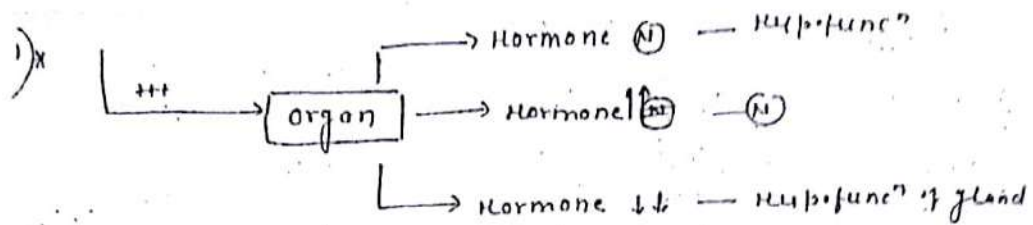
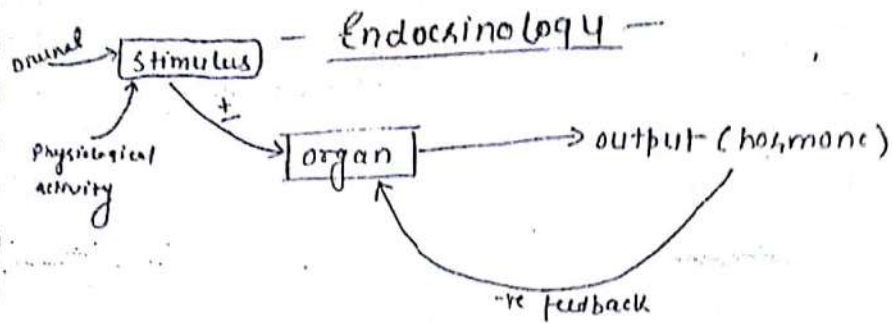
③ ocular problem (Ant. lenticonus)

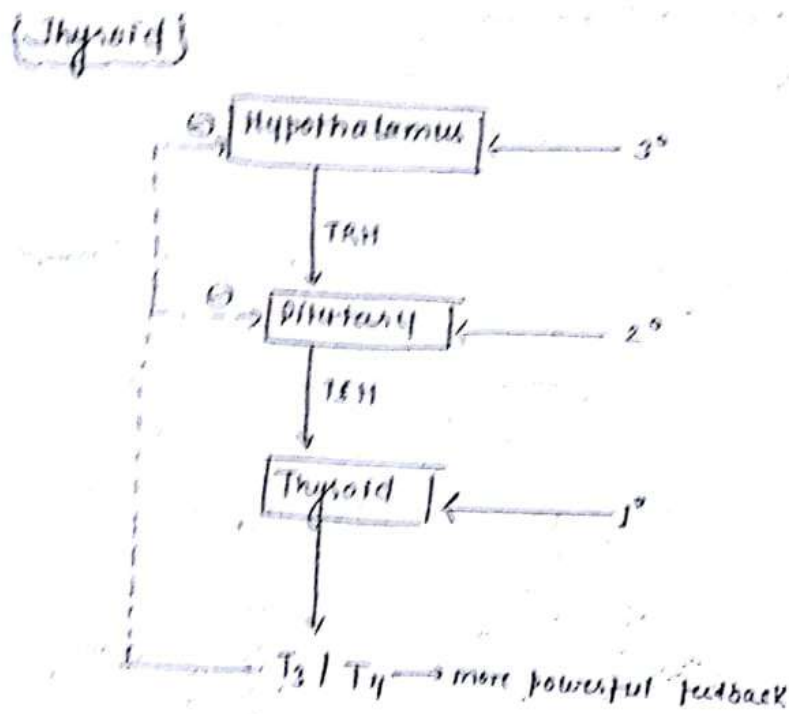
Inv - Basket weave appearance on EM

Rx - Transplant

Sometime pt. can develop Ab against $\alpha 5$ chain
after Tx.

(74)





Feedback inhibition & amount of hormone

24/24 axis control → metabolism

2 molecular homeostasis → controlled by 24/24 axis.

1 T₃-T₄ feedback gives more stronger feedback to Hypothalamus >> Pituitary.

1 (R) TSH = 0.3 - 4.12

(25)

Evaluation of Thyroid:—

① Thyroid funcⁿ test → Free T₄ + TSH

* TSH estimⁿ is helpful for 1st disorder to see for monitoring & diagnosis. so it is single most imp. test. Also overall it is best.

→ 2nd disorder → single best is Free T₄ for ^{Δsis} monitoring

* Free T₃ is not much useful.

→ Total T₄ + TSH → done in pregnancy only.

* Total T₄ / T₃ is not performed regularly bcz.

TBG₁ ↑ = Total T₄ ↑↑

↓
Bound T₄ ↑ ↑↑ Bound T₄ + free T₄ (N)

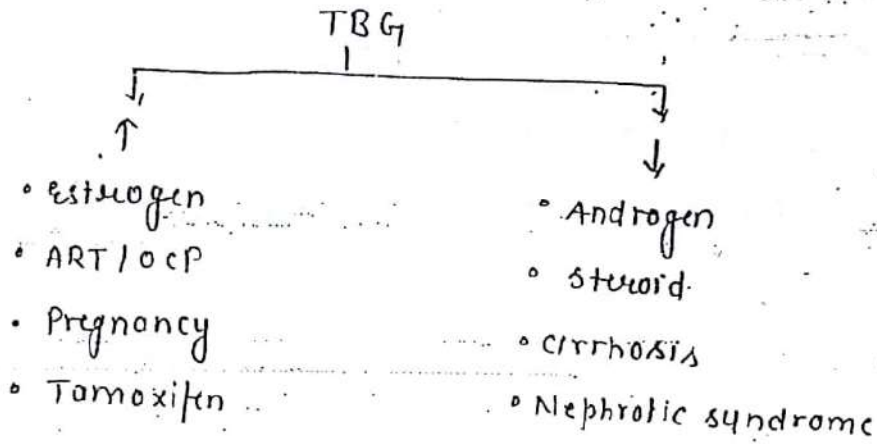
⇓
we misdiagnose pt. as hyperthyroid.

* TBG₁ ↓↓ = Bound T₄ ↓

Free T₄ (N)

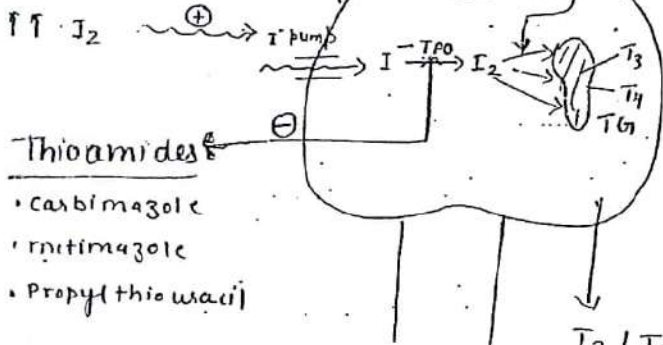
↓
Total T₄ ↓

⇓
Hypothyroidism

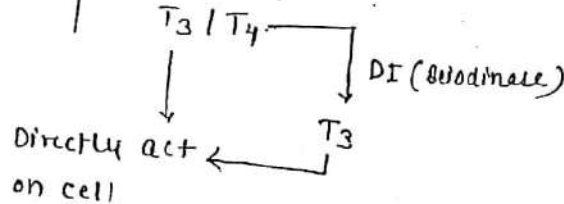


Thyroid

TSH when act on
Ⓡ, it act on I⁻
channel.



S/E - of ATT
Rath > Hypothyroidism



* T₃ is unstable & doesn't has ↓ T₁₁₂.

* so in cell T₄ is converted to T₃ & it acts

74

Thioamides —

Causima

Methimazole — 91 is DOC.

Propylthiouracil — weakest

Drug @ Incorporation of I_2 to TG —

* I_2

q. we give high dose of I_2 (acute) → ↓ Hormone

↓
Wolff chaikoff effect

* I_2 also @ proteolysis

* I_2 blocks both formation & release of thyroid hormone. → most potent

* Antithyroid drug only ↓ synthesis of thyroid hormone.

② Deiodinase — prevent conversion of $T_4 \rightarrow T_3$

① Propylthiouracil

② β blockers — Propranolol

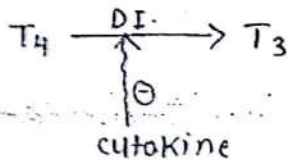
③ steroids

④ Amiodarone → contain ^{37%} I_2 → Produce Wolff chaikoff eff

⑤ I_2 (mild)

⑥ cytokine

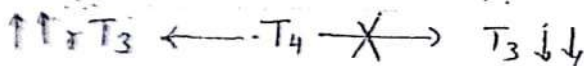
Cytokine — useful for non thyroid illness / sick euthyroid.



Cytokine storm occurs in — ICU pt.
starvation.

↓
So in these pt. cytokine ⊖ $T_4 \rightarrow T_3$

↓
In these pt.

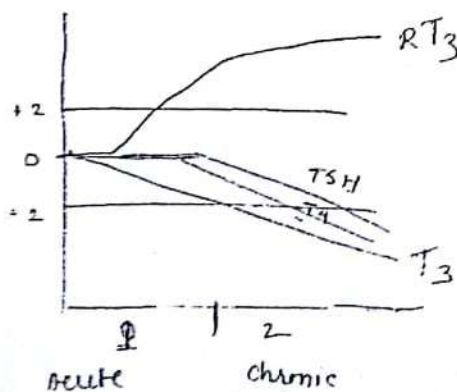


↓
∴ T_4 remain (N)

↓
So TSH is maintained (N)

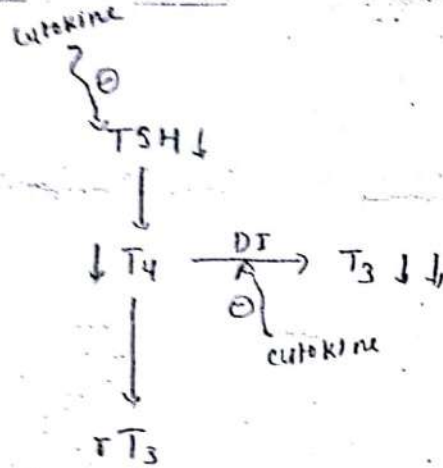
↓
Sick euthyroid. } i.e., no problem w/ Thyroid,
(Non-thyroid illness) hypothalamus, pituitary.

T_4 (N)
TSH (N)
T_3 ↓
rT_3 ↑



(77)

Chronic NTI — cytokine also $\ominus$ TSH release here.



— Here rT_3 is formed from T_4 which is already secreted in less amount.

- But in $\textcircled{N}$ person no rT_3 is found normally & it starts forming only once DI is $\ominus$. So we will find some amt. of rT_3 .

So here	In acute NTI
TSH ↓	TSH $\textcircled{N}$
T_4 ↓	T_4 $\textcircled{N}$
T_3 ↓	T_3 ↓
rT_3 ↑	rT_3 ↑↑

* So in TFT we don't use T_3 bcz its level can be altered in non thyroid illness also.

Jod Basedow effect —

Chronic micro ↑ in dose of I_2

↓
Act as stimulus for Iodide pump

↓
↑ Thyroid hormone synt

↓
Thyrototoxic

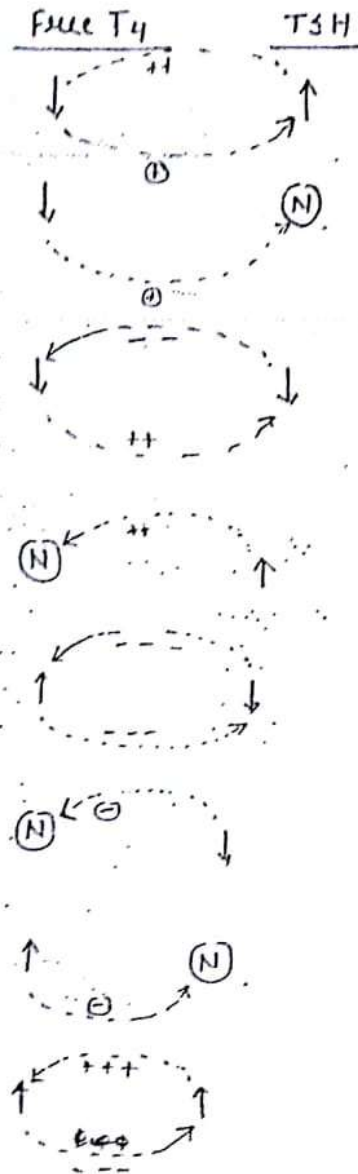
→ Acute dose of Amiodarone → Wolf chaikoff

→ if Prophylactically Amiodarone given for long time

↓
Jod Basedow effect

(78)

Interpretation of TFT-



Interpretation

1° Hypo T₄

2° Hypothyroidism

2° hypothyroidism

1° Hypothyroidism (subclinical)
as T₄ is (N) so (N) homeostasis

1° Hyperthyroidism

1° Hyperthyroidism (subclinical)

2° Hyperthyroidism

2° Hyper

* Pituitary Thyroid hor. Resistance —

Ⓡ ~~T₃, T₄~~

* Resist. to T₄ Ⓡ on pituitary

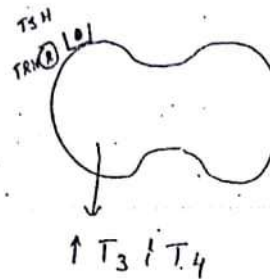
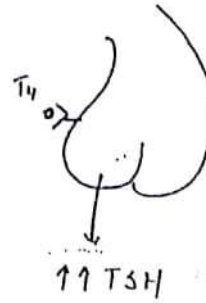
↓
so though there is T₄ but pituitary doesn't understand this

↓
so ↑ TSH is produced

↓
Act on TSH Ⓡ on thyroid

↓
↑ T₃ / T₄

↓
Hypothyroidism (2°)



- CIF —
- short stature
 - Bone problem
 - congenitally

* In pituitary tumor also there is ↑ TSH & ↑ T₃, T₄
but tumors are acquired & there will not be
any problem like short stature, bone problem.

(79)

Other Investigations -

Thyroid nodule — 1st test done is TFT.

Ultrasound — uses — ① to evaluate thyroid nodule
sp. to see if whether it is cystic / solid

② for characterizⁿ (size, number)

③ to guide FNAC

④ can do Doppler to see vascularity of gland.

FNAC — ① evaluate thyroid nodule

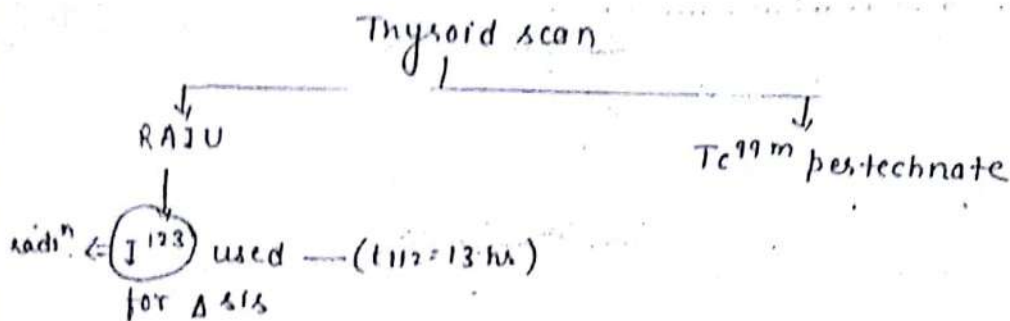
Disadv — can't differentiate b/w follicular adenoma
& follicular carcinoma

sis is based on — capsular & vascular invasion

↓
so Bx can detect it

Thyroid scintigraphy / scan — use

① to evaluate hyperthyroidism only.



* For ablatative purpose
 I^{131} used (half-life = 8 day)
 ↓
 (radiation) RAI A

RAIU

- High radiation
- accuracy ↑
- Breast feeding ? — X
- C/I in pregnancy

Tc^{99m}

- Low radiation
- ↓
- can be given
- C/I in pregnancy

(80)

Hypothyroidism

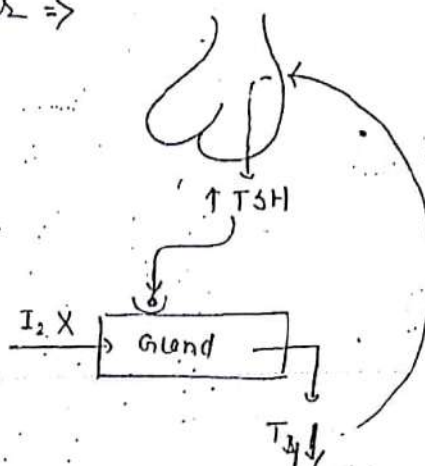
* mc is 1st Hypothyroidism.

mcc - Hashimoto's thyroiditis

• I₂ def → • Presents as goitre ⇒

• TFT is (N)

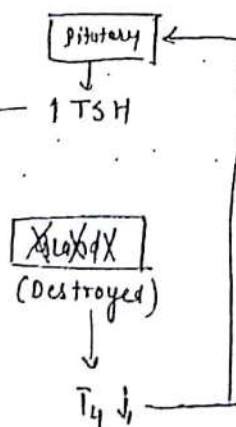
Here gland will
enlarge all stimuli
by ↑ TSH



I₂ def ⇒ Goitre

Hashimoto — no goitre

• But there is
no gland to
be acted by this
TSH
so there is no
goitre.



• At presentation there
is Hypothyroidism.

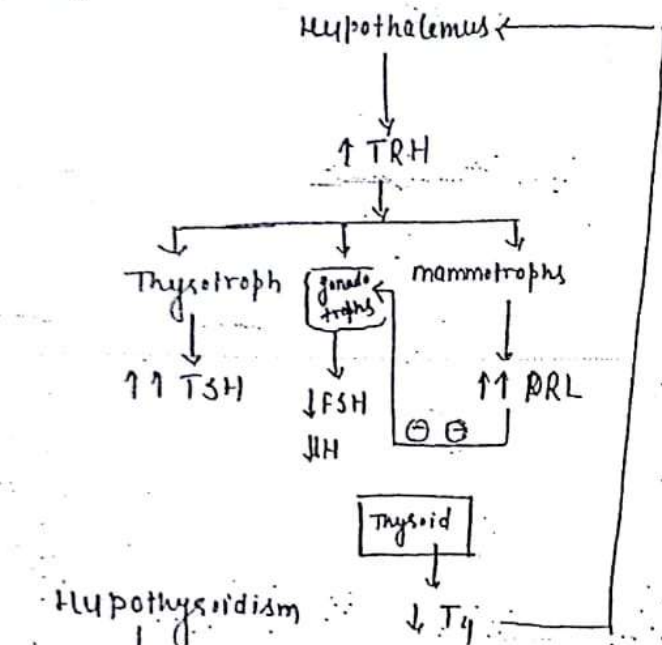
Endemic goitre — Goitre > 5%.

(1F of 1' Hypothyroidism: — moin 9

- (1) Alopecia
- (2) Dry skin, coarse, itchy
- (3) coarse facial feature
- (4) Hertoghe sign — madrosis
- (5) macroglossia
- (6) wt. gain
- (7) myxedema (pedal edema)
- (8) Pleural effusion
- (9) Pericardial effusion → chronic pericardial effusion
↓
so no tamponade.
- (10) Bradycardia
↓
no pulsus paradoxus
- (11) Diastolic Hypertension
- (12) constipation
- (13) menorrhagia (Hyperthy → oligomenorrhoea)
(practically ↓ menstrual cycle frequency)
- (14) Cold intolerance
- (15) Hypogonadism → infertility.
- (16) narrow pulse pressure.
- (17) macrocytosis (non megaloblastic)
- (18) Hyponatremia (sp. in myxedema coma)

(81)

Why Hypogonadism:-



Hypothyroidism

↑ Prolactine

gonadotrophs

∴ ↓ FSH / LH

Same mechanism for lactational amenorrhoea.

Why Hypo Na⁺ -

* Hypo Thyroid

↑ aquaporin exp in collecting duct

∴ ↑ H₂O absorpⁿ

∴ Euvolemic Hyponatremia.

$$\left[S.Na^+ = \frac{T.B.Na^+}{T.B.H_2O} \right] \text{ - Here total body Na}^+ \text{ is } \textcircled{N}, \text{ TB H}_2\text{O } \uparrow$$

∴ only Hyponatremia

(19) Hyperlipidemia ($\uparrow$ LDL)

familial Type II Hyperlipidemia

$\downarrow$
 $\uparrow$ risk of cardiovascular disease

(20) Somnolence.

(21) DTR — delayed. (Pseudomyotonic reflex)

— delayed relaxⁿ of contracted muscle $\Rightarrow$ myotonia

(22) Proximal myopathy

hypo T

hyper T

(23) sluggish thinking

Δ's — • TFT.

• s. prolactin $\uparrow\uparrow$

MIT —

1° Hypo T₄

over

T₄ $\downarrow$, TSH $\uparrow$

subclinical

T₄ (N) TSH $\uparrow$

Age < 65

NO CAD

DOC — L-thyroxine

Dose — 1 mg/kg/d

Age > 65 y^r

H/O CAD

DOC — L-thyroxine

Dose — start 25 $\rightarrow$ stable

(82)

Subclinical -

Indicⁿ of HT -

- ① TSH > 10
- ② Anti TPO +ve
- ③ Pregnancy / children
- ④ Symptomatic pt.
 - Dyslipidemia
 - wt gain
 - Amenorrhoea

R - start @ 50 μ g L-thyroxine
↓
titrate accordingly

Monitoring of R HT

1^o Hypothyroidism - TSH

check every 4-wk

til pt. become stable

Target

non pregnant

⑥ TSH is target
(0.3 - 4.12)

Pregnant

1st TM - TSH < 2.5

2nd TM - < 3

3rd TM - < 3.5

Target

TSH < 0.1 - trimester cut 1

↑ Risk of abortion in Hypothyroid —

- * qn 1st TH — (1) TSH > 2.5
(2) Anti TPO antibody

How to give thyroxine —

(1) At least 4 hr. of fasting should be there

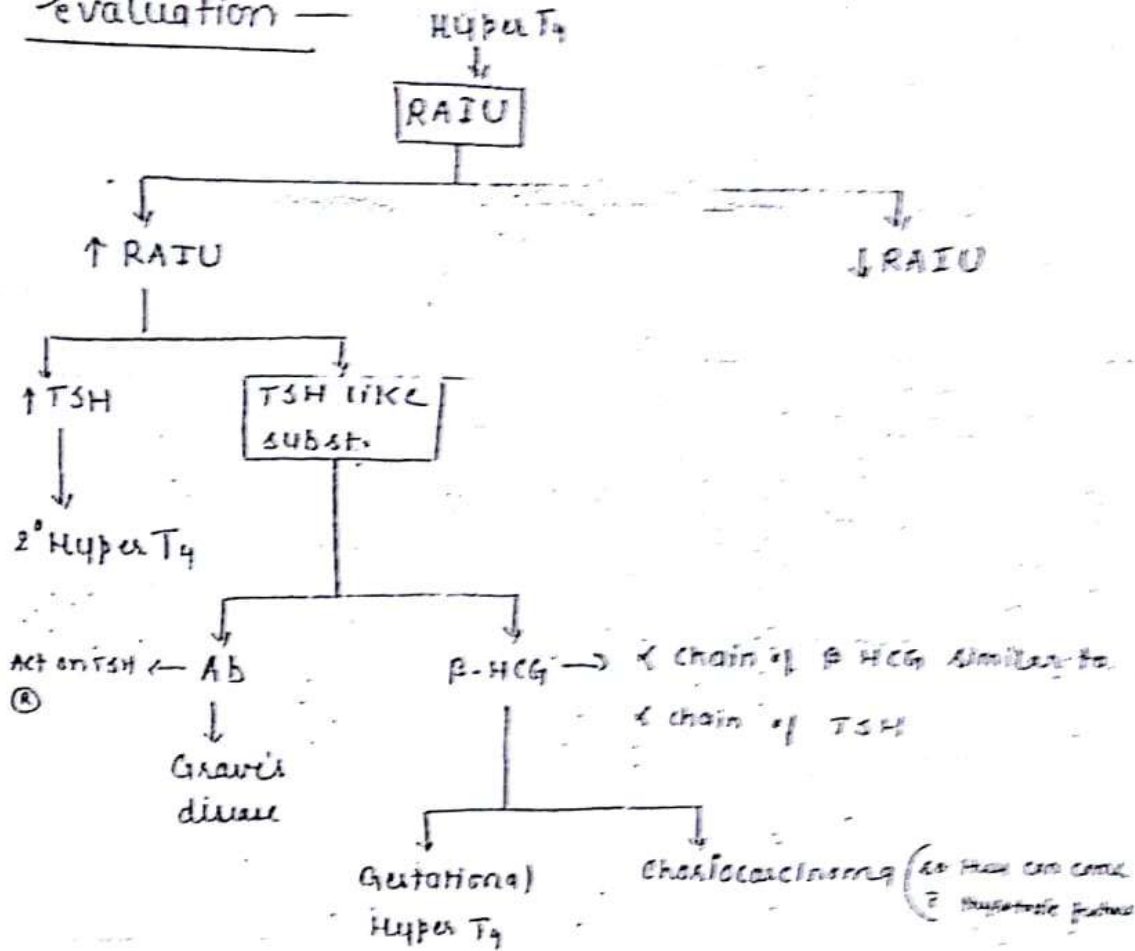
(2) After taking LT_4
↓ 30-60 min
No food

4 hr fast → LT_4 → 30-60 min → Food

(23)

Hyperthyroidism

Evaluation

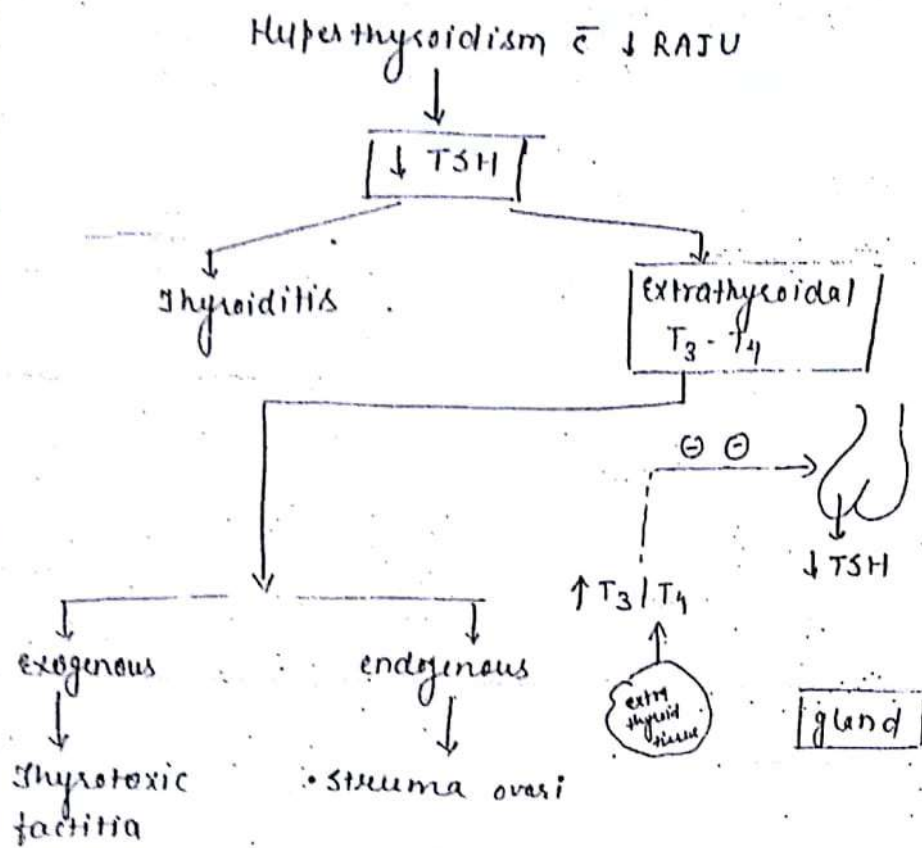


* Hyperthyroidism $\bar{c}$ $\downarrow$ TSH

Thyroid gland releases all its hormones after getting damaged

$T_3/T_4 \uparrow$

$\downarrow$ TSH from pituitary.



Special condition $\bar{c}$ $\downarrow$ RAU

① Toxic multinodular goitre / Plummer's ds.

② solitary toxic nodule.

(84)

* J₂ def

- ↑↑ TSH

↓
Act on gland
which is (N)

↓
↑ RAIU

* TOXIC MNG

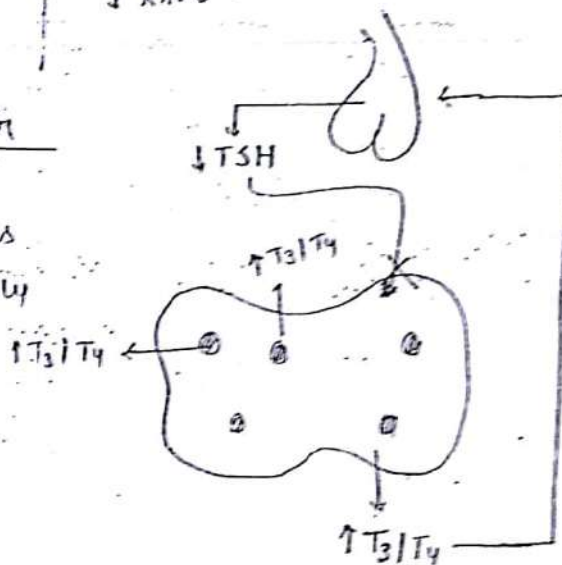
* few autonomous
nodule will only
take RAU

Hashimoto

- ↑ TSH

↓
No gland to act

↓
↓ RAIU



Clf of hyperthyroidism —

- (1) Anorexia
- (2) Hyperthermia
- (3) wt loss
- (4) Diarrhoea
- (5) oligomenorrhoea
- (6) tachycardia (sinus tachy. > Atrial fibrillⁿ)
- (7) Insomnia
- (8) Anxiety (Anxiety neurosis is not a hyperthyroidism)
- (9) exaggerated deep tendon reflex
- (10) prox. myopathy
- (11) systolic HTN — wide bounding pulse
- (12) ↑ pulse pressure
- (13) Mearns termen scratch → Rubbing sound produced by heart d/t tachycardia

Grave's disease — Clf

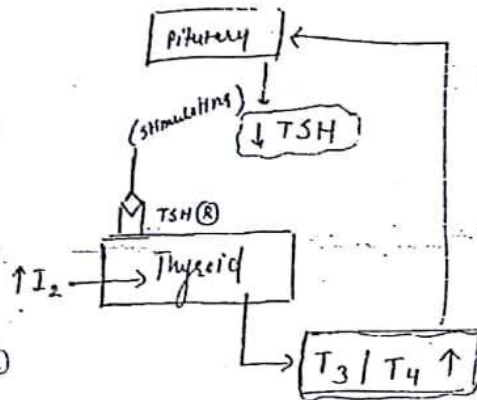
- (1) Grave's ophthalmopathy
 - (2) Pre tibial myxoedema / thyroid dermopathy.
 - (3) Thyroid acropachy
 - (4) Goitre
- * These are related to Ab in grave's ds, not due to thyroxine.

(85)

Grave's —

- ① Stimulating Ab
- ② Blocking Ab
- ③ modulating Ab

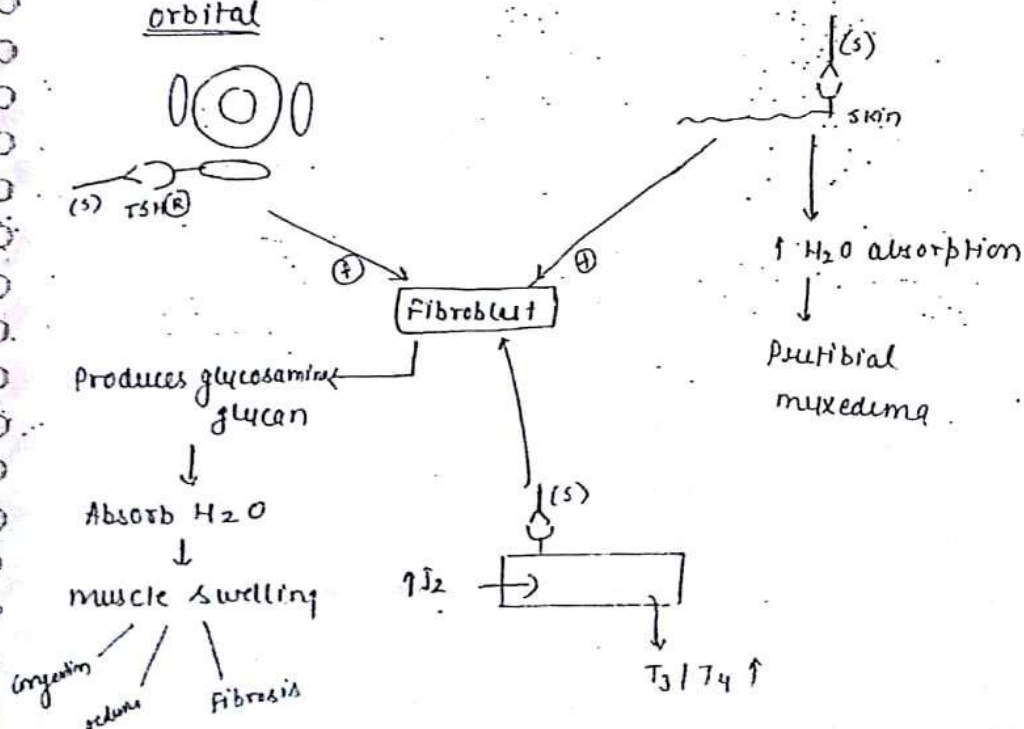
⇓
All action TSH R

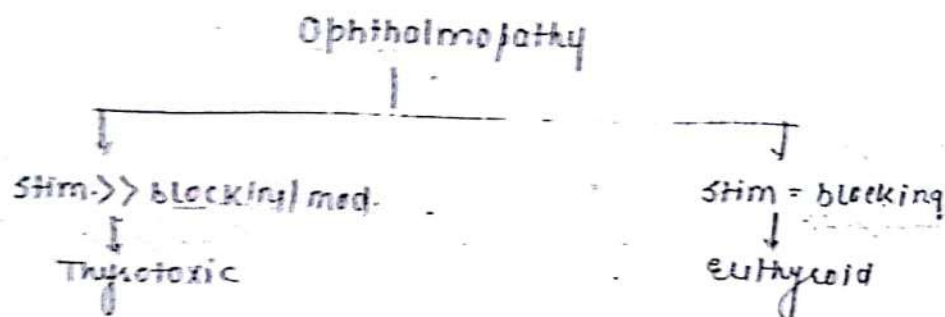


So in case of stimulating Ab

- | | |
|---|-----------------------------------|
| ① | T ₃ / T ₄ ↑ |
| ② | ↓ TSH |
| ③ | ↑ RAIU |

orbital





* Ophthalmopathy can be seen in euthyroid.

Features of Graves —

- ① Thyrotoxic state (optional).
- ② Ophthalmopathy $\left\{ \begin{array}{l} \text{Clinical} - 50\% \\ \text{MRI} - 80\% \end{array} \right\}$ incidence

* the muscle affected in ophthalmopathy $\rightarrow$ Inf. rectus
 - here elevator palsy is there. bcz muscle power is
 ③ here but elasticity is lost.

NOSPECKS — used for grading ophthalmopathy.

- ③ mce of ^{UL} proptosis — Graves (exophthalmos)
 $\downarrow$
 $\therefore$ Graves can be UL
 $\downarrow$
 measured by Hertel exophthalmometer

- ④ mce of B/L proptosis — Graves

(86)

Thyroid dermopathy — (pretibial myxedema)

* Inci — 10-20% untreated pt

• Occur late (after ophthalmopathy)

So it always presents w/ ophthalmopathy.

Acropachy — very less incidence

• severe clubbing d/t bone problem

Exophthalmopathy → d/t by steroids as it is d/t antibody.

1) TFT (N) / Ab (N)

Graves

↓
presents as 1st Hyper Ty.

2) RAIU ↑

3) USG doppler → ↑ vascularity (heard as bruit over goitre)

4) TSH (R) Ab → m-specific test

→ can be used for prognosis

5) Anti TPO Ab → +ve (as graves is autoimmune)

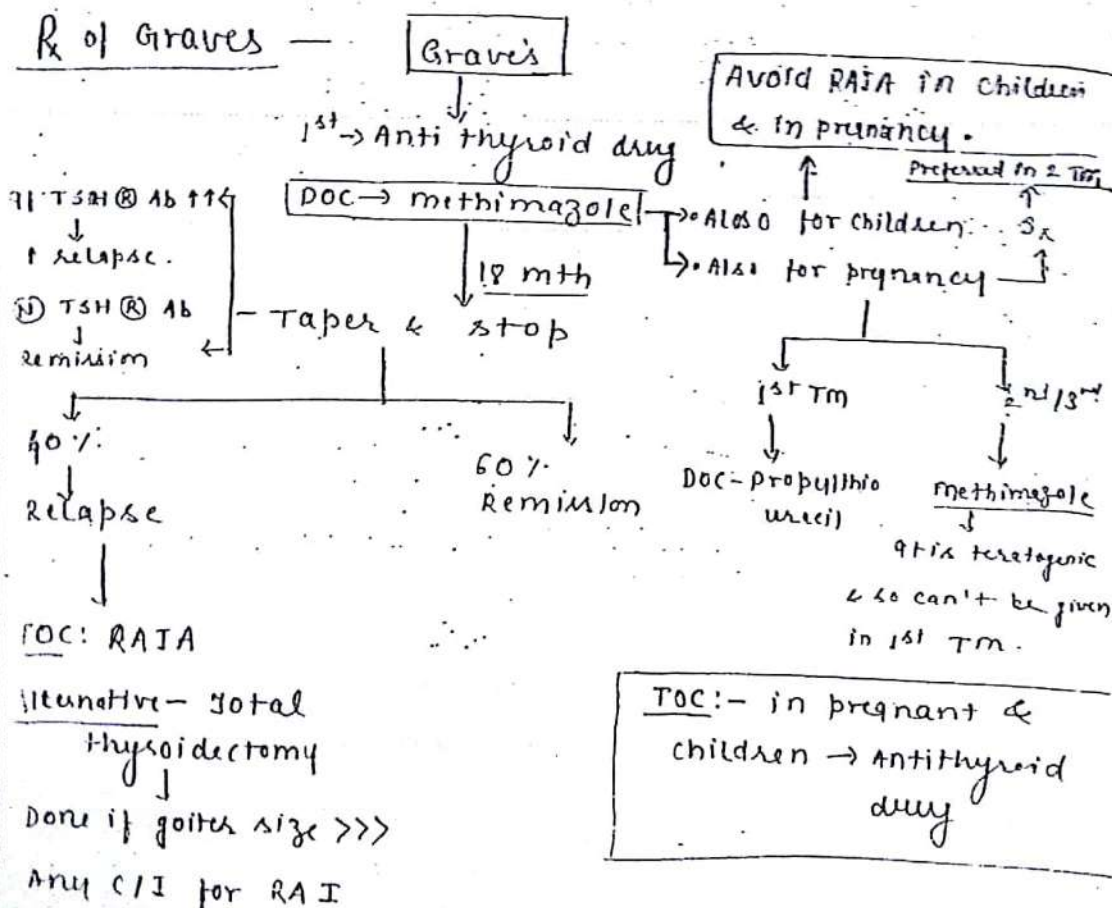
Graves

- Goitre & bruit
- ↑ RAIU
- Doppler — ↑ vascularity
- TSH ⊖ Ab
- Anti TPO ⊕

1st Hyper T_g

- Small goitre & no bruit
- ↓ RAIU
- ↓ vascularity (as gland is destroyed)
- TSH ⊖ Ab -ve
- Anti TPO ⊕

R of Graves



(87)

* Pre-requisite for RAJA → Pregnancy avoided for next 6 mth.

* Overall Toc for Grave's → RAJA

S/E of Anti thyroid-

• mc is rash

• Agranulocytosis is most threatening compliⁿ but it is rare.

↓
So if pt. getting URI or any infecⁿ immediately we ask him to report.

* symptomatic benefit → β -blockers

* Toc for Grave's ophthalmopathy — steroid

* RAJA flares up ophthalmopathy

↓
So in severe ophthalmopathy

↓
we avoid RAJA.

Thyroiditis - 1 RAJU

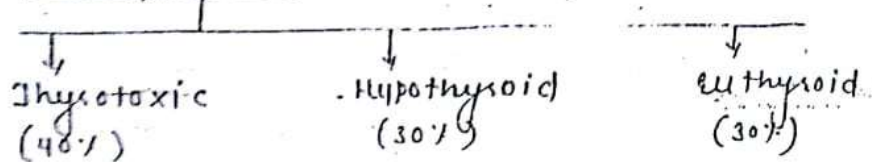
De Quervain's	Hashimoto's	Riedel's
- HLA B35 associ. CIF: H1O URI ↓ Loxace echo ↓ Thyrotoxicosis - Tender thyromegaly. ↓ 35% Euthyroid → nothing 15% Hypothyroid → L-T₄ Rx Rx: Pain → NSAID → 1wk → tail → steroid Thyrotoxic symptom → P-blocker on Bx - Granulomatous inflammation.	- Autoimmune Other ds. associated are - vitiligo pernicious anemia T₁ DM Addison's. → They generally don't presents in thyrotoxic state as the thyroid is non tender. Thyrotoxic ↓ 85% Hypothyroid → they present at this stage mostly. 15% Euthyroid → Inv: - mc. - 1st Hypothyroid on Bx → 1) CD4 ↑↑ 2) Hurthle (Askanazy) cell 3) RAJU ↓ 4) Anti TPO +ve → Rx - 1) L-T₄ replacement complicⁿ - Hashitoxicopathy ↓ Rx - steroid. "steroid responsive"	→ 91% ble of Fibrosis of thyroid gland. TFT ↓ 90% Euthyroid 30% Hypo T₄ CIF - ① They presents pressure symptoms like - stridor Dysphagia. ② Fibrosis of other places are also assoc. ex) RPF - (Ormond's ds) 2) mediastinal fibrosis 3) pyosonic's disease 4) PSC (1st sclerosing cholangitis) Inv - RAJU ↓ Rx - surgery PTM cancer • lymphoma.

"1st form" of Antinuclear Ab, glucose metabolism shut down & brain is affected.

(88)

Special thyroiditis —

(1) Post partum —



Inv: — • Tc^{99m} uptake ↓

(uptake is ↓^{ed} for I_{131} & Tc^{99m} but (N) in Breast feeding ♀, I scan is not done)

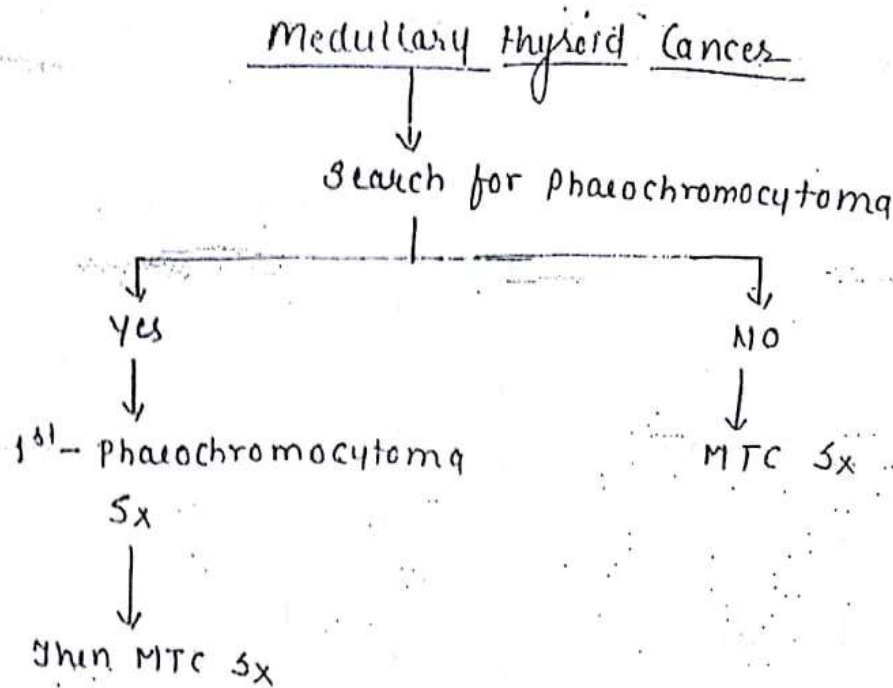
(2) Bacterial thyroiditis — ^{misnomer} It is actually a subcapsular abscess.

- It is U/L swelling
- Toxic symptoms like fever, pain.

Inv: — (1) TFT (N) (2) RAIU (N)

Rx — Drain abscess + Antibiotics.

(89)



* Prophylactic thyroidectomy is done in 5 yrs to a who is MEN-2 ⊕ & whose father is having MEN-2.

MEN			
MEN-1 (Weinreb)	MEN-2 (Sipple)	MEN-3	Casney Syndrome
AD	AD	AD	
MEN-1 gene	RET	RET	
Chr-11	Chr-10		
mc - Prolactinoma ✓	X	X	Pituitary
mc of death in MEN-1 ✓ Nonfunctional pheochromocytoma	X	X	Pituitary Pancreas
this is mc manifestation ✓ of MEN-1 hyperparathyroidism	✓	X	Parathyroid hyperplasia
X	✓	✓	MTC
X	✓	✓	Pheochromocytoma/paraganglioma
• Lipoma • Angiofibroma • Foregut Carcinoid	Lichen amyloidosis	• mastocytosis • mucosal neuroma	

Posterior pituitary doesn't have cells & so it doesn't form tumor. They generally undergo infiltration.
They cause blockage of ADH release.

90

Carney complex

- It is also a type of MEN syndrome.

① myxomas ———— cardiac
 extracardiac

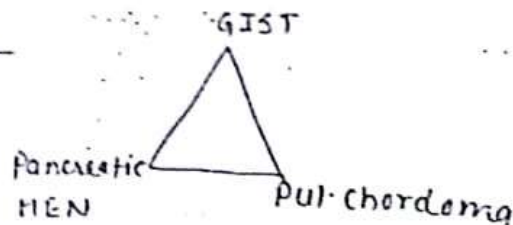
② Blue skin naevi

③ Psammoma-melanotic schwannoma

④ Pituitary tumor

⑤ Testicular tumor (mc - Sertoli cell tumor)

Carney triad -



Pancreatic NET

Insulinoma — • Benign (Gastrinoma → malign.)

↓
↑↑ Insulin

↓
↓↓ glucose (Hypo. < 40 mg/dL)

↓
Signs of Hypoglycemia

↓
Symptoms relieved by glucose

Whipple's triad.

qn insulinoma

⇒ glucose ↓↓ — Insulin ↑

DIFF — ① Insulinoma

② Sulfonylurea abuse

③ Insulin abuse.

	Insulinoma	SU abuse	Insulin abuse
1) C-peptide	↑	↑	↓
2) Urine sulfonyl-urea scan	-ve	+	-
↓			
only this test can differentiate b/w Insulinoma & sulfonylurea abuse.			
3) Pro-insuline	↑	↑	↓
4) Insulin - Ab	-	-	+
5) Insulin : glucose	> 0.3	> 0.3	> 0.3

(91)

Gold std. Inv: — ① 72 hr fasting

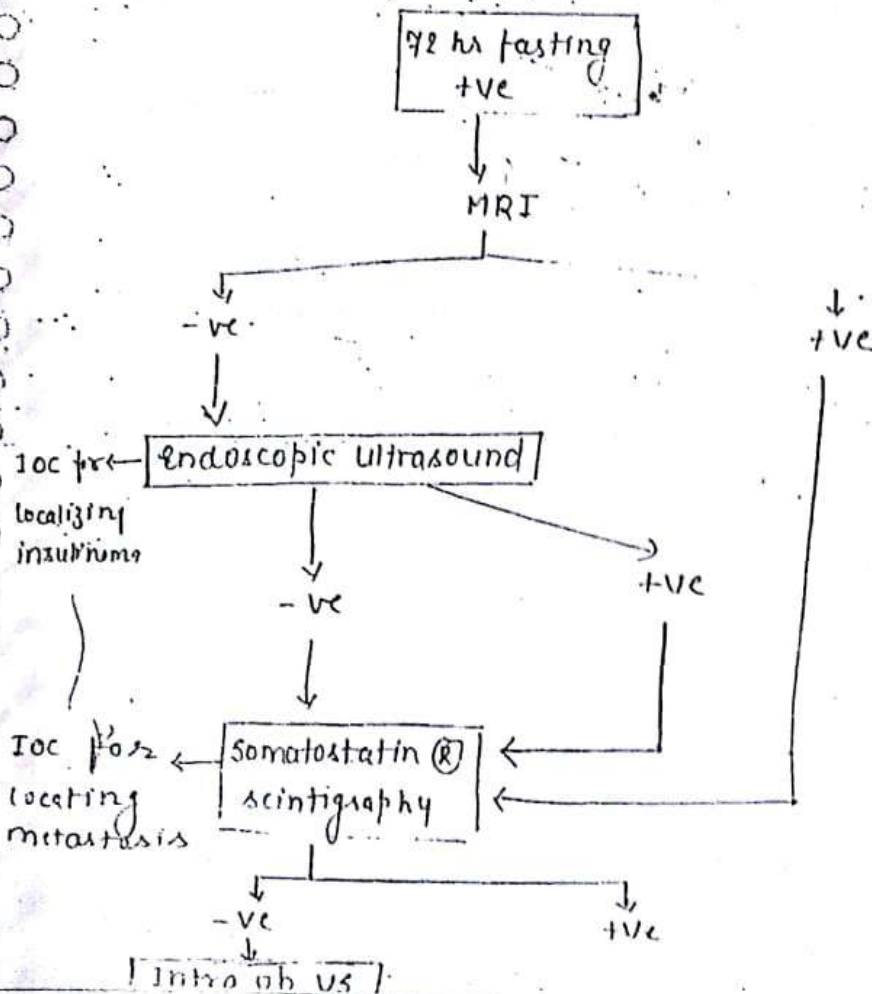
↓
[glucose ↓]

↓
So insulin should also be ↓
but in insulinoma after fasting

[Insulin ↑]

② C-peptide ↑↑ (to rule out insulin abuse)

③ Sulfonylurea screen -ve (rule out sulfonylurea abuse)



Rx → NEN's

TOC - surgery
malignant ↓ fail

Streptozotocin
+ 5FU

+ only 1 octreotide
everolimus
diazoxide

Glucagonoma → malignant

NME
Necrotic
migratory
erythema

Hyperglycemia

↑↑ glucagon
↓
Gluconeogenesis

⚡ (AA)

cachexia → BIC of protein breakdown
(severe)

Indic?

- β-blocker toxicity
- IV line can't be

TOC - octreotide (to suppress glucagon level)

↓ fails

AA + FA infusion

Vipomg

W } watery diarrhoea
D }
H - Hypokalemia
A - Acidosis

— X —

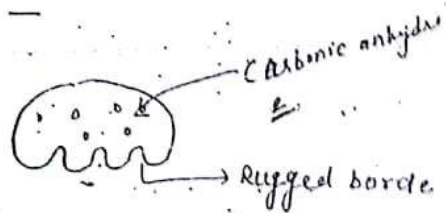
Osteoblast

- Bone forming
- Fibroblast lineage
- PTH / vit D (R)



Osteoclast

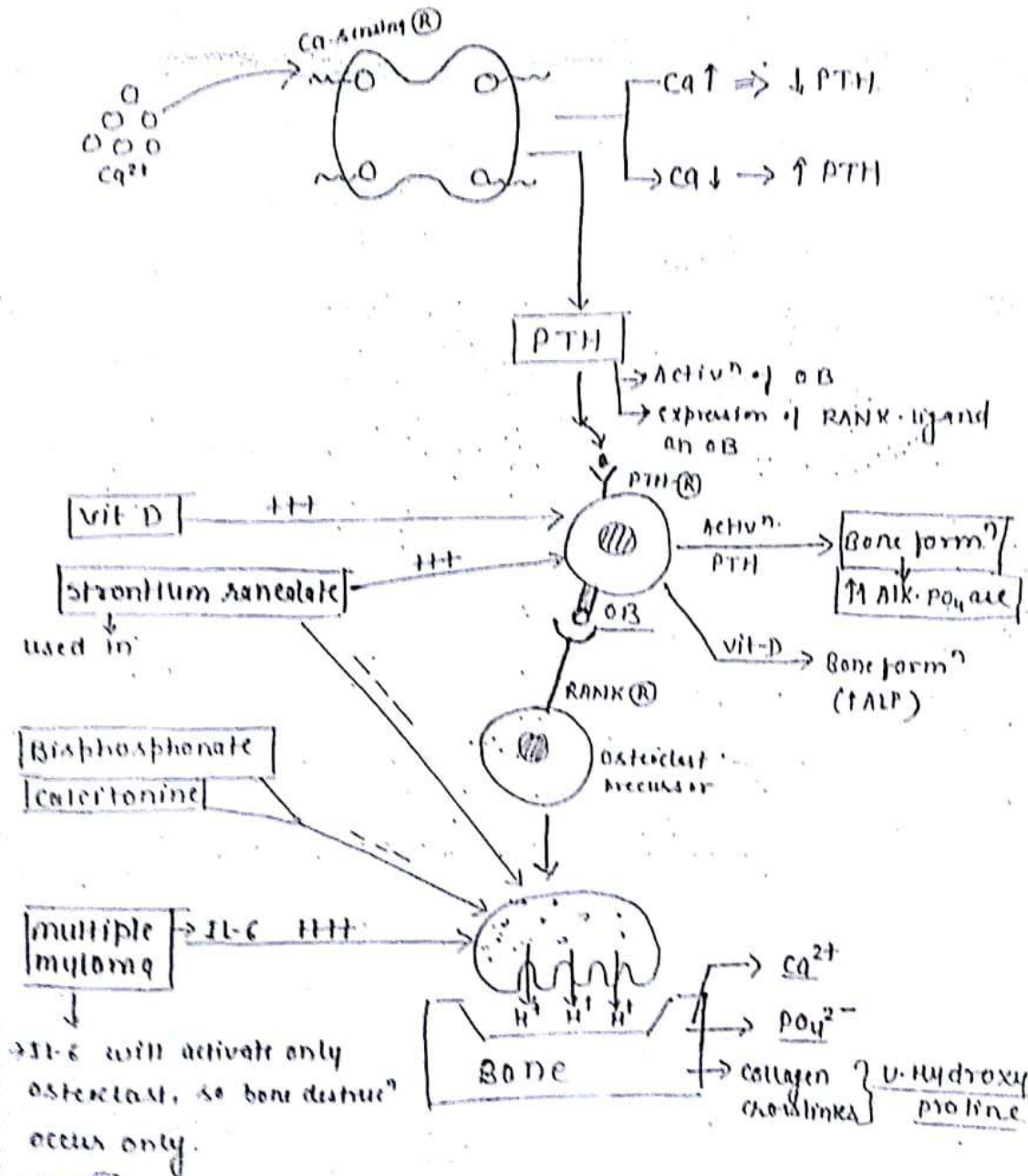
- Bone destroying
- macrophage



This CA-2 help in formⁿ of acid which help in bone dissoluti.

↓
In osteopetrosis there is def. of CA .

Parathyroid



$\rightarrow$ ALP $\uparrow$

$\rightarrow$ Bone scan -ve $\Rightarrow$ Bcz bone scan detect osteoblastic activity & in MM there is no osteoblastic activity.

$\rightarrow$ IL-6 inhibitor is Dexamethasone. So we give Dexamethasone + lenalidomide

(93)

* **PTH**

1) At physiological dose — $\uparrow B \approx \uparrow C \Rightarrow$ Remodelling

2) At low pulsatile dose — $\uparrow B \gg \uparrow C \Rightarrow$ Bone protector

Teriparatide $\rightarrow$ A recombinant PTH given in post menopausal $\varnothing$ at low pulsatile dose

3) At high continuous dose $\rightarrow \uparrow\uparrow\uparrow C \gg \uparrow B \Rightarrow$ Bone destroy
ex- osteogenic fibrosis cysts

* Vit-D — Bone forming agent.

↳ we give vit D in osteoporotic not to correct vit-D def. but to promote bone formⁿ.

Bisphosphonate
calcitonin

$\ominus$ osteoclast

So in hypercalcemic state d/t osteoclastic activity we can give these drug to low down $S. Ca^{2+}$ level.

9m MM —

* osteoblastic activity & pressure — Wolff law.

↳ it can be done by ~~stim~~ early mobilizⁿ in #.

Drug $\ominus$ RANK - RANKL interaction $\rightarrow$

- Osteoprotogerin (natural)
- Denosumab

Both are bone forming

PTH $\uparrow\uparrow$

- 1) • $\uparrow$ s. Ca^{2+}
- 2) • $\downarrow$ s. PO_4^{2-} (kidney)
- 3) • $\uparrow$ Urine Ca^{2+}

$\downarrow$
urinary Ca^{2+} is not dependent on PTH.
in DCT there are Ca^{2+} sensing (R)

$\downarrow$
if $\uparrow$ Ca^{2+} in urine
 $\downarrow$
 $\downarrow$ Absorpⁿ of Ca^{2+}
 $\downarrow$
 $\uparrow$ Ca^{2+} in urine

$\rightarrow$ if pt. has $\uparrow$ PTH $\rightarrow \uparrow$ Ca^{2+} will be in DCT.

$\downarrow$
so Ca^{2+} (R) will sense it

This is not bcz of action of PTH it is bcz of $\uparrow$ Ca^{2+} going to DCT. it is a protective mechanism

$\rightarrow \uparrow$ Ca^{2+} will pass out in urine ($\uparrow$ U. Ca^{2+})

(94)

Vit-D ↑

- 1) ↑ S. Ca^{2+}
- 2) ↑ S. PO_4^{2-}
- 3) ↑ U. Ca^{2+} (bcg of Ca^{2+} sensing (R))
- 4) ↑ ALP

→ Stim serum Ca^{2+} ↑ & it CASR will try to throw it out.

CAS(R) (protective funcⁿ)

- when s. Ca^{2+} is in (N) range level of PTH & Vit-D will operate.
- when s. Ca^{2+} ↑ / ↓ then CAS(R) will come to play role

CAS(R) range - 7.5 - 10.5.

	Blast	clast	Ca^{2+}	PO_4^{3-}
1) PTH (Physiol.)	↑	↑	↔	↔
2) Low / Pulsatile PTH	↑↑	↔	↔	↔
3) High / Continuous PTH	↑↑	↑↑↑↑	↑	↓
4) Vit-D	↑↑	↔	↑ (intestine)	↑
5) Bisphosphonate	↔	↓↓	↔	↔
6) Calcitonin	↔	↓↓	↓ (mild)	↔
7) Strontium Ranelate	↑↑	↓↓	↔	↔
8) Multiple myeloma	↔	↑↑	↑↑	↑↑

* Sarcoidosis → granuloma secretes 1- α -hydroxylase

↓
↑ 1,25 (OH) $_2$ CC

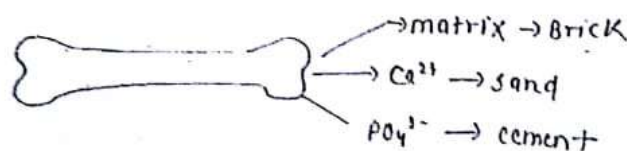
↓
So same features like vit D toxicity

* Osteoporosis →

↓
↓ matrix synthesis

↓
So minerals are (N) here.

→ DXA scan shows ↓ bone density.



(95)

	Ca^{2+}	PO_4^{3-}	PTH	ALP	Comments
1) 1 ^o Hyper PTH	↑	↓	↑↑↑	↑	U-Ca ²⁺ ↑ mcc - adenoma (Rt. inferior lobe)
2) 2 ^o Hyper PTH - Renal failure - vit-D. def.	↓(1) ↓(1)	↑ (↑) ↑↑↑ ↓	↑↑↑(1) ↑↑(1)	↑↑↑ ↑	Osteitis fibrosa cystica
3) vit-D toxicity	↑	↑	↓	mild ↑	U-Ca ²⁺ ↑ 25(OH)CC > ↑↑ 1,25(OH) ₂ CC
4) sarcoidosis	↑	↑	↓	mild ↑	U-Ca ²⁺ ↑ 25(OH)CC - (N) 1,25(OH) ₂ CC - ↑↑
5) 1 ^o Hypo PTH	↓	↑	↓↓↓	(N)	U-Ca ²⁺ ↓ mcc - Thyroid Sr
6) multiple myeloma	↑↑	↑↑	↓↓	(N)	purely lytic (clast)
7) PTHrP also like PTH	↑↑ ↑ Ca ²⁺ suppress endogenous PTH	↓	↓	↑↑	U-Ca ²⁺ ↑ [PNS] → se. cc of lung → RCC
8) osteoporosis	(N)	(N)	(N)	(N)	- matrix problem - Inv - DXA scan
9) Paget's	(N)	(N)	(N)	↑↑	urine. Hydroxyproline ↑
10) Benign familial Hyper Ca ²⁺ / Familial Hypercalcemic Hypercalcemia	↑	↓	↑	↑	CaS (R) is the problem. U-Ca ²⁺ ↓ → so differentiate from 1 ^o Hyper PTH

Scanned by CamScanner

(96)

* FHH - Ca^{2+} sensitivity become poor.

For ex. (N) threshold for Ca^{2+}

< 7.5

> 10

But here it will shift threshold to 9

so pt. has adequate Ca^{2+} actually but Ca^{2+} detect
if as $\downarrow Ca^{2+} \rightarrow$ so. in urine $Ca^{2+} \downarrow$ (to conserve Ca^{2+})

$\rightarrow$ Now PTH is (N)

AHO —

- short stature.
- obesity / round face.
- Brachydactyly (short 4th & 5th metacarpal)

$\downarrow$
Knuckle knuckle dimple dimple sign.

[1° Hyper PTH]

* 85 % cases dth adenoma, 15 % dth hyperplasia.

mc:- Rt. Inf. Lobe.

→ mc presentⁿ — asymptomatic Ca^{2+} ↑

mc symptom — Bone pain

CIF — 1) Stone → dth urinary ↑ Ca^{2+}

1) Abd. groans → serum Ca^{2+} ↑ — Contractⁿ ↓

↓
muscle weakness

↓
less peristalsis → constipⁿ

↑ serum Ca^{2+}

↓

* Also ↑ Histamine

↓
↑ acid

↓
↑ peptic ulcer disease

3) Psyc. moans → Calcifreⁿ of Basal ganglia (metast. calcifreⁿ)

↑ PO_4^{-3} can also cause metast. calcifreⁿ.

↓

In pseudohyper PTH

4) Band shaped keratopathy.

INV:- 1) ↑ Urine Ca^{2+} & other features of 1° hyper PTH

2) Sestamibi scan — Done to localize the gland which is abnormal so that the particular gland can be removed.

Page's

* Activⁿ of Blast >> clast.

→ ↑ in head sign.

* Presentⁿ → Asymptomatic ↑ level of ALP.

* 91 symptomatic — mc is bone pain (shin of tibia)

* mc neurological symptom — Headach

* " — " — sign — Deafness d/t involvement of 8th N.

(bcz of compression of N. bundle)

X-ray — mosaic appearance in IOM)

* Blade of grass appearance.

Tt — Bisphosphonate.

Osteoporosis

* DXA scan → Done at spine & femur.

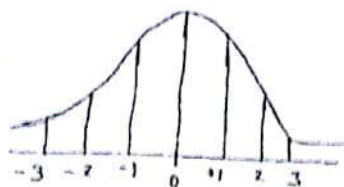
* Quantitative CT (QCT)

→ Result Interpretation in DXA is done by T-score.

Score -3

↓
Pt. is worst than
99% populⁿ

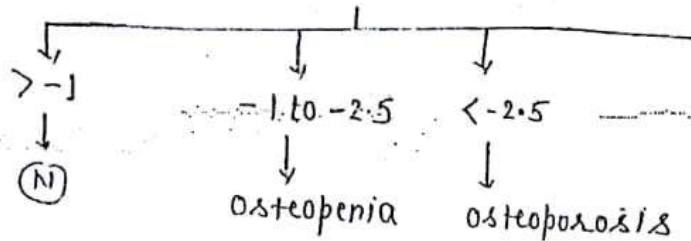
0
↓
Pt. is better
than 50% populⁿ
& worst than
50% populⁿ



(98)

Osteoporosis

T-score



* Post-menopausal osteoporosis, is: mc.

Rx —

↓
post-menopausal symptoms

Yes

↓
HRT

No

↓
Bisphosphonate+
vit-D & calcium

Alt. → Teriparatide (aPTH)

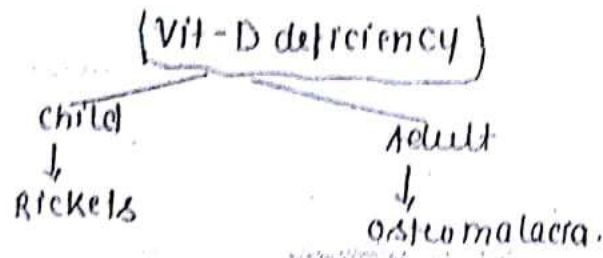
C/I of Bisphosphonate —

- Renal failure
- GERD

→ Bisphosphonate causes severe esophagitis (also caused by Doxycycline)

SIE — ① ↑ RISK of # femur

② osteonecrosis of jaw



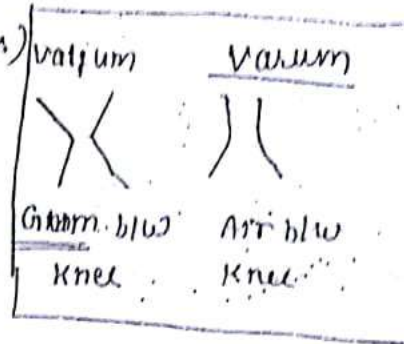
Infant — craniotables

child — pot belly.

• Harrison sulcus

• Costochondral beading (Painless)

• Genu valgum



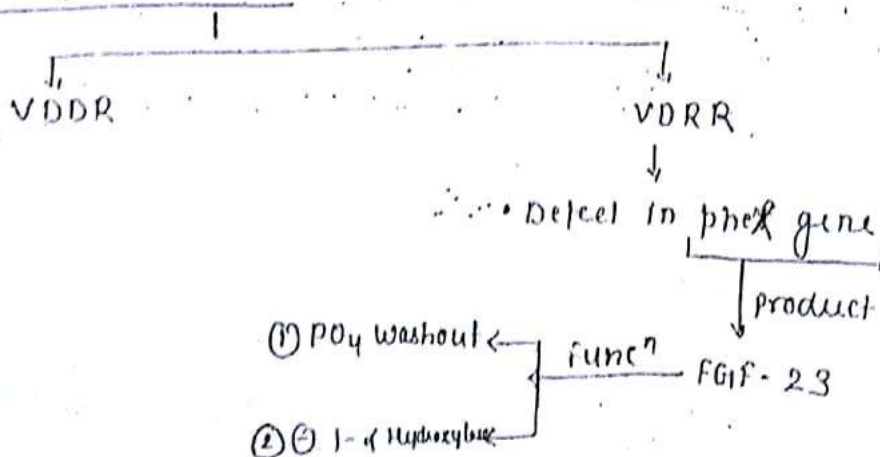
osteomalacia —

on x-ray — L — Looser's zone

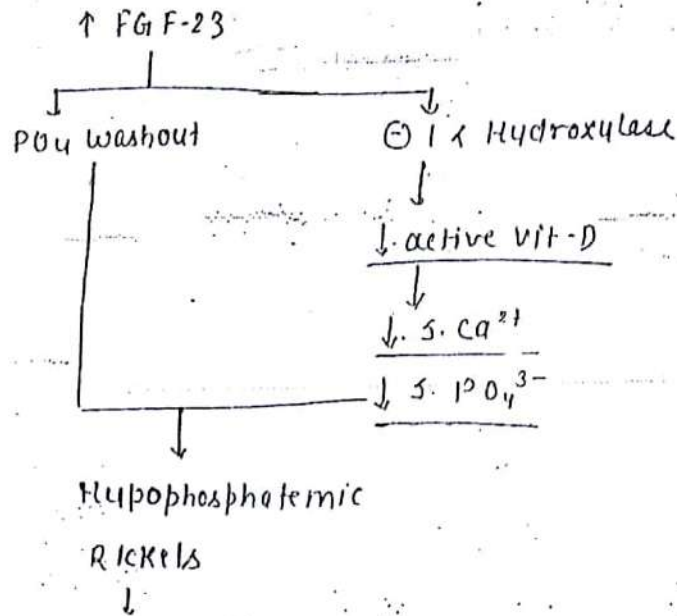
A — Acetabular protrusion

T — Trilateral pelvis

Types of Rickets —



(99)



$S. Ca^{2+} \downarrow$ $S. PO_4^{3-} \downarrow$ $vit-D \downarrow$
--

x q1 we give only Ca^{2+} for tit, it will not correct PO_4^{3-} deficiency. so PO_4^{3-} should also be corrected simultaneously.

→ After Rx → they get ^{renal} cal-store.

Malignant Hypercalcemia

Severe

$>13.5 \text{ mg/dl}$

Ca^{2+} (suprathreshold)

so they will not excrete urine

Distal
RTA

polyuria

Dehydration

($\because \text{Ca}^{2+}$ is toxic to distal nephron)

Aquaporin damage

severe dehydrⁿ

s. $\text{Ca}^{2+} \uparrow \uparrow$

vicious cycle $\rightarrow$ Death

Rx - 1st - IVF - give NS

hemodiluⁿ $\rightarrow \text{Ca}^{2+}$ start getting down

2nd -

I.V. Bisphosphonate (pre req - No renal failure)

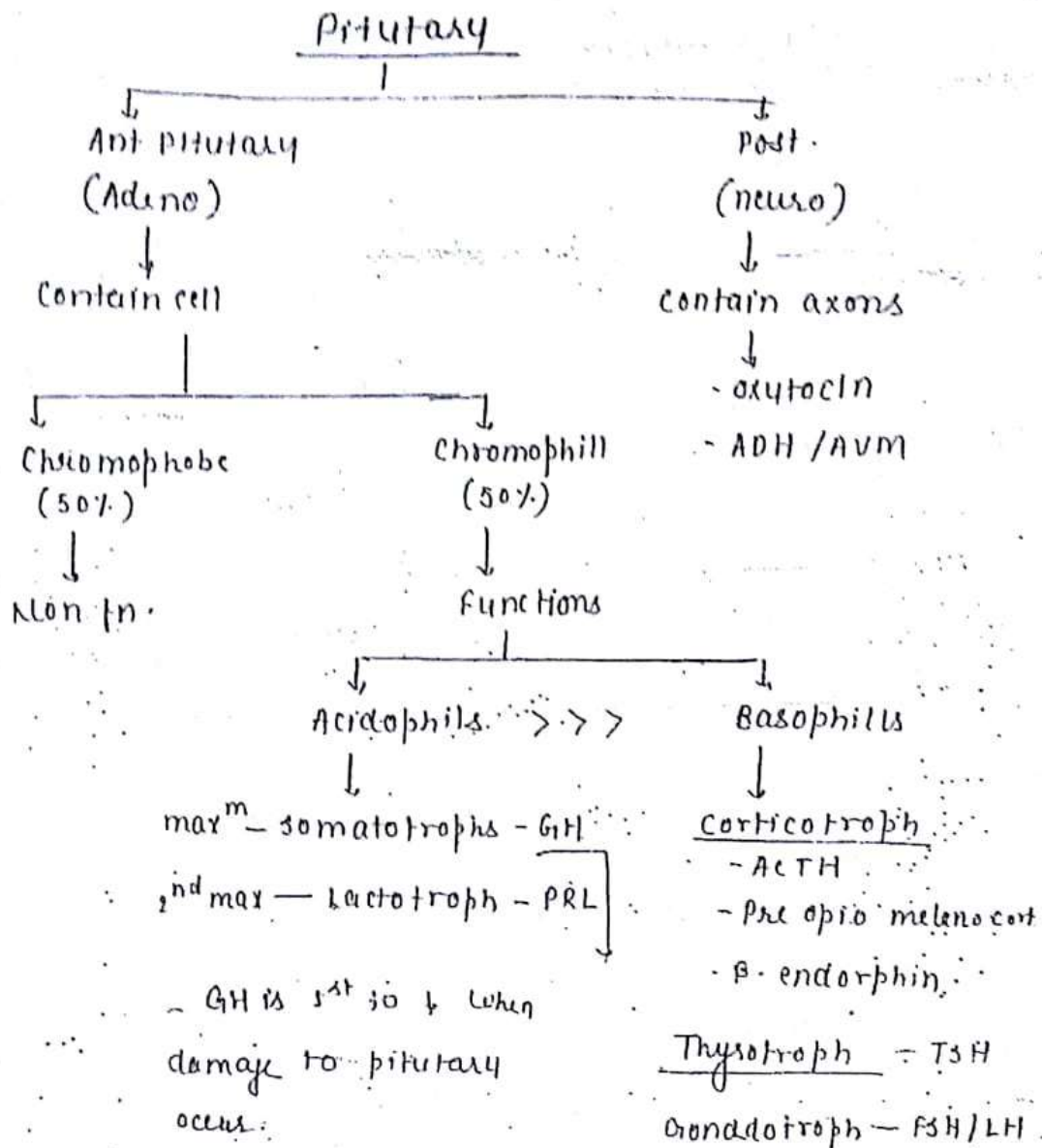
3rd -

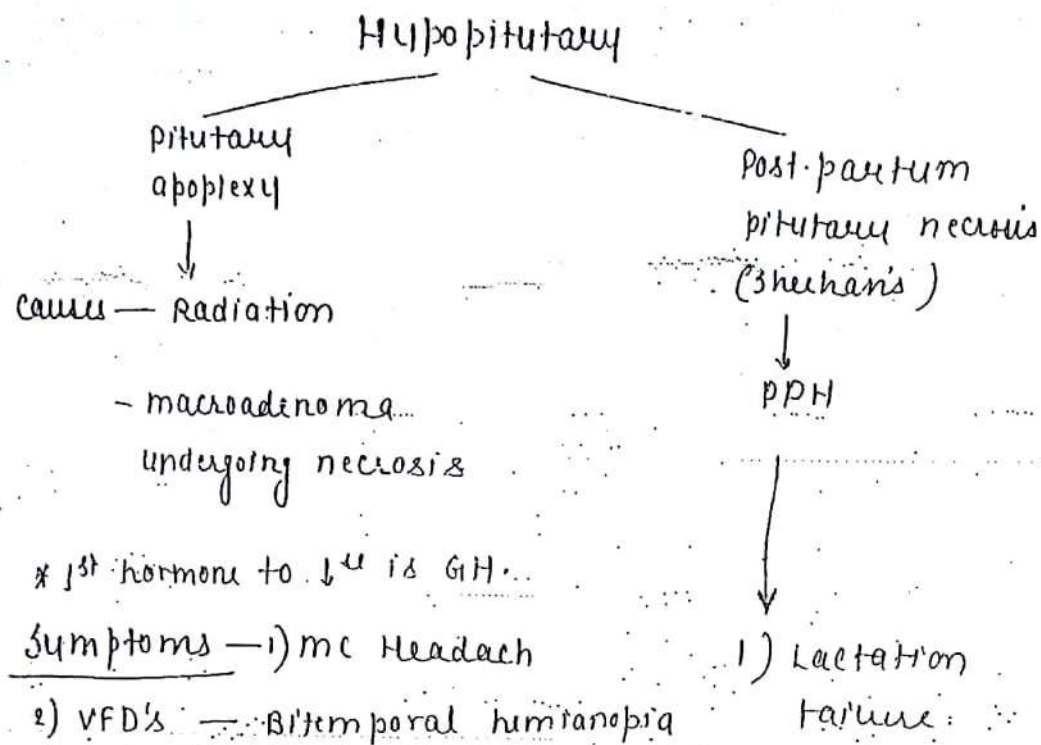
fosfamide ($\uparrow \text{U. Ca}^{2+}$)

4th -

calcitonin } $\rightarrow \uparrow$ sensitivity of $\text{CaS}(\text{R})$ to Ca^{2+}
cinacalcet }

(100)





↓

Rx — Give steroid bcz reduction in any other hormone doesn't cause any immediate problem.

GH def. → • Central obesity

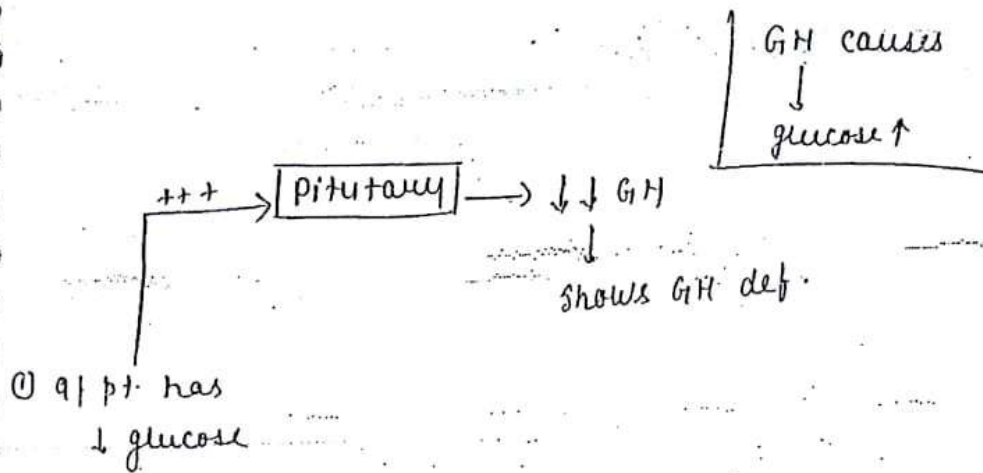
• ↑ sensitivity to Insulin

↓
more prone for hypoglycaemic attack.

* evaln of GH def. is done in few cases i.e. when there is risk assoc. to Hypopituitarism.

— INV:- Best test (gold std) → Insulin tolerance test (ITT)

(101)



* GH RH test —: / GH RH arginine test —>

Give GHRH

↓ ①

Pituitary

↓

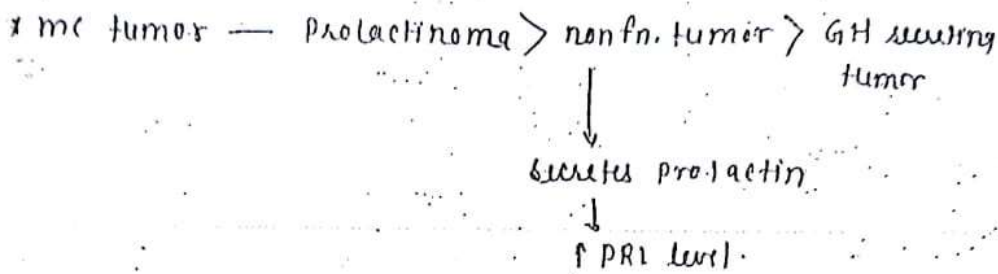
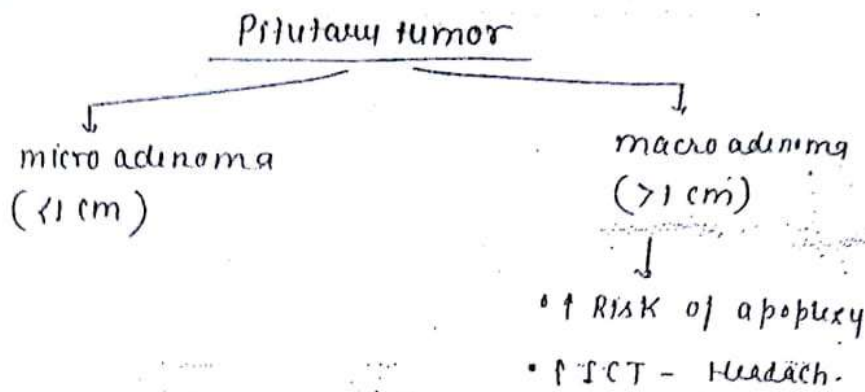
so GH should be released

↓

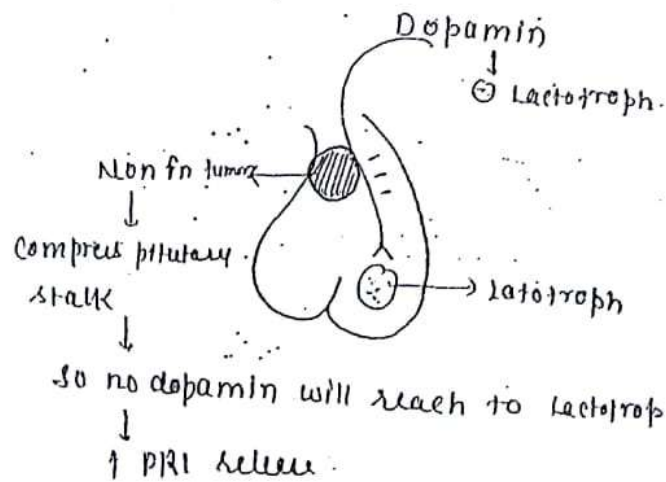
q1 still ↓ GH

↓

GH def.



Prolactinoma — • mc in ♀.
• mc pituitary tumor.



(102)

↑ PRL — ① micro/macro prolactinoma

② 1st Hypo T₄

③ stalk compression

④ empty sella

⑤ drugs — • neuroleptics
• metoclopramide
• Domperidone
• cocaine
• d methyl Depa.

CIF — ① mc — Hypogonadism

women

↓
Amenorrhoea

men

↓
- Loss of libido
- erectile dysfunction

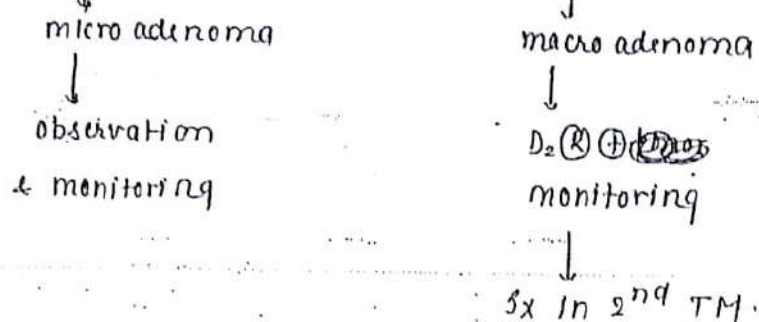
② 2nd mc — galactorrhoea

Inv! — 1) S. PRL ↑↑

↓
TOC ← MRI

R_x — TOC — DR ⊕ — Bromocriptine
• Cabergoline
• Pergolide
] — fails —> S_x
(Transsphenoidal)

Rx in pregnancy —



Acromegaly — m.c. GH secreting pituitary tumor.

CLF — 1) expansion of bone width & soft tissue

↑ in size of ring & shoes.

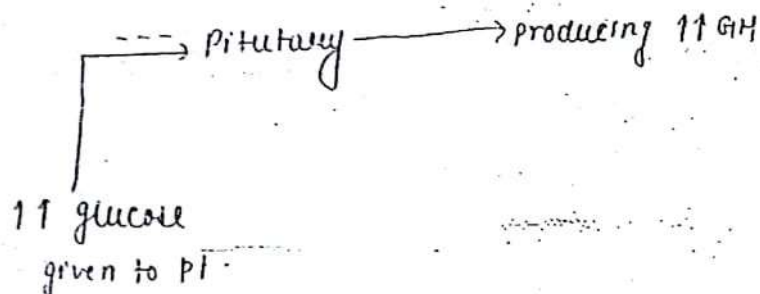
- 2) prognathism
- 3) frontal bossing
- 4) coarse facial features.
- 5) obs. sleep apnoea.
- 6) sweaty hand.
- 7) central obesity.
- 8) Glucose intolerance.
- 9) sys. HTN.

* m.c. of death — cardiovascular problem.

Rx — T_{oc} — Trans sphenoidal Sx.

I_{ac} — oral glucose tolerance test.

103

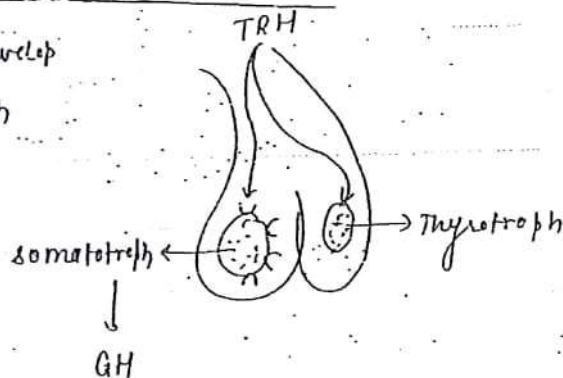


— even after giving 1 glucose there is 1 GH produced.

* Paradoxical response to TRH →

TRH (R) also develop
on somatotroph

↓
So when we give
TRH, GH starts
releasing.



Rx — T0C — Trans sphenoidal Sx

↓ fails

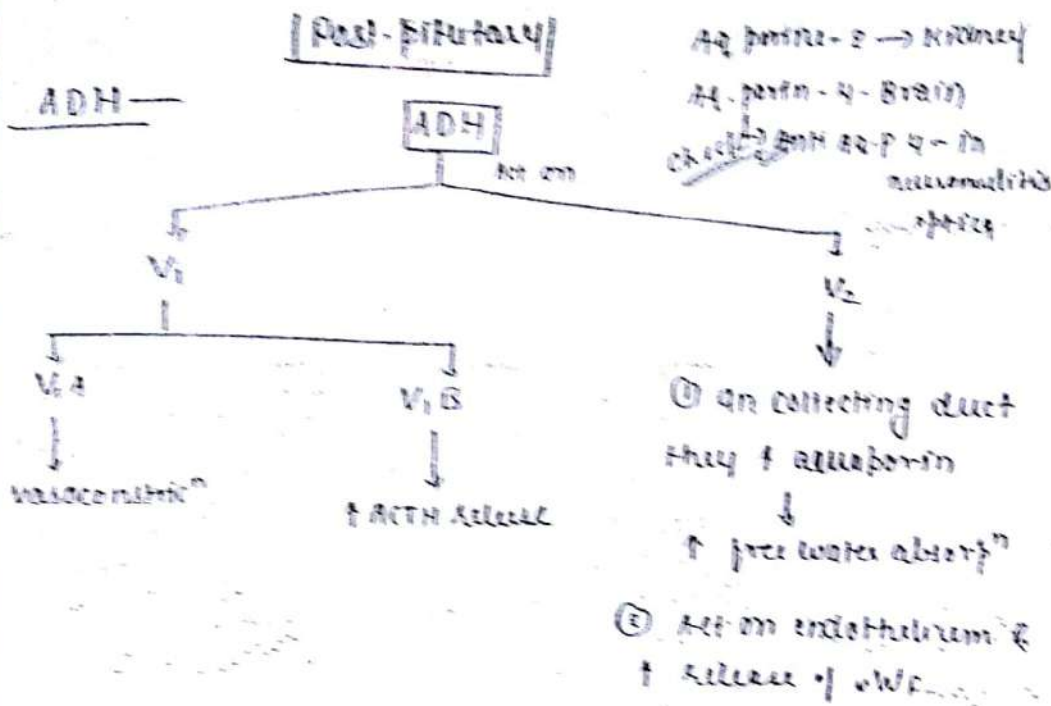
medical Rx ± RT

↓

- Octreotide
- Pasireotide

→ selective GHR ⊖

- Pegvisomant → stops action of GH.



* Vasopressin act on both V_1 & V_2 ①

* Desmopressin act on $V_2 \gg \gg V_1$

— selective V_2 ① → vaptans

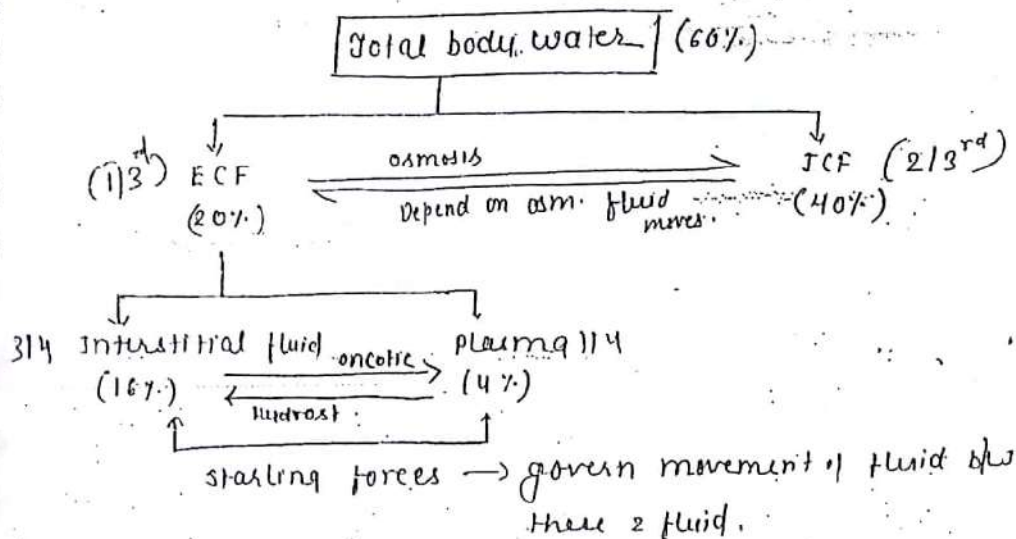
— selective V_1 ① agonist → Terlipressin

↑ DOC for Diab. Insipidus
VW disease } → Desmopressin → available intranasal form.

* DOC for vaptans & ADH — vaptans

* DOC for variceal bleed — Terlipressin (V_1 agonist)

(104)



1 Hydro-pressure — Heart failure → fluid shift to interstitial fluid.
Nephrotic to

$$S_{osmolality} = 2[Na^+] + \frac{BUN}{2.8} + \frac{glu}{18}$$

↓
285 - 295 mosm/kg

→ effective osmolality → doesn't consider urea.

* Na^+ is major contributor of osmolality.

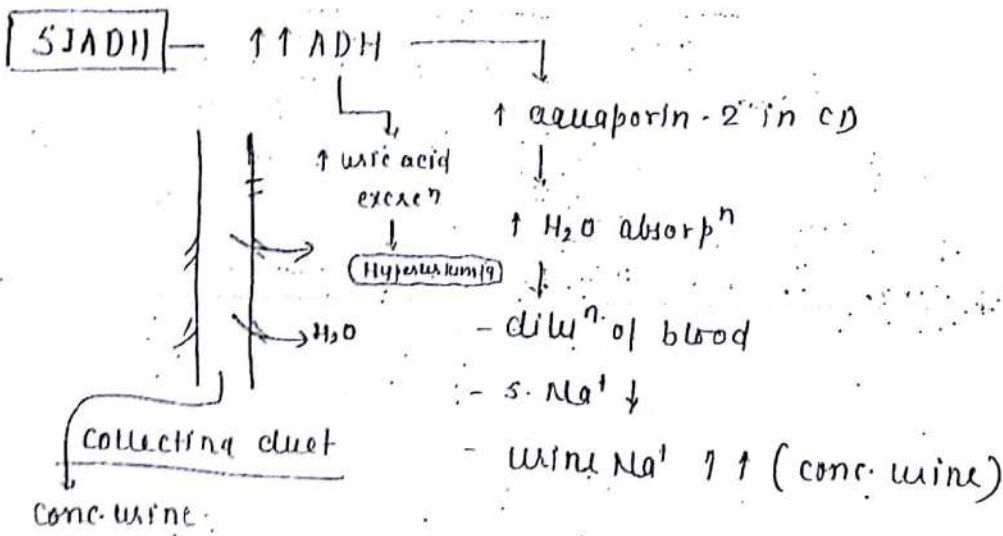
↓
even small change in Na^+ will cause big change in osmolality

↓
fluid movement occur b/w ICF & ECF.

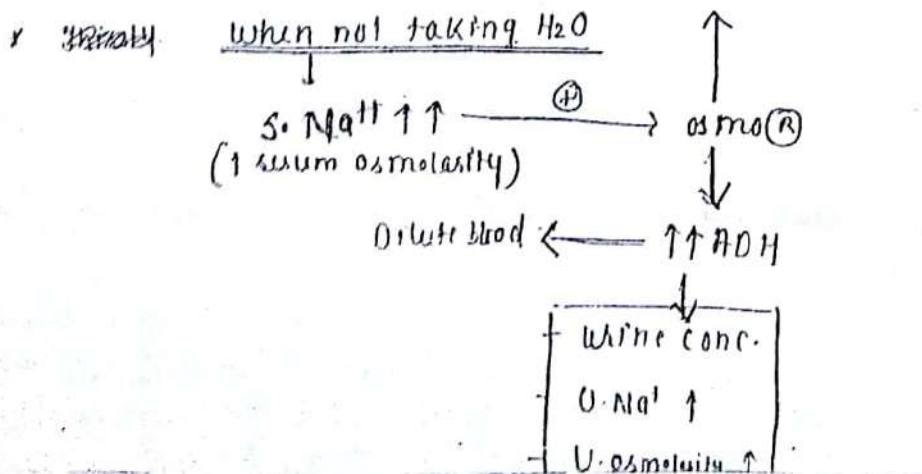
Total body Na^+ = full vol. status of body, not S. Na^+ .

$$\frac{\text{S. Na}^+}{\text{TBW}} = \frac{\text{TBNa}^+}{\text{TBW}}$$

→ S. Na^+ → reflects fluid shift, not fluid status of body.



S. Na^+ ↓↓	U. Na^+ ↑↑
S. osm ↓↓	U. osm ↑↑



(105)

Drugs producing SIADH —

- carbamazepine
- cisplatin
- cyclophosphamide
- thiazide
- SSRJ → Fluoxetine.

- small cell lung cancer → here the PNS is SIADH
- Any infection
- Any lung pathology pneumonia specially legionella.
- Acute inter. porphyrria.
- Neuro SA

CIF of SIADH — $\downarrow S.Na^+$ (dil. hypo Na^+) = $\frac{TBW Na^+}{TBW} \downarrow$ — (N)

① — Euvolemic

- no effusion
- no edema
- (N) B.P.

② — problem occur bcz $\uparrow$ Hyper Na^+

↓

$\downarrow$ S. osmolality

↓

Fluid movement.

③ → (N) TFT

④ → only S. Na^+ is affected, rest all ions are (N)

Rx — ↑ TBW causing ↓ S. Na⁺

① Fluid restriction → for mild-moderate cases

② Severe / symptomatic

↓
vaptans
+
Fluid restriction

Indicⁿ of vaptans —

① Any euvolemic hyponatremia (any condition)

② Hypervolemic hyponatremia

↓
used in CHF

Qn CHF — ↑ TBW

↑ TB Na⁺ (d/t RAAS)

So S. Na⁺ ↓↓

↓
By giving vaptans H₂O loss occur & Na⁺
also come back to (N) level.

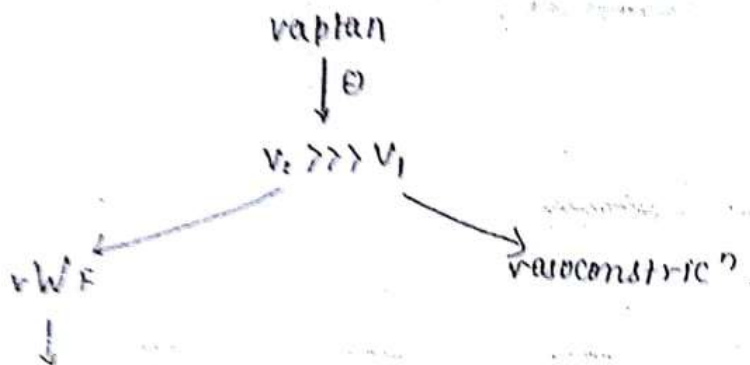
C/I — ① Hypovolemic hyponatremia.

↓ S. Na⁺ = $\frac{\text{TB Na}^+ \downarrow \downarrow}{\text{TBW} \downarrow}$ → Dehydrated

- If we give vaptan — $\frac{\text{TBW} \downarrow \downarrow \downarrow}{\downarrow}$ + S. Na⁺ ↑↑↑
more H₂O loss

(106)

② Hypertensive Hypotensive Diff. DCLD

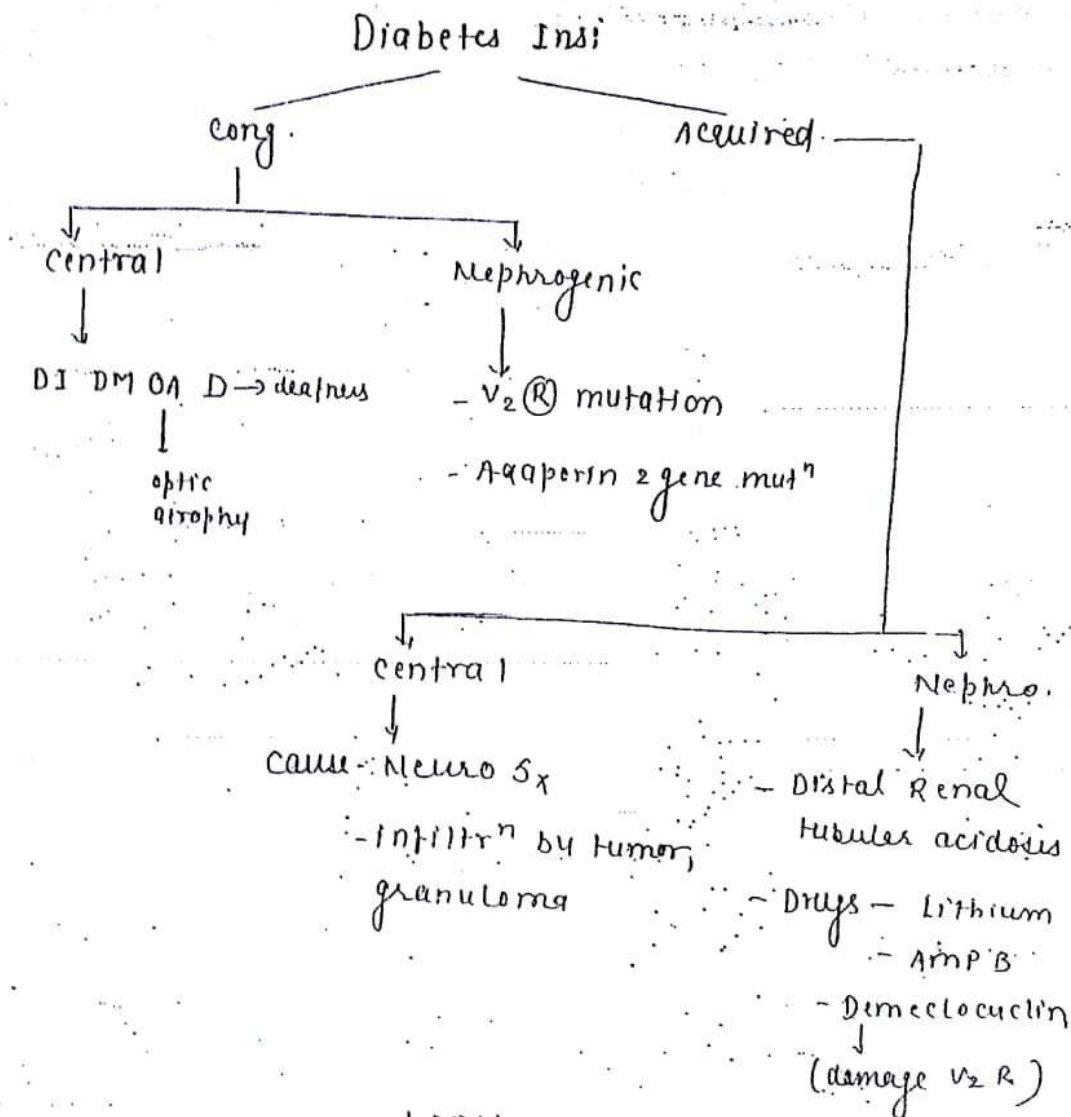


In DCLD pt already there are no coagulⁿ factor
only they depend on platelet plug for hemostasis.

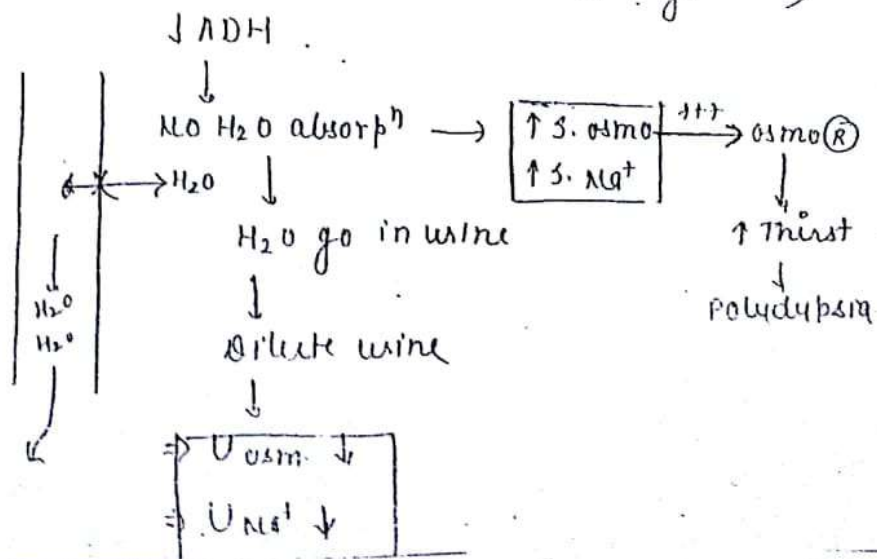
↓
By giving vaptan



Dmg - Tolvaptan - oral
Conivaptan - i.v.



Path:-



(107)

CIE - Polyuria ($>3\text{L/day}$ - Defⁿ)
polydypsia

R_x - T0c - Desmopressin acetate.

Psychogenic polydypsia - (1^o polydypsia)

$\rightarrow \downarrow \downarrow \text{S. Na}^+ = \frac{\text{TBW Na}^+}{\text{TBW}} \text{ (N)} \rightarrow \text{euvolemic}$

S. osmolality $\downarrow$
S. Na⁺ $\downarrow$

suppress ADH

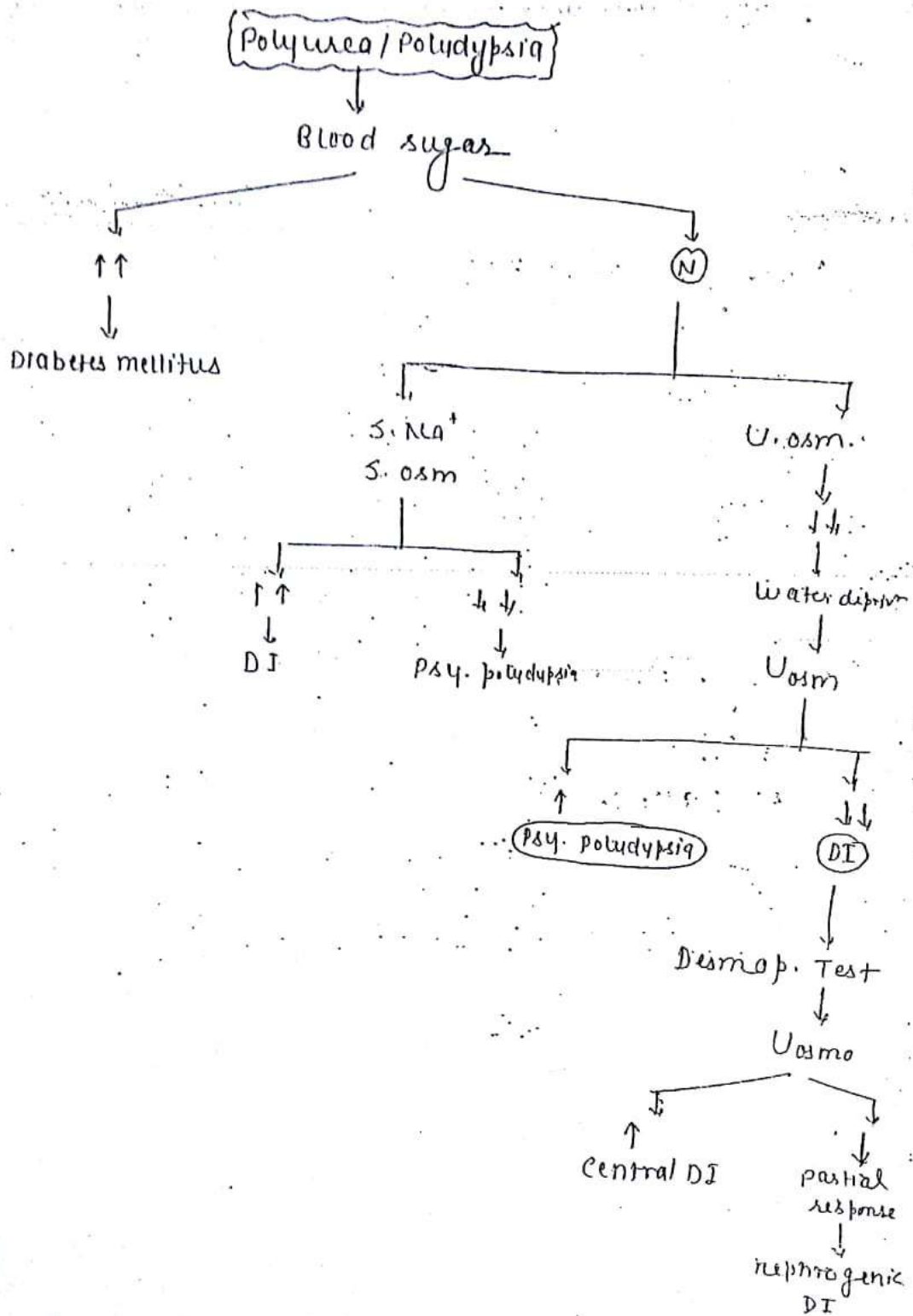
more H₂O loss in urine.

U. osmo $\downarrow$
U. Na⁺ $\downarrow$

Arrow in same direcⁿ
 $\downarrow$
mean
ADH axis is (N)

	U _{osm}	U _{osmolality} water depriv ⁿ	Desmopressin test
• Central DI	$\downarrow$	$\downarrow$	$\uparrow \rightarrow$ random is (N) $\leftarrow$ when ADH is given it corrects the difference
• Nephro. DI	$\downarrow$	$\downarrow$	$\downarrow$
• Psy. Polydypsia $\downarrow$ water depriv ⁿ	$\downarrow$	$\uparrow$	$\uparrow \uparrow$

$\downarrow \downarrow \text{TBW}$
 $\downarrow$
S. osm[?]
 $\downarrow$
ADH $\rightarrow$ $\uparrow$ H₂O absorpⁿ

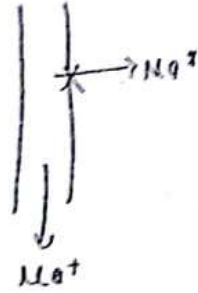


(108)

Cerebral salt wasting syndrome - mimics SIADH

↓
Brain lesion

↓
causing Na^+ loss



Path:- $\downarrow \downarrow \downarrow \text{Na}^+ \approx \frac{\text{TBNa}^+ \downarrow \downarrow \downarrow}{\text{TBW} \downarrow}$

↓
 $\downarrow \downarrow \text{Osmolar}$

urine $\left\{ \begin{array}{l} \text{Na}^+ \uparrow \\ \text{osmolality} \uparrow \end{array} \right.$

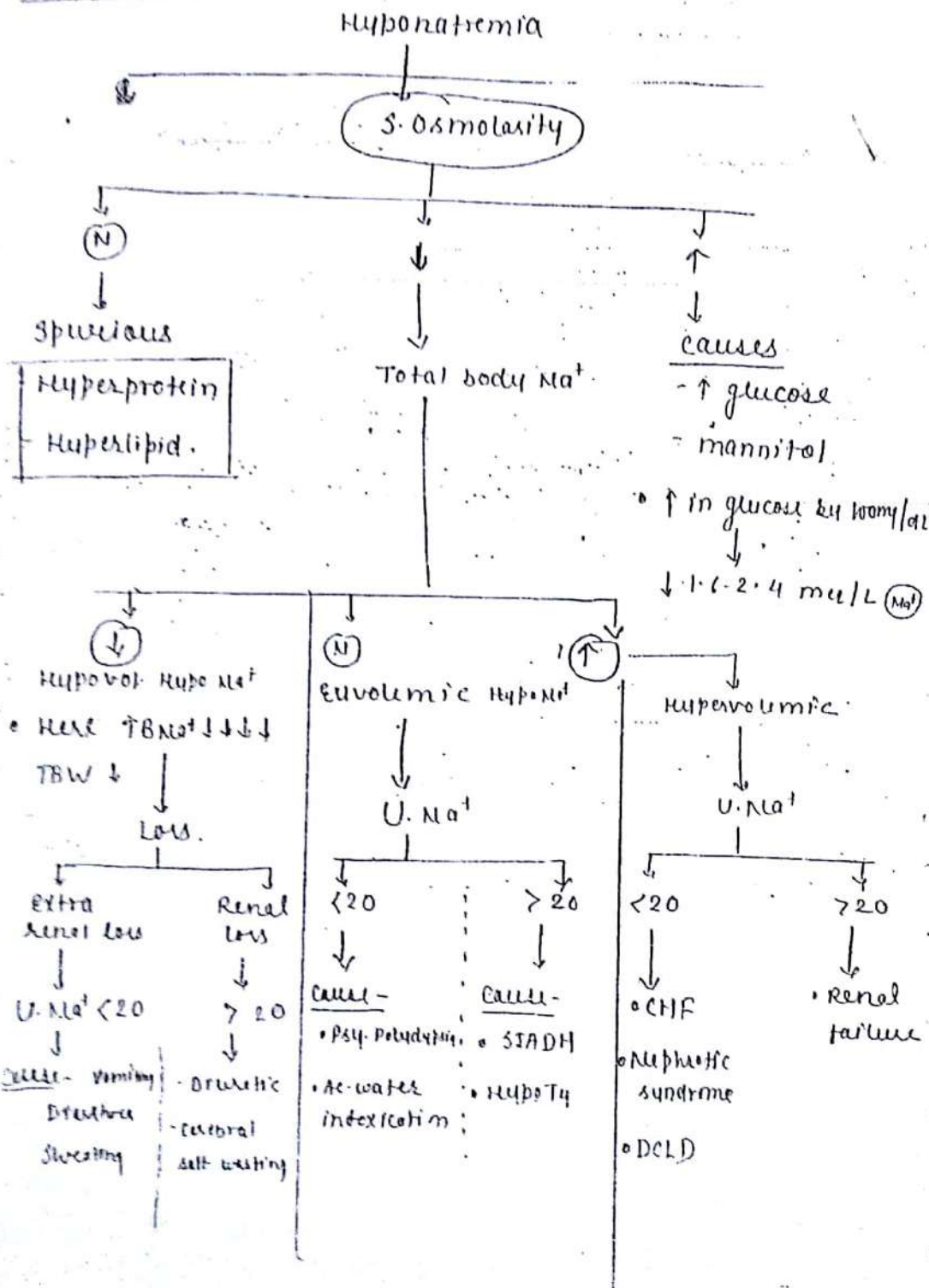
↳ same as SIADH

* only diff. is in this pt. $\text{TBNa}^+ \downarrow \downarrow \downarrow$ & they are dehydrated.

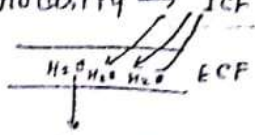
* here $\downarrow \downarrow \text{Osmolarity} \downarrow$
↓
no polydipsia ↓
↓
↓ $\downarrow$ ADH

* use acid (11)

Evaluation of Hyponatremia



(107)

* mannitol $\rightarrow$ $\uparrow$ osmolality $\rightarrow$ ICF

 $\uparrow$ H₂O causes Hypo Na⁺

Rx -

mild
(125-135)

- nausea + vomiting
- Lethargy
- cramps

moderate
(120-125)

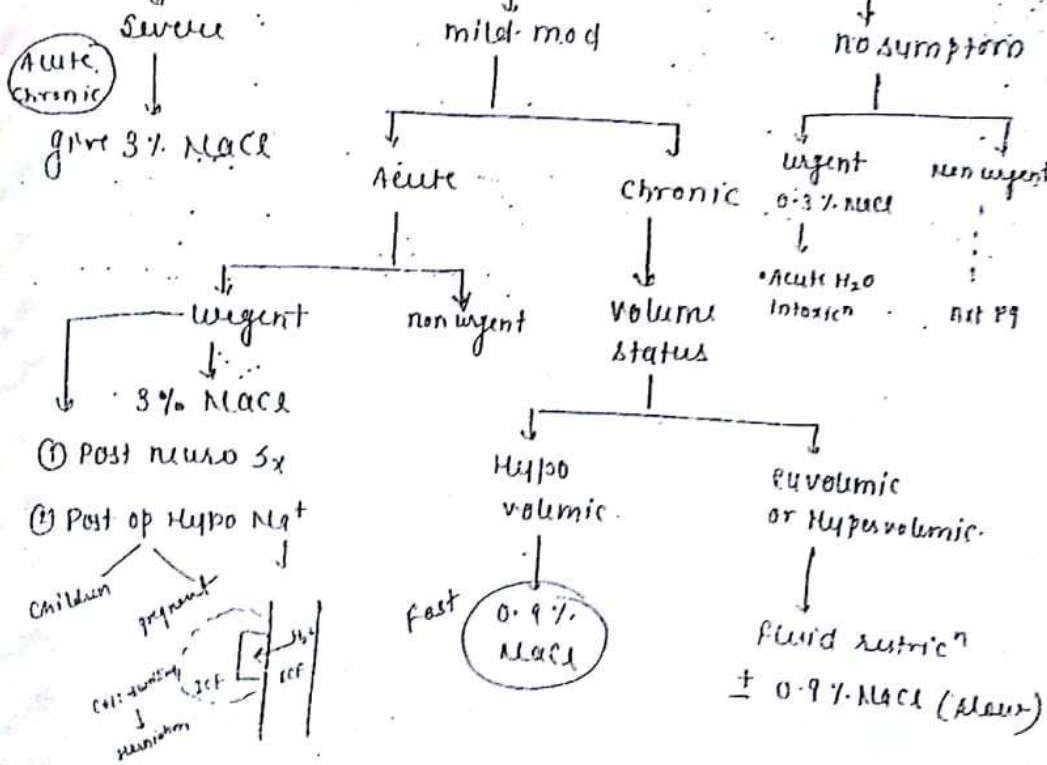
- Headach
- Delirium

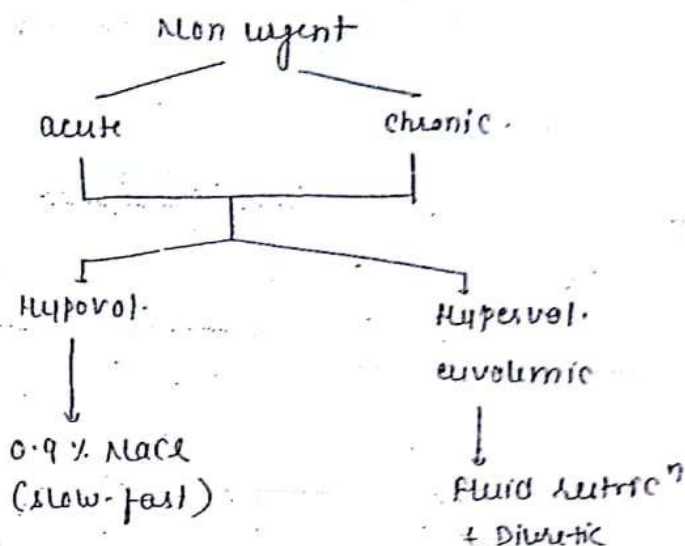
severe
(<120)

- Seizure
- coma

Rx -

symptoms





Correction of Na^+

I - In acute $\rightarrow$ should ~~not~~ correct $< 1-2 \text{ mEq/L/hr}$
 chronic $\rightarrow$ Not correct beyond $0.5-1 \text{ mEq/L/hr}$

II - $8-12 \text{ mEq/day}$ $\leftarrow$ 1st day
 $< 18 \text{ mEq/48 hr}$

||
 * This ^{1st} correctⁿ is ^{m.} imp otherwise

Osmotic demyelination syndrome will occur if 1 day corrⁿ
 (Previously central pontine myelinolysis)

* If there is seizure $\rightarrow$ $4-6 \text{ mEq/hr}$ ^{rise $> 6 \text{ mEq}$}
 (acute)
 3 hr

$\downarrow$
 For next 21 hr we should follow the old protocol
 i.e. $< 8-12 \text{ mEq/day}$

(110)

ex. pt is assigned Na^+ = 110

↓ (1.2 meq/L/hr)

Follows hb. protocol ← 110 in 3 hr → 116 (i.e. 6 in Na^+ by 4-6 meq)

not (21 hr) ↓ 8-12 meq/day ≈ 1

Rest of the deficit Target: —

120

fulfilled after initial 3 hr.

How to correct Na^+ deficit —

Sod. deficit = 0.6 × BW × Correction

ex. ∴ pt Na^+ = 115

Target = 120

$$\boxed{\text{Sod. deficit} = 0.6 \times 80 \times 5}$$

$$= 240 \text{ meq.}$$

↓

∴ 80 meq/hr

0.9% NaCl (1-1.5 meq/L)

8% NaCl — 500 meq/L

Q. $\text{Na}^+ = 118$ mild symptoms.

wt = 80 kg

we want to tit $\approx 0.9\%$ NaCl.

goal = 120 meq in 8 hr.

Correcⁿ = 10

$$\text{Na}^+ \text{ def} = 0.6 \times 80 \times 10 = 480 \text{ meq}$$

for this we need Na^+ (0.9% NaCl)

~~for~~ 150 meq — 1000

$$480 \text{ — } \frac{1000}{150} \times 480$$

$\approx 3.2 \text{ L in } 24 \text{ hr.}$

3200 mL $\longrightarrow$ 24 hr.

$$\text{infusion rate} = \frac{3200}{24} = 125 \text{ mL/hr}$$

Q. $\text{Na}^+ = 105$ seizure $\oplus$, wt = 60 kg

31 F $\approx 3\%$ NaCl

105
1 hr $\downarrow$ 2 meq
107

23 hr $\downarrow$ 8 meq
115

$$\Rightarrow \text{Na}^+ \text{ deficit} = \frac{0.6}{14} \times 60 \times 2 = 92 \text{ meq}$$

to correct this 150 ml
of 3% NaCl is given.

$$\text{Na}^+ \text{ deficit} = \frac{0.6}{14} \times 60 \times 8 = 288$$

(iii)

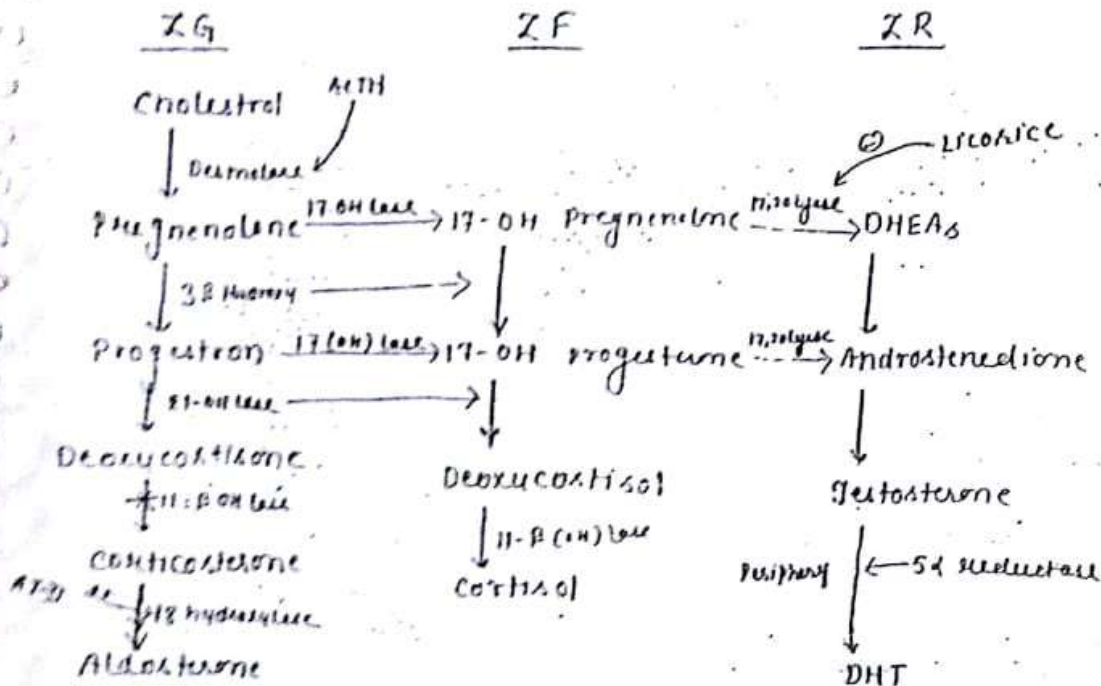
go correct this -

we need

$$300 \text{ mg} \rightarrow \frac{100 \text{ ml}}{23 \text{ hr}}$$

$$\frac{300}{23} = 20 \text{ ml/hr}$$

Adrenal gland



- Dehydrocorticosterone
 - Corticosterone
- most potent

Deficiency of 21-OH laie — (non classical → mimics PCOS)
prog ↑ 17-OH Progesteron ↑

Deoxycortisone ↓ Deoxycortisol ↓

cortisol ↓

- | |
|--|
| <ul style="list-style-type: none"> • 17 OH prog ↑ • glucocorticoid ↓ • mineralocorticoid ↓ • sex st. ↑ |
|--|

C/F — • Child has shock at birth

• Hypoglycemia

• 1 sex hormone → in ♀ ambiguous genitalia

Def. of 11 β hydroxylase —

① • 17 OH progesteron ↑

② • mineralocorticoid + glucocorticoid ↑ } → HTN

③ Androgen ↑

C/F — • HTN

• Ambiguous genitalia in ♀

(112)

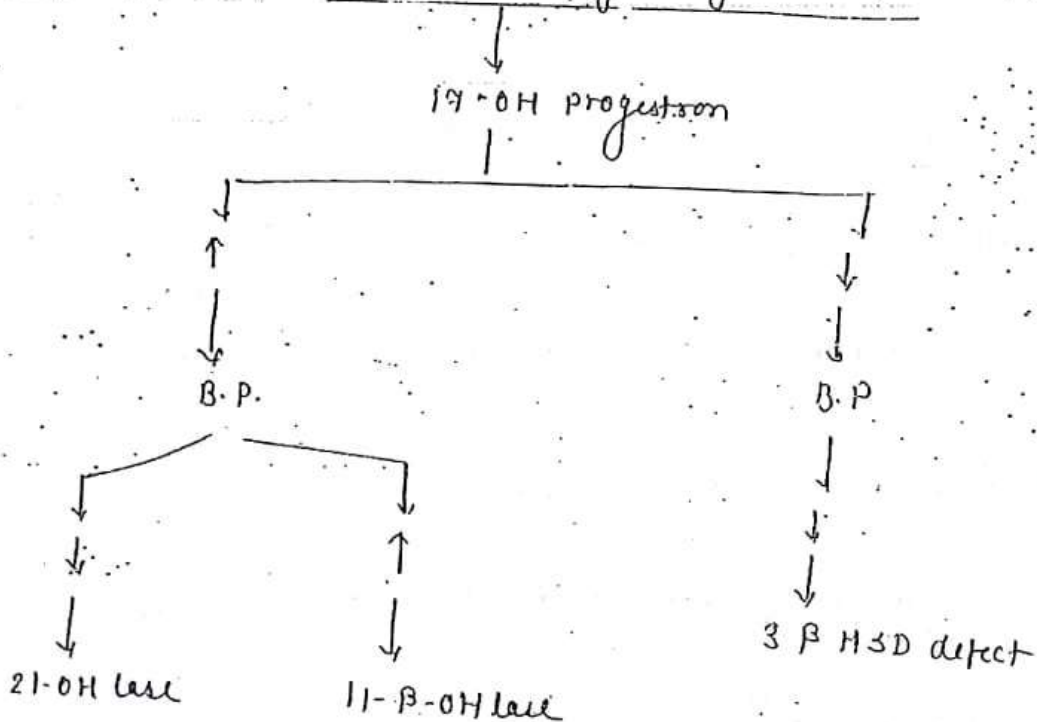
3 β -HSD deficiency —

- 17-OH prog ↓
- mineralocort. + glucoc. ↓
- sex hormone ↑ (Androgen)

C/F — • Shock & refractory hypoglycemia
• Ambiguous genitalia

Adrenogenital syndrome

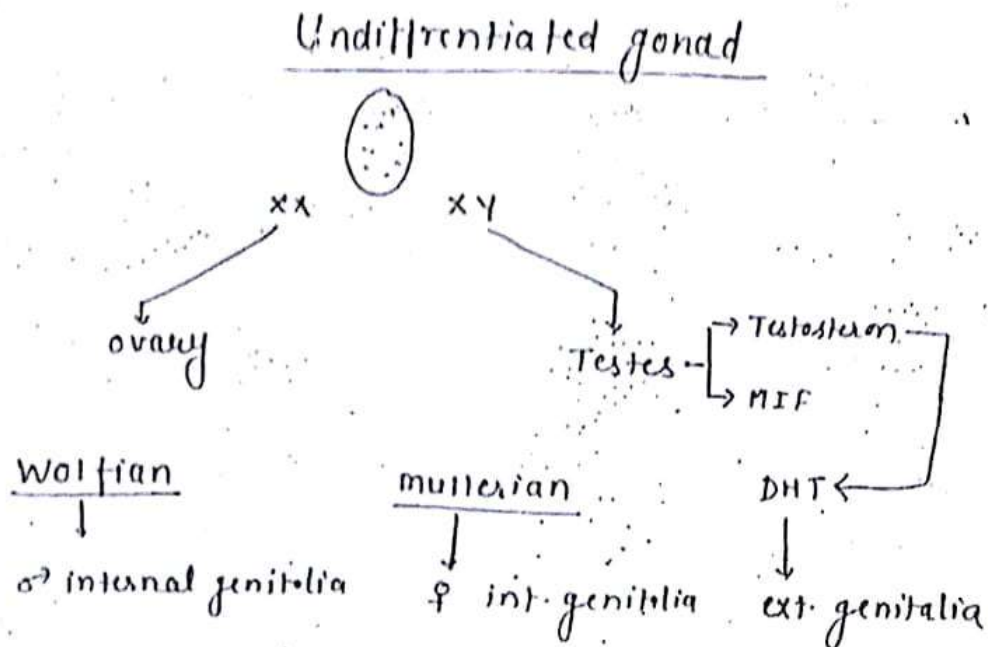
Child with Ambiguous genitalia



9/11 - Steroids — Patient shock & HTN.

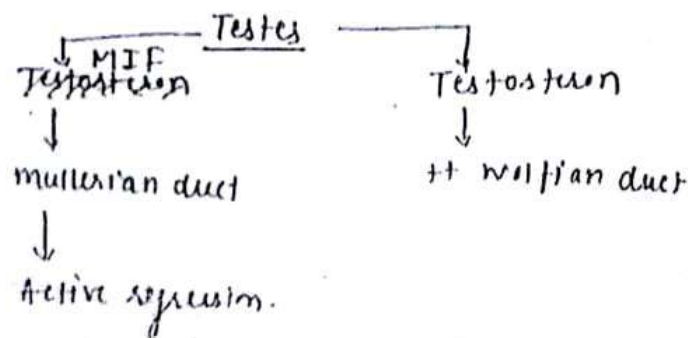
↓ ⊖
ACTH
↓
Adrenal shut down

* Give life long till steroids.

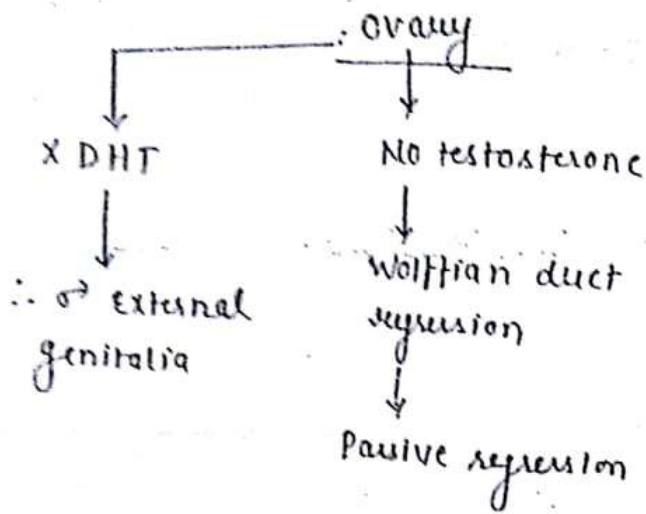


* Testosterone — ++ Wolffian duct

* MIF → Active suppression of Mullerian duct.



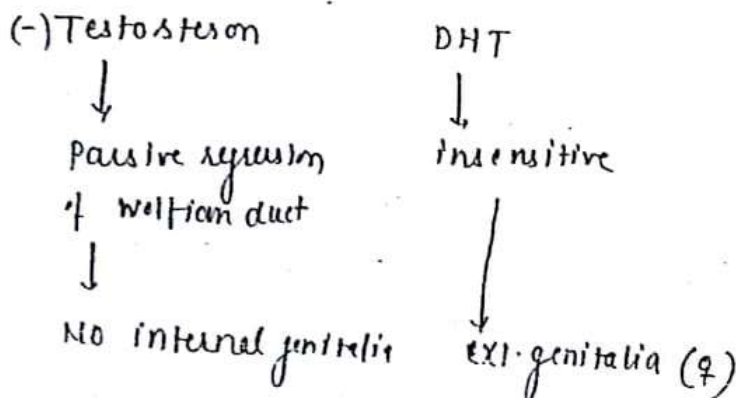
(113)



* Congenital adrenal hyperplasia — (virilization)
int. genitalia are ovary

- DHT coming from androgen causes ambiguous genitalia (male like)
- All these changes occur at the time of adrenarcheal (growth of pubic & axillary hair)

* Androgen Insensitive —



→ Female (ext. genitalia female)

→ Testes → male testosterone

↓ Aromatase

Breast development ← Estrogen

→ No internal genitalia — so come ♂ 1° Amenorrhoea

→ ext. genitalia are like female so Intercourse is possible. Here vagina is like a blind sac.

→ Adrenarchae not happen because adrenal androgens are also not working.

MRKH syndrome —

→ Mullerian duct go for passive regression in -nce of MIF

→ They are ♀ & have ovary.

→ Mull. duct regression
↓
no internal organ.

→ ext. genitalia ♀. — intercourse possible

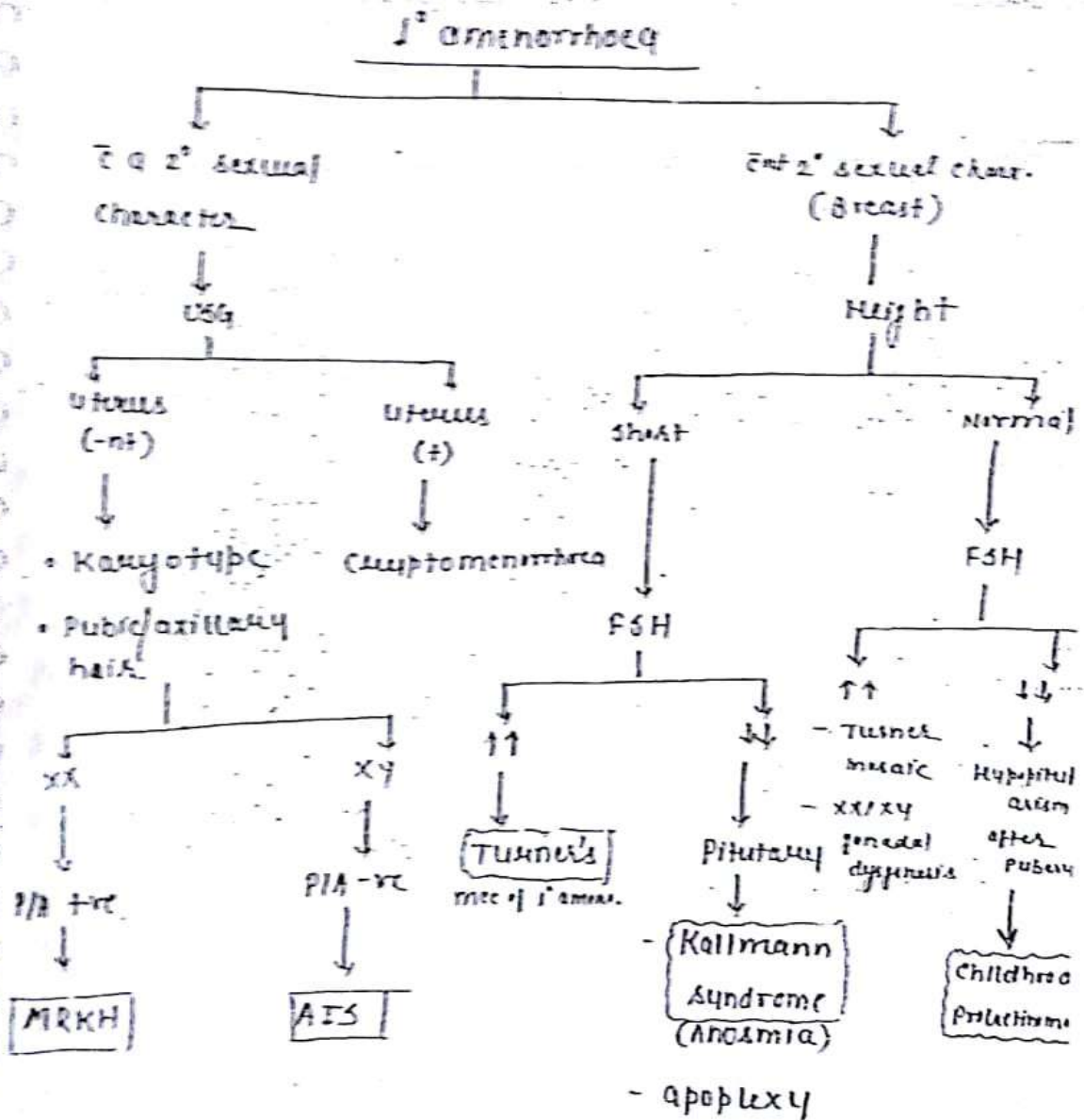
→ Breast development (N).

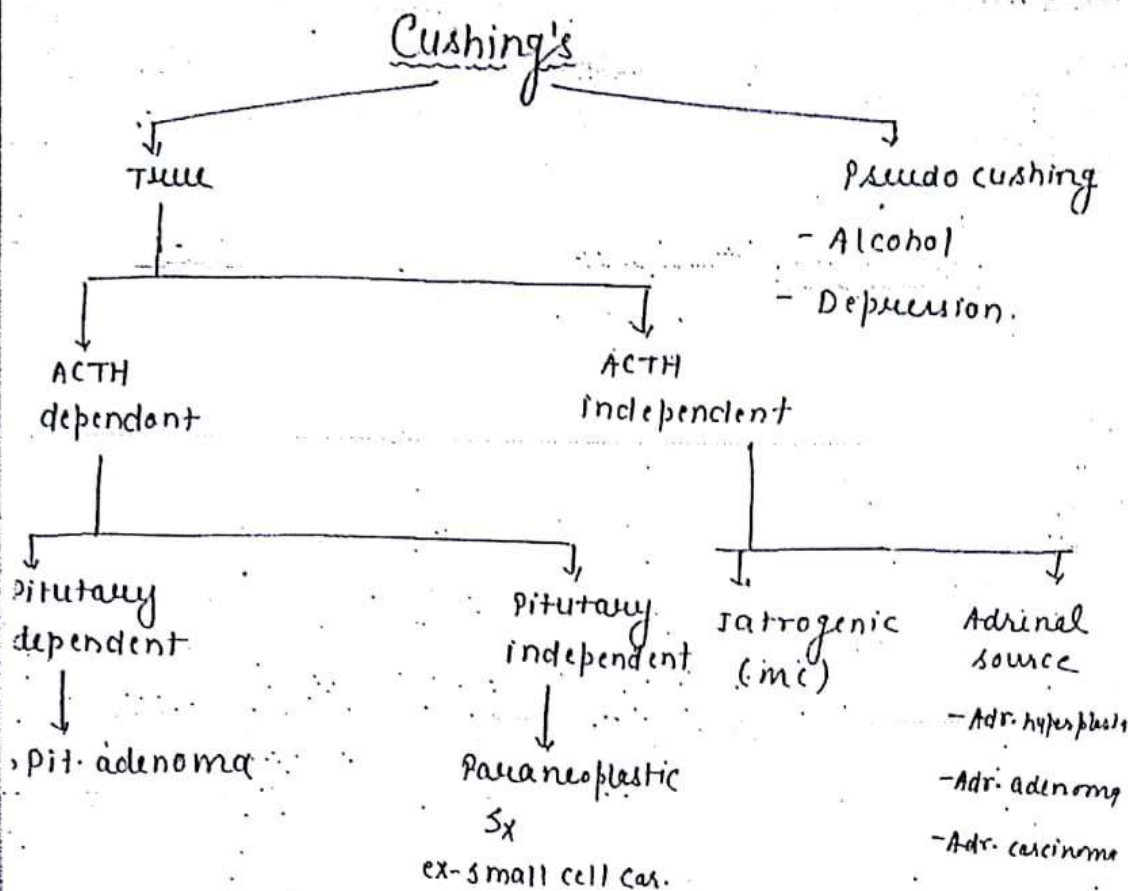
→ Presents ♂ 1° amenorrhoea.

(117)

* Adrenarche is (N) in this pt.

→ on USG → ovary seen in proper position in abdomen.





CIF - • wt gain (truncal, central)

- Buffalo hump
- Round face
- Purple abdominal striae
- DM
- HTN
- Cardiovascular disease
- capillary fragility causes easy bruising
- Thin skin d/t loss of s.c fat
- Glaucoma

(115)

Evaluation—Screening:In Pt.OP

• midnight salivary
cortisol
(Cortisol)

• 24 hr urinary
Cortisol

max^m

min

8-9 am

12 am

For screening
of Addison's
morning sample
taken.

so midnight sample
taken

↓
S/O steroid excess

confirm

LDST / ODST

cushing

Localize

check ACTH

ACTH dependent

ACTH independent

Adrenal

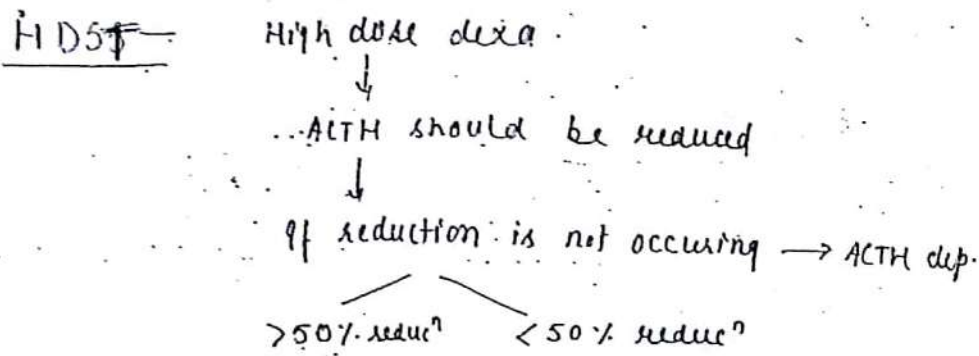
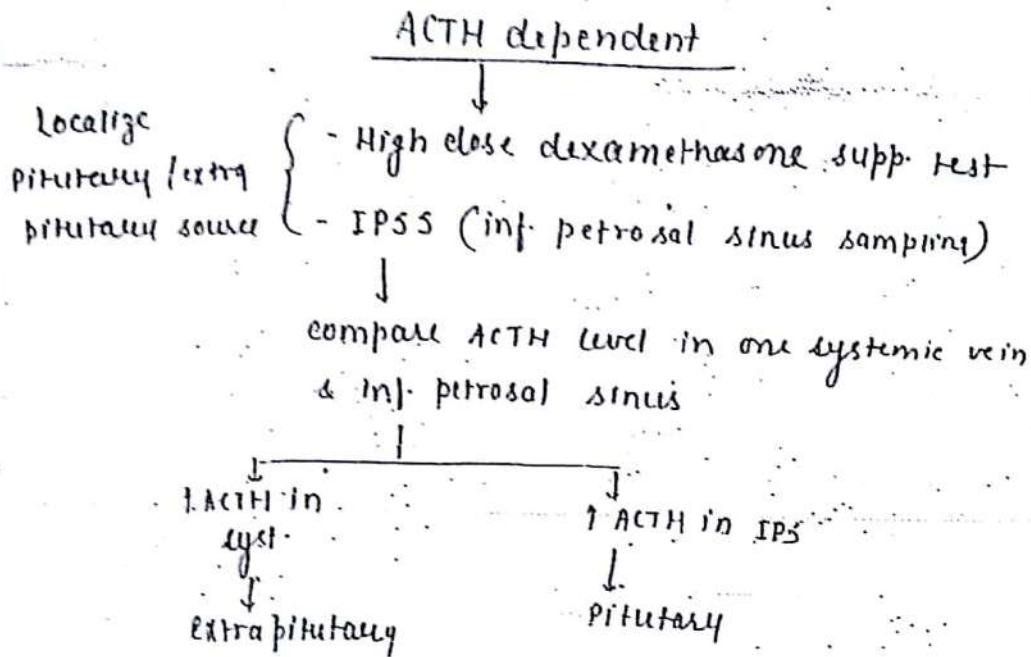
MRI

+ve
adenoma-ve
Adrenal vein sampling

Localize

* For Δ⁵C₁₉ purposes
dexamethasone is used
as it can't be detected
by (M) method & so
levels ^{to be measured} are not altered

* Take sample from both adx. vein & check out the level in both.



Rx — Surgery — Remove pituitary / adrenal

↓ Radio

medical Rx —

metoprolol

metoprolol

metoprolol

metoprolol (adult)

metoprolol (children)

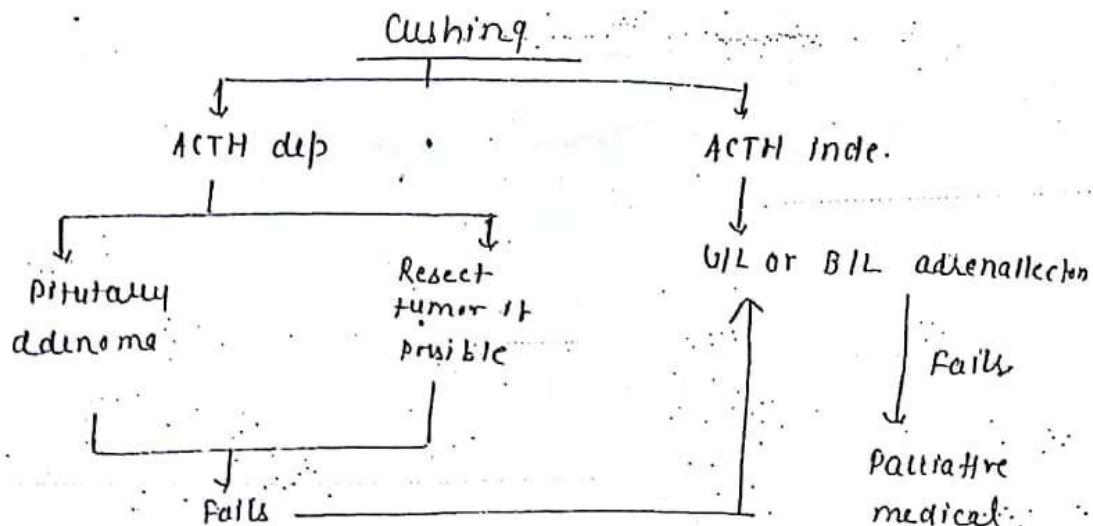
For non carcinomatous

(116)

Adult
metopirone
>>>
mitotane

child
Ketoconazole

carcinoma
mitotane >
metopirone



Nelson syndrome—

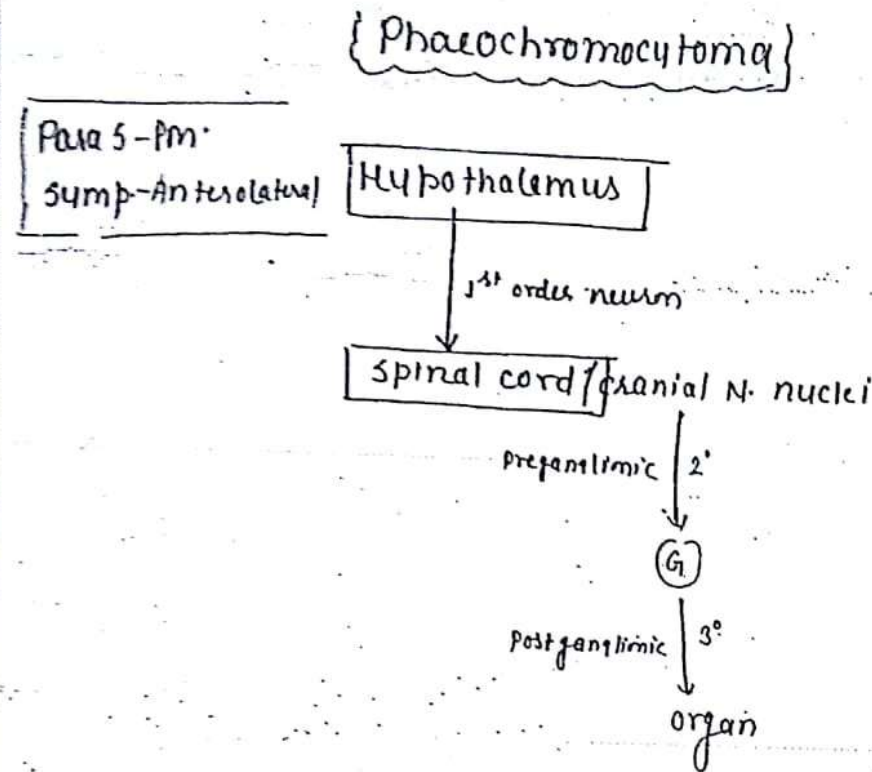
while doing pituitary adenoma
resectⁿ of tumor

↓
if we do adrenalectomy.

↓
no hormone will be produced to

* feedback the pituitary

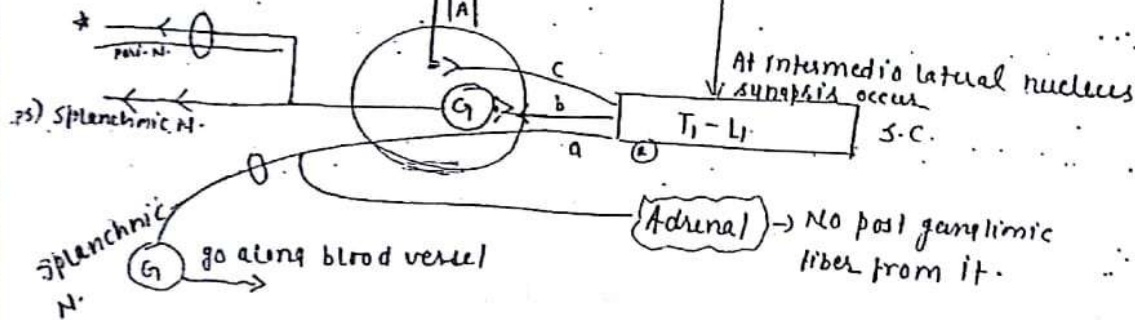
↓
so pituitary cell hyperplasia



Sympathetic

Supply sympathetic in head
↑ & neck

aceticid
symp.
nucleus

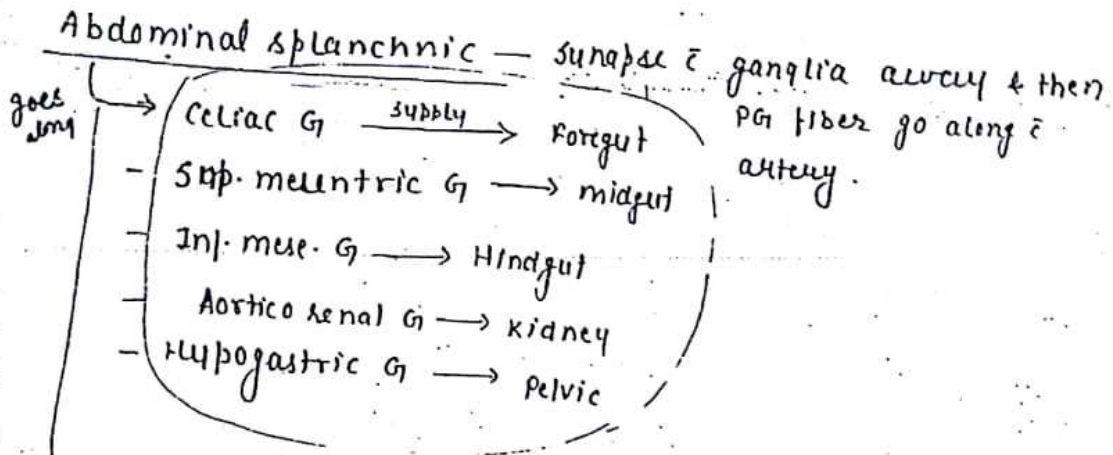


* N. joining peripheral N. goes to limb & trunk.
& produce

- vasomotor
- sudomotor funcⁿ
- pilomotor funcⁿ

117

Cardiopul. splanchnic (CPS) — From T₁ - T₅
— supply thorax



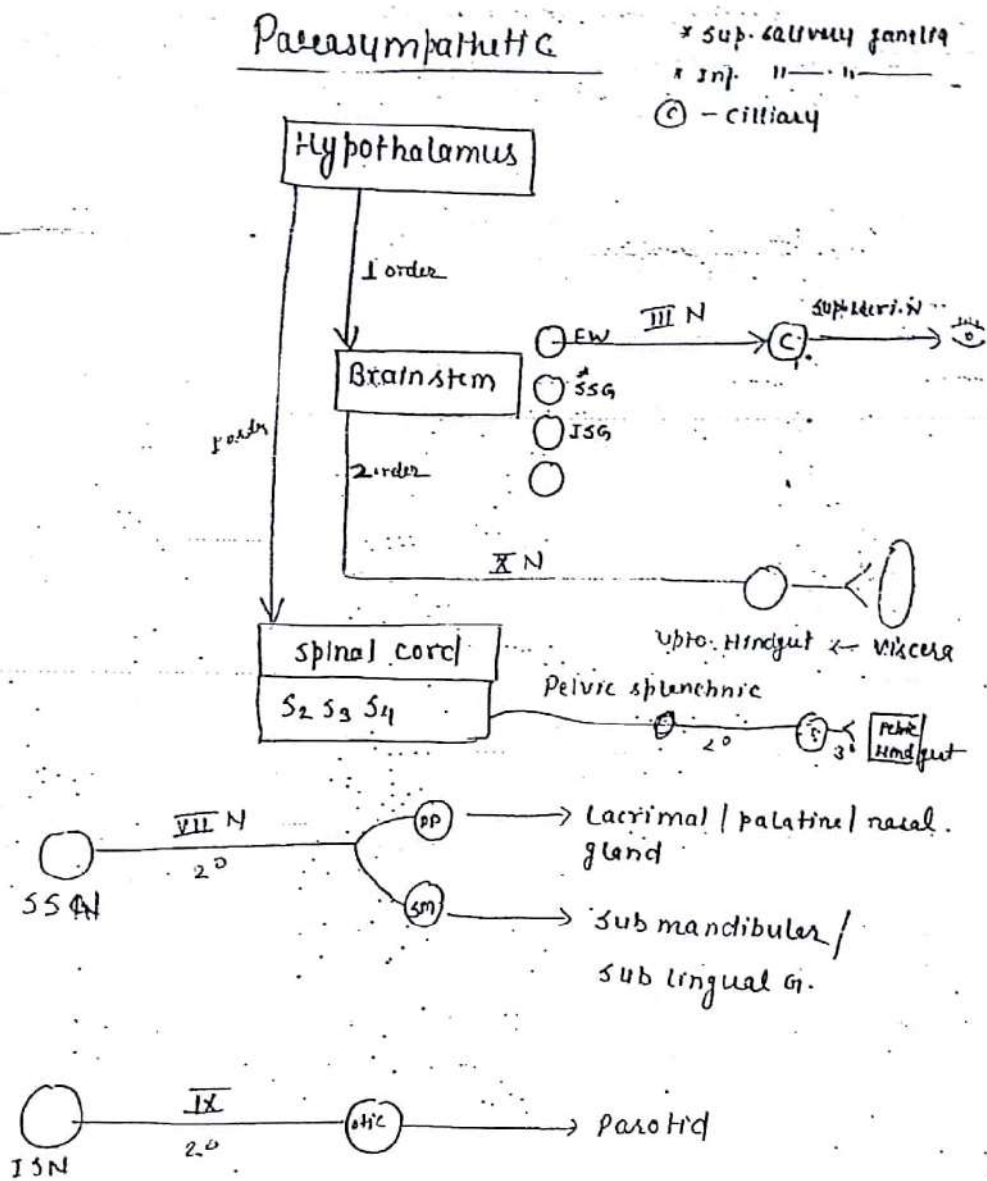
exception → Adrenal → directly releases catecholamine in blood

→ Tumors of adrenal (sp. ganglia) → pheochromocytoma

→ Tumors of other ganglia → paraganglioma

* Thus pheochromocytoma is a type of paraganglioma.

• Glomus is also paraganglioma but it is non-chromatin type.



→ an parasympathetic system → ganglia are embedded in viscera
← post ganglionic fibres are very small.

* S₂-S₄ PS supply Hindgut & pelvis.

118

Ganglia/ Brain/ S.C./ adrenal → Common in all

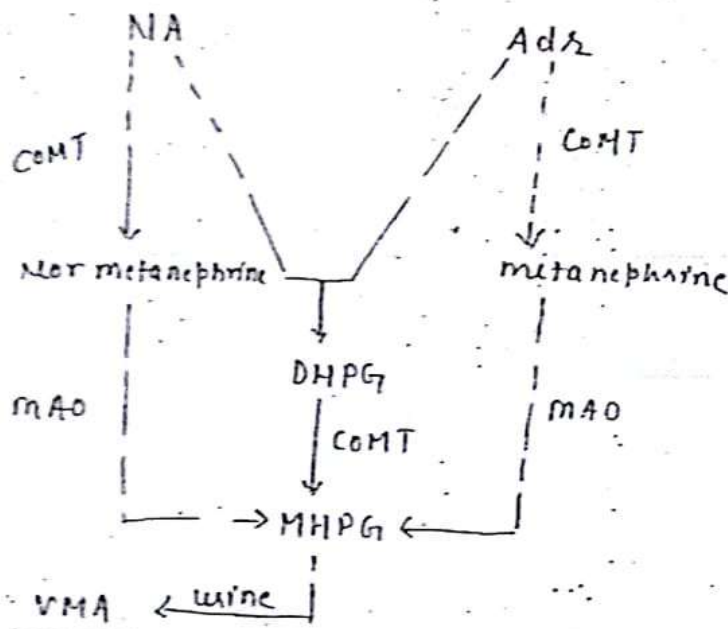
Tyrosine → DOPA → NA → Adrenaline

PNMT enzyme → depend on cortisol level

All these str. can release NA only but Adrenaline

occurs only in Adrenal

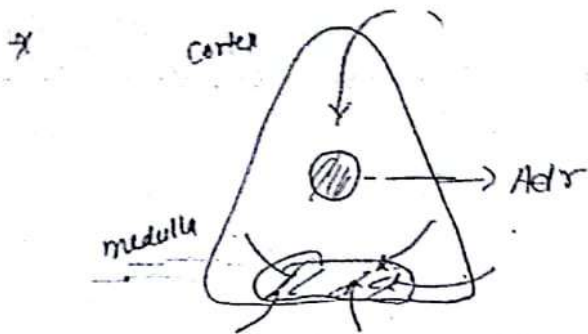
is released only from adrenal.



* metanephrine is m-specific for pheochromocytoma as it is exclusively formed by Adr.

* VMA can be released in both pheochro. & paraganglione

Even in pheochromocytoma main neurotransmitter is NA. but Adr. is only secreted from pheochromocyt any paraganglione / even pheochro → NA is released



→ q1 tumor is small

- It takes blood from native area only.
- This blood contain cortisol

↓
① PNMT

↓
Secretes (Adr)

→ Large tumor — neovascularization occurs

- These new vessels have ↓ cortisol

↓
NO PNMT activity

↓
Large tumor will secrete — NA

Associaⁿ of Pheochro.

1) NF-1

2) VHL

3) MEN-2 (mucosal neuroma)

(119)

C/F- Phaeochromocytoma —

(1) Labile blood pressure.



(2) Phaeo spell —

Paroxysm of sudden
(episodic)

- HTN
- Sweating
- Tachycardia
- Headache

(3) Constipation.

(4) Postural hypotension → when standing

on phaeochro —

The NA/AdA (R) undergo
tachyphylaxis.

↓
So released NA/AdA will
not act on (R)

↓
diff venous pooling

↓
Release of NA/AdA to
cause vasoconstrictor?

↓
↑ v. return

↓
maintain blood...

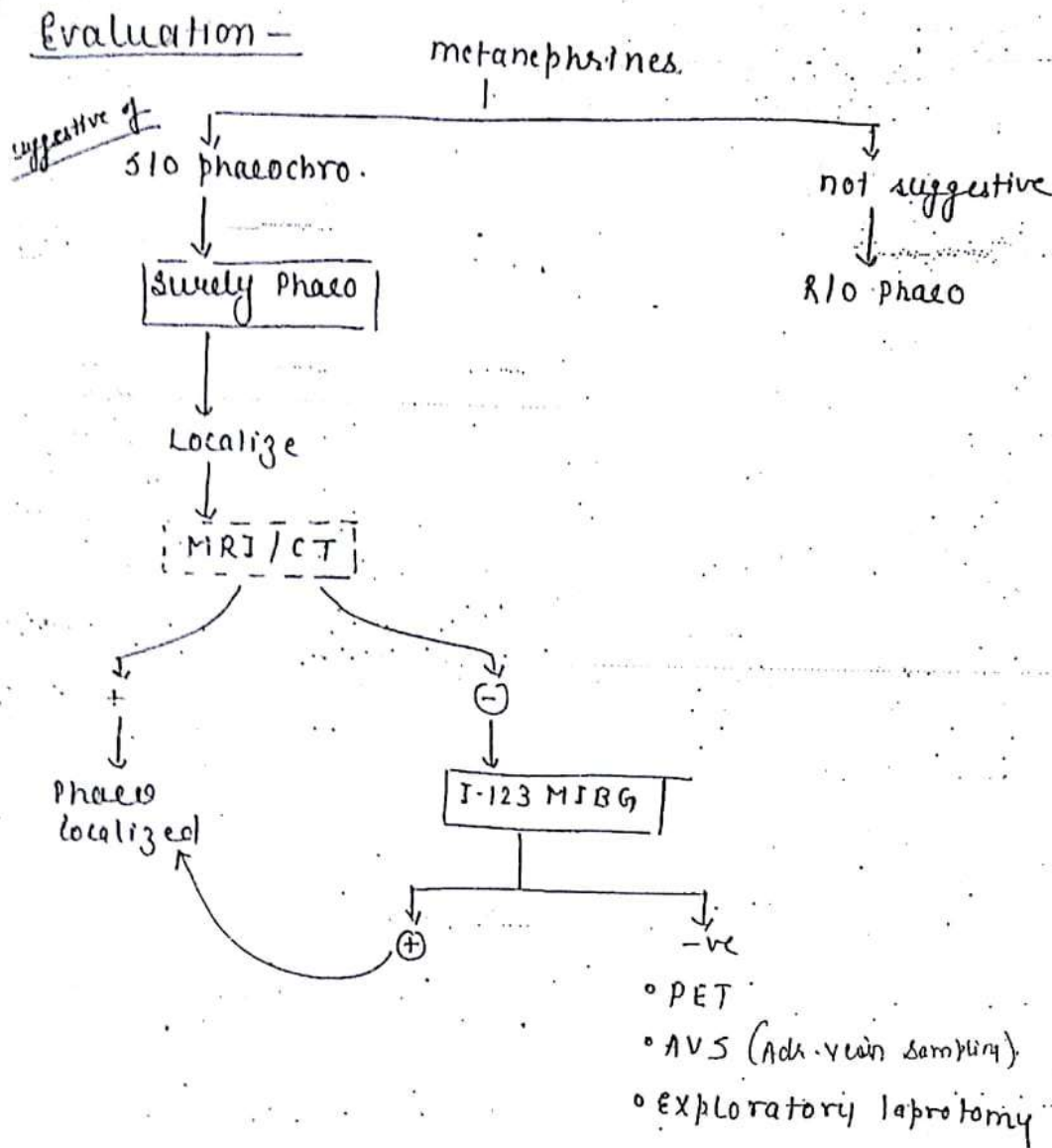
Inv: — (1) Plasma free metanephrine (>90% sp)

(2) M-sp 24-hr urinary fractionated metanephrine
Imaging —

(3) CT, MRI both are equally sn.

(4) ^{123}I MIBG most specific

(5) Fluorodopa - PET



* Biopsy / FNAC → "Never do".

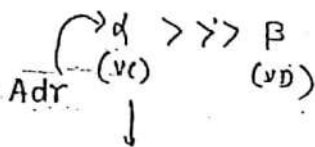
Rx -

- capsular invasion occur in benign tu. itself
- only the mets can tell whether tumor is benign or malignant.

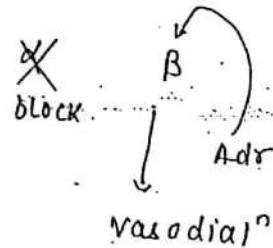
(20)

Preprⁿ of Sx -

① α -blockade (Phenoxybenzamine)



- α are more in no.
- whole Adr will act on α
- & ve occur



② β -blockers - Given after 48-72 hr

Target BP
< 160/90

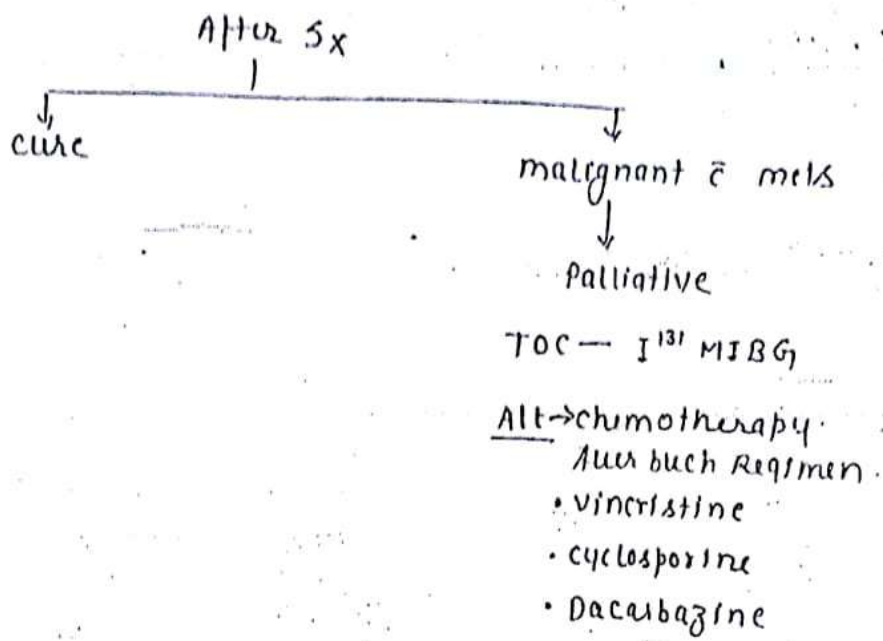
③ Surgery

Prazosin → Paroxysm spikes of ↑ B.P. during Sx
↓
give prazosin to treat

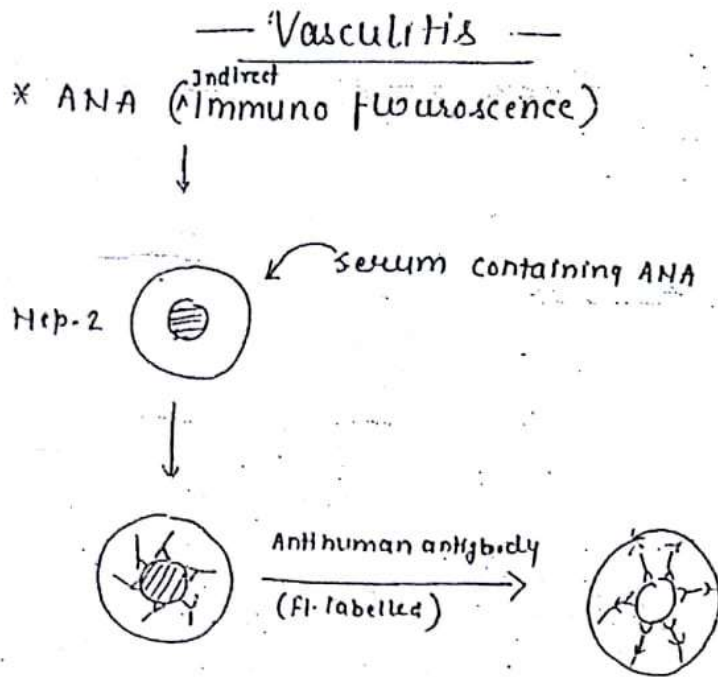
while manipulating BP ← Nitroprusside

After tumor removal

Hypotension — Rx → I.v. fluid + ephedrine



(121)

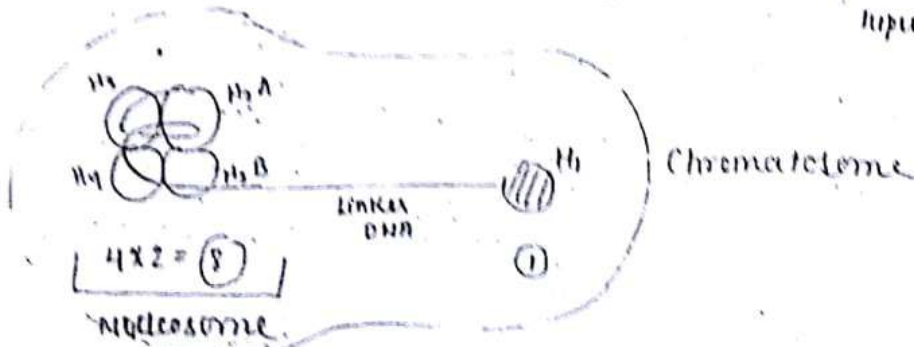
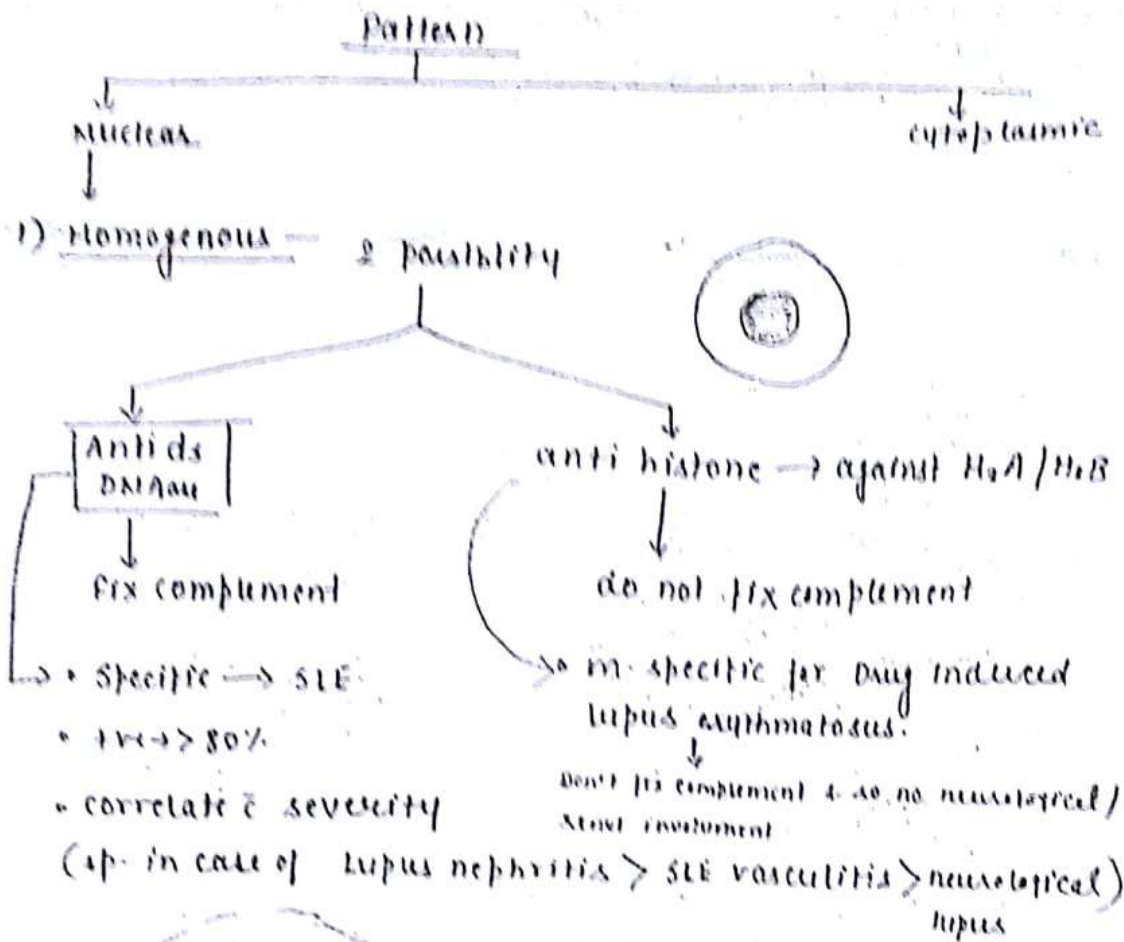


* ANA ⊕
↓
end point titre — ≥ 1:160

→ ANA alone is most sp. for SLE → if 2 times it is ANA
[Always SLE is ANA ⊕] if is never SLE ←

→ for SLE SLICC criteria is used now.
↳ 1 clinical + 1 immunological criteria

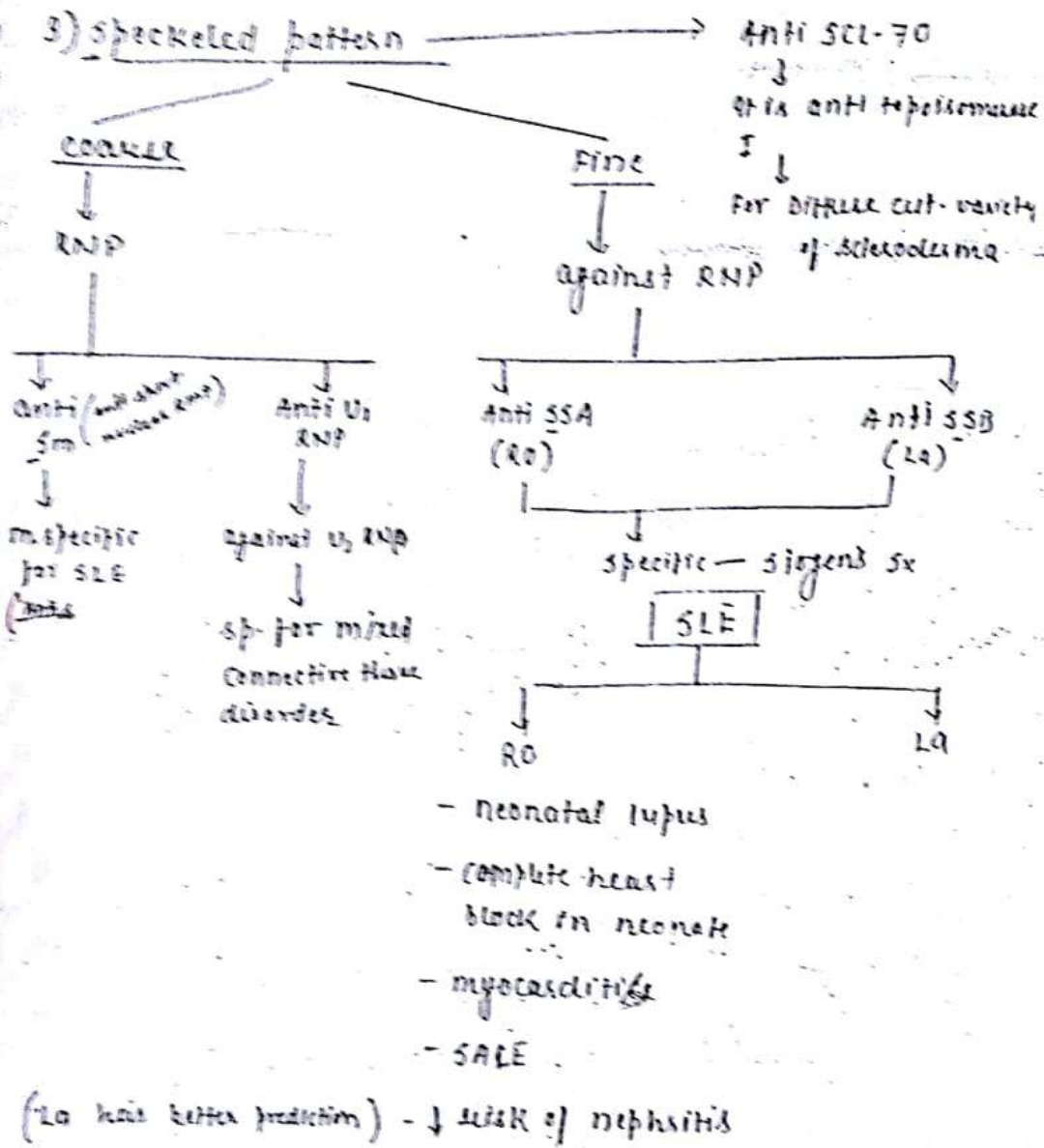
Pattern of ANA ⊕ —



2) Rim pattern —

* Anti ds DNA abs





4) Centromeric pattern —

- Against centromeric proteins (CENP)

- Seen in → limited cutaneous variety of scleroderma (Anti centromere Ab)



5) Nucleolar pattern — AKA Antiexosomal Ab

or
Anti pML-SL ab

Polymyositis

Scleroderma

- Seen in pML-SL overlap syndrome

Cytoplasmic —

① Ab against
anti histidyl t-RNA
synthetase

• Anti histidyl t-RNA
Synth. Ab

• Anti synthetase Ab

• Anti Jo-1

↓
Polymyositis

② Anti mitochondrial
Ab

Sp: - Pri-biliary
cirrhosis

Also true in
Scleroderma
(DIP for Biliary)

③ Ribosome

anti Ribosomal -P
Ab

↓
SLE v.s.p.

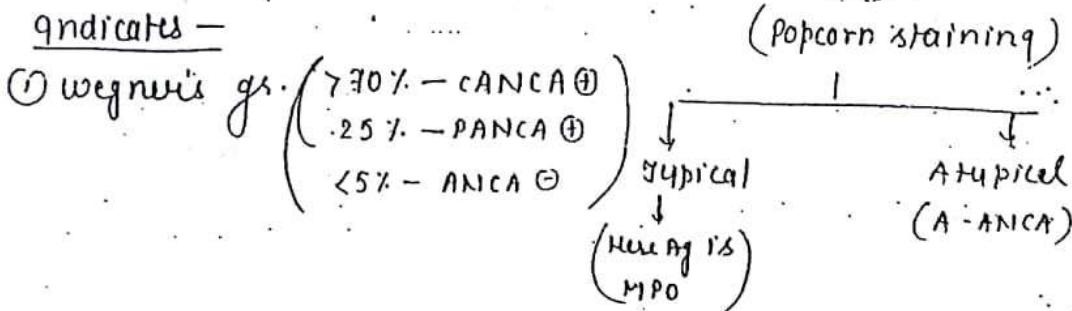
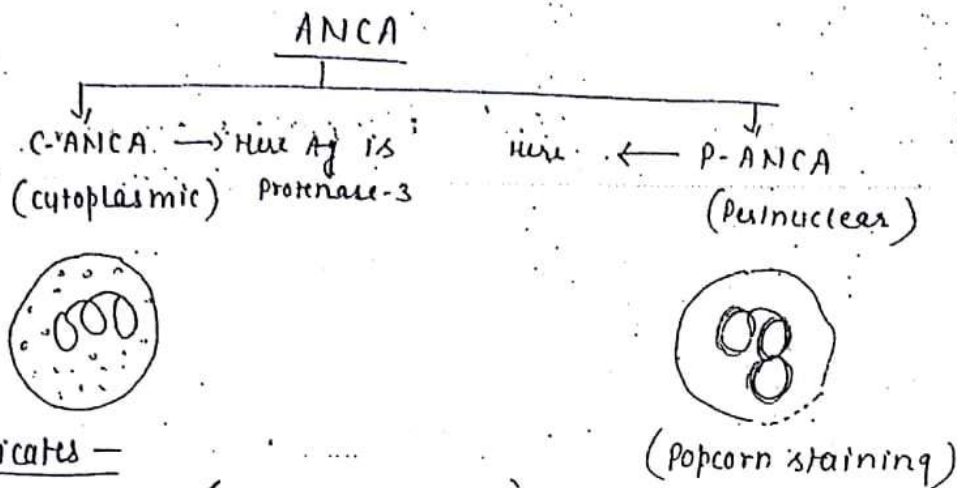
↓
neurological lupus

esp- psy / depression

⑤ Anti Mi-2 - +ve in Dermatomyositis (V-neck sign)
- It shows good prognosis (shawl sign)

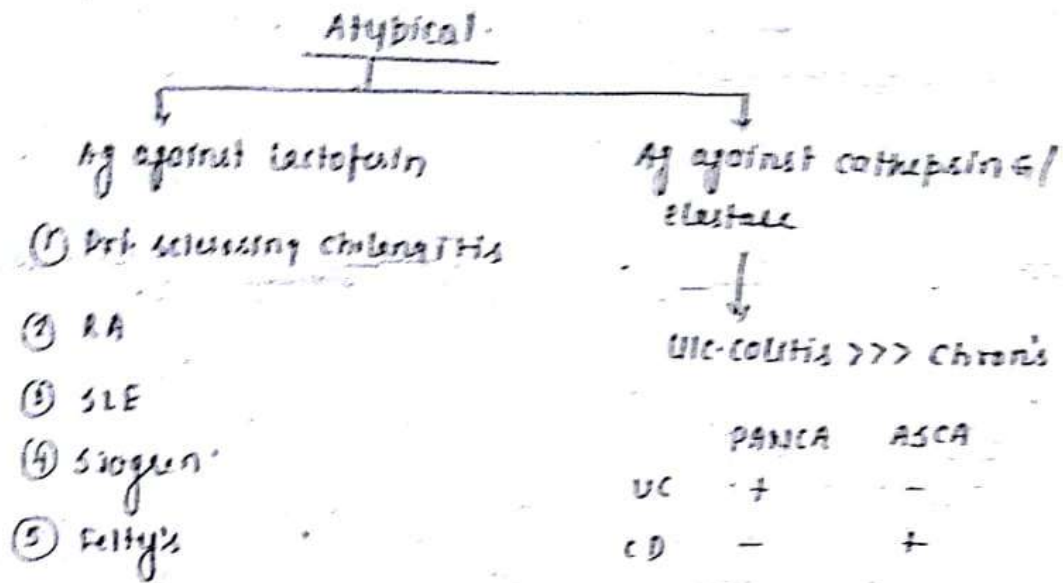
⑥ Anti NXP-2 - • Shows calcinosis

⑦ Anti P155/140 (Anti TIF-1 γ) $\rightarrow$ Dermatomyositis
+ malignancy

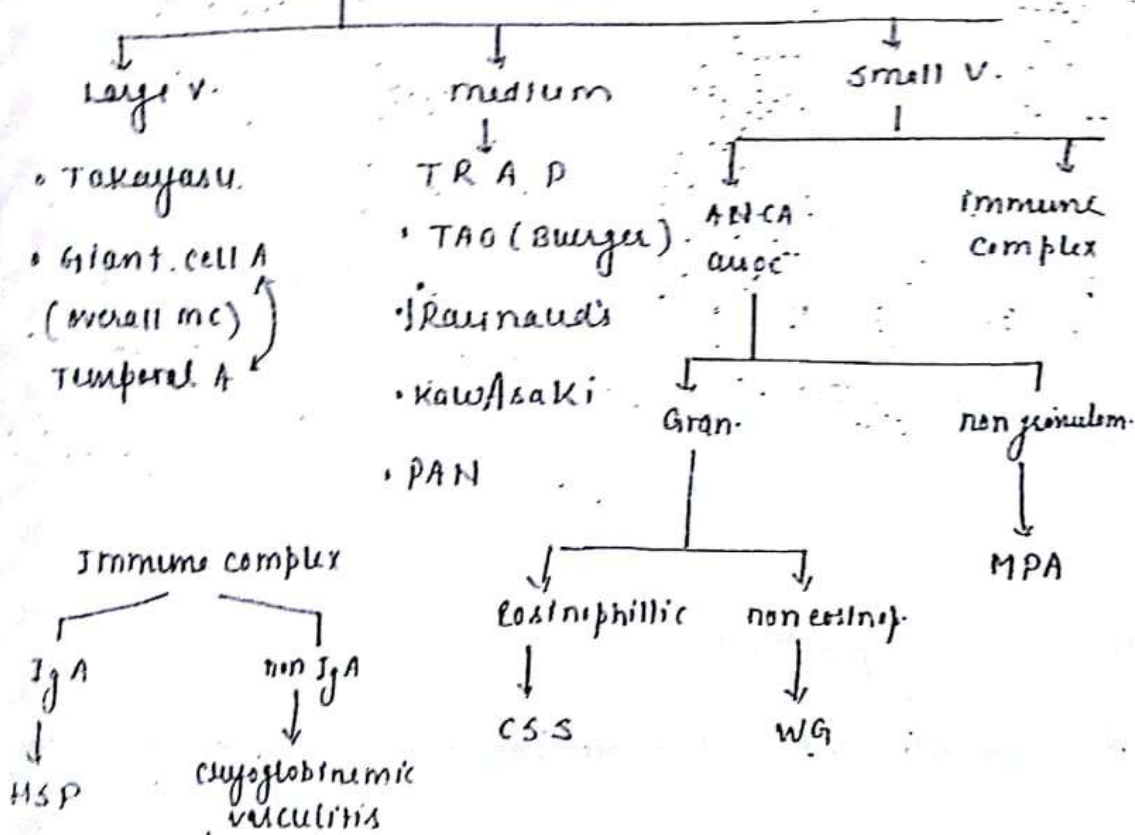


- Indicates
- ① microscopic polyangiitis
 - ② Churg Strauss
 - ③ 1 $^\circ$ RPGN
 - ④ Good pasture (w/ association)

(124)

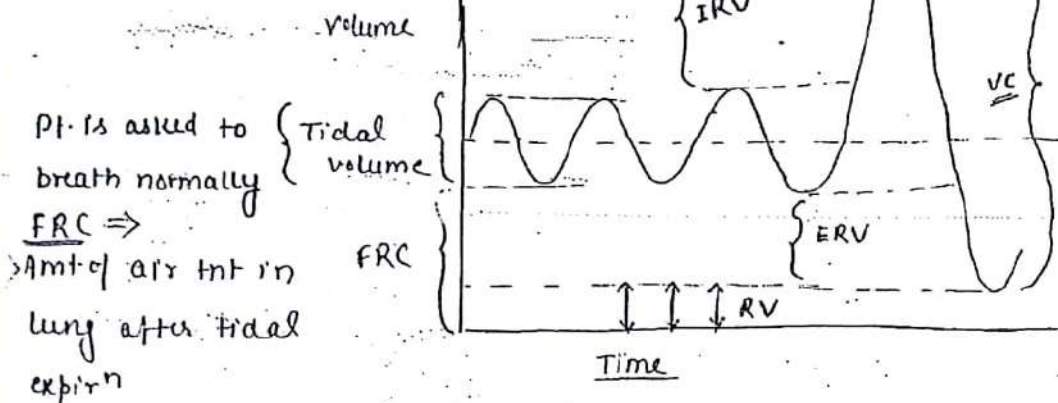


Vasculitis — Chappel Hill classification



Respiratory System

Spirometry —



Pt. is asked to
breathe normally

FRC $\Rightarrow$

Amt. of air in lung
after tidal
expirⁿ

VC $\Rightarrow$

= Amt. of air that can be exhaled after max^m inspirⁿ.

TLC $\Rightarrow$ Amt. of air in lung after max^m inspiration.

I.e. $\Rightarrow$ Inhaled after (N) expirⁿ
Insp. capacity $\rightarrow$

After (N) tidal expirⁿ, amt. of air that can be
inhaled.

* To measure RV

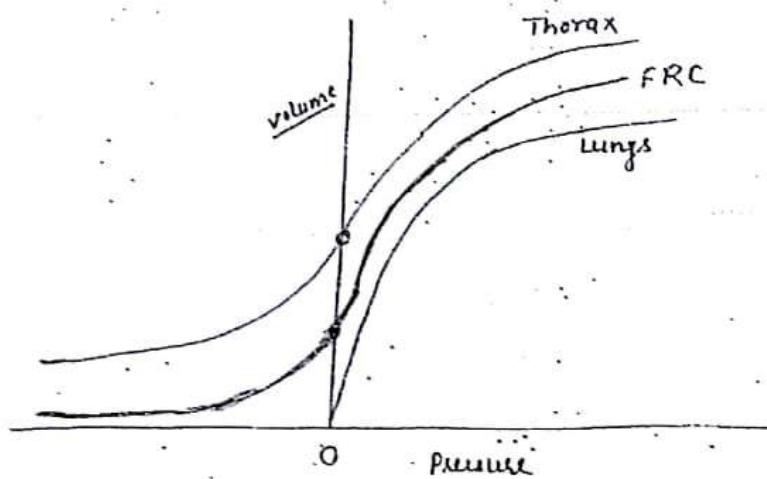
- Body plethysmography (best)
- Helium dilution technique (inert gas dilution technique)

* TLC & FRC can't be measured by spirometry.

(125)

Funcⁿ of FRC —

- ① to continue gas exchange during expirⁿ
 - ② During expirⁿ → to prevent collapse of alveoli
- * FRC should be more than closing capacity
 → if closing vol >> FRC
 ↓
 collapse will occur



At FRC $\Rightarrow$ collapsing of lung = distandibility of thorax
 ↳ i.e At FRC both of them become equal.

Inspiration —

* contraction of diaphrag.

↑ V ↓ P

↓
air moves

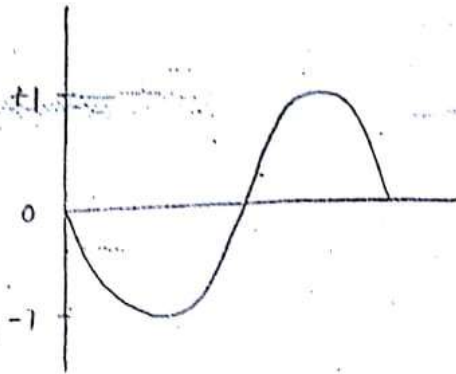
↓
inhaled

↓
vol. of air ↑
in lung

* elastic recoil of
lung

↓
vol ↓, P ↑

so air move out from
lung & neutralizes P.



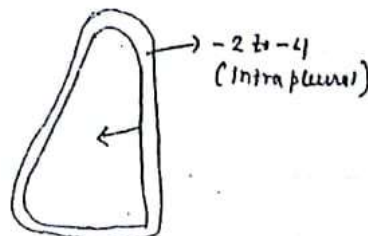
Intrapul pressure

Intrapleural pressure —

- it is always -ve.

① * Lungs are elastic & always
try to collapse.

② Surface tension in alveoli.
beg of fluid → so alveoli
want to get collapse.

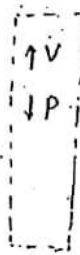
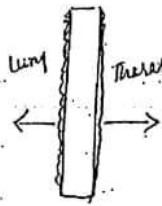


(126)

* The Intrapleural pressure act in opposite direction & prevent collapsing of alveoli.

⇓

∴ Intraparenchymal pressure is 0.



Transpul. pressure =

Intra pul. - Intrapleural press

0 - (-4)

* TPP = 4. mmHg.

↳ Pressure that keep alveoli open.

Intrapleural press -

Inspirⁿ - thorax expand

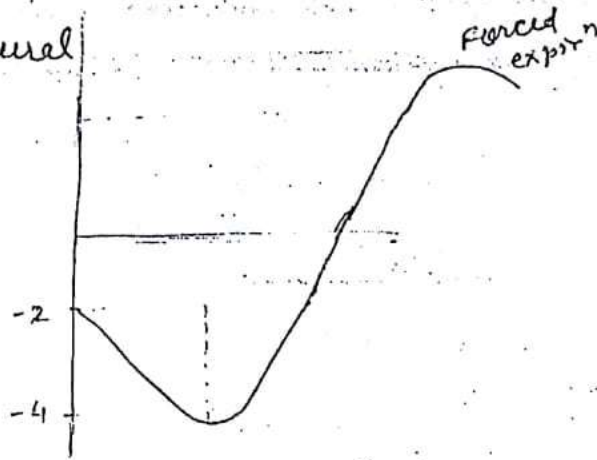
↓
pleural expand

↓
V ↑ P ↓

so pleura press. become → Reach upto -6 mm more -ve.

expirⁿ - contractⁿ of pleural space

↓
P ↓



* When pl. press become +ve (fluid mass)

↓
TPP become -ve

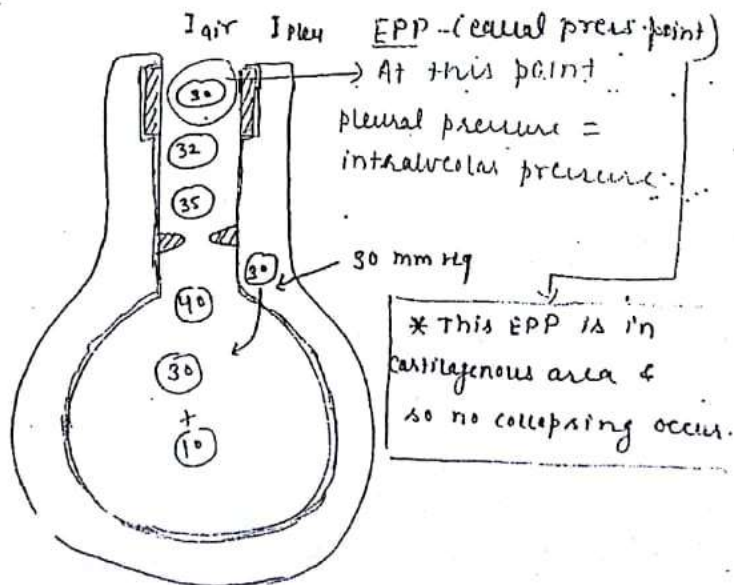
↓
Collapse of that segment

* During forced expirⁿ / valsalva

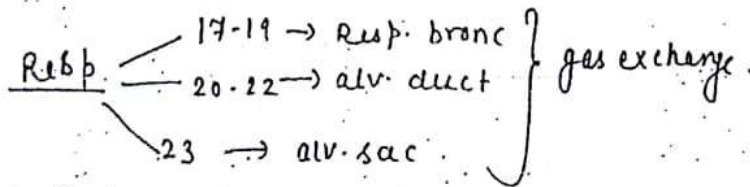
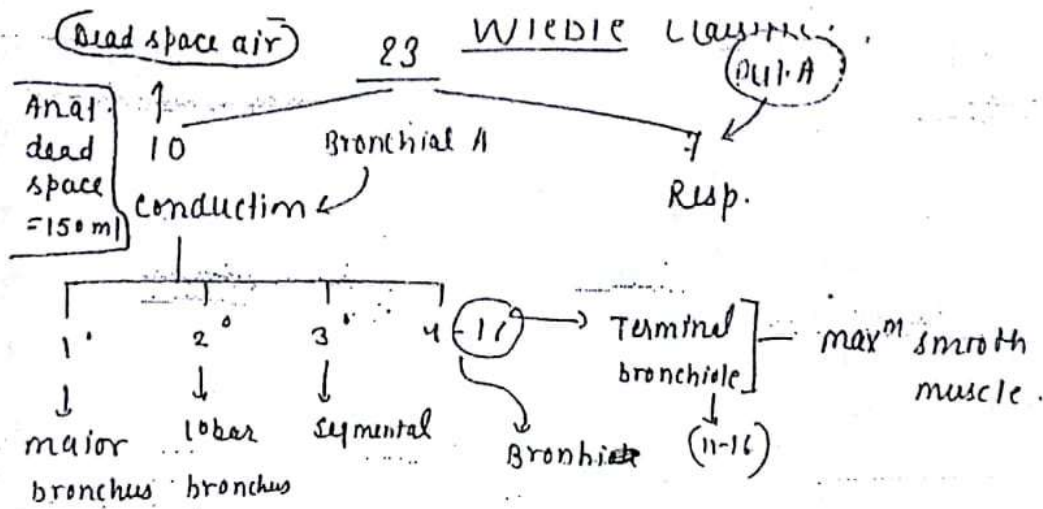
pl. press = +ve } so collapse should occur, but
TPP = -ve } it doesn't occur. bcz...

ex- 30 mmHg pressure
given to expire
the air out
↓
goes to alveoli

↓
It recoil in
alveoli some extra
pressure created (10 mmHg)



(127)



Alv. dead sp + Anat. D.S

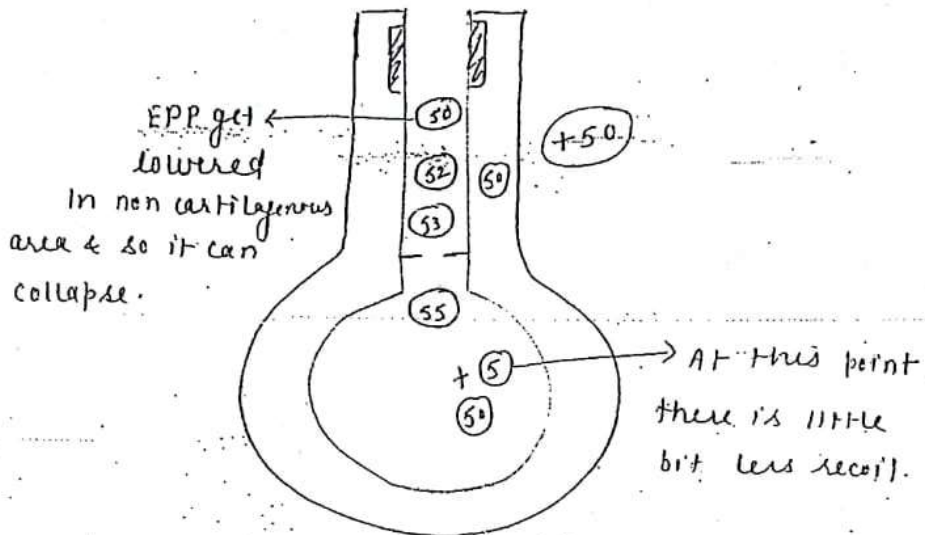
↓
Physiological D.S.

↓
Bohr eqⁿ

Conducⁿ
turbulent flow
↓
series array.

Resp.
smooth
↓
11th array.

When trying to forcefully expire —



As the pressure ↑

↓
EPP comes more lower (upto alveoli)

↓
so lung can't collapse.

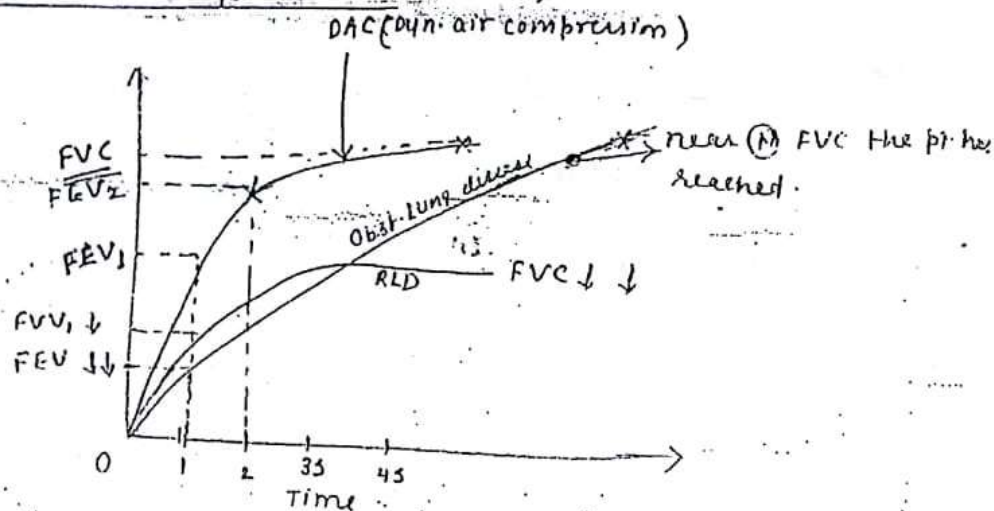
* In COPD pt EPP is at much lower level.

i.e. at alveoli at (N) exp. pressure

↓
So they collapse easily have difficulty in expiration.

(28)

Timed vital capacities :- (TVC)



When expiring (N) → followed by forceful expiration

* Amt. of air expired in 1st sec is FEV₁ & is max^m

FEV₁ > FEV₂ > FEV₃

RLD

	FVC	FEV ₁
(N)	10L	4L
Red. L.D	5L	3.5L

Here ratio remain same but FVC & FEV₁ both reduced.

Tiffeneau index —

$$\frac{FEV_1}{FVC}$$

	OLD	RLD
$\frac{FEV_1}{FVC}$	$\frac{\downarrow\downarrow\downarrow}{\downarrow} \Rightarrow \downarrow\downarrow$	$\frac{\downarrow\downarrow}{\downarrow\downarrow} = (N)$

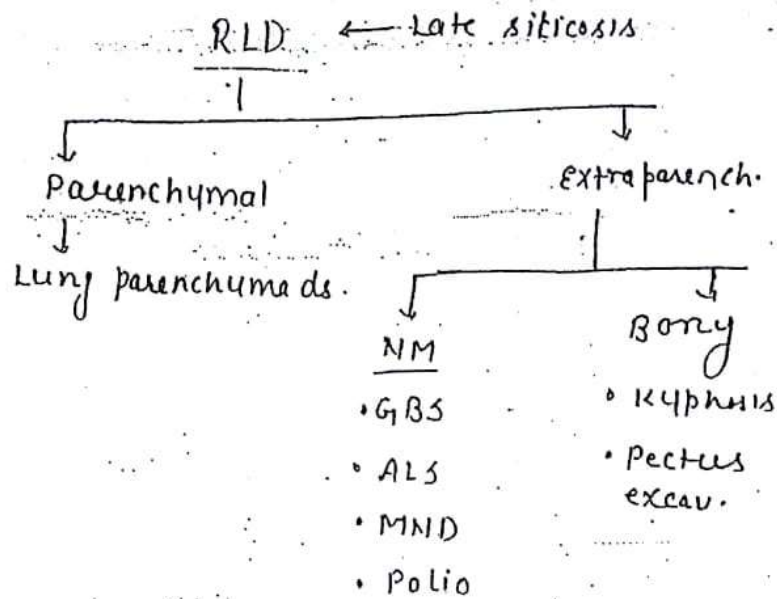
* T.I will tell whether the disease is OLD or RLD

but FEV₁ reduced in both.

* FVC ↓ (mild) in OPD, ↓↓↓ in RLD

OLD -

- Cystic fibrosis
- COPD
- Bronchiectasis
- BA
- Early silicosis



DLCO

Diffusion barrier (N)

↓
CO is inhaled when
exhaling in container

↓
So in container CO
level go down

not intact

↓
CO in container
doesn't drop down.

$$\text{Diffusion} \propto \frac{1}{\text{thickness}} \propto \text{area}$$

Condition. ↑ DLCO -

②A) when there is more pul. blood flow -

- 1) supine
- 2) exercise
- 3) obesity
- 4) L → R shunt
- 5) mild LVF

(129)

B) ↑ Surface area —

- Chronic bronchitis
- Asthma

Emphysema → Here in lung many
scared areas formed & so it
doesn't ↓ DICO

c) Polycythemia

b) Spurious causes → Pul. hemorrhage.



Condition ↓ DICO —

A) ↓ Pul. blood flow —

- Standing
- R → L shunt
- Pul. HTN
- RVF

B) ↓ Surface area —

- Emphysema

c) ↑ T —

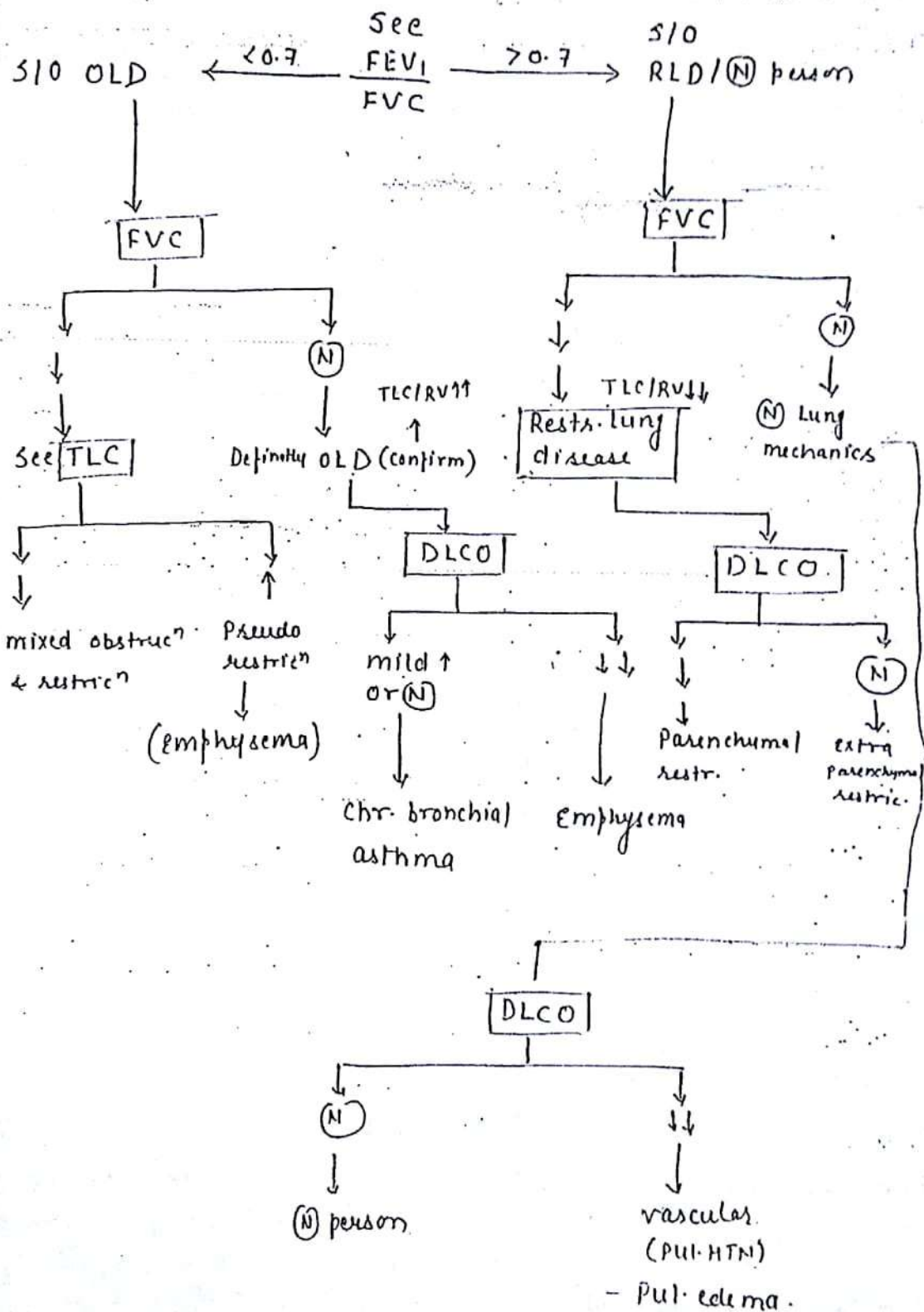
Pul. edema —
 LVF (mod. severe)
 (cardi)
 non cardiogenic (ARDS)

D) Fibrous — JLD

— Connective tissue disorder

(Extraparenchymal RLD will not cause ↓ DICO)

E) Anemia.



(20)

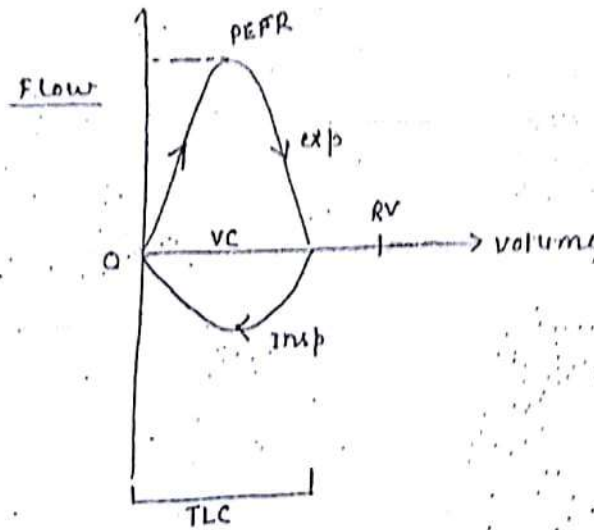
Flow volume loops — ① shape of curve

② PEFR

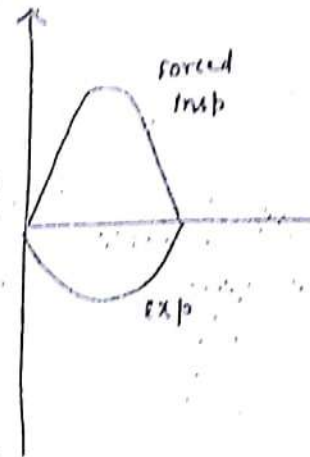
③ VC

* See only for forced
expir'n & forced vital
capacity.

① (N) shape of curve —

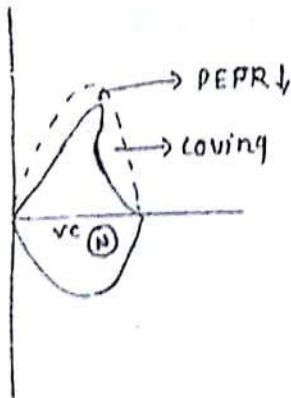


② Mechanical ventillⁿ

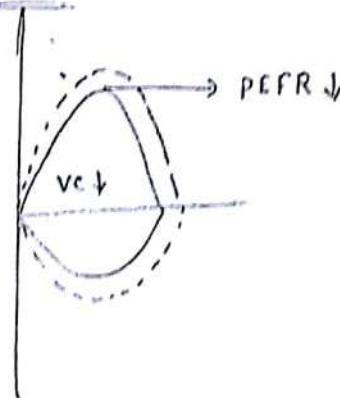


forced inspiration &
③ expir'n seen in
mechanically ventilated
pt.

③ OLD



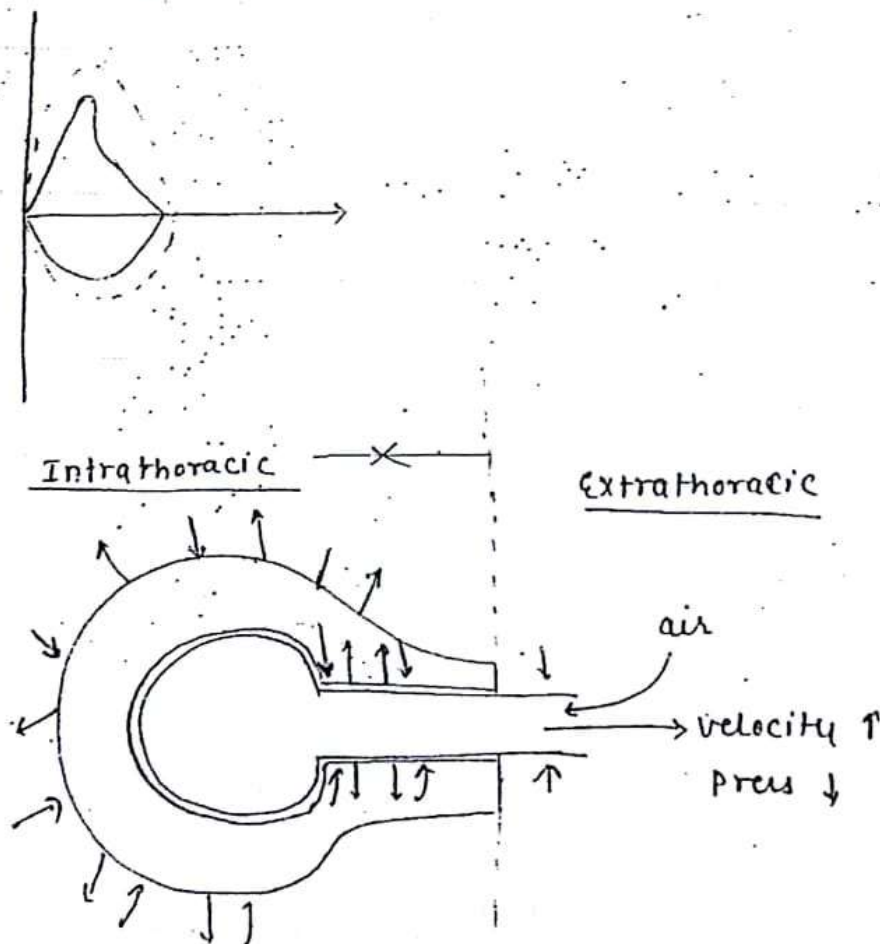
④ RLD



* PEFR is best for home monitoring. It is not best to differentiate b/w OLD & RLD. bcz in both PEFR ↓.

— In OLD shape of curve may become (N) & HYPER. & also PEFR can become (N) & tilt.

(5) mixed—



↑ Inspirⁿ

↑ Expirⁿ

(131)

	Insp.	expir ⁿ
ET	↓	↑
IT	↑	↓

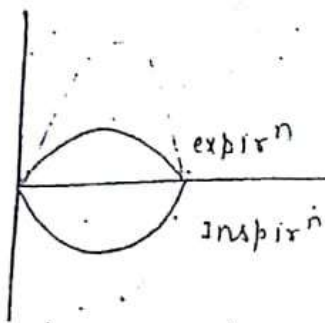
IT size least during expirⁿ

↓
Problem in IT region

↓
causes problem in expirⁿ



(1)* Intrathoracic variable —

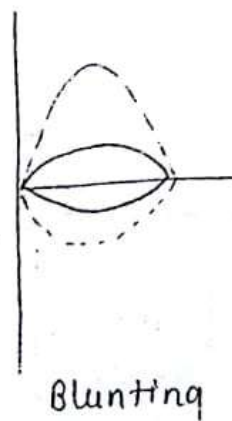
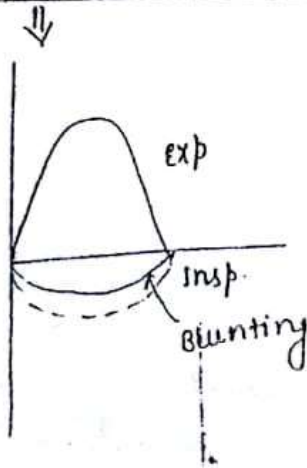


ET size least in inspirⁿ

↓
Problem in ET region

↓
Difficulty in inspirⁿ

(2)* Extra thoracic variable obstruct (3)* Fixed obstruct



Respiratory failure

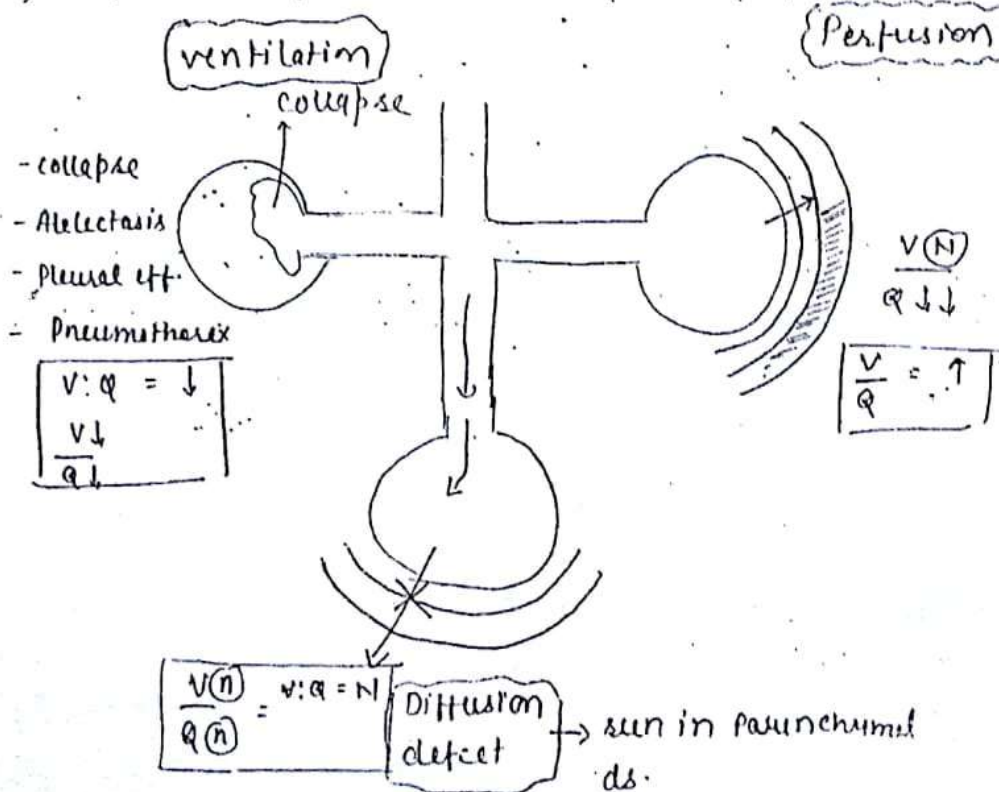
<u>Type-I</u>	<u>II</u>	<u>III</u>	<u>IV</u>
<u>Hypoxic R.F</u>	<u>Hypercarbic</u> <u>R.F</u> (Hypercarbic Hypoxic)	Post op atelectasis	Shock

Type-I

Type II

- $\downarrow PaO_2$
- 3 types of defect
 - 1) ventilⁿ defect
 - 2) Diffusion defect
 - 3) Perfusion defect

• $\uparrow PaCO_2$

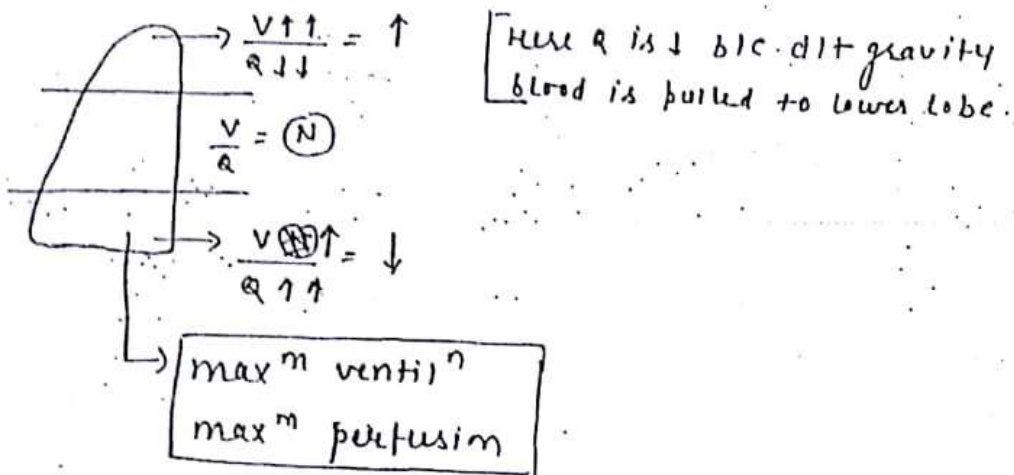


(132)

Ventilⁿ defect —

- (1) collapse
- (2) atelectasis
- (3) Pleural effusion
- (4) Pneumothorax

V/Q mismatch in (N) Lung — Waste zone
It is seen in (N) lung also



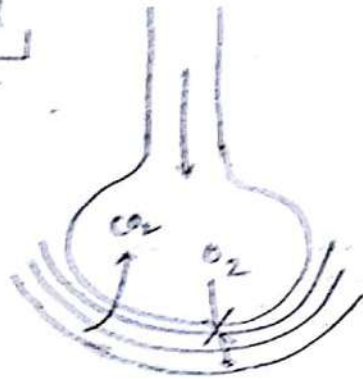
* V/Q is max^m in upper lobe

— But max^m V & max^m Q are in lower lobe.

* TB bacilli grow in upper zone bcz there is poor perfusion.

Type-1 Resp failure

- BA
- emphysema
- (w) obstruct



only problem is O₂ transport.
CO₂ is moving (w)

↓ PaO₂ → Resp centre
PaCO₂ (w) ↓
↓ Hyperventilation

→ (Blue bloater)

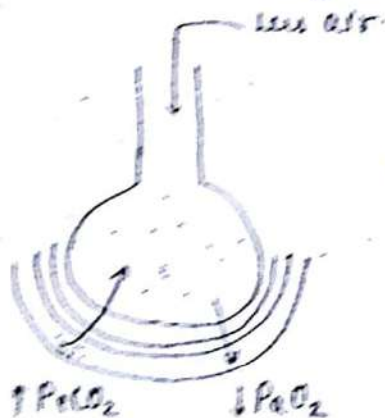
Type-2 Resp failure

ex- Alveolar hypoventilation

↓
Pt is not breathing

• chronic bronchitis

• BA
• asthma
↓
Jawing cause?

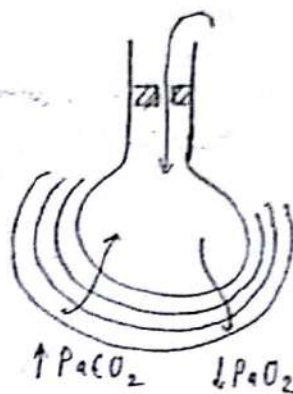


Neither Pt inhaling O₂ nor exhaling CO₂

(22)

Obstructive lung disease:—

only during exacerbation, they behave like type-II failure

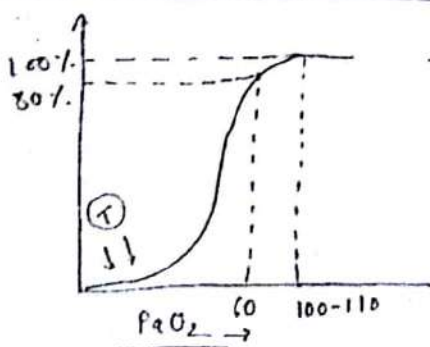


Type-3 RF— mixed type-1 & type-2

- DIF neuromuscular blockade pt. not breathing properly (type-2)
- Also the pt. is bed ridden & there is fluid accumulⁿ in alveoli (type-1)

$\downarrow PaO_2$ means < 60

Hb-O₂ Dissocⁿ curve—



* Beyond 60 the saturⁿ will dramatically fall. So $\downarrow PaO_2$ is < 60

Tense form



Addition of 1st O₂ is difficult as Hb is in tense form.

After that conformⁿ changes & addition of other O₂ become easy.

Later on when saturⁿ occurs again, it become difficult to join O₂

→ when move st. → we need more PaO_2 to produce similar saturⁿ. of 55%

ex on (N) graph 50% saturⁿ at — 60

on R1 shifted graph 50% saturⁿ at — 70

Causes of shift to R1 — (R1) shift for (R)elease

(1) ↓ p^H

(2) Temp. ↑ ⇒ more O_2 needed.
↓
curve shift to st.

(3) 2,3 DPG ↑ → when poor perfusion

↓
poor glycolysis

pregnancy → ↑ 2,3 DPG

↓
↑ Release O_2

Causes of L1 shift —

(1) myoglobin (max^m L1 shift)

(2) HbF

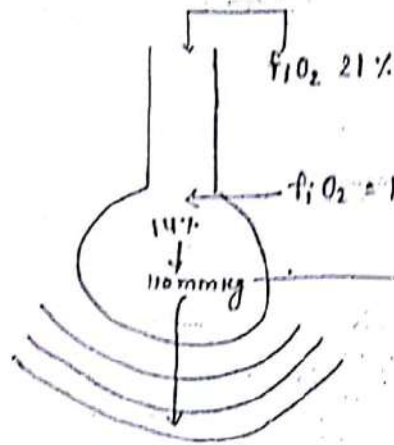
(3) ↑ p^H

(4) Hypothermia

(5) ↓ 2,3 DPG

(134)

A-a₂ gradient / Alveolar arterial gradient



This 110 mm Hg will not go to capillary. Some spillage will occur. The efficiency of this syst is 90% & so 10% spillage will occur. So 100 mm Hg will reach capillary.

This spillage is A-a₂ gradient.

$$PA-aO_2 \text{ gradient} = PAO_2 - PaO_2$$

(1) In diffusion defect - PAO₂ (N)

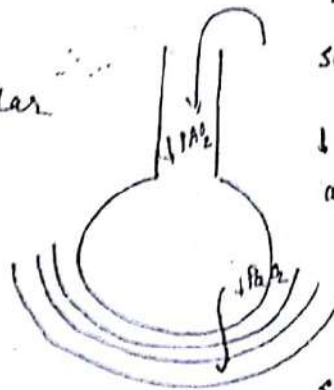
cause - Parenchymal disease PaO₂ ↓

∴ PA-aO₂ gradient ↑↑

(2) Alveolar hypoventilation -

(N) PA-aO₂ gradient

causes - Any neuromuscular problem.



Pt. not breathing
↓
so ↓ PAO₂
↓
↓ O₂ will go to artery
↓
↓ PaO₂
↓
so gradient is (N)

How to calculate $PA-aO_2$ gradient —

$PAO_2 - PaO_2 \rightarrow$ calculated by ABG

$$PAO_2 = (713 \times f_{iO_2}) - \frac{PaCO_2}{0.8}$$

$$\frac{Age}{4} + 4 = A-aO_2 \text{ gradient}$$

$A-aO_2$ $\begin{cases} > 30 \rightarrow \text{Grossly } \uparrow \text{ sed} \\ < 30 \rightarrow \textcircled{N} \end{cases}$

* In $\textcircled{N}$ person there should be less $A-aO_2$ gradient
(no spillage should be there)

Q. $f_{iO_2} = 21\%$

$PaO_2 = 100 \text{ mm Hg}$

$PaCO_2 = 40 \text{ mm Hg}$

$$PAO_2 = \left(713 \times \frac{21}{100} \right) - \frac{400}{0.8}$$

$$= 159 - 50$$

$$PAO_2 = 99.100$$

$$Q. f_{iO_2} = 50$$

$$P_{aO_2} = 200 \text{ mm Hg}$$

$$P_{aCO_2} = 48$$

$$PAO_2 = \left(713 \times \frac{50}{100} \right) - \frac{480}{0.8}$$

$$= 350 - 60$$

$$350 - 60 \neq 180$$

$$\begin{aligned} \text{Gradient} &= 296 - 200 \\ &= 96 \end{aligned}$$

$$PAO_2 = \left(713 \times \frac{50}{100} \right) - \frac{48}{0.8}$$

$$= 356 - 60$$

$$= 296$$

(135)