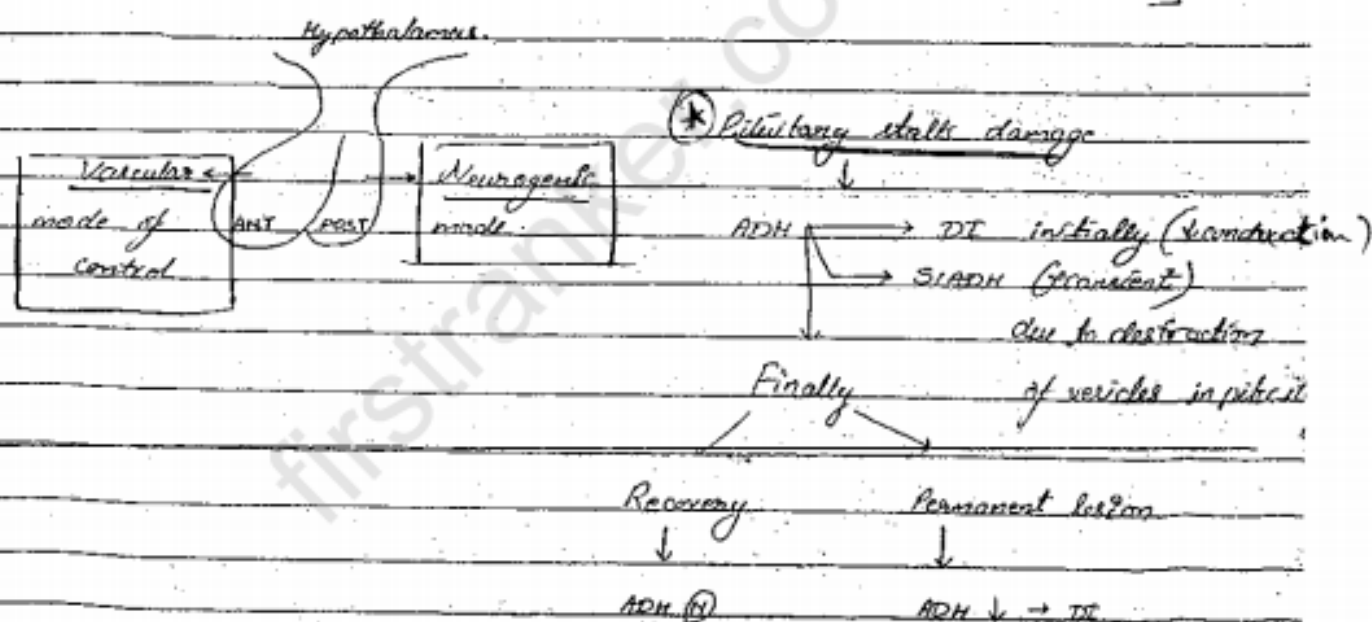


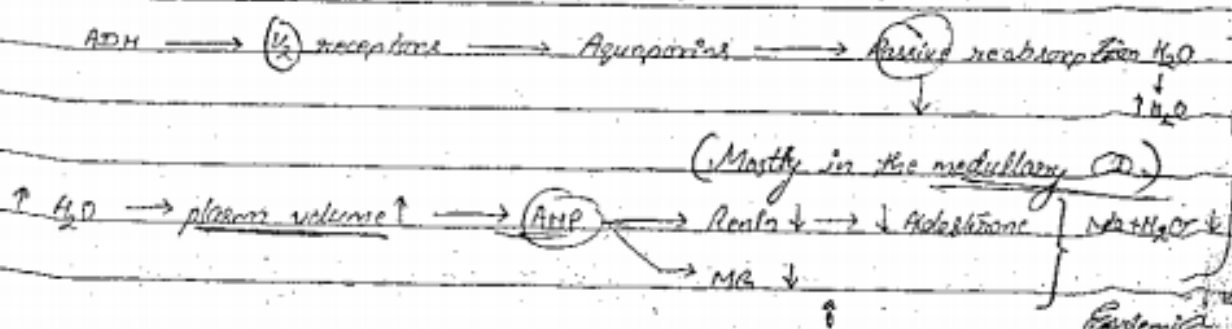
## Diagnosis of Endocrine disorders

### PITUITARY GLAND

All anterior pituitary hormones are under stimulatory control of hypothalamus except Prolactin (under -ve influence of Dopamine)  
[PROLACTIN → Under -ve influence of DOPAMINE]



### SIADH



Patients of SIADH generally do not have edema



SIADH → \* Euvolemia

\* Hypouricemia

\* True Hyponatremia (due to ANP)

\* Urine  $\text{Na}^+$  ↑ (H) → 20-40 mEq/l (Should be above 20)

\* Urine osm > Plasma osm

Single most imp parameter for plasma osmolality →  $\text{Na}^+$

$$\star \text{ PLASMA OSM} = 2(\text{Na}) + \frac{\text{Glu}}{18} + \frac{\text{BUN}}{2.8}$$

$$\text{OR } 2(\text{Na} + \text{K}) + \frac{\text{Glu}}{18} + \frac{\text{BUN}}{2.8}$$



Testing for SIADH :-

Water loading test → ADH remains high (normally ADH ↓)

Confirms diagnosis of SIADH

True about SIADH are ALL

- 1) Vasopressin analogs are class of drugs approved for R
- 2) Urine  $\text{Na}$  is 14 to ↓
- 3) The plasma  $\text{Na}$  can be as low as 125 mEq
- 4) Water loading test can be used for diagnosis

CF :-

1) Headache

2) Anorexia

3) Altered sensorium

4) Seizures

R :- Fluid restriction

$\text{Na}^+$  Correction

Vasopressin

(CONIVASOL)

(TEL VASOL)

Selective  $\text{V}_2$  receptors

blockers

Desmopressin

\* Rapid Correction of Sodium may cause "Central Pontine Myelinolysis"



★ Polyuria :  $> 40 - 50 \text{ ml/kg/day}$

$> 3 \text{ litres/day}$

Urine osmolality

$< 300 \text{ mOsm/L}$

Free water loss

Primary polydipsia

1) Psychogenic polydipsia

★ Plasma  $\text{Na}^+$  conc :  $\downarrow$

may be @ but never  $\text{Na}^+$

★ Water deprivation test

(1hr & 3hrs after water deprivation)

Urine osm  $\uparrow$

(Should improve by at least

50% to say primary polydipsia)

$> 300 \text{ mOsm/L}$

Solute loss

Diabetes Insipidus

Central

Nephrogenic

★ Plasma  $\text{Na}^+$  conc :  $\uparrow$

or @ but never  $\text{Na}^+$

Urine osm  $\leftrightarrow$

or  $\uparrow$  by  $\sim 50\%$

Central

Nephrogenic

↓ Post Dehydration

Urine Osm  $\uparrow$

q:- Desmopressin

Spray

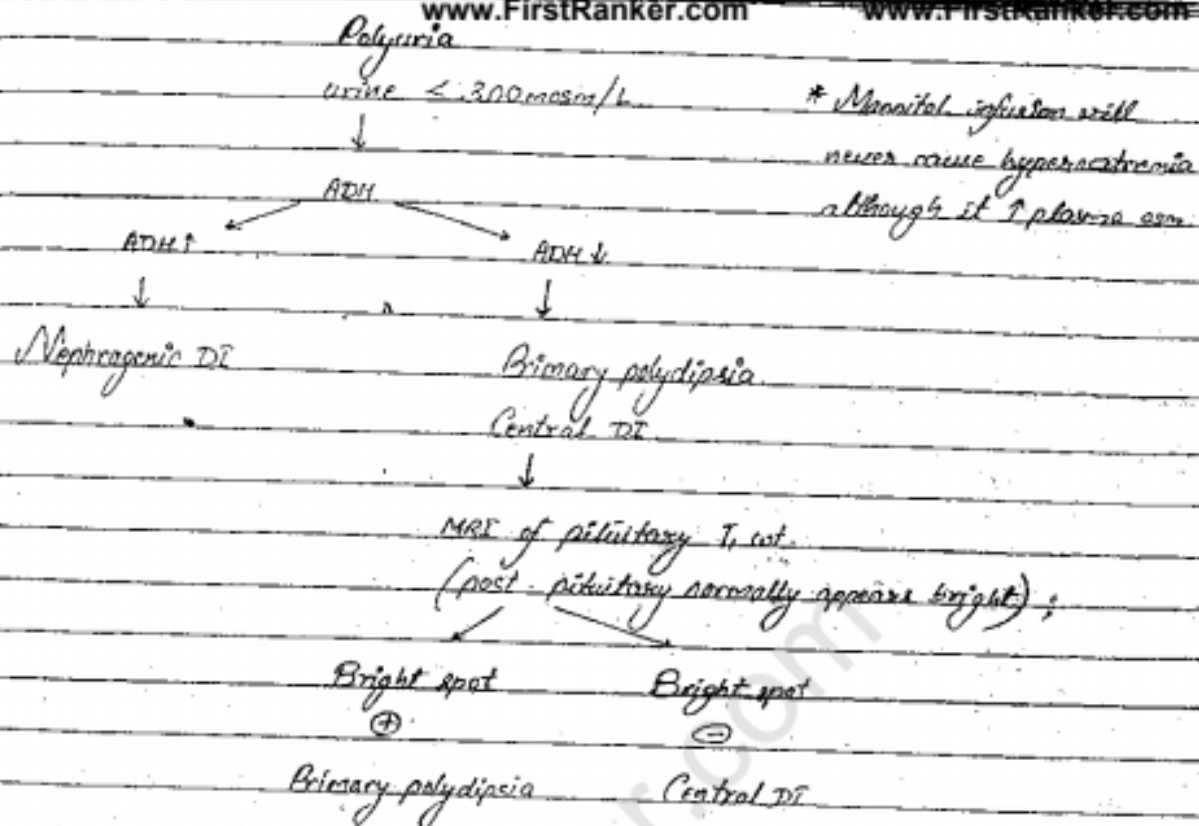
Urine Osm  $\leftrightarrow$

q:- Thiazide

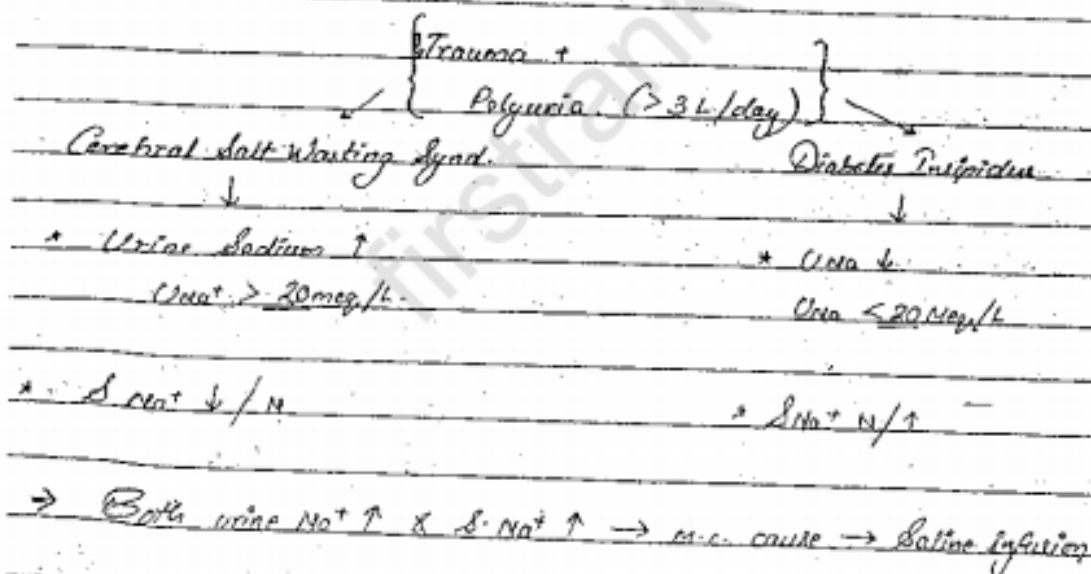
Thiazides help by causing  $\text{Na}^+$  loss in urine

Reffer  $\text{Na}^+$  absorption in PCT

$\text{H}_2\text{O}$  is absorbed along with

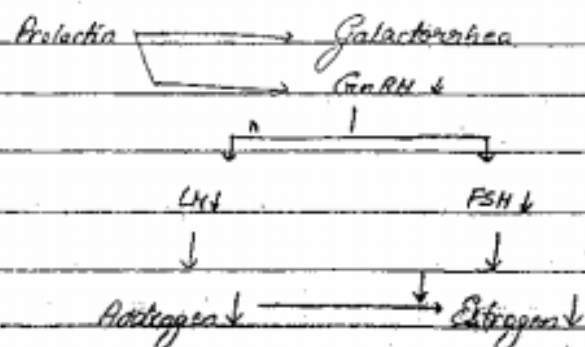


\* Mannitol infusion will never cause hypernatremia although it ↑ plasma osm.



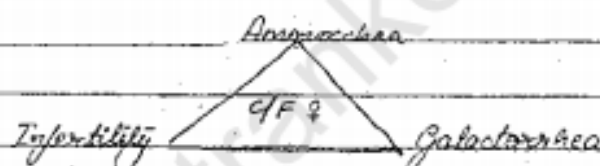
PROLACTIN:

✓ M.c functional tumor of pituitary: Prolactinoma



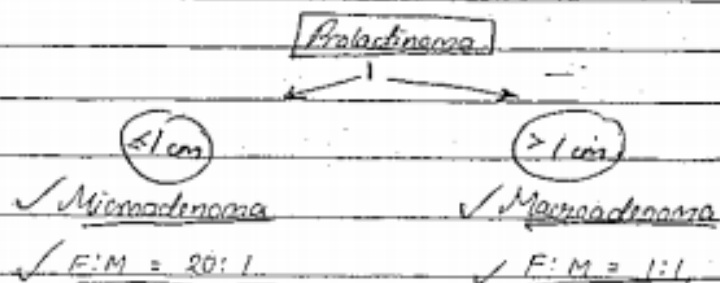
- ⊗ Prolactin levels ( $>100 \text{ ng/ml}$ )
- \* Prolactinomas (MC)
  - \* Physiological state
  - \* Dopamine blocker  $\rightarrow$  drug history
  - \* Hypothyroidism  $\rightarrow$  TSH levels
- ↑ prol.  $\rightarrow$  Prolactinoma

PROLACTINOMA



♂  $\rightarrow$  Erectile dysfunction  
Galactorrhea (55%)

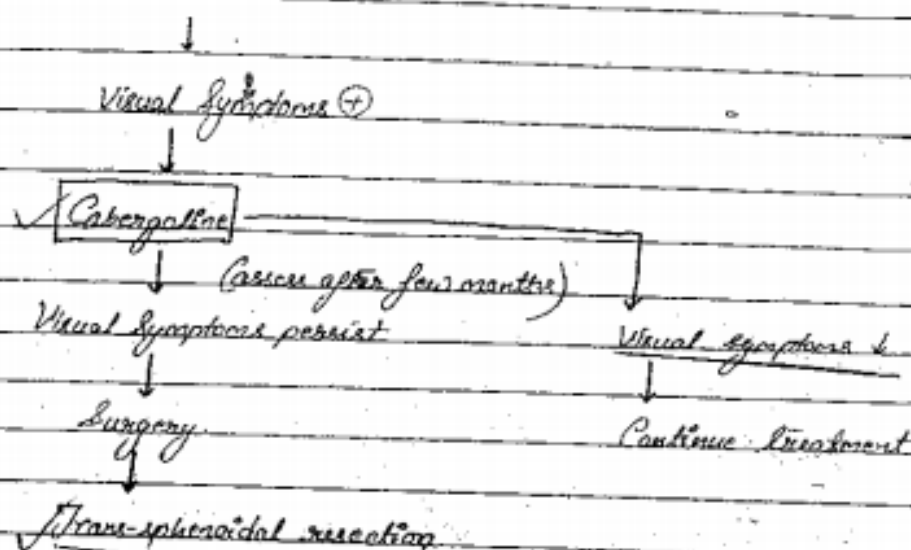
⊗ Prolactinoma doesn't cause Gynaecomastia



q1 - q.o.c. in Dopamine agonists: Cabergoline (D.o.c. in non-pregnant)  
Bromocriptine (D.o.c. in pregnancy)

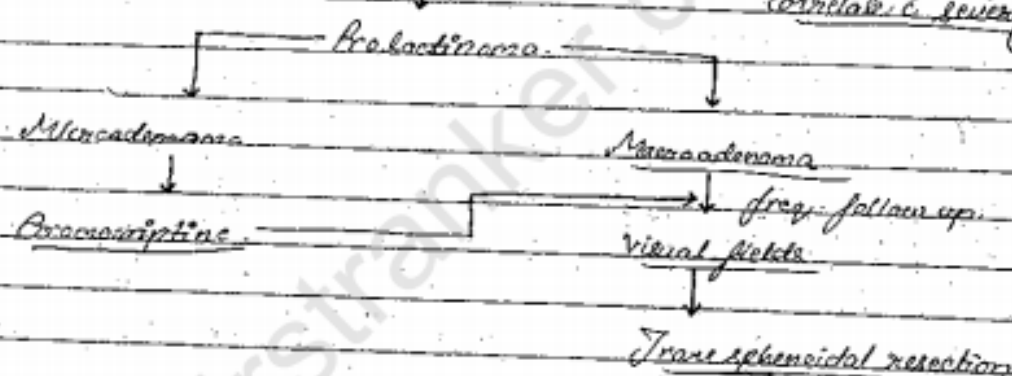


Macroadenoma



Pregnancy

↓ Prolactin levels in pregnancy don't correlate to severity/magnitude



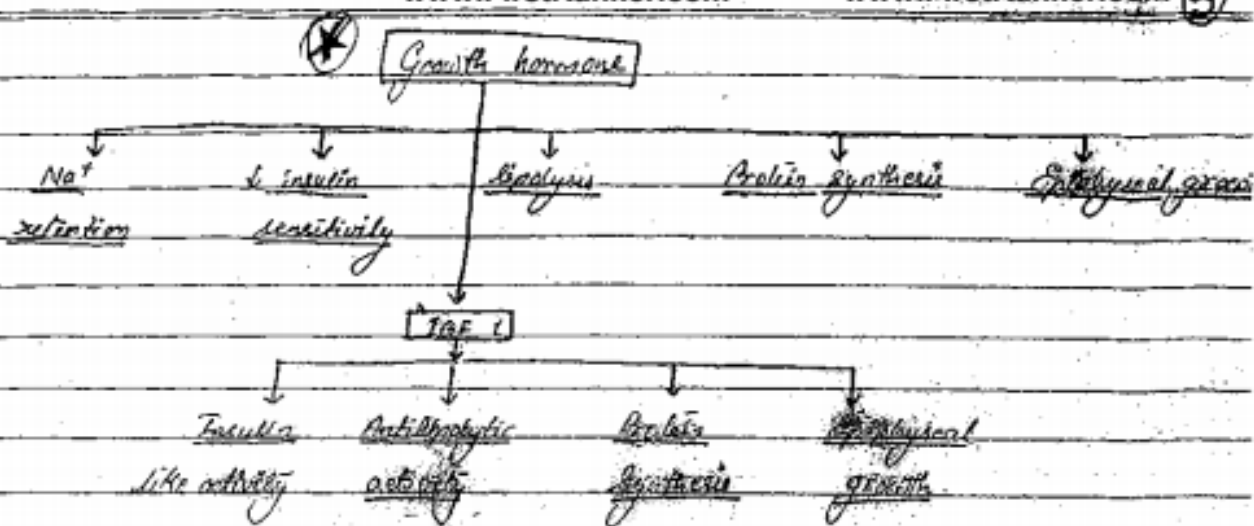
ACROMEGALY

Growth Hormone

Liver

→ IGF-1

↓  
Epiphyseal growth → Bone size/length ↑  
↑ protein synthesis



Arginine  $\rightarrow$   $\uparrow$  GH  $\rightarrow$  Muscle mass  $\uparrow$   
Fat  $\downarrow$

**C/F** - \* Skull size  $\uparrow$   $\rightarrow$  Mandible growth  $\uparrow$   $\rightarrow$  gaps b/w teeth  
\* Finger "  $\uparrow$   $\rightarrow$  Squaring of Mandible  
\* Foot "  $\uparrow$  ENGLISH MAN'S CHINAMAN HOT DISEASE

Enlarged Skull size  $\leftrightarrow$  Paget's disease  $\rightarrow$  Sella turcica (H)  
 $\rightarrow$  Acromegaly  $\rightarrow$  Enlarged sella turcica

\* Heart pad thickness  $> 20\text{mm}$

\* Fleeshy palate

\*  $\uparrow$  Glucose + Insulin resistance  $\rightarrow$  Diabetes Mellitus

\*  $\text{Na}^+$   $\uparrow$  + Systemic vascular resistance  $\uparrow$   $\rightarrow$  Hypertension

\* LVH  $\rightarrow$  Cardiomyopathy  $\rightarrow$  Ischaemic heart disease

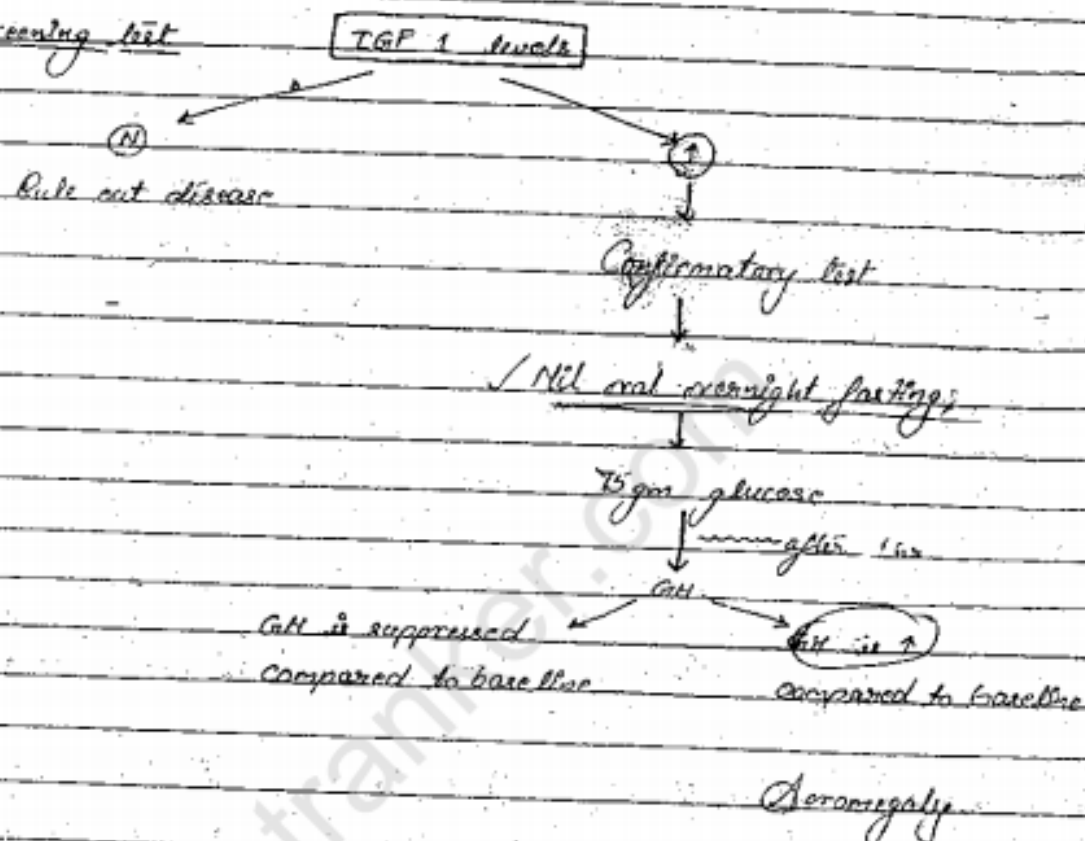
\* Colonic polyps  $\uparrow$   $\rightarrow$   $\uparrow$  risk of CA Colon

\* Moist doughy handshake

## Investigations

2. Growth hormone levels are not useful in assessment.

## Screening test



(OGTT may be also used to describe the confirmatory test)

[R] : A.o.c is surgery

Drugs: somatostatin analogues (Octreotide, Lanreotide)

**MRT**

```

    graph TD
      MRT --> Resectable[Resectable]
      MRT --> NonResectable[Non Resectable]
  
```

Trans Sphenoidal Resection

Gamma Knife Surgery

↓ (as benefit)

GH receptor blocker → (pegvisomant)



CUSHINGS

⑥

Cushing disease: Corticosteroid excess due to pituitary adenoma

Cushing syndrome: Entire spectrum of Corticosteroid excess disorders

M.c. cause of Cushing syndrome:- Iatrogenic

ACTH ↑

\* Pituitary adenoma

\* Ectopic ACTH syndrome

\* Pigmentation ⊕

ACTH ↓

\* Adrenal suppression/atrophy ↑

\* No pigmentation

Pituitary adenoma

Ectopic ACTH

\* Insidious

\* Rapid onset

\* Hypokalemic  
metabolic alkalosis

\* Hypokalemic  
metabolic alkalosis

~40%

~90%

ACTH ↑

Cortisol ↑ → Mineralocorticoid

↓ 11β-Hydroxylase

Cortisone → No mineralocorticoid

\* Insidious course leads

\* Rapid course

→ No induction of 11β-HLase

to induction of 11β-Hydroxylase

which doesn't lead to rise in mineralocorticoids

↑ mineralocorticoid activity

\* F:M = 4:1

\* F:M = 1:1

\* F:M = 4:1

\* Obesity ⊕

\* Obesity ±

\* Obesity +

(if obesity is absent it  
is due to malignant carcinoma)

\* Earliest manifestation of Cushing's → lab → loss of diurnal variation of cortisol levels

\* next manifestation / earliest cl → wt gain (after constitutional features)

cl → \* Central obesity

\* Thin skin

\* Moon faces

\* Striae abdomen, Easy bruisability

\* Thin extremities

\* Buffalo hump

\* Osteoporosis / arthralgia

Pseudo Cushing

→ Alcohol (the most common)

→ drugs

Investigation

Cushing suspected

Overnight / low dose Dexamethasone test

↓ 1 mg Dexamethasone 11 pm

8 am Cortisol

Cortisol ↓

Rule out Cushing

↑ Cortisol

ACTH

↑ ACTH

Pituitary adenoma

Ectopic ACTH

↓ ACTH

Adrenal cause

NCCT - abdomen

High dose Dexamethasone test

6 mg Dexamethasone / 24 hrs

< 6 cm

Benign

> 6 cm

Malignant

17 ketosteroid ↑↑

↓

Pituitary

↑

Ectopic

\* (ambiguous)

Petrous vein  $\rightarrow$  ACTH

Peripheral vein  $\rightarrow$  ACTH



Petrous : Peripheral  $> 2:1 \rightarrow$  Pituitary  
 $< 1:1 \rightarrow$  Ectopic

[R] : \* Passerolide  $\rightarrow$  acts through Somatostatin receptors.

\* Ketocanazole

\* Metyrapone  $\rightarrow$  11 $\beta$  hydroxylase inhibitors.

R.O.C  $\rightarrow$  Surgery

## DISORDERS OF SEXUAL DIFFERENTIATION (DSD)

XX DSD

XY DSD

XY DSD : SRY gene on Y-chromosome  $\rightarrow$  development of testis

Testis  $\rightarrow$  Mullerian Inhibiting Factor.

Testosterone

$5\alpha$  Testosterone reductase

Dihydroxy testosterone

Androgen receptors (X-chr. codes for androgen receptors)





Müllerian duct → female structures

Wolffian duct → male structures

External Genitalia → develops from common Embryonic Structures

{ If there is no Y-chromosome the internal and external genitalia will by default form female structures }

\* MIF → blocks the Müllerian development

\* Testosterone → promotes development of Wolffian duct

\* DHT → required for the external genitalia to become male

5 $\alpha$  reductase deficiency

MIF + → No müllerian development

Testosterone + → Wolffian development ⊕ }  $\delta$  internal genitalia

No DHT → Ambiguous ext. genitalia (since the action of testosterone to develop ext. genitalia is weak)

Androgen Receptor Insensitivity

Testosterone + → No action on receptors → Wolffian Duct absent

MIF + → Müllerian duct ⊖ → No müllerian system

DHT + → No action on receptors →  $\delta$  external genitalia

Testis are present in the abdomen / undescended

\* 125% present at puberty with primary amenorrhea and blind vaginal pouch

- \* Breast development will be normal (estrogen dependent)
- \* Axillary / pubic hair will be absent (androgen dependent)

Testicular feminization syndrome → Karyotype XY

- \* The testes are either undescended / atrophic & secrete regular amount of androgen and have a 30 fold higher risk of malignancy (Seminoma)

Testicular Feminization Syndrome  
XY

MURK Syndrome  
Müllerian agenesis XX

- \* T-G → Absent
- \* Ext. genitalia → ♀
- \* Breast → (N)
- \* Axillary / Pubic hair → Absent
- \* inguinal hernia +

- \* Int. genitalia → Absent
- \* Ext. genitalia → ♀
- \* Breast → (N)
- \* Axillary / Pubic hair → (N)  
(Androgen receptor (N))

Gonadal Dysgenesis :  
→ Pure gonadal dysgenesis  
→ Mixed gonadal dysgenesis

Pure gonadal dysgenesis :- streak testis

↓  
No testosterone, No MIF

↓  
Both int. & ext. genitalia are female by default

- \* Breast development - absent
- \* Axil / Pubic hair growth - N (due to androgens from adrenal)

## Mixed Gonadal Dysgenesis

- \* One testis (gonad) & streak, one gonad is normal.
- \* General masculine picture, not proper masculinization because just one gonad is present (virilization is not complete)
- \* Hypospadias is common

Range  $\rightarrow$  Normal female  $\leftarrow$  to  $\rightarrow$  Male  
any phenotype in between

## XX DSD

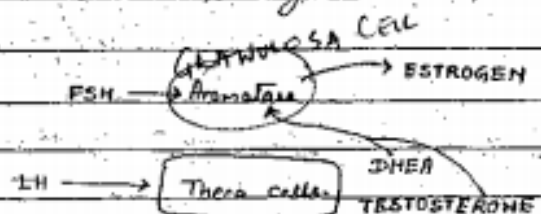
- \* Maternal cause  $\rightarrow$  Androgen producing tumor } during pregnancy  
Androgenic drugs

- \* Fetal cause  $\rightarrow$  Congenital Adrenal Hyperplasia  
 $\left. \begin{array}{l} 21 \alpha \text{ OH deficiency} \\ 11 \beta \text{ OH deficiency} \\ 3 \beta \text{ HSD deficiency} \end{array} \right\} \uparrow \text{ Androgen}$

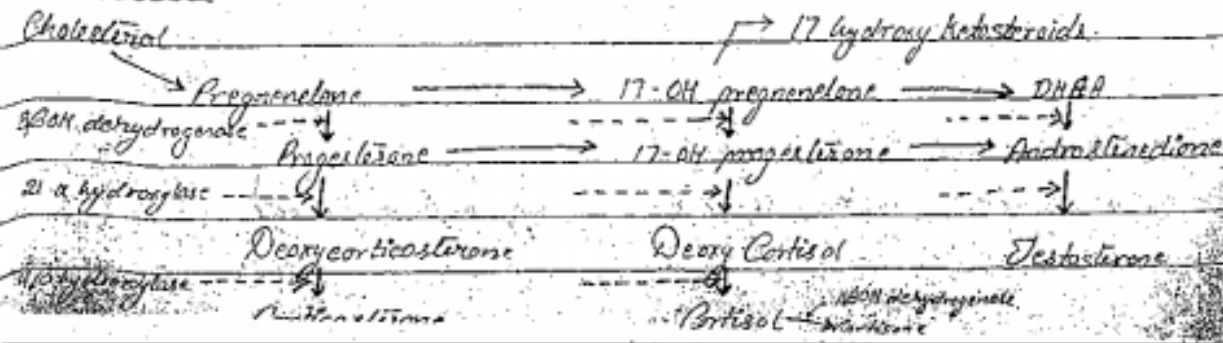
Cytochrome P450 oxidoreductase

- \* Aromatase defect Glucocorticoid receptor gene mutation

- \* NNT-4 Mutation



## CAH







Most common enz defect  $\rightarrow$  21 $\alpha$  hydroxylase deficiency

Autosomal recessive

Any defect of horizontal enz will  $\downarrow$  formation of Cortisol

ACTH will constantly stimulate adrenal cortex

CAH

21 $\alpha$ OH / 11 $\beta$ OH deficiency  $\rightarrow$  17 $\alpha$  ketosteroid levels will  $\uparrow$

Can be used for evaluation in case of ambiguous genitalia

(17-OH progesterone more preferred than 17-OH pregnenolone)

Deoxy corticosterone (DOC) has mineralocorticoid action

21 $\alpha$ OH

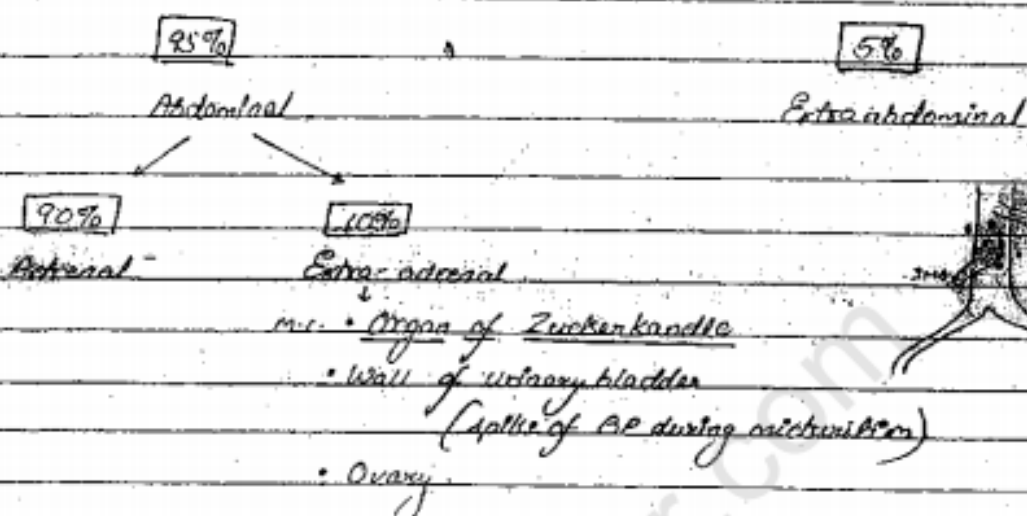
- Androgens  $\uparrow$
- XX  $\rightarrow$  Ambiguous genitalia
- XY  $\rightarrow$  precocious puberty
- Metabolic acidosis
- Hypertension

11 $\beta$ OH

- Androgens  $\uparrow$
- XX - ambiguous genitalia
- -de-
- Metabolic alkalosis
- Hypokalemia
- HTN  $\oplus$

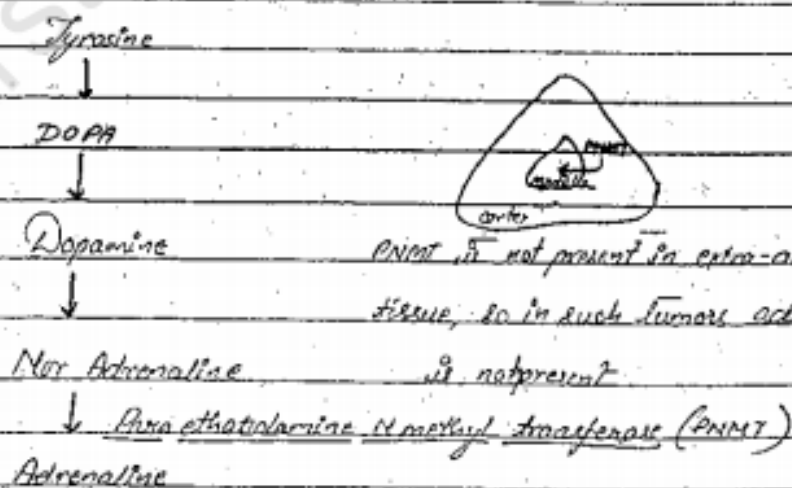
## PHAECHROMOCYTOMA / PARAGANGLIOMA

Phaeochromocytoma is for tumours of adrenal & extra-adrenal regions.  
Paraganglioma is for head and neck tumours.



Rule of 10:

- 10% Extraadrenal
- 10% Bilateral
- 10% Children
- 10% are malignant at the time of diagnosis



Extra-adrenal  
Non-adrenaline

Adrenal Pheo

$\leq 3\text{cm}$

Epinephrine

$> 3\text{cm}$

Noradrenaline

avg size - 4 to 5  
↓  
MOR

In MEN syndrome, Pheo are adrenal  $\rightarrow$  so adrenaline is produced.

Malignant Pheo :- N/c ratio

Mitotic spindle

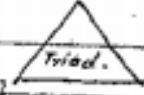
Capsular invasion

Metastases  $\rightarrow$  only way to differentiate

$\uparrow$  production of embryonic / primitive metabolites like

DE :- Headache (m.c. symptoms)

Palpitation



Sweating

Wt. loss (differentiated for wt. loss)

Pheochromocytoma

\* Catechol  $\uparrow$

$R_2 \leftrightarrow (N)$

\* Hyperadrenergic features

\*  $\uparrow$  BMR

\* Wt. loss

\* Tachycardia (SVT + AF)

\* HTN  $\leftarrow$  Sustained  
Episodic

\* Tremor - occasional

Thyrotoxicosis

\* Catechol (N)

$T_3 \rightarrow R_2$

\* Hyperadrenergic features

\*  $\uparrow$  BMR

\* Wt. loss

\* Tachy (SVT +

\* Sustained

\* Tremor



\* Orthostatic hypotension (+)  
(due to volume contraction)

\* absent

\*  $\ominus$

\* RAG deposition (+)

Low → 24 hr urine → catecholamine & Metanephrine assay + T.O.C.  
(fractionated)

\* Plasma → catecholamine & free metanephrine assay

\* Chromogranin A levels ↑ in plasma

\* Optimal test for pheochromocytoma → abdominal MRI (sensitivity 91%)  
localization if +ve → MIBG (to look for mets)  
if -ve → MIBG (sensitivity 81%)  
T.O.C. for localization

\* Best investigation :- DOBA PET

R:-  $\alpha$  Blockers

Phenylephrine (2 weeks to achieve full effect)

→ Nifedipine

→ Phentolamine

$\alpha$ -Blockade

$\beta$ -blockers → Surgery

CANN'S - PRIMARY HYPERALDOSTERONISM

Aldosterone ↑

→  $\text{Na}^+$  ↑ +  $\text{H}_2\text{O}$  ↑ → ANP ↑ →  $\text{Na} + \text{H}_2\text{O}$  ↓

→  $\text{K}^+$  ↓

→  $\text{H}^+$  ↓ (metabolic alkalosis)

→ HTN

Renin ↓

Pts. with primary hyperaldosteronism (Conn) do not have oedema.

Rx :: Spironolactone, Eplerenone (Aldo. receptor blockers)

Primary hyperaldosteronism (+ Aldo. + renin)

↓  
Abdominal imaging

↓  
A/E - adrenal enlargement (70%)

Conn's → Should only be used for Adrenal adenoma (30%)  
not for adrenal hyperplasia.

Autoimmune Polyglandular Syndrome

APS 1

APS 2

\* Early Childhood, infant

\* Adult Adolescent

\* Hypo parathyroidism

Celiac Sprue, Dermatitis herpetiformis

\* Asplenia

Graves disease

\* Mucocutaneous candidiasis

Hyperparathyroid.

\* Hypogonadism

- do -

\* Autoimmune thyroiditis

- do -

\* Alopecia

- do -

\* Hypogonadism

- do -

\* Type I diabetes

- do -

\* Addison's disease

- do -

\* Vitiligo

- do -

| MEN-1                        | MEN-2A             | MEN-2B             | MEN-4                |
|------------------------------|--------------------|--------------------|----------------------|
| Werner Syndrome              | Sipple Sydnr.      |                    |                      |
| * Parathyroid adenoma (n.c.) | * MTC              | * MTC              | * PTH-adenoma        |
| Multi-centric                | * Pheochromocytoma | * Pheochromocytoma | * Pheochromocytoma   |
| * Enteropancreatic problems  | * PTH adenoma      | * Medullary        | * Gastric Int. tumor |
| Gastrinoma                   | * Lichen-Amyloid   | * Mucosal/Int      | * Renal tumor        |
| Insulinoma                   | cutaneous lesion   | neurofibroma       | * P.C.               |
| * Pituitary adenoma          | * Hirschprung's    |                    | * ? Adrenal tumor    |
| * Carcinoids                 |                    |                    |                      |
| * Pheochromocytoma (rare)    |                    |                    |                      |

M.c. entero-pancreatic tumor in MEN-1 → Gastrinoma

M.c. pancreatic tumor in MEN-1 → Insulinoma

M.c. tumor in MEN-1 → Parathyroid adenoma

Gastrinoma → ↑ Gastrin  
↓  
↑ Basal acid output  
↓  
Peptic ulcer disease.

↑ Serum Gastrin can be due to :-  
1) PPT  
2) Pernicious anaemia  
3) Atrophic gastritis

If Stomach pH  $\leq 2.0$  Serum Gastrin is  $\geq 1000$  pg/ml

\* M.c. site for Gastrinoma  
Duodenum > 1st part of duodenum

Gastrinoma

[Rx] - PPT, Surgery

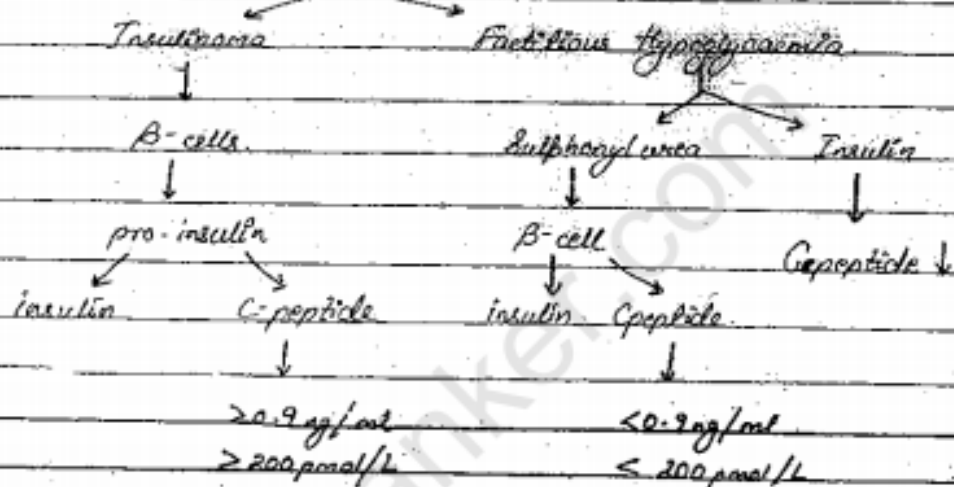


Insulinoma: Episodes of hypoglycaemia

72 hr fasting (I.O.C)

Insulin: Glucose  $\geq 0.3$  (Check insulin: glucose ratio every hour)

possibility of insulinoma.



[Q]: \* Diazoxide + Carbohydrate diet

\* Surgery (Insulinoma occurs equally in all parts of pancreas)

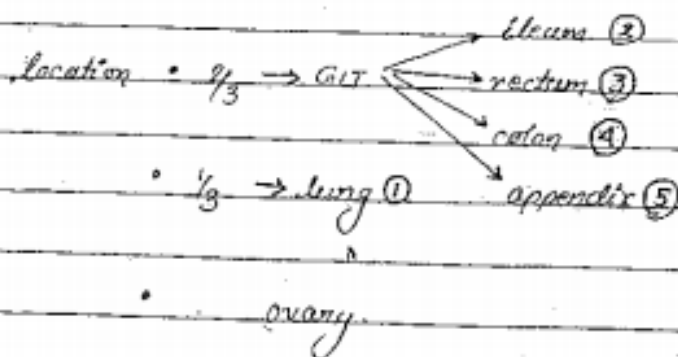
\* Metastatic :- Streptozocin + 5FU

Surgery → Localisation of Tumour in pancreas

- EUS
- CT (Contrast CT) → I.O.C.
- Intra-operative Ultrasound

Gold Standard → Arteriography

## CARCINOID



(Carcinoid syndrome is rare in rectal carcinoids)

\* M.c. complaint of Carcinoid tumor: Abdominal pain

\* M.c. complaint of Carcinoid syndrome: Flushing & diarrhea

## Carcinoid Syndrome

[CF] : \* Diarrhea

\* Flushing

\* Asthma like wheezing episodes

\* Endomyocardial Fibrosis - RV

\* TR > TS > PR > PS

Serotonin

↑ (tumor)

Tryptophan

↓

Niacin ↓

→ Pellagra

→ Diarrhea

→ Dermatitis

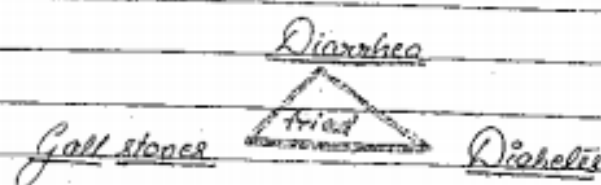
→ Dementia

[Tx] : Asx : PET Scan

I.O.C : Scintigraphy

[Rx] : Surgery

Samab stationoma

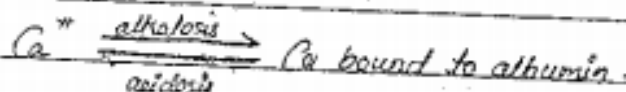
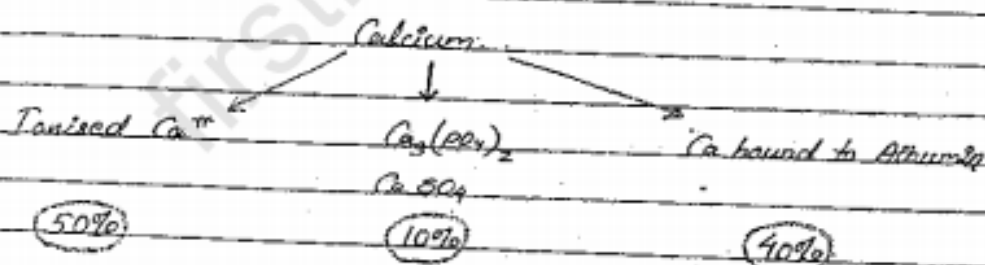


VIPoma

- \* Werner Morrison Syndrome
- \* WDHA syndrome
  - Watery diarrhea
  - Hypokalemia
  - Hypochlorohydrata
- \* Stool osmotic gap  $< 50 \text{ mOsm/L}$
- \* Stool sodium content  $> 90 \text{ meq/L}$

(in case of secretory diarrhea  $\rightarrow$  Stool osmotic gap  $> 50 \text{ mOsm/L}$ )

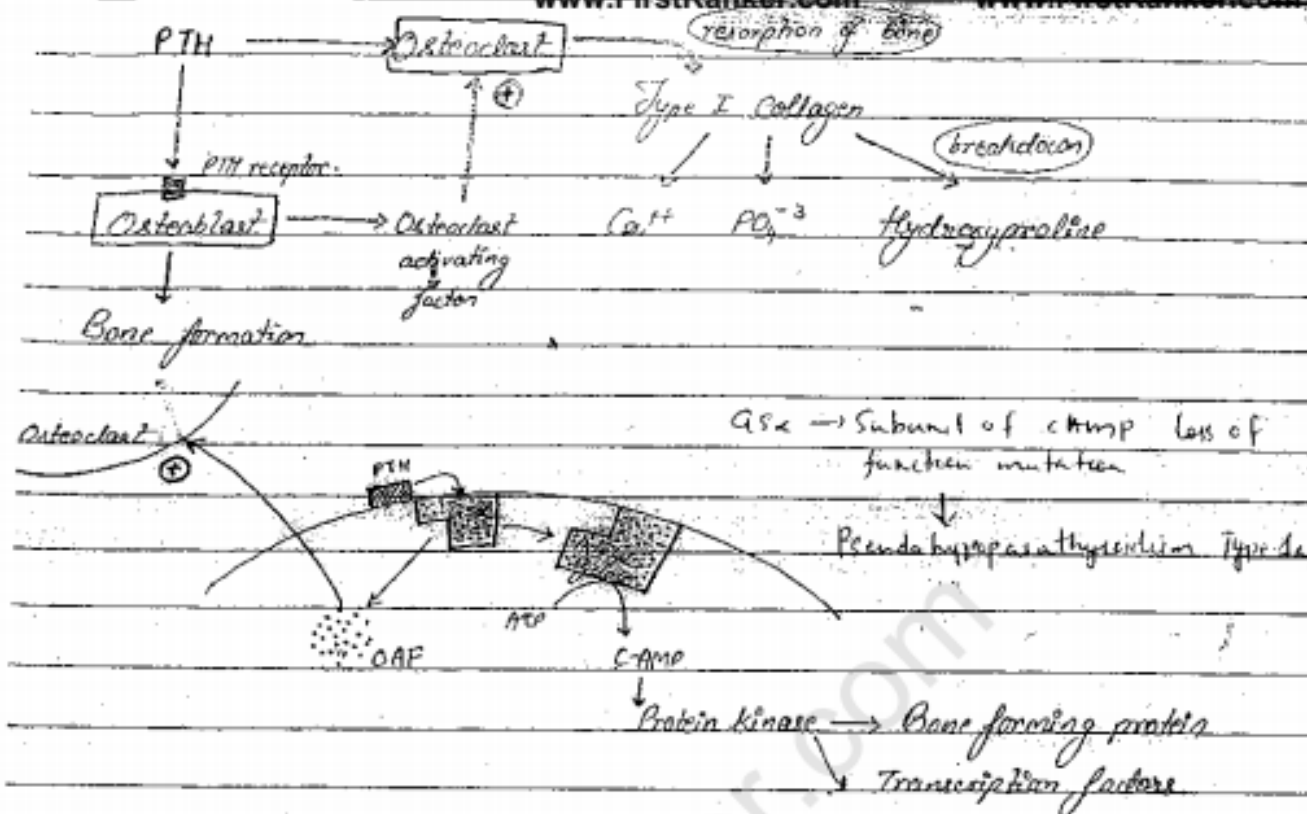
### CALCIUM DISORDERS.



(in case of hyperventilation  $\rightarrow \text{CO}_2$  wash out  $\rightarrow$  alkalosis  $\rightarrow \text{Ca}^{++} \downarrow \rightarrow$  Carpopedal spasm)

Hypocalcaemia  $\rightarrow$  cells become hyper excitable  $\rightarrow$  Exaggerated jerks  
 Spasms, Tetany  
 Ticks, Seizures.





### Pseudo hypoparathyroidism

Defect in  $\text{G}\alpha$  receptor.

PTH  $\uparrow$

Loss of function mutation  $\rightarrow$  Albright Osteodystrophy

### Pseudo Pseudo hypoparathyroidism

✓ Defect in bone forming protein or cAMP control.

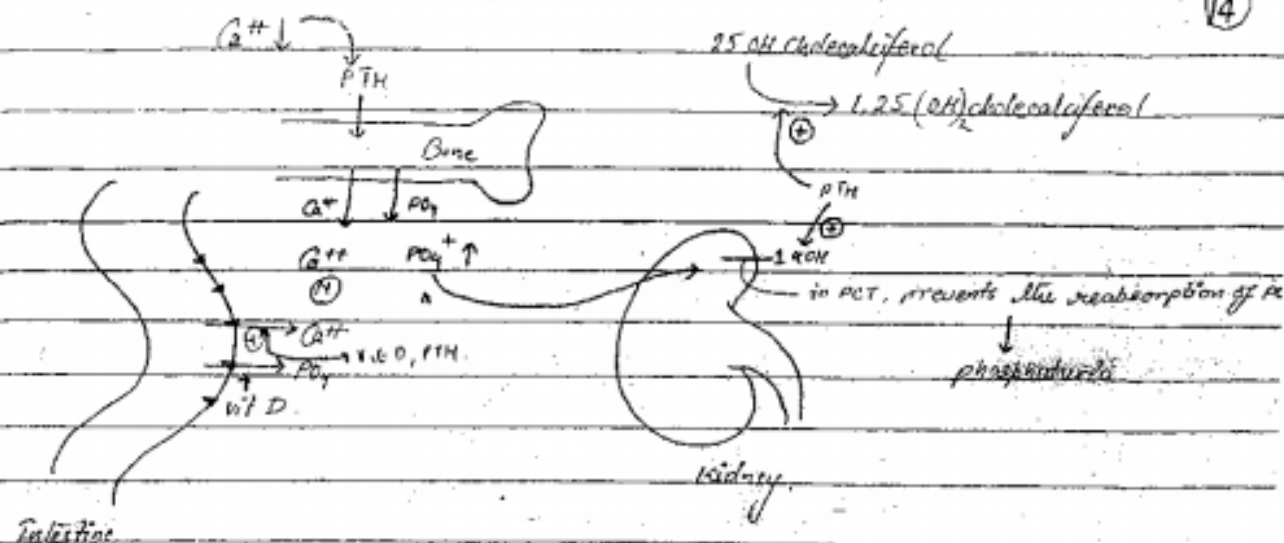
✓ Osteoclastic activity (N) cAMP is unaffected.

✓  $\text{G}\alpha$  activity (N)

McCune Albright Syndrome :- Gain of <sup>function</sup> mutation  
 $\text{G}\alpha$  overactivity.

✓ Poly-ostotic fibrous dysplasia.

✓ Precocious puberty



If there is vit. D toxicity  $\rightarrow Ca^{++} \uparrow, PO_4^{--} \downarrow$

If there is hypoparathyroidism  $\rightarrow Ca^{++} \downarrow, PO_4^{--} \uparrow$

Hypoparathyroidism

$\downarrow Ca, PO_4^{--} \uparrow$

Vit. D dependent Rickets

$\downarrow Ca, \downarrow PO_4^{--}$

Chronic Renal Failure :- vit. D is not formed.  $Ca \downarrow$   
phosphate is not excreted  $PO_4^{--} \uparrow$

Normal values :-  $Ca :- 9-11 \text{ mg/dl}$

$PO_4^{--} :- 2.5 - 4.5 \text{ mg/dl}$

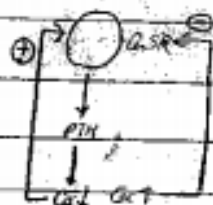
$ALP :- \geq 130 \text{ SI} / \geq 13 \text{ KA}$  is indicative of ALP.

ALP & Osteocalcin are osteoblastic / bone forming markers.

Proline / Hydroxyproline are osteoclastic / bone resorption markers.

Granulomas have 1 $\alpha$ OH activity  $\rightarrow$  formation of vit. D.

|                                               | Ca  | PO <sub>4</sub> | PTH | ALP |
|-----------------------------------------------|-----|-----------------|-----|-----|
| <u>Primary hyperparathyroidism</u>            | ↑   | ↓               | ↑   | ↑   |
| <u>Hypoparathyroidism</u>                     | ↓   | ↑               | ↓   | N/↓ |
| <u>Rickets/Osteomalacia</u>                   | ↓/N | ↓               | ↑   | N/↑ |
| <u>Sarcoidosis</u>                            | ↑   | ↑               | ↓   | N   |
| <u>Malignancy/PTHrP</u><br>(eg. cell Ca lung) | ↑   | ↓               | ↓   | ↑   |
| <u>Osteoporosis</u>                           | N   | N               | N   | N   |
| <u>Paget's</u>                                | N   | N               | N   | ↑↑  |



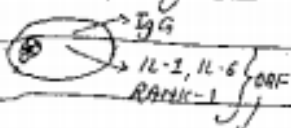
↓ Mg is required for PTH production. So persistent Mg↓ can cause PTH↓ although generally Mg has feedback action on PTH like Ca i.e.

↑ Ca / ↑ Mg → PTH ↓    or    ↓ Ca / ↓ Mg → PTH ↑

↓ Small Cell Carcinoma can cause hypocalcaemia but generally doesn't cause hypercalcaemia unless there is metastasis i.e. osteoclastic activity

⊗ Paget's disease  $\left\{ \begin{array}{l} \text{Osteoblastic } \uparrow \\ \text{coupled hyperactivity} \\ \text{Osteoclastic } \uparrow \end{array} \right.$

|                         | Ca | PO <sub>4</sub> | PTH | ALP |
|-------------------------|----|-----------------|-----|-----|
| <u>Multiple myeloma</u> | ↑  | ↑/N             | ↓   | N   |



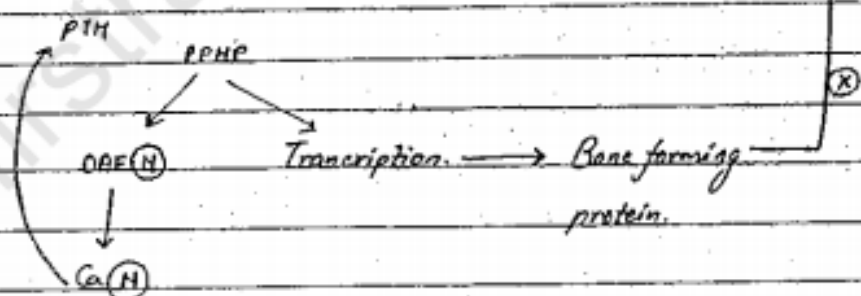
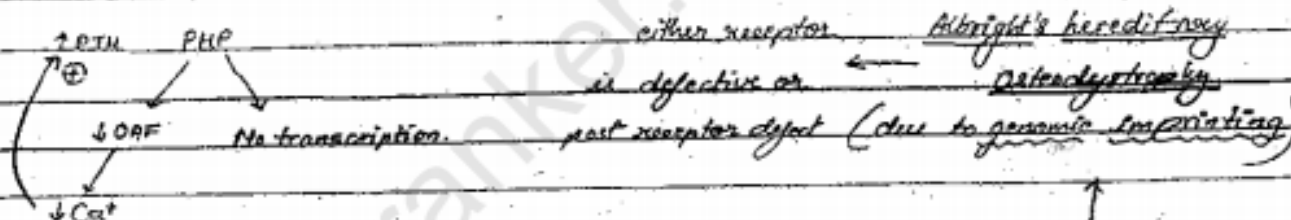
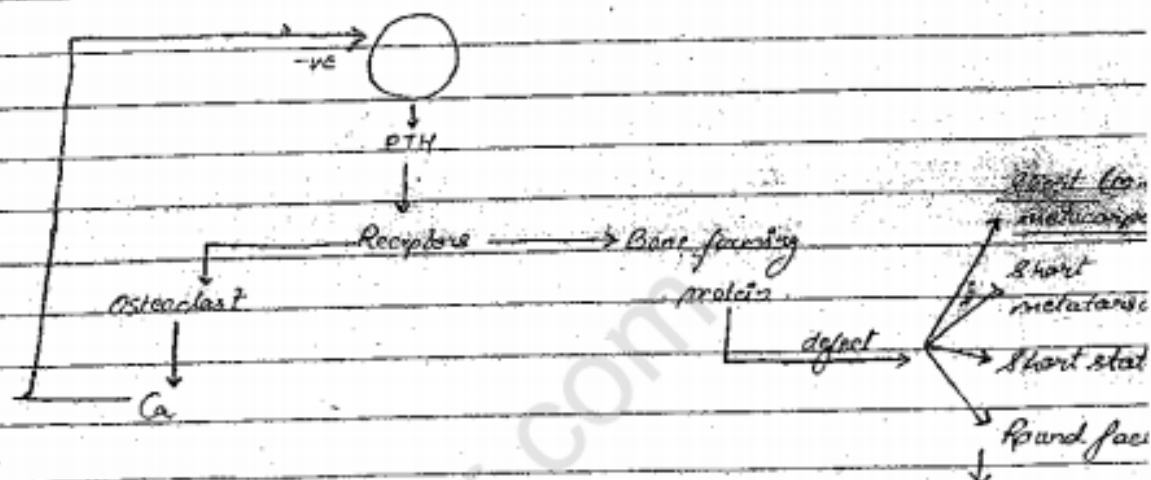
osteoclast activating factor

Pickoff genes → silenced

Feedback of Osteoblastic activity is suppressed.



|                                         | Ca                                     | PTH | PTH | ALP |
|-----------------------------------------|----------------------------------------|-----|-----|-----|
| ★ <u>Pseudohypoparathyroidism</u>       | ↓                                      | ↑   | ↑   | N/x |
|                                         | due to deficiency of receptor activity |     |     |     |
| ★ <u>Pseudopseudohypoparathyroidism</u> | N                                      | N   | N   | N   |



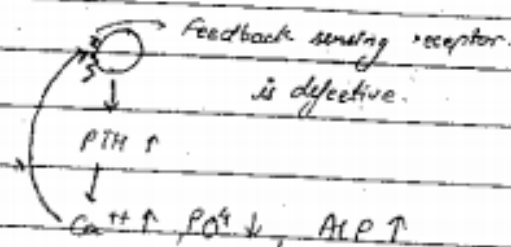
✓ Maternal deletion → PHP

✓ Paternal deletion → PPHP (maternal isodisomy)

✓ In PHP  $Ca^{++}$  is ↓ In PPHP  $Ca^{++}$  is ↑

\* Familial hypocalcaemic hypercalcaemia

| Ca | PO <sub>4</sub> | PTH | ALP |
|----|-----------------|-----|-----|
| ↑  | ↓               | ↑   | ↑   |



\* Hyperparathyroidism

\* Familial Hypocalcaemic hypercalcaemia

✓ 4<sup>th</sup> decade

✓ Autosomal Dominant  
1<sup>st</sup>/2<sup>nd</sup> decade

✓ Renal stones

\* ⊖

✓ Urine Ca ↑

\* Urine Ca<sup>++</sup> ↓

\* Urine Ca > 2%

\* Urine Ca < 2%

Urine Creat

Urine Creat

In hyperparathyroidism, the Ca<sup>++</sup> sensing receptors on the vascular endothelium of the kidneys stop Ca<sup>++</sup> absorption after a certain level of hypercalcaemia, so Ca<sup>++</sup> excretion ↑ leading to renal stones.

Hypercalcaemic crisis > 13.5 mg/dl → M.C. cause is Malignancy

\* Thiazide diuretics never unmask the diagnosis of hyperparathyroidism due to their Ca retaining action as a long term effect.

⊛ Vit D Dependent Rickets

16

⊛ Type I :-

25 OH cholecalciferol

↓  
(1α OH)

→ 1, 25 (OH)<sub>2</sub> CCF

→ Receptors

↑

deficiency

↓

↓ Ca, ↓ PO<sub>4</sub> (due to ↓ absorption from gut)

R :- Vit D supplementation life long

⊛ Type II :-

25 OH CCF

↓  
(1α OH)

→ 1, 25 (OH)<sub>2</sub> CCF

→ Receptors (Receptors unresponsive)

↑

↑ ↑

responds

(acts on the receptors)

very high dose of vit D

R :- Vit D supplementation life long

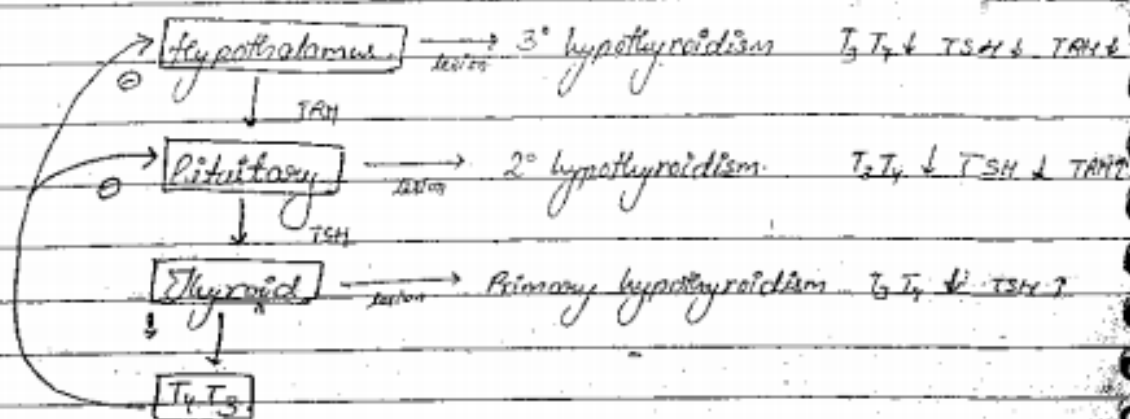
⊛ Vit D resistant Rickets :-

✓ Hypophosphatemic Rickets → PO<sub>4</sub> lt.

Inheritance → XLD

✓ R :- Vit D supplementation + PO<sub>4</sub> supplementation  
(only vit D won't help)

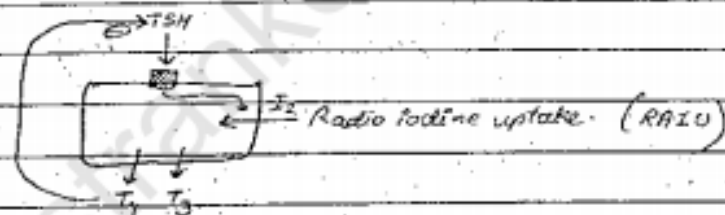




if TSH is ↓ then it is Central hypothyroidism.

In 1° hypothyroidism → ↑ TRH → causes ↑ Prolactin from pituitary (due to direct axodendritic stimulation)

Normal TSH → 0.5 - 5 IU



Radioiodine / Iodine uptake is dependent on TSH

So for RAIU → TSH has to be high → Stop Thyroxine (T<sub>4</sub>)

↑ RAIU } Iodine deficiency  
Hypothyroidism

Toxic } Exogenous administration of Thyroxine  
RAIU ↓ } Thyrotoxicosis

Thyrotoxic } a) Hashimoto's Thyroiditis  
RAIU ↑ } b) Choriocarcinoma → release HCG → TSH, HCG, LH, FSH  
c) Struma Ovarii  
d) Thyrotoxicosis factitia

## \* Graves Disease

- \* Toxic
- \* Autoimmune Ab.
- \* TSH receptor Ab  $\rightarrow$  most specific (LMS)



(Anti TPO Ab  $\rightarrow$  also seen)

- \* TSH  $\downarrow$
- \* GAG ++
- \* proptosis ++
- \* Thyroid acropachy (finger tips)
- \* Pre-tibial Myxoedema

- \* RAIU  $\rightarrow$  homogeneous

- \*  $\beta$  blockers

- $\downarrow$  Anti thyroid drugs
- Carbimazole
- Propylthiouracil

$\downarrow$  Surgery

$\downarrow$  RI ablation

[Surgery has to be done in Retrosternal goitre.]

because if RI ablation is given in Retrosternal goitre  $\rightarrow$  Blood may happen  
 $\downarrow$   
Compress the airway

## \* Toxic Adenoma

(17)

- \* Toxic

- \* Adenomatous part of thyroid producing excess thyroxine

- \* TSH  $\downarrow$

- \* absent

-ve

-ve

-ve

- \* Nodular uptake

- \*



## ★ Hashimoto's

## ★ Subacute

## ★ Riedel's

✓ Autoimmune

✓ De Quervain's

• Idiopathic

✓ Viral thyroiditis

Fibrosis

✓ Antinuclear Abs  
Anti TPO Abs• Fever, Cold  
Sore throat

• Nerve pain

• Vitiligo, Addison's

{ Pain } in  
{ Tenderness } thyroid.

• Hypothyroid (becomes hypothyroid very early)

• Type I DM

May have silent

Dysphagia

• Pernicious anaemia

Thyroiditis (-ve pain)

Hard mass

★ Fibrosis can also happen in

✓ Atoms - Dupuytren's contracture

✓ Retroperitoneum - Ormond's

✓ Benign - Peyronie's (ED)

✓ Mediastinal fibrosis

? If toxic → β blocker

Rx: NSAIDs

Rx: T<sub>4</sub>

• Antithyroid

• Steroids

• Tamoxifen (to reduce fibrosis)

(PRV)

Hypothyroid → T<sub>4</sub>(T<sub>3</sub> is not given due to

upregulated receptors)

★ Carbimazole if given in the 1<sup>st</sup> trimester may cause Cretin's Aplasia

Acute thyroiditis is caused by Bacteria → Subcapsular abscess

Thyroid function is Normal

(Euthyroid)



Wolff Chaitoff's Phenomena:  $T_2 \uparrow \rightarrow T_3, T_4 \downarrow$

(13)

Aded Basedow Phenomena:  $T_2 \uparrow \rightarrow T_3, T_4 \uparrow$

Endemic Iodine deficiency  $\rightarrow$  Thyroid is overactive

$\downarrow$   $T_2$  is given

$T_2$  is not preserved

$\downarrow$

Aded Basedow effect  $\leftarrow T_4$  is produced

✓ Excess Iodine

✓ Propylthiouracil

✓ Steroids

✓  $\beta$  blockers

✓ Azathioprine

$T_1$  (crosses blood brain barrier better)

$T_3$  (active moiety)

## DIABETES MELLITUS

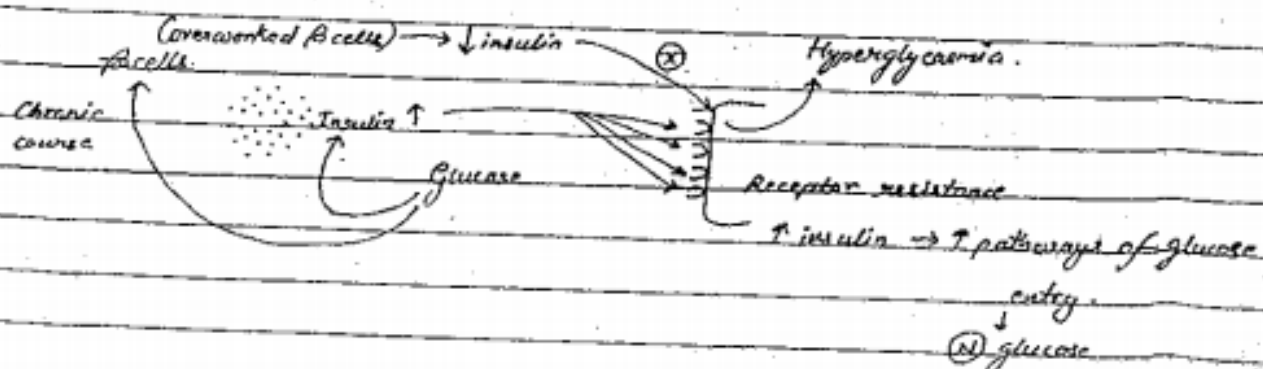
⊗ Pre Diabetes:  $\downarrow$  FBS - 100 - 125 mg/dl

Impaired Fasting Glucose

$\downarrow$  PPBS - 140 - 199 mg/dl

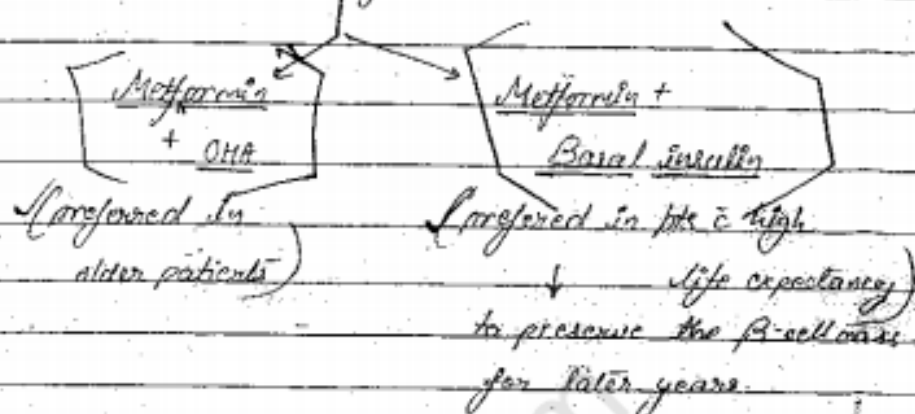
Impaired Glucose tolerance

$\downarrow$  HbA1c - 5.7 - 6.4



Drug of Choice: Metformin (do & glucose, receptor resistance to & work load on the  $\beta$  cells)

if not controlled  $\times$  Metformin



### ★ Gestational Diabetes Mellitus

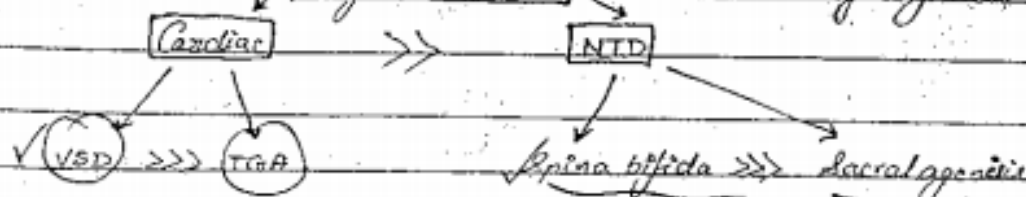
50% loss of  $\beta$ -cell mass is required to be lost to develop type II DM.

(if  $\beta$  is at threshold level before pregnancy)

(during 2nd trimester  $\rightarrow$  Glucose  $\uparrow$  due to HPL  $\uparrow$ )

★ (Gestational DM)  $\rightarrow$  high risk of development of type II DM

(No congenital Malformation) (by 2nd trimester organogenesis has happened)



TYPE I DM :

19

- ✓ Autoimmune
- ✓ viral infection - coxsackie (m/c)
- enterovirus
- rubella
- ✓ HLA DR3/DR4

⊗ Type I

⊗ Type II DM

- ✓ < 25 yrs
- ✓ Autoimmune
- ✓ Non-obese
- ✓ T cell Ab.
- ✓ Glutamic acid Decarboxylase Abs (GADA)
- ✓ CMI  $\left\{ \begin{array}{l} \text{Cytotoxic T cells} \\ \text{T Apoptosis} \\ \text{Nitric oxide metabolites} \end{array} \right\}$
- TH<sub>1</sub>
- ↓ T cell destruction
- Insulinitis

- ✓ > 45 yrs
- ✓ Peripheral resistance
- ✓ Insulin resistance phenotype
- ✓ Obesity Male  $\geq 102$  cm  $\geq 88$  cm
- Female  $\geq 90$  cm  $\geq 80$  cm (Asian)
- ✓ Dyslipidemia
- ✓ HTN

✓ Amyloid deposition in  $\beta$  cells

@ the time of diagnosis almost 80% of  $\beta$  cells are lost.

- ✓ Ketoacidosis ++
- ✓ Family history +  $\rightarrow$  3-4 times increase

- ✓ Ketoacidosis late manifestation
- ✓ Family history +  $\rightarrow$  20 times increase

⊗ MODY

(Autosomal Dominant)

- Type I  $\rightarrow$  HNF-1 $\alpha$
- Type II  $\rightarrow$  Glucokinase
- Type III  $\rightarrow$  HNF-1 $\alpha$
- Type IV  $\rightarrow$  TCF
- Type V  $\rightarrow$  HNF-1 $\beta$

Most frequent

Most Common



$\beta$ -cell mass is normal

No peripheral resistance to insulin

Non-obese patients

Defect - Glucose Sensing Defect

[R] - low dose of Sulphonylureas

Type 1 DM

MODY

- < 25 yrs
- Non-obese

- < 25 yrs
- Non-obese
- Family 4/5 t/c 3 generations
- AD - penetrance > 80%

- Ketonoidosis
- No OHA (SUR)
- Abs ++

- Non-ketotic (KA 2/3 cases)
- Sulphonylureas
- No Abs

⊗ LADA (Latent autoimmune Diabetes of adults)

- ✓ Abs +  $\rightarrow$  TCA, GADA
- ✓ HLA  $\rightarrow$  DR3/DR4
- ✓ > 25 yrs.
- ✓ Initially OHA can be administered, but rapidly become unresponsive to OHA and require insulin
- ✓ Non obese.

[R] :  $\rightarrow$  Treat as with Type 1 DM.  
 $\rightarrow$  Immunosuppressants.  
 $\rightarrow$  Steroids.

DIABETIC COMPLICATIONS

20

| <u>Microvascular</u>                                                                                         | <u>Macrovascular</u>                                                                     | <u>Non vascular</u>                                                                                                             |
|--------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>• Retinopathy</li> <li>• Nephropathy</li> <li>• Neuropathy</li> </ul> | <ul style="list-style-type: none"> <li>• IHD</li> <li>• Stroke</li> <li>• PVD</li> </ul> | <ul style="list-style-type: none"> <li>• Dyslipidemia</li> <li>• Glaucoma</li> <li>• Cataract</li> <li>• Gastropathy</li> </ul> |

✓ Pts  $\rightarrow$  tight control of blood sugar  $\rightarrow$  Significant prevention of microvascular complications

Not significant improvement in macrovascular (only long term benefit may be improved)

✓ There is 5-10 fold increase in risk of IHD in Diabetic than non diabetic

✓ HbA1c  $\rightarrow$  controlled  $\rightarrow$  twice a year  
 $\rightarrow$  uncontrolled  $\rightarrow$  four times in a year

Metformin

$\swarrow$  GFR  $\rightarrow$   $< 45$  ml/min Reduce the dose  
 $\searrow$   $< 30$  ml/min Stop metformin

$\swarrow$   $\rightarrow$  Creat  $> 1.4$   
 $\searrow$   $\rightarrow$  Creat  $> 1.5$

Stop metformin

Thiazolidinediones  $\rightarrow$  PPAR $\gamma$  agonists

Can be used in Renal failure

Need to be stopped in heart failure (NYHA 3,4)

Low wt. gain

Pioglitazone

- LDL ↑
- HDL ↑
- TG No effect/↓
- May be implicated in Ca Bladder

Rosiglitazone

- LDL ↑↑↑
- HDL ↑
- TG ↑

Saraglitazone

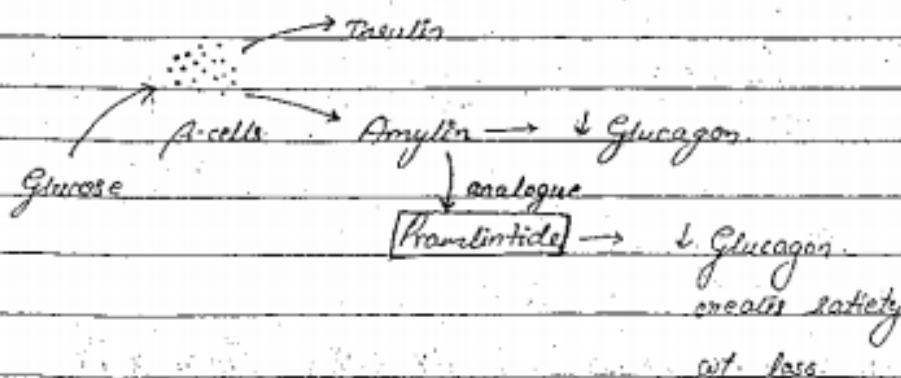
Dual PPAR  $\alpha$  } agonist  
PPAR  $\gamma$  }  
↓ insulin resistance

SGLT-2

↳ required for reabsorption of glucose from PCT.  
↳ Blockade → No glucose reabsorption.  
↳ Glucosuria  
↳ Better control of HbA1c.

Eg: Cagliflozin, Dapagliflozin

assoc. ~ risk of vaginal infections, UTI



can be used in both Type I & II



## Incretins

"Oral glucose is better handled by the body than IV glucose"

### INCRETIN EFFECT

$\left. \begin{matrix} \text{GIP} \\ \text{GLP-1} \end{matrix} \right\}$  Incretins released by the L-cells of duodenum.  
 $\rightarrow$  is  $\downarrow$  in type II DM patients

GLP-1 may cause  $\uparrow$  in insulin release from  $\beta$  cells (Glucose dependent)

- Safety
- slows gastric emptying
- $\downarrow$  Glucagon
- $\downarrow$  Apoptosis  $\rightarrow$   $\beta$  cell preserving effect

GLP-1 inactivated by DPP-IV

GLP-1 analogues  $\left\{ \begin{array}{l} \text{Exenatide} \rightarrow \text{Modified GLP-1} \rightarrow \text{not inactivated by DPP-IV} \\ \rightarrow \text{derived from Gila Monster} \\ \text{Liraglutide} \\ \text{Dulaglutide} \end{array} \right.$

DPP-IV inhibitors  $\left\{ \begin{array}{l} \text{Linagliptin} \\ \text{Anagliptin} \\ \text{Vildagliptin} \\ \text{Saxagliptin} \end{array} \right. \quad \left\{ \text{Sitagliptin} \right\} \text{ older generation}$

A/E: - Pancreatitis / MTC reduces

$\uparrow$   
 GLP-1 analogues are more efficacious, cause wt loss, Route - s.c.  
 DPP-IV inhibitors are less efficacious, Route - oral

Dose should be modified in Renal Failure for both.

## LIPIDS

Formula for calculating LDL:

$$LDL = TG - \left( HDL + \frac{TG}{5} \right)$$

↓  
Total cholesterol

Non HDL cholesterol is the most atherogenic > LDL cholesterol.  
(ASCVD - atherosclerotic coronary vascular disease)

## Framingham Risk Calculator

- Age
- Sex
- BP (Systolic)
- HDL levels
- Total Cholesterol
- Smoking

Pooled Cohort Equation / Score

- \* Gender      \* Age      \* Race      \* Diabetic Mellitus
- \* HDL Cholesterol      \* Total Cholesterol      \* Systolic BP      \* Smoking

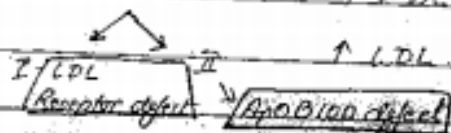
## Individual Risk assessment factors

- ✓ HSCRP + TC:HDL
- ✓ HSCRP (best single parameter for future risk of MI)
- ✓ TC:HDL
- ✓ Non HDL (TC-HDL)
- ✓ Apo B / Apo A<sub>1</sub>
- ✓ LDL
- ✓ Lp(a)

Targets LDL < 100  
Non-HDL < 130

Type I → Familial Chylomicronemia → ↑ Chylomicrons  
(Lipoprotein lipase deficiency)

Type II → IIa - AD - Hypercholesterolemia → ↑ LDL (isolated ↑ in LDL)  
IIb - polygenic



Type III → Dysbetalipoproteinemia → ↑ LDL  
(Apo E defect)

Type IV → Hypertriglyceridemia → VLDL ↑  
TG ↑

Type V → Combined → LDL, TG, VLDL ↑

Type IIb and IV are the most common.

Xanthomas are not seen in IIb and IV.

✓ Tendon Xanthoma → IIa

✓ Palmar + Tuberoeruptive xanthomas → III

✓ Tuberoeruptive xanthomas are seen in type IV (rare)

| Rx           | LDL       | HDL       | TG        |
|--------------|-----------|-----------|-----------|
| Statin       | ↓↓↓ (max) | ↑         | ↓         |
| Fibrate acid | ↓         | ↑         | ↓↓↓ (max) |
| Niasin       | ↓         | ↑↑↑ (max) | ↓         |



ApoA<sub>1</sub> :- Associated  $\bar{E}$  HDL (LCAT)

ApoB<sub>100</sub> :- Derived from ApoB<sub>100</sub> by RNA editing  
 $\rightarrow$  assoc.  $\bar{E}$  Chylomicrons

Chemical change

Cytosine is replaced by Guanine. Uracil  
 Stop codon is formed

absent ApoB<sub>48</sub>  $\rightarrow$  Abetalipoproteinemia

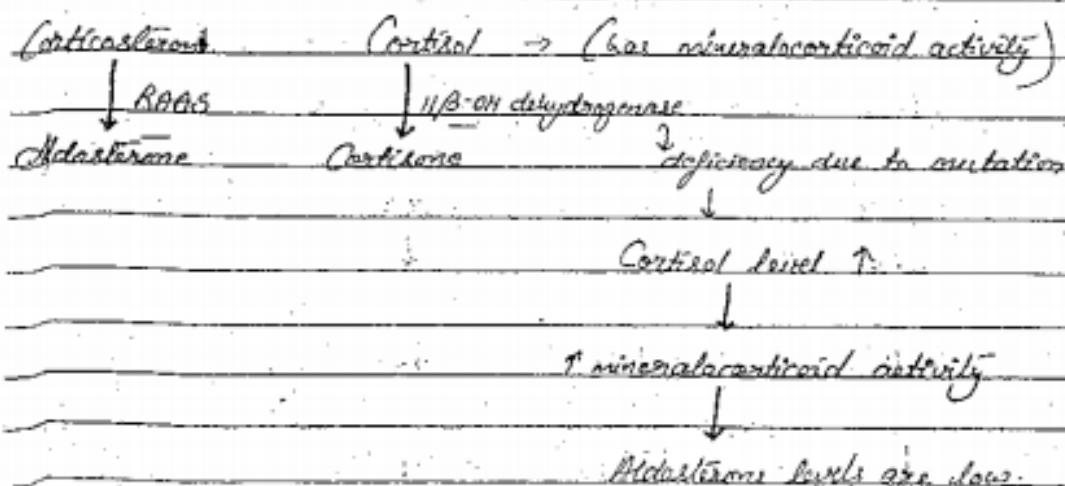
• presents like Friedrich's Ataxia

• lipid instability  $\rightarrow$  irregular membrane  
 $\rightarrow$  Acanthocytes  
 $\rightarrow$  Spur cells

$[R]$  - large doses of vit E

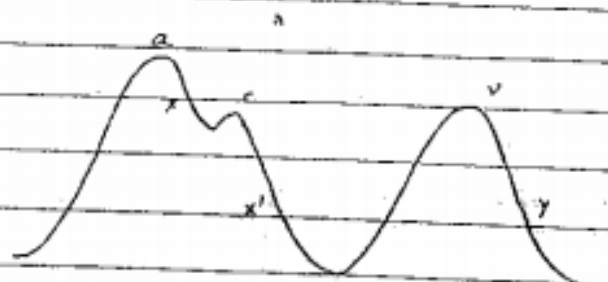
Type IIa has the highest risk of CAD/IMD  
 Type IIa type 1  $\rightarrow$  homozygous  $\rightarrow$  death in 1<sup>st</sup>/2<sup>nd</sup> decade  
 $\rightarrow$  heterozygous  $\rightarrow$  death in 3<sup>rd</sup>/4<sup>th</sup> decade

SAME :- Syndrome of Apparent Mineralocorticoid Excess



## CARDIOLOGY

JVP



a-wave - atrial contraction

c-wave - bulging of Tricuspid valve - is isovolumetric contraction

x-descent - atrial relaxation

x'-descent - ventricle contraction  $\rightarrow$  wall b/w atria & ventricle is sucked by the ventricle  $\rightarrow$  atrial expansion

v-wave - venous reflux into RA.

y-descent - Early diastolic filling (70-80% of filling occurs by this)

v-wave is taller in II, atriuni due to compliance of II, atriuni

Giant 'a' wave :- TS, PS, PAH, RV diastolic dysfunction

Cannon 'a' wave :- AV dissociation, V. Ectopic (m.c. cause) } irregular  
VT, Complete heart block (very frequently) } cannon 'a' wave

Functional reflux } regular cannon 'a' wave

'CV' waves - TR (normal x-descent is missing)

prominent 'u' wave :- 'u' wave taller than 'a' wave

TAPVC

ASD

Rapid x-descent :- Tamponade

Rapid y-descent :- Constrictive pericarditis

Square root sign } Constrictive pericarditis  
M pattern JVP

Equalisation of pressures in heart (RA, RV, diastole, pulm art pressure)

↓  
Seen in Cardiac tamponade & pericarditis

Cardiac Tamponade

Constrictive Pericarditis

• Rapid x-descent

• Rapid y-descent

• Absent 'y' descent

• Normal x-descent

Kussmaul's sign

• No Kussmaul sign

• present

• JVP decreases on inspiration

Pulsus paradoxus

• present

• 1/2 of pts & present

VSD, regurgitant lesions will

not allow a pulsus paradoxus

in tamponade





Pulsus paradoxus is seen in airway disease, because of the greater pressure generated in the pleural cavity & the lungs holding back a greater volume of blood.

### Blood pressure Measurement:

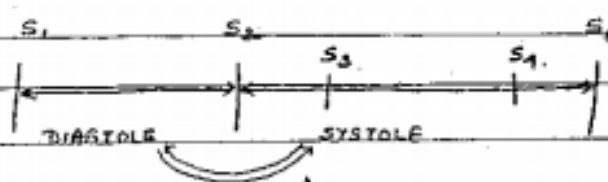
- \* Arm at heart level
- \* Cuff length/width should be 80% / 40% of arm circumference
- \* Cuff should be deflated at 3 mmHg per second
- \* Column or dial should be read nearest to 2 mmHg
- \* First audible ~~loud~~ Korotkoff sound - SAP, last audible - DAP

### BLOOD PRESSURE MEASUREMENT

|           |   |                    |          |
|-----------|---|--------------------|----------|
| Systolic  | { | Arterial           | ↑ higher |
|           |   | Automated          |          |
|           |   | Manual             |          |
| Diastolic | { | Manual / Automated | ↑ higher |
|           |   | Arterial           |          |

Manual measurement underestimates the SAP while it overestimates the Diastolic BP, compared to intra-arterial measurement.

## HEART SOUNDS



Conditions for loud  $S_1$  :-

- 1) The valve leaflets shut at greater speed.
- 2) The valve leaflets are wide open.

seen in :- \* Tachycardia / Tachysystole

\* Mitral Stenosis

(in MS, soft  $S_3$  may be seen in :- \* MS + MR

\* Short PR interval

\* calcified valve commissures

in pts. with soft  $S_1$  & MS → don't do Balloon Mitral valvotomy

- because MS will worsen

and calcified commissures won't yield

$S_2$  :

$A_2$  occurs earlier than  $P_2$

$P_2$  is delayed in inspiration } inspiration :- splitting is more  
 $A_2$  is early in inspiration } prominent

During expiration -  $S_2$  appears as a single sound due to close splitting ( $< 20$  msec)

$A_2$  is early  $P_2$  is late



| $A_2$                             | $P_2$           | $S_2$ split                       |
|-----------------------------------|-----------------|-----------------------------------|
| $\leftarrow  $                    | $ $             | Severe MR $\rightarrow$ wide      |
| $  \rightarrow$                   | $ $             | AR $\rightarrow$ Narrow           |
| $  \rightarrow$ $\rightarrow$ $ $ | $ $             | AS $\rightarrow$ Narrow, reverse  |
| $  \rightarrow$                   | $ $             | LBA $\rightarrow$ Narrow, reverse |
| $ $                               | $  \rightarrow$ | PS $\rightarrow$ wide             |
| $ $                               | $\leftarrow  $  | Pulm HTN $\rightarrow$ Narrow     |
| $  \rightarrow$                   | $ $             | PDA $\rightarrow$ Narrow          |
| $  \rightarrow$                   | $ $             | HTN $\rightarrow$ Narrow          |
| $ $                               | $  \rightarrow$ | ASD $\rightarrow$ Wide fixed      |

In **PDA**  $\rightarrow$  The blood flowing from Aorta to PA doesn't go to RV  
 it goes to lungs and then to RA and LV.  
 LV is volume overloaded, Aortic closure will be delayed  
 Splitting will be narrow.

In **ASD**  $\rightarrow$  The split is fixed because the RV volume doesn't change  
 in expiration or inspiration.

In **Pul. HTN**  $\rightarrow$   $P_2$  occurs early because the  $\uparrow$  pressure in PA shuts the  
 pulmonary valve early overcoming the pressure in RV.

In **Sys. HTN**  $\rightarrow$   $A_2$  occurs late because Aortic pressure can't close the valve  
 even LV and LV takes a longer time to pump the  
 blood against  $\uparrow$  pressure.



$S_3$

$S_4$

\* assoc.  $\uparrow$  pre load

assoc.  $\uparrow$  after load

\* Early diastolic filling

atrial contraction

$S_3$  will not be seen in MS.

$S_4$  will not be seen in R. fib.

Lt.  $S_3$

Rt.  $S_3$

Lt.  $S_4$

→ Chd. MR, AR

→ TR, PR

→ HFN

→ PDA, VSD

→ ASD

→ A.S.

→ Hyperdynamic condition

→ Co. A.

• exercise, anaemia,

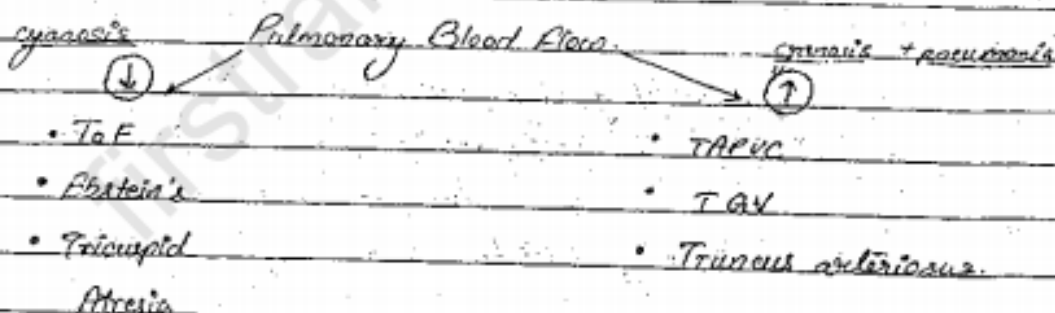
→ MI

• pregnancy

→ Physiological  $< 30$  yrs of age

→ IHD - MR

## Cyanotic Congenital Heart Disease

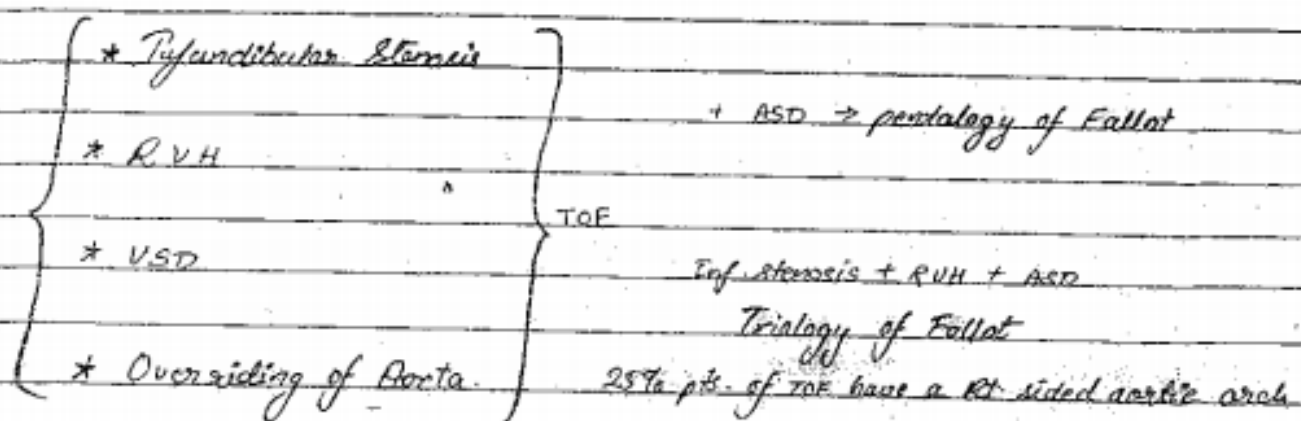


M.C. cyanotic HD :- TdF

M.C. cyanotic HD at birth :- TAV.

M.C. cyanotic HD in children :- TdF

## TETRALOGY OF FALLOT



(Pulmonary valve stenosis is not a component of tetrad, but might be present)

Blue TOF  $\rightarrow$  Silent Chest

Pink TOF :- Murmur is present

Infundibular Stenosis is inversely related to Murmur.

Blue TOF  $\rightarrow$  Cyanosis  $\rightarrow$  Catecholamines  $\uparrow$



Infundibular contraction



Less blood flow  $\rightarrow$  No Murmur

Cyanotic Spell:

RVOT  $\uparrow$

SVOT  $\downarrow$   $\leftarrow$  vasodilation

Rt to left shunt

$\left\{ \begin{array}{l} O_2 \downarrow \\ pH \downarrow \\ PCO_2 \uparrow \end{array} \right\}$

②  $\rightarrow$

Medulla

Ventilatory drive

Hypoxia

carotid chemoreceptors

Squatting  $\rightarrow$  folds the femoral artery  $\rightarrow$   $\uparrow$  pressure in Aorta



RV starts pushing blood into PA

[Q] of cyanotic spell :- \*  $\beta$  blockers

\* Humidified Oxygen

\* Morphine (depress the respiratory centre)

\*  $\alpha$  agonists (vaso-constrictors)

Features not occurring in TOF :-

→ Cardiomegaly

→ COF

→ New born Cyanosis

X-Ray :- Boot shaped heart

RV apex

Pulmonary oligemia

Aortic apex - diaphragm angle

Q. of TOF :- Surgical correction

Ketamine is the anaesthetic agent of choice

Stents :- Blalock - Taussig Shunt

→ PA - SA (done on the opposite side of Aortic arch)

Pott's Shunt → PA - desc. aorta

Celatorson's Shunt → PA - Asc. aorta

Ebstein's Anomaly :-

\* Atrialization of the Rt. Ventricle

- the septal leaflet is present inferior to its normal location leading to atrial enlargement.

Sail like leaflet :- ECHO finding



There is no Pulmonary stenosis

Functional pulmonary blockade is present.

Ductus arteriosus (patent) is required for the child to survive

At Tricuspid Regurgitation is +ve

There is huge cardiomegaly in children

ECG  $\rightarrow$  tall P waves (due to RA enlargement)

X-Ray: Box-shaped

Massive Cardiac

megaly

### Tricuspid Atresia

ASD is a must in Tricuspid Atresia and TAPVC

Left axis deviation in the ECG  $\neq$  Cyanotic Heart Disease  $\rightarrow$  TA  
(because the LV dominates in TA)

### Total Anomalous Pulmonary Venous Drainage

$\rightarrow$  Supracardiac  $\rightarrow$  SVC

33% have a rt. sided aortic arch

Not a ductus dependent condition

$\rightarrow$  Cardiac  $\rightarrow$  Rt atrium

$\rightarrow$  Infra-cardiac  $\rightarrow$  IVC

Portal vein (worst prognosis)

$S_2$  - wide-spread

X-Ray: Snowman's appearance

Figure of 8 appearance

## Transposition of Great Arteries:

The baby will present with cyanosis at birth.

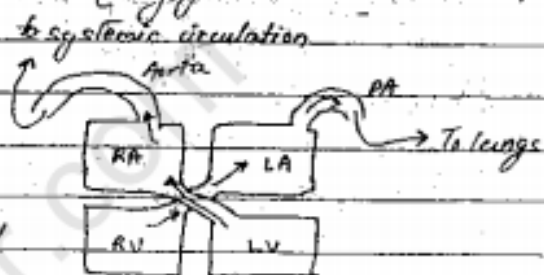
Initial procedure → Atrial Septostomy

later - Switch procedures

[X-Ray] Egg on side/string appearance (only for uncorrected transposition)

Corrected transposition

The R ventricle is connected with LA, so that de-oxygenated blood goes to the lungs & the LV is connected to the RA.



\* D-transposition is corrected.

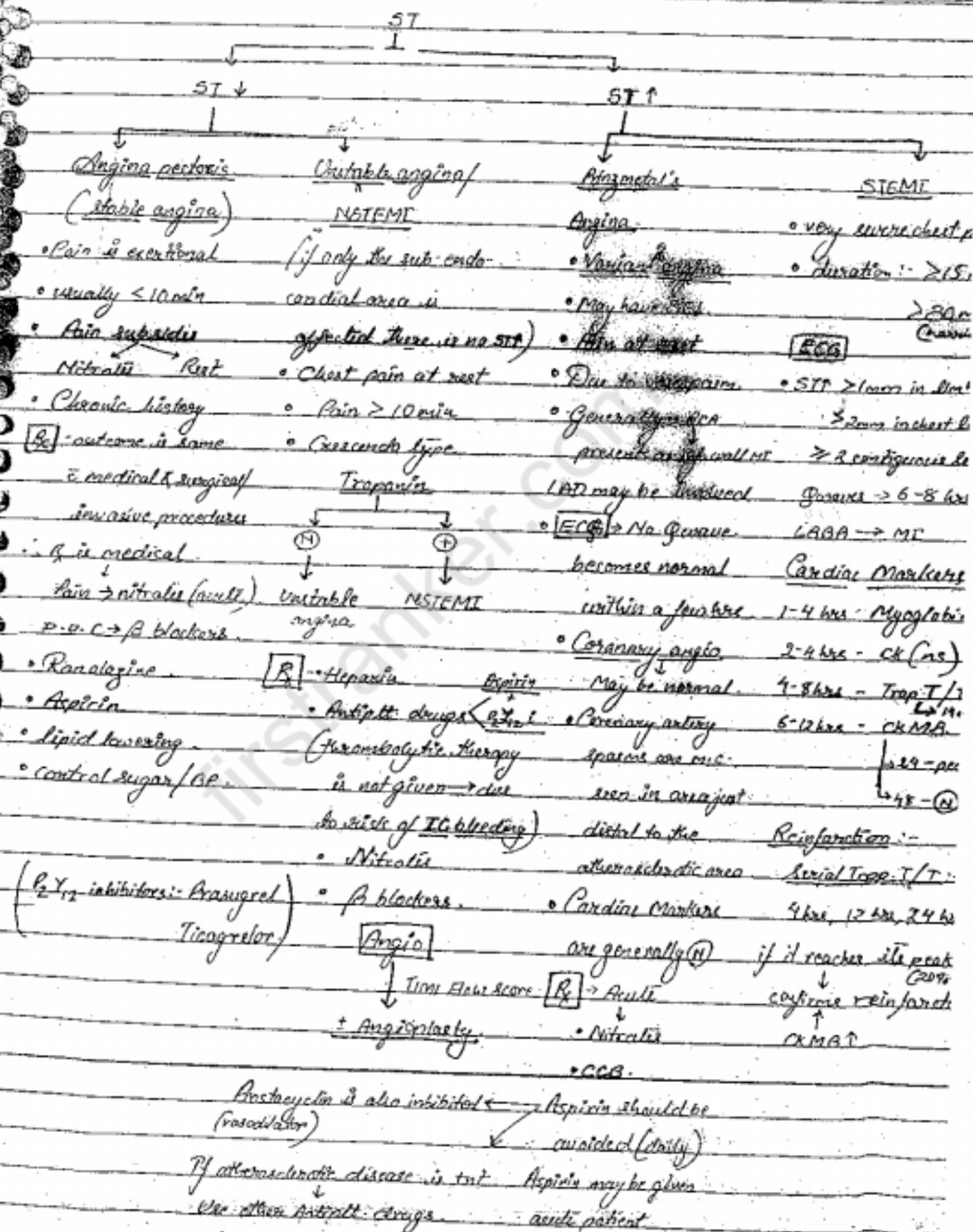
\* L-transposition is uncorrected.

## ISCHAEMIC HEART DISEASE

Chest pain → Chest pain varying {  
• inspiration → pericardial disease  
• position → pericardial disease  
(supine → ↑, erect → ↓)}

{ • palpitation → Musculoskeletal }

Cardiac chest pain :-  
• Compressive (if Inferior cervical a. is damaged)  
• Radiating - jaw  
- arm  
- epigastric (never below umbilicus)  
- back





Serum troponin should be reported  $\rightarrow$  Treatment/prognosis depends on Troponin level

### New Onset Regional Wall Motion Abnormality (RWMA)

\* Aknetic segment due to defense mechanism preventing further damage to the ischemic area

\* RWMA is detected earlier than ECG or ECHO

No RWMA (new onset) - Myocardial dysfunction is severe

New onset RWMA  $\rightarrow$  not specific but sensitive for MI

### Classification of MI

**Type 1B** - Sudden Cardiac death

Any 1

TYPE 1 :- Coronary

1) Ischaemic pain

TYPE 2 :- Hypoxia

2) ECG changes (ST-T changes or New QBBB)

TYPE 3 :- Sudden death

3) ECHO - RWMA (new onset)

TYPE 4 :- PTCA  $\rightarrow$

4) Angiography - Coronary thrombosis

TYPE 5 :- CABG  $\rightarrow$  Troponin  $> 10$  times above (N)

**Rx** :-

1) Rest

2) Oxygen therapy

3) Aspirin - 325 mg (can be given before any procedure like ECG, thrombolysis)

$\rightarrow$  Reduces mortality

4) Nitrates - don't reduce mortality

5) Morphine - IV (control of pain)

6) IV  $\beta$  blockers  $\rightarrow$  with modified dose CCB are not to be used

7) Heparin (Nitroglycerine increases mortality)

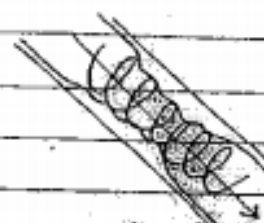
## Thrombolytic therapy

- Thrombolytic therapy is faster and requires less facilities
- Earlier the procedure  
↓  
More muscle can be saved.

\* If it is not feasible to do PCI  $\leq$  2 hrs, then do thrombolytic therapy

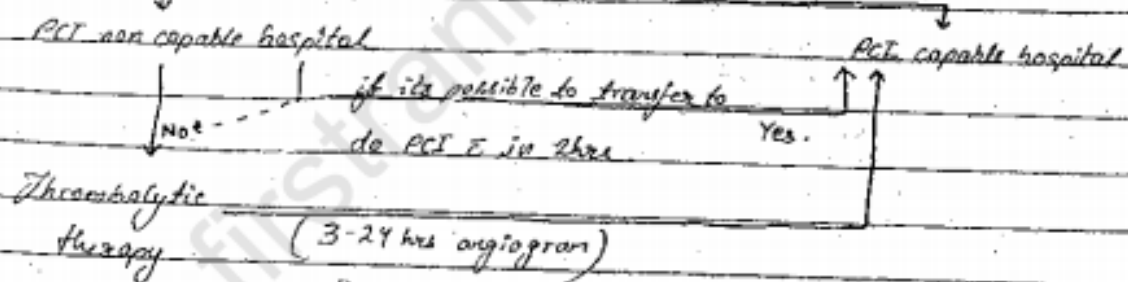
- \* Door to needle time  $\leq$  30 min. } Goals
- \* Door to balloon time  $\leq$  90 min. }

## Primary Percutaneous Coronary Intervention



- Ballooning with permanent stent placement can be done.
- Superior than thrombolytic therapy

### STEMI - 2013

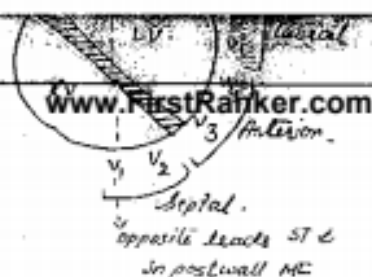


After 12 hrs  $\rightarrow$  Thrombolytic therapy should not be done

it may be done between 12-24 hrs in case there is

- 1) ongoing chest pain.
- 2) Hyper acute changes on ECG.

If the pt. is hemodynamically stable  $\rightarrow$  PCI after 24 hrs is of no benefit  
hemodynamically unstable  $\rightarrow$  PCI always has a benefit.



ST ↑

Anterior wall MI → I, aVL

Anterior wall MI → I, aVL

Lateral wall MI → I, aVL

Anterior wall MI → II, III

Septal wall MI → I, aVL

Lateral wall MI may be missed on ECG

↓

if the heart is rotated slightly

↓

current coming flowing in the heart will be perpendicular to the leads

↓

No change in ECG

AWMI → LADCA

LWMI → LCxCA

ALWMI → LMCA

IWMI → RCA

Hypotension

LMWI

Ant/ALMI

→ Vagal ↑

\* → Pump failure

- Bradycardia

Rx: Intra-aortic Balloon pump (IABP)

Rx: Atropine

IABP should be done after

RV Infarction

PCI or thrombolytic therapy

→ no pulm. edema

IABP just provides symptomatic

Rx: ZV fluids

benefit

Biventricular

No mortality benefit of IABP



→ Left Main Coronary > 50% blocked } CABG (better than PCI)  
Triple vessel disease

Restenosis rate

CABG :- Laphorous graft → 60-70% / 10 yrs.  
Tubular Innominary Artery → 20-30% / 10 yrs.

PTCA :- Only clot removal & out stent → 40% / yr.  
Bare metal stent → 20% / yr.  
Drug Eluting Stent + Dual anti-plt therapy → 10-15% / yr.

Restenosis :- PTCA >> CABG

CABG is not done due to :- 1) Sternotomy / Scar on chest  
(not preferred) 2) Hospital stay / mortality surgical is ↑

Bare Metal Stent

- \* Endothelialization of the stent is complete
- \* Indication → pts. intolerant to Anti-plt. stent drugs.

Drug Eluting Stent

- Paclitaxel.
- Sirolimus.
- Everolimus.
- Endothelialization of stent is not complete
- For min 1 yr 2 Anti-plt drugs should be given.

Regional wall motion Abnormality post MI:-

Viabile tissue      Scar tissue  
(angiogram doesn't help in differentiating b/w alive/dead tissue)

viability indicated by :- \* Stress ECHO (Dobutamine scan)

\* Nuclear perfusion studies

-  $Tl^{201}$

-  $Tl^{201}$  / Sesta MIBI

inter observer

variability

\* MRI - T.O.C

\* PET scan - Best investigation

MRI  $\rightarrow T_2$  wt :- Scar  $\rightarrow$  Bright (late enhancement)

Viable Myocardium

Stunned Myocardium

Coronary flow - good

Hibernating myocardium

hypoperfusion of myocardium

Reperfusion is beneficial.

\* In Technetium pyrophosphate scan  $\rightarrow$  scar is bright \*

$Tc$  pyrophosphate chelates  $Ca^{++}$

$Ca^{++}$  is  $\uparrow$  in dead / scar tissue

Scar is bright

## ARRHYTHMIAS

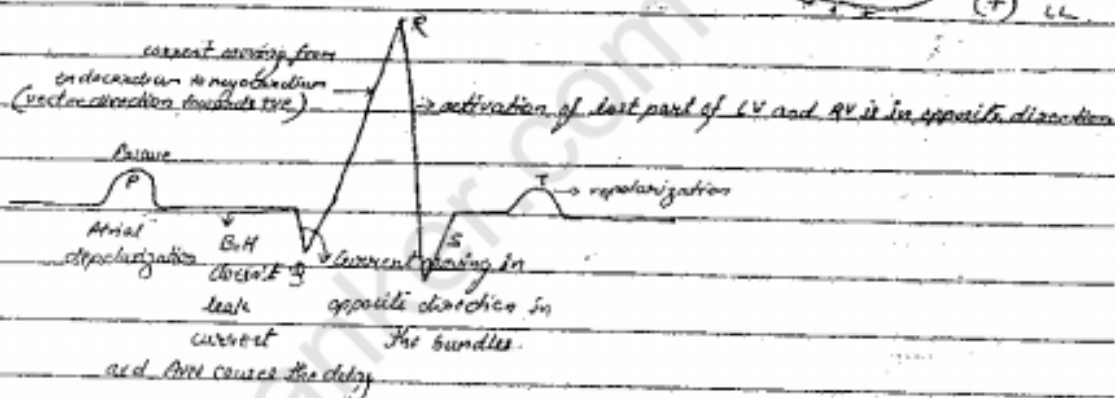
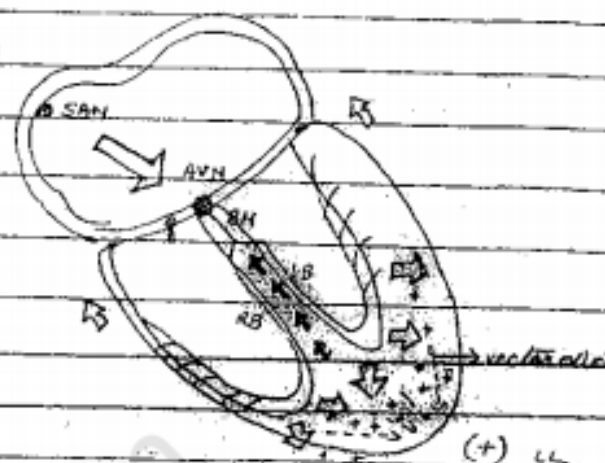
Speed of current across

- 1) Muscle:  $2.5 \text{ m/s}$
- 2) Bundle of His:  $1 \text{ m/s}$
- 3) Purkinje fibres:  $4 \text{ m/s}$

AVN is the slowest conducting tissue of the heart

RUL

(-)

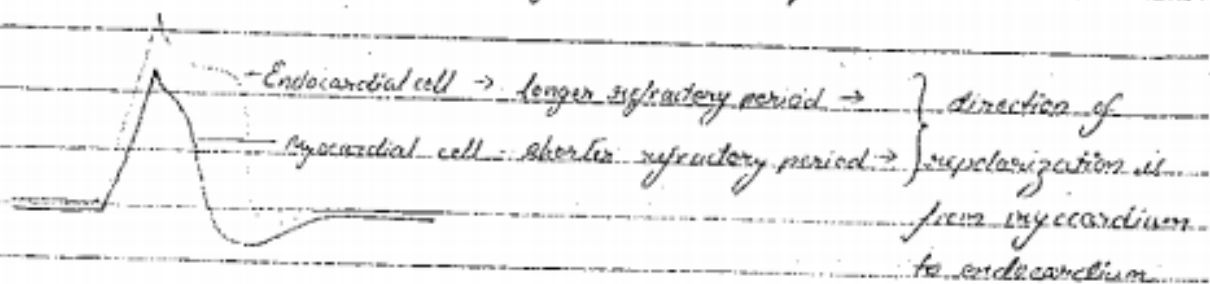


1st part of septum to be excited: IT leaves TV septum

last part to be activated LV  $\rightarrow$  posterior basal part of LV (last)

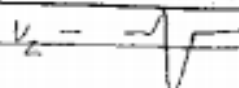
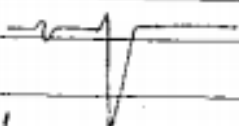
RV  $\rightarrow$  pulmonary cone

If QRS width  $\leq 0.125 \text{ sec}$   $\rightarrow$  Current is entering the ventricles through the bundle of His and the left and right bundles

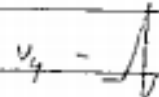
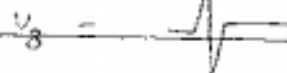
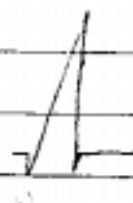




$V_1$  electrode  $\rightarrow$



$V_6$  electrode  $\rightarrow$



Poor progression of R wave - if the R wave doesn't progressively increase in height from  $V_1$  to  $V_6$

Re-entrant :-  $\rightarrow$  1 automaticity  
 $\rightarrow$  Re-entry

(Defibrillatory shock will not work if there is no re-entry)  
will not work in case of a flat line

because defib homogenises the current in the heart into the same phase

a rhythmia/flat line already in the same phase  
won't be affected by defib

Atrial fibrillation

Idiopathic

Hypertension

Ischaemic Heart Disease

Mitral Stenosis

Thyrotoxicosis

Alcohol (Holiday Heart Syndrome)

Electrolyte imbalance

Rate :- 350-550/min - due to multiple re-entry currents  
around the pul vein openings or in the LA

**ECG**: No p-wave or irregular p-waves (wavy baseline)  
 QRS wave is normal/narrow  
 R-R interval fluctuates (due to erratic conduction by AVN)

**Rate control**  
 - outcome is same  
 - safer and easier  
 but generally both are done

**Rhythm reversal**

- do -

{ Ibutilide } Class III antiarrhythmic  
 { Dofetilide } → D.C. for rhythm reversal

Slow the AV node conduction

→ Adenosine ( $T_{1/2}$  - 1 sec)

used for AF {  
 →  $\beta$ -blocker  
 → Verapamil, Diltiazem  
 → Digoxin

A-fib: > 48 hrs → left atrial clot

↓ Rate control

Anticoagulation

(Do not do rhythm reversal)  
 ↓  
 ↑ chances of embolism

min 3 wks anticoagulation

↓  
 Rhythm reversal

Continue anti-coag for 4 wks after

(Anticoagulation is given because Electrical activity might be recovered but mech. activity is not restored - Electro mechanical dissociation)

#### CHADS<sub>2</sub> VASCULAR SCORE

Cardiac failure → 1

Score: Min :- 1

HTN → 1

Max :- 10

Age > 75 → 2

DM → 1

Score: ≤ 2 → Aspirin

Stroke/TIA → 2

> 2 → Anticoagulation \*

Vessel - Carotid → 1

Age 65 - 75 → 1

Sex Female → 1

\* Conventional anticoagulants &

Dabigatran → Direct thrombin inhibitor

Rivaroxaban } Factor Xa antagonist  
Apixiban }

For any arrhythmia → Electro-physiological study

↓  
Radiofrequency ablation

Cox Maze technique :: to prevent recurrence after radiofrequency ablation

ATRIAL FLUTTER :- Single Macro Re-entry tract  
Usually in the Rt-atrium

ECG → Multiple P-waves → Saw tooth appearance

QRS wave is narrow

R-R interval is fluctuant

[R] :- Same as atrial fibrillation

except Radiofrequency ablation is quite easily done  
compared to Atrial fibrillation

PSVT :- mechanisms :- AVNRT (Atrio-ventricular reentry tachycardia) 60-70%

AVRT (Atrio-ventricular reentry tachycardia) 20-30%

Atria & ventricles are not contracting simultaneously → no cannon 'a' wave

ECG :- P wave is inverted (since current is coming from AVN)

\* Retro - P wave (P-wave is after QRS)

\* Atrial rate = ventricular rate

\* No blocking in AVN



- QRS will be normal (narrow)
- Absent P-wave may be there - buried in the QRS complex
- Rate  $> 150/\text{min}$
- R-R interval is regular (not fluctuant)

AVRT: Inverted or retro P-waves

P-waves are always present (never absent)

always occur after the QRS complex

**Q** :- Control Measure

\* inj Adenosine (6mg) - D.O.C.

$\left\{ \begin{array}{l} \beta\text{-blockers} \\ \text{CCB} \\ \text{Digoxin} \end{array} \right\}$

to prevent further episode

fails

→ Ibutilide + AV node Blocker

Procainamide + AVN Blocker

↓ fails

Cardioversion

↓

Radiofrequency Ablation

↑ Type A :- Accessory pathway b/w LA & LV (rare)

→ Type B :- Accessory pathway b/w RA & RV

WPW Syndrome :- Most pts. are hemodynamically stable

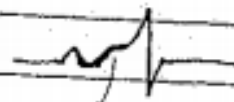
Impulses are generated by SAN - (HR 60-100/min)

ECG :- QRS is broad -  $> 0.12 \text{ sec}$

PR-Interval is same as P-wave

Delta wave is present (due to

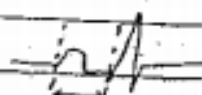
= conduction by the band of muscle)



WPW syndrome

Delta wave (delta wave)

(mostly in  $V_1, V_2$ )



PR interval

If AVN blockers are used → Only conduction through muscle band

Eccentric conduction

Cardiac output ↓

Hence avoided

$\left\{ \begin{array}{l} \text{Adenosine} \\ \beta\text{-blockers} \\ \text{CCB} \\ \text{Digoxin} \end{array} \right\}$

→ Sotalol can be used

worst

After RF ablation  $\rightarrow$    $\rightarrow$  

Group: Class I, II, III  
mild symptoms → Severe symptoms

Unifocal Ectopic - localized pathology

Multifocal Ectopic -- Electrolyte Imbalance

- Drugs
- Alcohol
- Inflammatory processes
- Toxins
- Diffuse irritation of Myocardium

Compensatory pause is seen in ventricular ectopic.

Run of Vent. Ectopics  $\rightarrow$  VT

Rate  $> 100/\text{min}$

Run  $> 30$  sec  $\rightarrow$  Sustained VT  $< 30$  sec  $\rightarrow$  Non Sustained VT

Ventricular Ectopic  $\rightarrow$  VT / VFib  $\rightarrow$   $\beta_1$  - **A Blockers**  
Catecholamines

|            |                                                               |
|------------|---------------------------------------------------------------|
| Risk of    | >10 Ectopic/yr                                                |
| Conversion | Couplet Ectopics                                              |
| to RT/VF   | R-on-T phenomenon (Ectopic is present where T wave should be) |

\* Synchronised Defibrillation  $\rightarrow$  Cardioversion

Shock should be given at R-wave

\* Non-Synchronised defib may be given in:-

$\rightarrow$  Pulseless VT

$\rightarrow$  Ventricular fibrillation

Q:

\* (Only  $\beta$  blockers have benefit in Ventricular Ectopics)

\* Intra-Cardiovascular Defibrillation

Indications  $\rightarrow$  Multiple Vent. Ectopics

$\rightarrow$  Mobitz type II & III heart blocks

$\rightarrow$  Ejection fraction  $< 30\%$  ( $< 35\%$ )

$\rightarrow$  Congenital heart blocks

### Ventricular Tachycardia

Monomorphic VT

Morphology of QRS complexes is identical

Polymorphic VT

QRS complexes are different

Broad QRS is seen in:-  $\rightarrow$  Bundle Branch block  $\rightarrow$  p-wave before every QRS ( $> 0.125$ )

$\rightarrow$  VT  $\rightarrow$  no p-wave before QRS

$\rightarrow$  WPW Syndrome

$\rightarrow$  Idiopathic  $\rightarrow$  Automaticity

No p-wave before QRS

VT rate  $> 120/\text{min}$

Acc. Idioventricular 40-120/min

Idioventricular  $< 40/\text{min}$

Transient

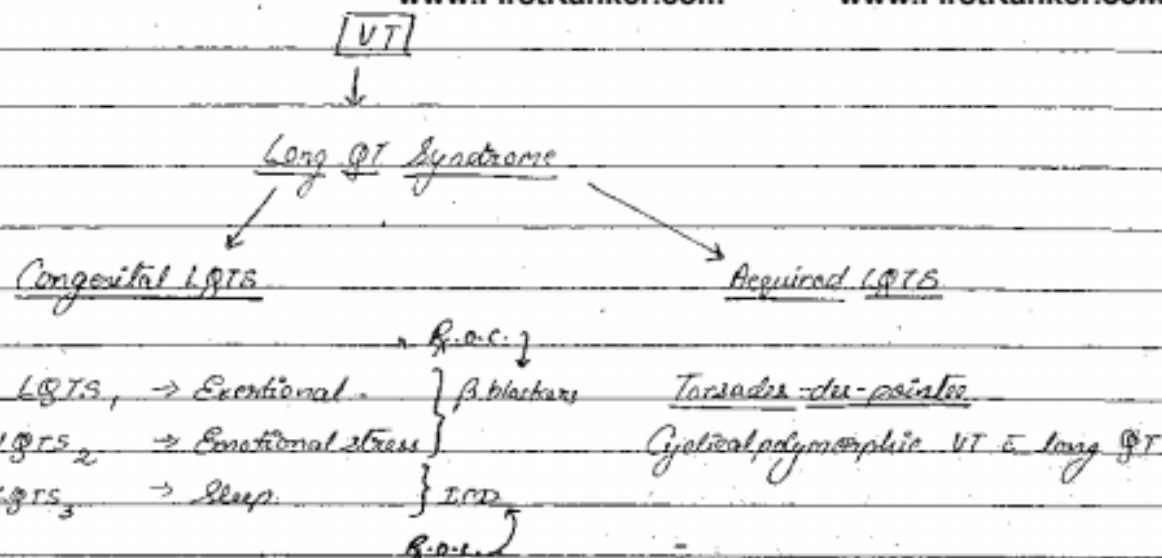
M.C. cause is reperfusion arrhythmia

SAV takes over

if persist

AV node defect





80-90% of Cong LQTS is LQTS<sub>1</sub>

Firstest β-blocker or ablated pt: **ICD**

**R** → Acute VT → β-blockers

VT + Stable → Procainamide  
+ ECHO Normal

VT + ECHO Abnormal → Amiodarone

Polymorphic VT: Magnesium Sulfate

Ventricular Fibrillation

Multiple and numerous re-entry currents

None of the GRs complexes are similar

Conversion rate

Shock → 1min → 90%

10min → 30%

AED: Automatic Electrical Defibrillator

Cardio-Pulmonary Resuscitation:

→ Not 15:1, Multiple ppl giving CPR: 15:2

C Chest Compression → 30:2 (Chest compression first then ventilation)

A Airway Rate - 100/min

B Breathing Depth:- Sternum should go down by 4-5 cm.  
( $\frac{1}{3}$  of A-P diameter in all age groups)

Heart Blocks

Type I:- Prolonged PR Interval (m.c. type of heart block)  
PR > 0.20 sec

Type II:- Mobitz I → Wenckebach → Progressive prolongation of PR  
Mobitz II → Fixed PR interval

Type III:- Complete heart block, R-R interval is regular, P-P interval is regular  

|                                                                                                                          |                                                                              |
|--------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>- Palpitations</li> <li>- Dizziness</li> <li>- Syncope</li> <li>- Pain</li> </ul> | <p>↓<br/>Stokes Adams attacks<br/>↓<br/>More likely to occur on exertion</p> |
|--------------------------------------------------------------------------------------------------------------------------|------------------------------------------------------------------------------|

Pacemaker implantation:- Mobitz II & Type III

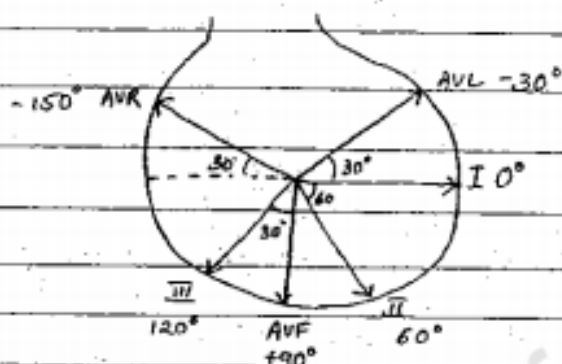
Pacemaker implantation is not done in Type I.

Current towards +ve Electrode - positive deflection

Current towards -ve Electrode - negative deflection

Current  $\perp$  to the Electrode axis - Biphasic (near base line) -  $\downarrow$

Axis determination of ECG



P wave : 2.5 small boxes.

PR segment : 2.5 small boxes

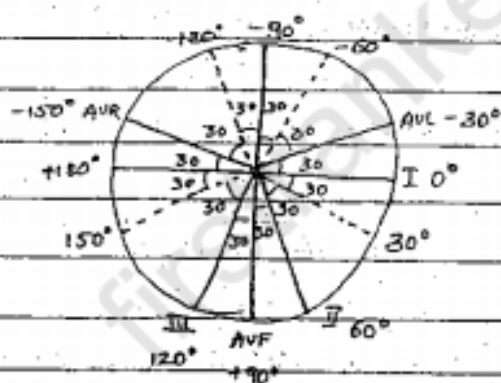
QRS : 2.5 small boxes

ST interval : 7.5 small boxes.

QT interval : 10 small boxes.

$\delta$  : 0.44 sec upper limit

$\phi$  : 0.46 sec upper limit

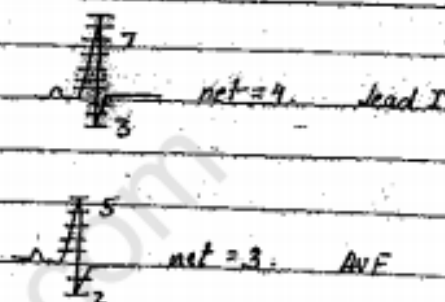
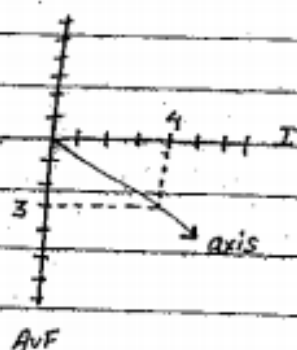
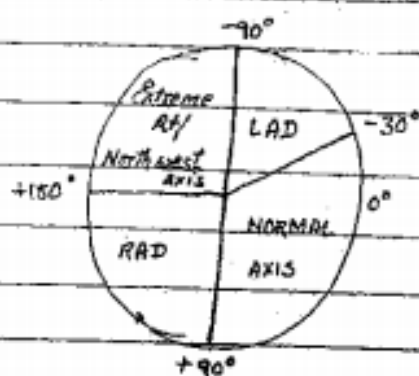


$$\star \text{ Heart rate} = \frac{300}{n(\text{large})} \text{ or } \frac{1500}{n(\text{small})}$$

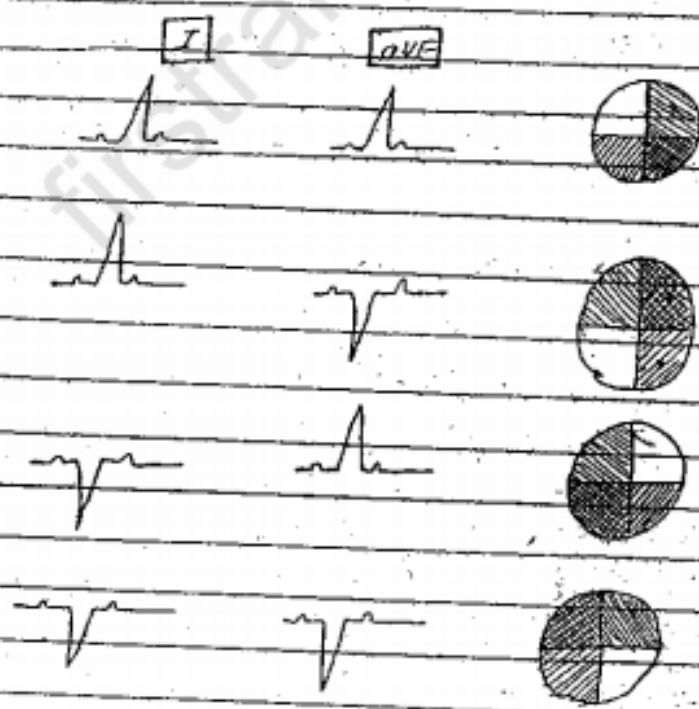
15 large boxes = 3 sec

No. of R-waves in 3 sec  $\rightarrow$   $\times 20 \rightarrow$  Heart Rate





Quadrant method: The overlapping quadrant gives an indication of the axis.



### Biphasic wave Method.

Look for the wave that's most biphasic among I, II, III, aVR, aVF, aVL.



In the vector diagram look for the 1<sup>st</sup> lead of the most biphasic wave.



If the 1<sup>st</sup> lead is mostly +ve then the axis is the axis of the 1<sup>st</sup> lead.



If the 1<sup>st</sup> lead is mostly -ve then the axis is in the opposite direction of the 1<sup>st</sup> lead.

### Atrial Enlargement:-

→ If the P-wave is > 2.5 small boxes → indicates Atrial Enlargement

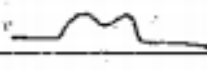
Lead I, aVF → upright P-wave → Source is from SAN.

Morphology of P-wave is different in 3 leads → Multifocal P-wave.

Height of P-wave I → > 2.5 small boxes (> 3 small boxes) (lead II)

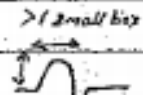


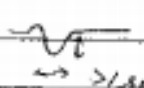
Rt. Atrial Enlargement

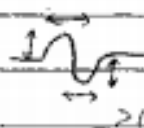
Width of P-wave ↑ →  > 2.5 small waves (lead II)  
Notch > 1 small box.

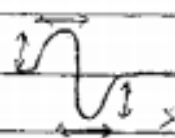


Left atrial enlargement

 > 1 small box  
V<sub>1</sub> P-wave → Rt. atrial Enlargement

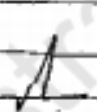
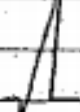
$V_1$    $\rightarrow$  Lt. atrial enlargement  
 $> 1$  small box

$V_1$    $\rightarrow$  bi-atrial enlargement?  
 $> 1$  small box

$II$    $\rightarrow$  bi-atrial enlargement  
 $> 3$  small boxes

RT atrial enlargement - P pulmonale (seen in cor pulmonale)  
 - Himalayan P waves.

Left Ventricular Hypertrophy :-

$V_1$  Normal  LVH   
 $V_6$  Normal  LVH 

Criteria :-  $S_4 + R_{(V_5/V_6)} > 35$  small boxes :- LVH. (voltage criteria)

If there is T wave inversion in  $V_5$  or  $V_6$  it indicates LV enlargement + strain.

\* LV enlargement + strain  $\rightarrow$  indicative of LVH.

(cause due to  $\uparrow$  afterload, HTN, Aortic stenosis)

Boxer criteria for Ventricular Enlargement / Hypertrophy :- ESTES

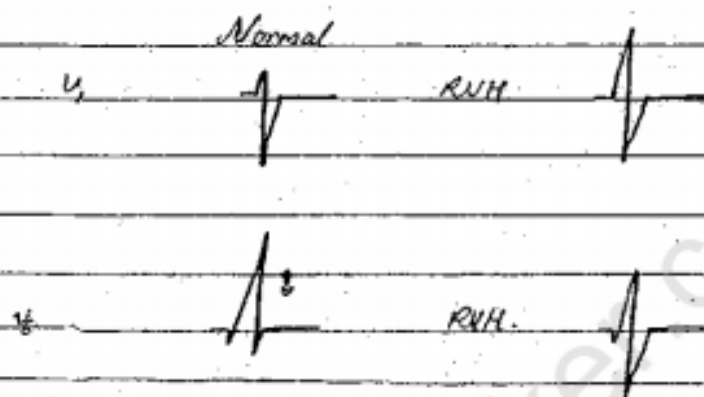


$aVL \rightarrow$  taller than 12 small boxes  $\rightarrow$  LVH.

Voltage criteria is useful for pts  $> 35$  yrs old.

a.k.a. Sokolow Lyon Criteria

Right Ventricular Hypertrophy:-

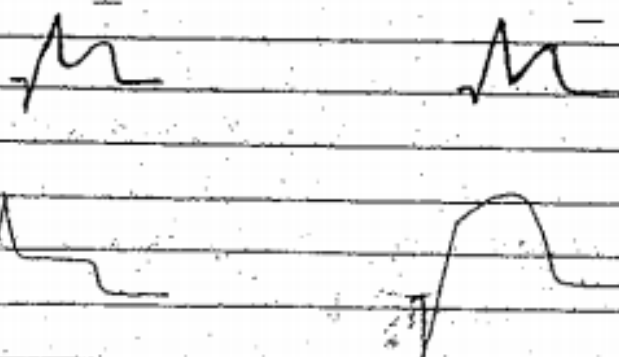


$R_{V1} + S_{V5/V6} > 10$  small boxes  $\rightarrow$  indicative of RVH.

Rt. ventricular strain  $\rightarrow$  Tented T wave in  $V_1$  or  $V_2$ .

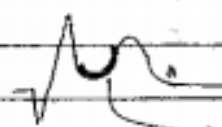
Rt. vent. enlargement + strain = Rt. vent. Hypertrophy

MYOCARDIAL INFARCTION ECG:-



In pericarditis there is Pan-ST elevation.

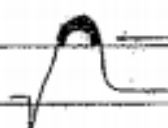
Concavity of ST-elevation is suggestive of pericarditis



Concavity upward

Saddle type ST elevation

Pericarditis

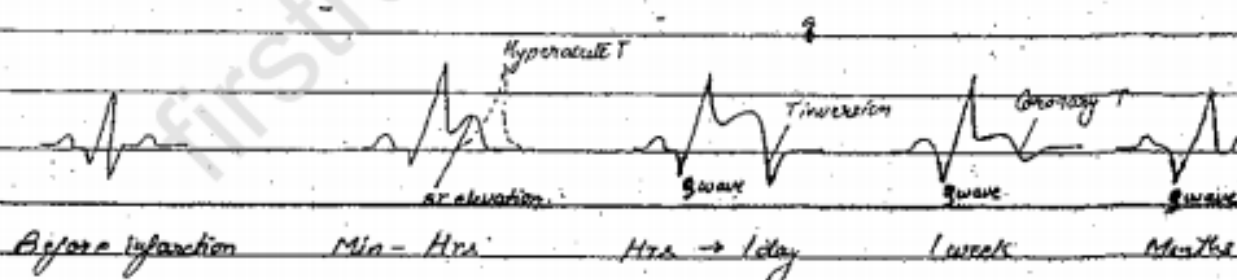


Concavity downward → Myocardial infarction

Acute pericarditis :-

- PR ↓ (PR segment depression)
- Widespread concave (saddle shaped) ST elevations
- Reciprocal ST depression & PR elevation in aVR & V1
- Absence of reciprocal ST depression elsewhere

Evolution of STEMI



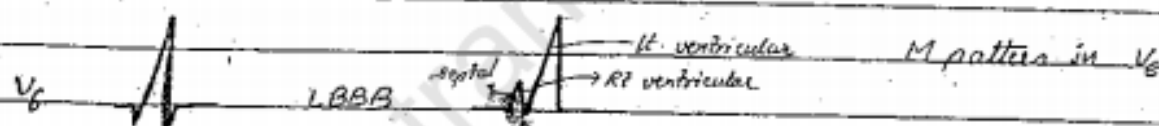
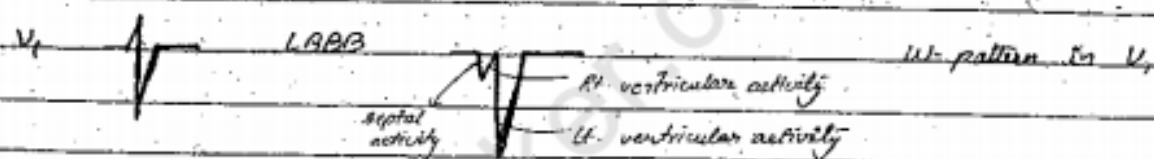
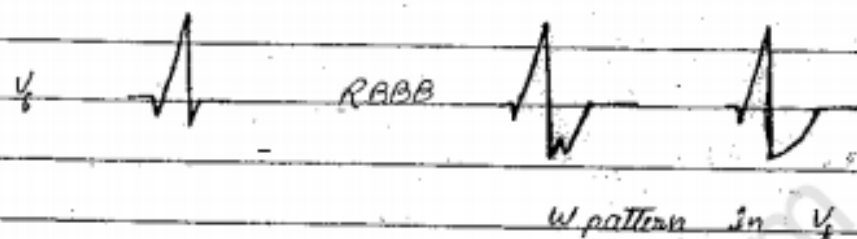
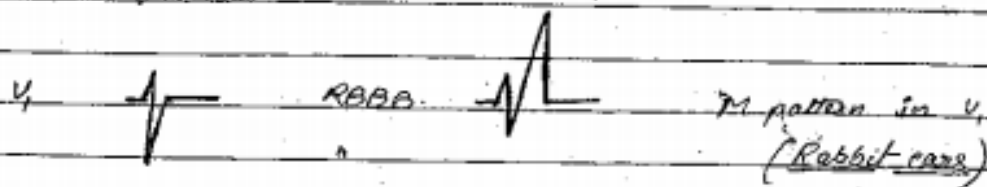
1st change in MI :- hyperacute tall T waves

In ST elevation MI → Reciprocal changes should be seen in the opposite leads

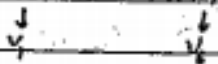
(for pericarditis reciprocal changes are absent)

## Bundle Branch Block

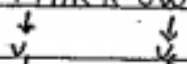
Normal



WILLIAM



MARROW



RBBB  $\rightarrow$  last part of QRS in  $V_1$   $\rightarrow$  Rt. ventricle.  
last part of QRS in  $V_6$   $\rightarrow$  Rt. ventricle

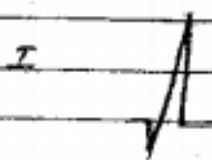
LBBB  $\rightarrow$  last part of QRS in  $V_1$   $\rightarrow$  Lt. ventricle.  
last part of QRS in  $V_6$   $\rightarrow$  Lt. ventricle



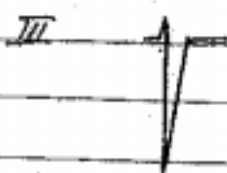
## Fascicular Block

In fascicular Block - no lead should have broad QRS ( $>3$  small)

Fascicular Block is decided only by limb leads (Not chest leads)



Left anterior fascicular Block (left ant. hemiblock)



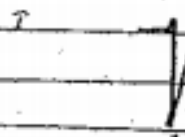
(will always have left axis deviation)

usually beyond  $45^\circ$

Small q in leads I & aVL

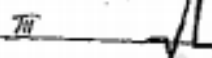
Small r in leads II, III, aVF

Tatracoid deflection in aVL  $> 9.5$  mm



Left posterior fascicular Block (left post. hemiblock)

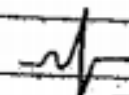
(will always have RBD)



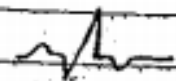
## Pulmonary Embolism:-

M.C. presents in sinus rhythm.

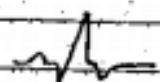
S, Q, T<sub>3</sub> → S wave in lead I



Q wave in lead III



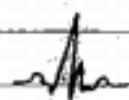
Inverted T waves in lead III



May also have RBBB along w features of Pulmonary Embolism  
T wave inversion may be present in V<sub>1</sub>, V<sub>2</sub>, V<sub>3</sub>

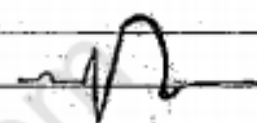


Osborn waves :- Seen after QRS at the J-junction.  
Seen in hypothermia  
Seen in the lateral chest leads



Brugada Syndrome RBBB  $\bar{c}$  ST elevation in  $V_1-3$   
RBBB  $\bar{c}$  ST elevation in  $V_1-3$

Sudden death is a possibility  
Sodium Channelopathy  
SCN5A gene mutation.



- \* Concave ST elevation in  $V_1, V_2$
- \* J point elevation
- \* Inverted T wave
- \* Broad P wave & some PQ prolongation

Functional Rhythm: Rate 40-60, no p-wave, narrow QRS complex.

Concordance is a feature of Ventricular tachycardia  
Capture beat is a feature of VT.

SVT & conduction defects

VT

- |                       |                    |
|-----------------------|--------------------|
| • I-VR                | • Cannon 'a' waves |
| • Conducted message ↓ | • -VR              |
| • -VR                 | • QRS concordance  |
| • -VR                 | • Capture beats    |
| • -VR                 | • Fusion beat      |

Electrical Alternans is seen in Effusion.

## Cardiomyopathy:-

M.C. type of Cardiomyopathy is Dilated.

DCM: Idiopathic

THD

Viral Infections

Alcohol

Toxins

Drugs - Doxorubicin, Daunorubicin

Eosinophilic Cardiomyopathy

Connective tissue Disorders

Heart failure & reduced ejection fraction.

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

Systolic dysfunction

IR: Diuretics

ACEI

$\beta$  Blockers (low dose)

Inotropes  $\leftarrow$  Dobutamine

Digoxin

Synchronization  $\rightarrow$  Dual Chamber Pacing

ICD ( $< 35\%$  EF)

Correct the underlying cause.

RCM: Amyloidosis

Sarcoidosis

Connective tissue dis: RA

SLE

Hemochromatosis (both DCM & RCM)

Parasites (Chagas)

Endomyocardial Fibrosis

(Carinoid)



$$EF = \frac{SV}{EDV} = 25\% EF$$

Distolic dysfunction

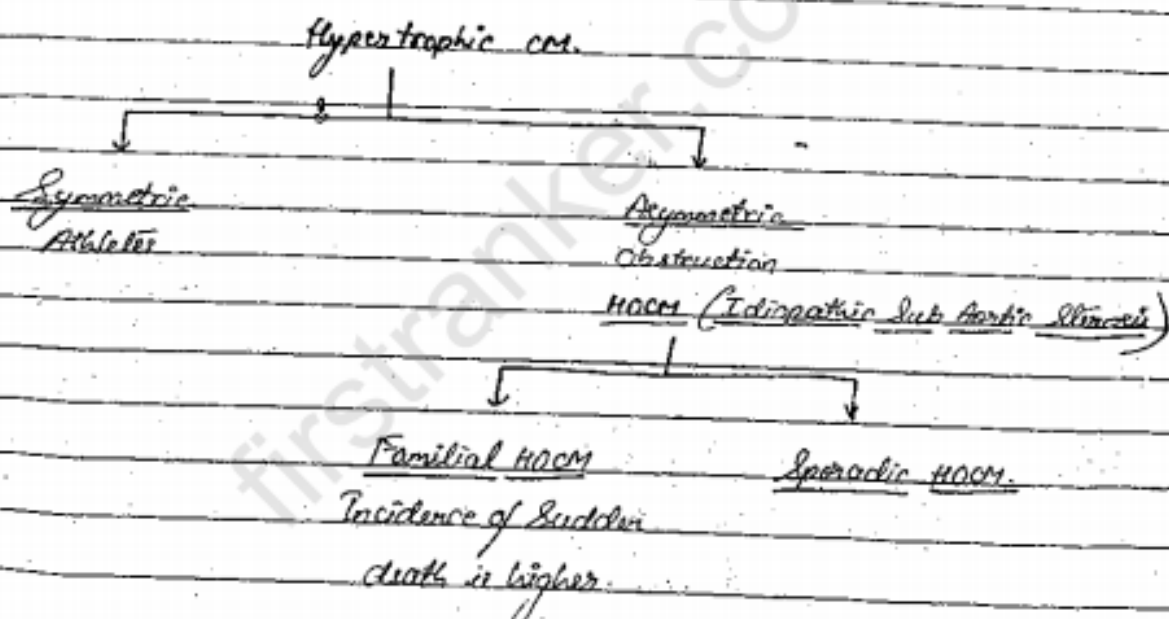
Heart failure & preserved ejection fraction

[Rx]: Diuretics

$\beta$  Blockers

ACEi

Correcting the underlying condition



[HOCM]:

- SAM - Systolic anterior motion of Mitral valve
- Mitral regurgitation

HOCM

Irregular muscle fibres

Muscle fibre disarray

Fibrosis (pockets of scar)

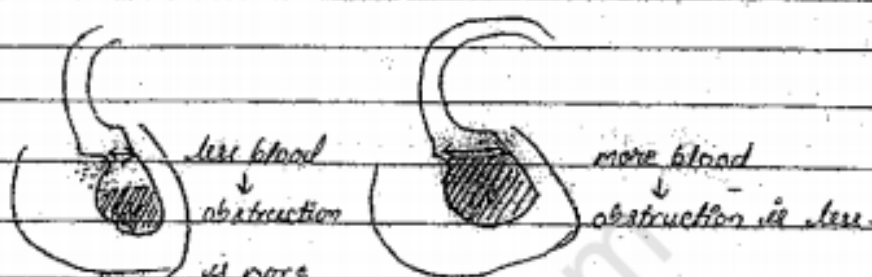
Arrhythmogenic RV Cardiomyopathy  
Fat (adipose) in muscle biopsy

### Murmur HOCM :

- less the blood, ↑ the murmur (peculiar to HOCM)
- lower the EDV, the louder will be the murmur.

Louder murmur :- ↓ EDV

↑ EDC



∴ in standing - pooling of blood in lower extremities

↓ venous return

↓ LV filling

Murmur increases

Valsalva → ↑ve pressure in thorax ↑

↓ LV filling

↑ murmur

Squatting → Femoral is flexed, Gastrocnemius contracts

↑ LV filling

↓ murmur

Handgrip :- ↓ murmur

Nitrate :- ↑ murmur (contraindicated)

Digoxin :- ↑ murmur (avoid)

HOCM - Both diastolic & systolic dysfunction

R: - Survival benefit is improved by  $\beta$ -Blocker D.O.C.

↓  
protect against sudden death

- CCB (Diltiazem, Verapamil)
- Disopyramide
- Septal Myectomy / Myotomy
- ICD

Mitral valve Prolapse

↓ EDV → ↑ Murmur

Physiology of loudness of murmur  
will be similar to HOCM.



less blood → lax chordae

↓  
More prolapse

More blood → tight chordae

↓  
less prolapse





## ARTHRITIS

⊗ Inflammatory

- R.A.
- Spondyloarthropathy
- Gout / Pseudogout
- Connective tissue D.
- Post viral

⊗ Degenerative

- Osteoarthritis
- DISH (Diffuse idiopathic skeletal hyperostosis)

X-Ray - Bone loss

Osteopenia

Osteoporosis

Erosions

New bone formation

Osteosclerosis

Osteophytes

Synovial:TLC  $> 2000/\mu\text{L}$  $> 50000/\mu\text{L}$  (lytic)TLC  $< 2000/\mu\text{L}$ • ESR  $\uparrow > 50$ 

• CRP +ve

• ESR  $\leq 50$ 

• -ve

Morning stiffness  $> 1\text{hr}$ (M.S.  $< 1\text{hr}$  can be either inflammatory or degenerative)RAOACriteria: Classification Criteria

- |                            |                                   |
|----------------------------|-----------------------------------|
| ① No. of joints            | } Total score is<br>↓<br>≥ 6 → RA |
| ② Duration $< 6\text{wks}$ |                                   |
| ③ Anti CCP's               |                                   |
| RA factor                  |                                   |
| ④ ESR, CRP                 |                                   |

Excisions, Subcutaneous nodules,  
morning stiffness are not included  
in new criteria

\* PIP, MCP, Wrist  
(C/C)  
DIP is spared.

Base of thumb - most common  
MCP } spared  
Wrist }

PIP and DIP are involved.

\* Inflammatory Conditions  
involving the DIP joint ←

{ Psoriatic  
Reiter's

\* Elbow, knee, MTP is  
involved in RA.

PIP - Bouchard's  
DIP - Heberden's

\* Shoulder joint is involved  
in ♂ and elderly ♀

Hip

Knee

} involved.

\* Ankle is involved.  
Cervical vertebrae  
(C4-C7)

Acromio-Clavicular

Lower C, lumbar vertebrae

\* **1. IHD**

Ocular :- • Scleritis • Episcleritis

• Uveitis (Anterior/Posterior/IR)

mostly in spondyloarthropathy

Lung :- • Pleuritis

• Pleural Effusion (Glu < 30mg/dl)

• TLD

• Caplan's - Coal workers + RA  
+ Progressive fibrosis

Heart :- Pericarditis

Restrictive CM (diastolic)

infection most common valve lesion.

splenomegaly

Anaemia of chr. disease.

DLBCL

Neutropenia + Splenomegaly + RA - Felty Syndrome.

Neurologic Syndrome: Compressive neuropathy

Mononeuritis multiplex is rare.

Kidneys: Membranous nephropathy

Interstitial nephritis (due to drugs for RA)

Rx: DMARD

|                          |                                                    |              |                         |
|--------------------------|----------------------------------------------------|--------------|-------------------------|
| Cat. X<br>↓<br>c/p prog. | • HCG                                              | • Anti TNF   | • Anakinra IL-1         |
|                          | • MTX $\begin{cases} TC, DC \\ LFT \end{cases}$    | • Infliximab | • Tacizumab IL-6        |
|                          | • Leflunomide                                      | • Etanercept | • Abatacept FcR blocker |
|                          | • Sulfasalazine $\begin{cases} TC, DC \end{cases}$ |              | ↑ the risk of infection |

Leflunomide - Dihydro-orotate dehydrogenase inhibitor.

\* Oligospermia is seen in Sulfasalazine, MTX  
(reversible)

TNF $\alpha$  antagonists 2/E :- Reactivation of TB (TB should be ruled out

- Neuropathy before starting Rx)
- Lupus like markers.
- Avoided in HIV (Given to HIV if CD4 > 200)



## Spondyloarthritis:

- Ankylosing Spondylitis
  - Reiter's (Reactive arthritis)
  - Psoriatic arthritis
  - IBD associated arthritis
- \* M > F
  - \* Sacroiliac / low backache
  - \* Enthesitis - Ant. longit. lig of the vertebrae
  - \* Assoc.  $\bar{c}$  HLA B27
  - \* assoc.  $\bar{c}$  Uveitis
  - \* Sex negative (No RA factor)  
(Psoriatic may have RAP 5-10%)
  - \* Syndesmophytes are present in all.

### Ankylosing Spondylitis

### Ankylosing hyperostosis (DISH)

- |                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |                                                                                                                                                                                                                                                                                                                               |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>* Male &lt; 40 yrs</li> <li>* Low backache &gt; 3 months</li> <li>* Sacroiliitis +++ (symmetric)<br/>↳ ↑ in the morning</li> <li>* HLA B27 &gt; 90% pts.<br/>↳ not specific, very sensitive</li> <li>* Schobers' Test :-<br/>↳ 5 cm movement → lower vertebra</li> <li>* Uveitis → 3.3%</li> <li>* RA → &lt; 10%</li> <li>* X-Ray :- Bili. sym. sacroiliitis<br/>Bamboo spine<br/>Dagger sign<br/>Trolley track</li> </ul> | <ul style="list-style-type: none"> <li>* &gt; 50 yrs</li> <li>* Backache (morning)</li> <li>* Sacroiliac spared</li> <li>* No HLA assoc, assoc. <math>\bar{c}</math> DM</li> <li>* Syndesmophyte formation<br/>↓<br/>Non marginal Syndesmophyte formation</li> <li>* Acl involved } No neuropathy<br/>PLL spared }</li> </ul> |
|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
- DISH → Frozen shoulder

\* Neuro deficit because  
both ACL, PL both are involved.

\* X-Ray:- Wax-dumping  
Candle dripping appearance

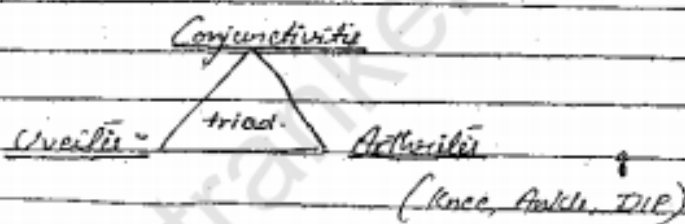
\* Marginal lymphocyte formation

\* Bamboo spine - due to marginal involvement

\* Dagger sign - ossification of interspinous ligaments

Reiter's / Reactive Arthritis

\* Low back ache (asymmetric sacro-iliitis)



\* Vesicles  $\rightarrow$  Crusting on palms & soles  
Keratoderma blennorrhagica

\* Penile vesicles  $\rightarrow$   
Balanitis circinata

Rx:- NSAID, steroids, Mts (common for all)  
+ Doxycycline (only for Reiter's)

Infections causing  
Chlamydia (m.c.)  
Salmonella  
Shigella  
Yersinia

Ureaplasma urealyticum  
Mycoplasma genitalium  
HIV

## Psoriatic Arthritis

- 20-40% pts - joint problems may precede skin lesions

→ Oligoarticular ( $\leq 4$  joints) → Asymmetric / Symmetric

→ Polyarticular ( $> 4$  joints)

\* Arthritis mutilans (destructive arthritis)

\* DIP inv. is classical, asymmetric sacro ilitis

\* Nails → pitting → splitting (dystrophy)

X-Ray → Periost in sup deformity

→ Mouse Ear appearance

R :- Psoriasis + Arthritis :- Mtx (D.O.C)

Arthritis :- Etanercept (D.O.C)

## GOUT

M.C :- 1<sup>st</sup> MTP involvement - Podagra

→ More cooler the joint → more chances of being affected.

→ Serum uric acid has a relationship with acute gout

Synovial :- \* TLC  $> 2000/\mu l$  (may be as high as 50000)

|                                                                       |                   |
|-----------------------------------------------------------------------|-------------------|
| { Negative BF<br>Needle shaped<br>Bistouris white<br>Yellow amorphous | } Crystallography |
|-----------------------------------------------------------------------|-------------------|





Rhomboid shaped CPPD crystals are seen in pseudogout.

Q :- Acute :- \* NSAIDs

\* Intra-articular steroids

\* Colchicine

doesn't affect uric acid.

just reduces inflammation.

S/A :- dose dependent  $\rightarrow$  diarrhea

Don't use in acute :-

Allopurinol

Probenecid

Aspirin

Chronic :- Uric acid is  $> 7\text{mg/dl}$

X Ray findings in Chronic gout :-

- Marginal erosions  $\pm$  sharp spikes (Marsel's sign)
- Tophi (hazy joints) (G. sign)

S. Uric acid  $> 7\text{mg/dl}$

Over producer

10%

Urine uric acid  $> 800\text{mg/day}$

Under excretor

90%

Urine uric acid  $\leq 800\text{mg/day}$

R :- Allopurinol

Febuxostat

R :- Probenecid

Benzbromarone, vit. C.

New drugs :- Canakinumab :- IL-1 blocker

Pegloticase

Rasburicase

Urate oxidase

Benbromarone

Allopurinol

Pseudogout :- Synovial fluid

WBC  $> 2000$

Rhomboid CPPD crystals

{ Hypothyroidism

{ Hyperparathyroidism

Hemochromatosis

as seen in

pseudogout

X-Ray:- Knee joint calcified

R:- NSAIDs, Intra-articular steroids

### VASCULITIS

| <u>Large</u>         | <u>Medium</u> | <u>Small</u>               |
|----------------------|---------------|----------------------------|
| - Takayasu           | - PAN         | - Microscopic polyangiitis |
| - Temporal arteritis | - Kawasaki    | - Wegener's (GPA)          |
|                      |               | - Churg-Strauss (EGPA)     |
|                      |               | - HSP                      |

Granuloma: Takayasu arteritis  
Temporal arteritis  
Wegener's (GPA)  
Churg-Strauss (EGPA)

Immune Complex:- Polyarteritis Nodosa  
Henoch-Schönlein purpura

| <u>Takayasu</u>                          | <u>Temporal</u>                |
|------------------------------------------|--------------------------------|
| • Large + medium                         | • Large + medium               |
| • Granuloma                              | • Granuloma                    |
| • Aorta                                  | • Aorta                        |
| • Skip lesions                           | • Skip lesions                 |
| • Age < 40 yrs                           | • Age > 50 yrs                 |
| • E: M = 8:1                             | • E: M = 2:1                   |
| • Extra-cranial vessels are not involved | • - do -                       |
| • m.c vessel:- Subclavian                | • m.c vessel:- Temporal artery |
| • l.c vessel:- Coronary                  |                                |
| Asymmetric pulses                        |                                |

- Difference in BP  $> 10$  mmHg
- Abd. pain, bowel ischaemia
- ↑ Creat, HTN (Renal vessel inv.)

Classification

- I: Arch of aorta I - Arch of aorta
- II: Asc. aorta II - asc. aorta + br
- III: Desc. aorta III - thoracic aorta
- IV: Aorta. art. IV - Abd. aorta.

II: Overlapping  
(aorta)

- Rx:- Initially steroids  
After fibrosis - steroids don't work  
Surgery:- Stenting or  
Re-anastomosis

- Headache, scalp tenderness (46)
- Polyarthralgia Rheumatica  
↳ stiffness + pain → proximal muscles
- Ant. ischaemic optic neuropathy (irreversible)

• Mean ESR  $> 90$

• Ocular problems:- Blindness

Diagnosis

Altitudinal field defect

Rx:- High dose steroids

Tx:- USA of the temporal artery

Rx:- 4cm segment of temporal a.

Polyarteritis Nodosa

Microscopic Polyangiitis

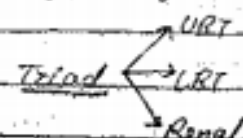
Wegener's Granulomatosis

-ve

p-ANCA

c-ANCA (70%)

HBsAg +ve (20%)



Medium vessels + capillary  
never venule

Capillaries + Venule

Capillaries + Venule

Lung - Spared

ILD

ILD

Bronchial artery

Alveolar haemorrhage

Alveolar haemorrhage

may be involved.

No cavities

Cavities ++ (peripheral lower lobe)

URT ⊖

URT ⊖

Nodules URT ++

Musculo skeletal (joint problem)

Glomerulonephritis ⊕

GN ⊕

Arthritis/Arthralgia

Focal necrotizing GN

- do -

M.a. organ - Renal  
No GN.

Crescentic GN

Crescentic GN



|                                  |                                 |                                 |
|----------------------------------|---------------------------------|---------------------------------|
| <u>Polyarteritis Nodosa</u>      | <u>Microscopic Polyangiitis</u> | <u>Wegener's Granulomatosis</u> |
| -                                | RBC casts in urine              | RBC casts in urine              |
| <u>Mononeuritis Multiplex</u> ++ | + (not common)                  | + (not common)                  |
| <u>Mesenteric - Abd pain</u>     | ⊖                               | ⊖                               |
| <u>Malena</u>                    |                                 |                                 |
| <u>Coronary - IHD</u>            | ⊖                               | ⊖                               |
| <u>Gangrene of digits</u>        | very rare                       | very rare                       |
| ⊖                                | ⊖                               | Granuloma ⊕                     |

2. Steroids ✓

Cyclophosphamide ✓

Should not be given for more than 6 months (Hemorrhagic cystitis, Ca bladder)

Maintain :- Mtx

Rituximab (Anti CD20)

Mycophenolate Mofetil, Azathioprine (Steroid Sparing)

HSP :- Usually < 20 yrs

can occur > 20 yrs

Tetrad :- \* Palpable purpura (Essential feature), m.c. feature

Starts in - buttocks

\* Trunk

\* Lower limbs

\* Arthralgia

- knee / ankle

\* Mesenteric → Abd pain, Malena

\* Hematuria + Proteinuria (IgA nephropathy) 20-40% pts



- ⊗ Biopsy:- Neutrophilic infiltrate  
→ leucocytoclastic vasculitis  
\* Anaphylactoid purpura

Immunofluorescence → IgA

R:- Steroids

M.c. vasculitis in children HSP (AHIS, NRE)  
KAWASAKI (PGL)

### KAWASAKI DISEASE

- \* Exclusively Children
- \* Peak - 1 to 5 yrs (1 to 2 yrs old children m.c.)
- \* Coronary involvement - Myocardial dysfunction
- \* Fever x 5 days (unrelieved)

Four out of 5 criteria:-

- 1) Conjunctivitis (perilimbal sparing)
- 2) LN+ (Cx → 1 or 1.5 cm in size)
- 3) Polymorphic Rash (on trunk)
- 4) Peripheral Sign  $\left\{ \begin{array}{l} \text{Swelling} \\ \text{Desquamation} \end{array} \right.$
- 5) Mucosal Sign  $\left\{ \begin{array}{l} \text{Strawberry tongue} \\ \text{Dry Cracked lips} \end{array} \right.$

R:- IV immunoglobulin + Aspirin

Steroids can be given after 3 wks of IVIg

M.c primary vasculitis - Cutaneous Vasculitis

↓  
Hypersensitivity Vasculitis  
(Post capillary Venules)

SLE

F:M = 9:1

New criteria

\* Skin

Immunological

\* Alopecia

→ ANA

\* Synovitis (arthritis)

→ Anti-Sm

\* Oral ulcers

→ Anti dsDNA

\* Renal

→ Anti phospholipid

\* Neurological

→ Complement

Blood

→ Coombs test +ve

Old criteria

\* Malar rash

\* Blood Ab(n)

\* Discoid rash

\* Renal

\* Serositis

\* ANA

Anti-Sm

\* Oral ulcers

\* Tumor

→ Anti dsDNA

\* Arthritis

\* Neuro

\* Photosensitivity

Malar rash :- Butterfly pattern. Naso labial area should be spared.

Discoid rash :- Scarring + Alopecia

Oral ulcers :- Hard palate, generally painless



Neurological:- Behavioural  
Seizures  
Focal deficits

Arthritis:- Non Erosive

Blood:- Anaemia, neutropenia, pancytopenia, thrombocytopenia  
↓  
Pancytopenia

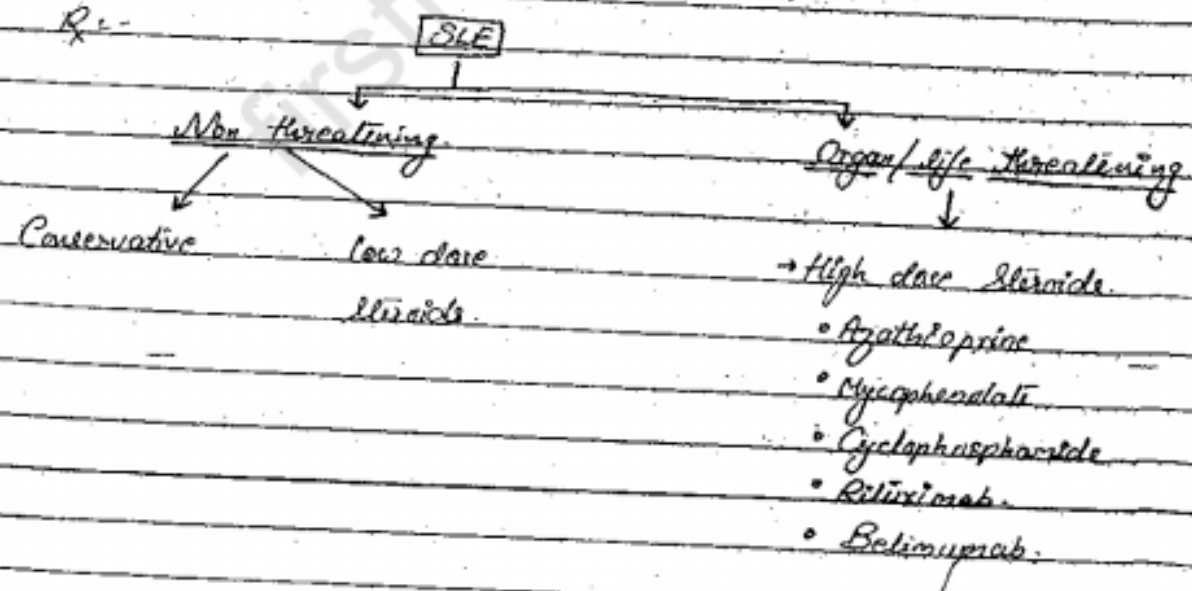
ANA:- Sensitivity 90% Specificity 10-15%

Anti Sm:- 20% 98-100%

Anti dsDNA:- 60% 95% Most accurate

Anti dsDNA titres correlate  $\pm$  disease severity

Rx:-



M.c. presenting complaints of SLE:- Systemic/Constitutional  
Arthritis/Musculoskeletal  
Haematological

## APLA Syndrome

LUPUS      Anticoagulant X  
↓                    ↓  
50%                Thrombosis

$\beta_2$  glycoprotein Ab is the most imp. Ab.

Anti-Cardiolipin Ab

Assoc.  $\pm$  SLE in 50% of the cases.

Thrombogenic state (don't present a bleeding)

Pregnancy:- Thrombosis in placental bed.

Abortion (10 wks)

DUGR

Still birth

Utero-placental insufficiency

Bad Obstetric History

Aspirin + Heparin

↓  
Warfarin (2nd trimester)

Steroids are not to be given in APLA syndrome

↓  
Heparin 3rd trimester

Warfarin in 1st trimester:- Craniofacial anomalies (common)

Chondrodysplasia punctata (characteristic)

Asymptomatic:- PT (N)

APTT  $\uparrow$  (m.c. cause of isolated PTT

in an asymptomatic person.

2nd: Factor II deficiency)

Mix Sample test:- PTT  $\uparrow$  (proceed inhibitors in the pt sample)

Thromboses      Arterial - Stroke / TIA  
                          Venous - DVT  
                                          CVT

Russell viper venom test time - prolonged

+ phospholipids (freeze dried platelets /  
 thawed platelets)  
 RVVT becomes normal

Confirms APLA syndrome.

VDRL +ve      FTABs -ve  
 ↓  
 due to anti-cardiolipin Ab.

Rx :- Anti-coagulation

TNR :- arterial thrombosis      2.5 - 3.5

venous thrombosis      2.0 - 3.0

Only in APLA, Prosthetic valves TNR > 3.0



## Systemic Sclerosis

### Localised CREST

### Diffuse SS.

|       |      |                                     |    |      |
|-------|------|-------------------------------------|----|------|
|       | +    | Calcinosis                          | +  |      |
| Early | +    | Raynaud's                           | +  | late |
|       | +    | Esoph. dysmotility                  | +  |      |
|       | +    | Sclerodactyly                       | +  |      |
|       | +    | Telangiectasia.                     | +  |      |
|       |      | (peri-ungual)                       |    |      |
|       |      | Also seen in dermatomyositis        |    |      |
|       | +    | { Skin +<br>Face, Fingers, Feet }   | +  |      |
|       | -ve. | Above Elbow Trunk.                  | ++ |      |
|       | ±    | { Joint, Arthralgia,<br>Arthritis } | ++ |      |

4%

Renal involvement

15%

1° PAH

lung involvement

ILD

ILD - rare

PAH

M.c. cause of death in Scleroderma is lung disease

Anti-Centromere

Abs.

Anti Scl 70

Anti RNA poly III

Ant. Ia (SSG) → more specific

Inv: Ant Ro (SSG)

PBC

MTCD

→ 91E

→ RA (m.c.)

Secondary Sjogrens: Ray STD Assoc. & Sjogrens

M.C. Lymphoma: MALTOMA (Marginal Cell Lymphoma)

Tubulointerstitial nephritis - Type I RTE

Hepato-splenomegaly

Dry vaginal mouth

Dry Mouth

Dry Eye

P:M = 9:1

M.C. Extra glandular manifestation  
Arthritis / Arthralgia

Sjogrens Syndrome

Supportive Treatment

Sympathetic

Excretion

PRB

Raynaud's: csg

↓ the thickening of skin

R: D penicillamine (slowly)

Thrombotic condition

Assoc. w/ HLA-B\*57:01

Pathology Test +ve

Demyelinating condition of CNS - looks like MS

*Cryptosporidium parvum* (causes diarrhea)

Genital ulcers

Acute/painful ophthalmic ulcers - recurrent (essential)

Oral - conjunctivitis / keratitis

Behcet's

Stomach - limited sites

Lymphoma - R. CHOP

RTA - HCG

Endocrine

Artificially

Supportive

Lymphoma in glands & organs

Oral lymphoma - difficult to treat

lobular biopsy - Minor salivary gland



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## IMMUNOLOGY

### Innate immunity / Non specific

### Adaptive / Specific / Acquired immunity

- Anatomical barriers

- T helper cells

- Physiological barriers

- Humoral  $\rightarrow$  Igs  $\rightarrow$  B cells

- Biochemical barriers

- CMI - T cells

- Barrier - skin pH

- Switch on/off

- cilia

- Highly specific

- lysozymes

- Memory  $\oplus$

- pH stomach

- Lag phase  $\oplus$

- Neutrophil, NK cells

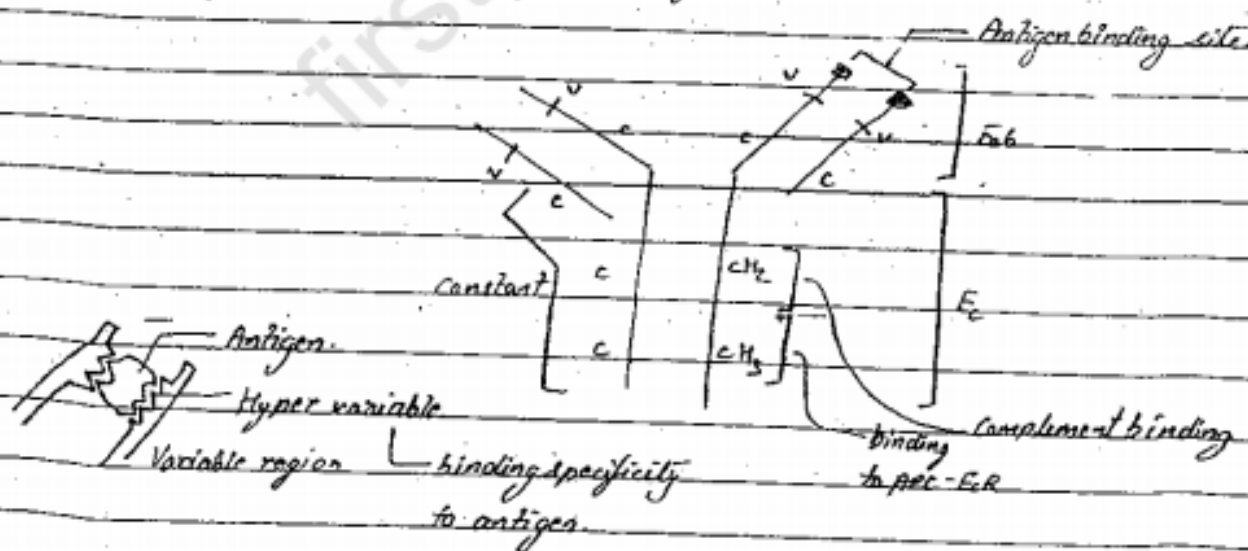
- Complement, Macrophages

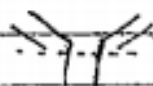
- Dendritic cells

- "Toll-like receptors"

- No memory, no lag phase

### Antibody





$Ab + \text{papain} \rightarrow 2 Fab + 1 Fc$

$Ab + \text{pepsin} \rightarrow 2 F(ab)_2$  (Fc destroyed)

Isotypes:-

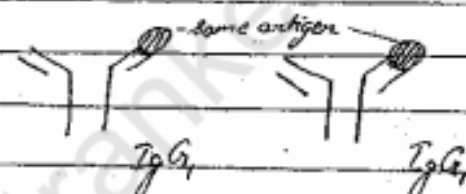
|            |                              |
|------------|------------------------------|
| $\gamma$   | $IgG_1, IgG_2, IgG_3, IgG_4$ |
| $\alpha$   | $IgA_1, IgA_2$               |
| $\mu$      | $IgM$                        |
| $\delta$   | $IgD$                        |
| $\epsilon$ | $IgE$                        |

Total no. of isotypes:- 18

due to K & L chain in each.

Idiotypic:- Specificity of Ab:- Variations in variable site

Allotype:-



bind to same antigen

but difference in the heavy chain / structural differences

Allelic polymorphism - between 2 individuals of same species.

Ab diversity:-

Heavy:  $V, D, J, C, H, C, H$

Light:  $V, J, C, L, C, L$

$V_1, V_2, V_3, V_4, \dots, D_1, D_2, D_3, \dots, J_1, J_2, J_3, \dots$

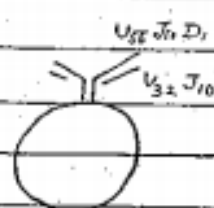
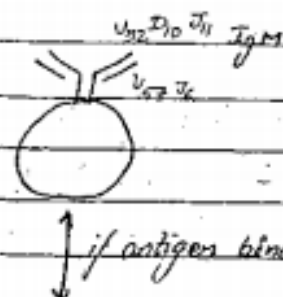
$\xrightarrow{RAG} V_{H5} D_1 J_6 \xrightarrow{\text{Jolt} \leftrightarrow \text{isolate}} V_{H5} D_1 J_6$

Random splicing and shuffling by RAG enzymes.



Any sequence of V, D, or J can be joined to each other leading to a different pattern of VDJ sequence.

Tdt is only present in immature cells.



Every B cell will have receptors for a specific type of Ag

if antigen binds

Clonal selection, clonal amplification



Mitotic bursts



Plasma cells with the same antibody type



After antigen binding if there is further variation in the antibody structure (variable region, hypervariable region) in the daughter cells it's called somatic hypermutation.

Weak binding



less/no proliferation

Stronger binding than the parent cell



More proliferation of the same type of cells



further mutation/changes in the hypervariable region



Selection & proliferation of the best antibody forming cells.

Affinity maturation is done by Somatic hypermutation

\* IgM is a poor marker for fetal toxoplasma.

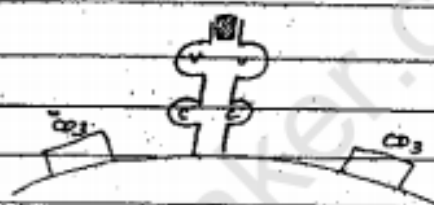
For fetal toxoplasma better marker is IgG (but IgG appears late)

To detect Toxoplasma in mother, IgG is used.

If affinity is very good  $\rightarrow$  remote infection.

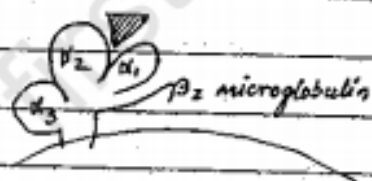
If affinity is less  $\rightarrow$  recent infection  $\rightarrow$  ↑ chances of fetal toxoplasma.

T cell receptors:-

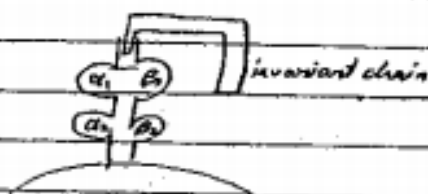


$\alpha\beta$  - T cell receptor /  
Antigen - T cell marker

HLA receptors



Ag binding site is b/w  
 $\alpha_1$  and  $\alpha_2$



- Two chains, two domains in each  
- Invariant chain protects against binding of any antigen unless specific antigen is recognised.

### HLA - I

### HLA - II

### HLA - III

A ↓  
150  
B ↓  
250  
C ↓  
100  
subtypes

low genetic polymorphism - B  
inherited in co-dominant  
pattern

\* DP, DQ, DR  
max. chances of graft rejection  
much more polymorphic  
in HLA-II than HLA-I

\* C, C<sub>2</sub>,  
TNF- $\alpha$   
Factor B / properdin  
HSP

For individual identification best is :- Fingerprinting

- 1) DNA fingerprinting
- 2) HLA typing

All nucleated cells and  
platelets

\* All antigen presenting cells  
- dendritic cells (most potent APC)  
- Macrophages  
- B cells  
- Activated T lymphocytes  
(Plasma cells don't have HLA-II)  
(Naive T cells don't have HLA-II)

Intracellular defence

\* Extracellular defence

CD8

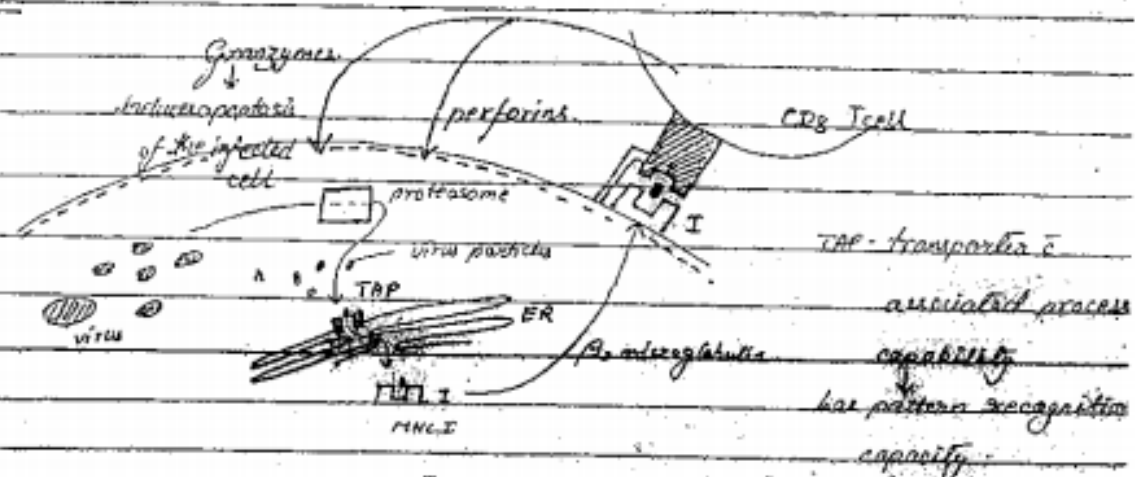
\* CD4

$\beta_2$  Microglobulin

\* Transmembrane chain



## HLA-I



Virus infects a cell  $\rightarrow$  proliferates

proteasome breaks the virus  
into protein particles.

presents to the TAP receptor.

viral particles are presented to MHC I.

MHC I recognizes particle as foreign.

Migrates to surface (via  $\beta_2$  microglobulin)

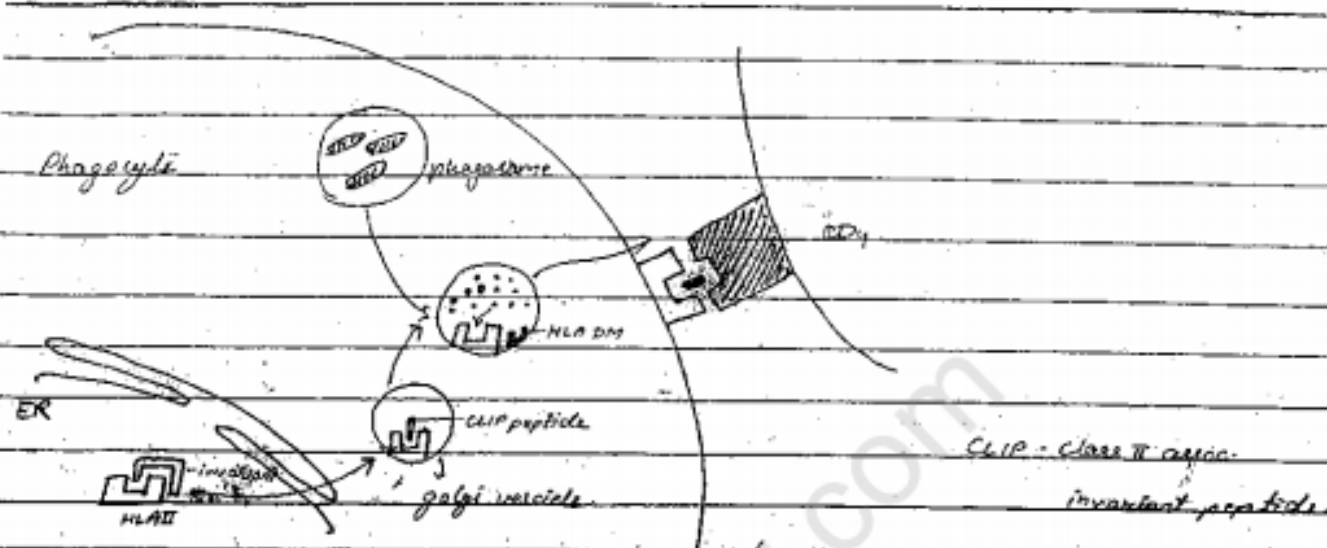
CD8 recognizes the MHC I and the viral particle.

CD8 induces apoptosis of the infected cell.

via perforins and Granzymes  $\rightarrow$  release cytokines  
activates caspases.

M.C. method of evasion of viral particles is blocking of the TAP receptors

## HLA-II

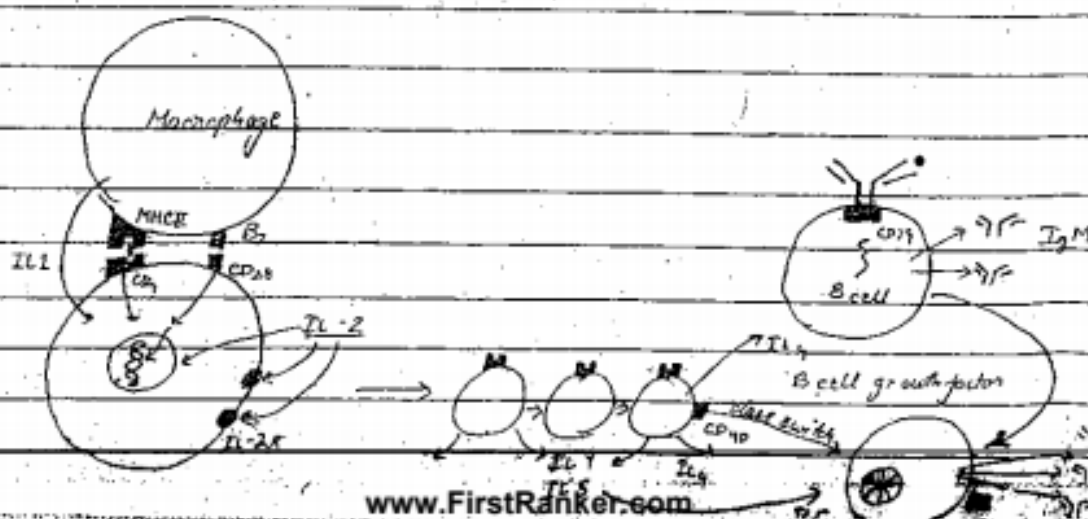


Progressive acidification of the golgi vesicle degrades the invariant chain to CLIP peptide.

After fusion of the vesicle vesicle with the phagosome HLA DM removes the CLIP peptide.

The bacterial particles bind to the MHC II.

MHC II migrates to surface and presents to CD4 cells.

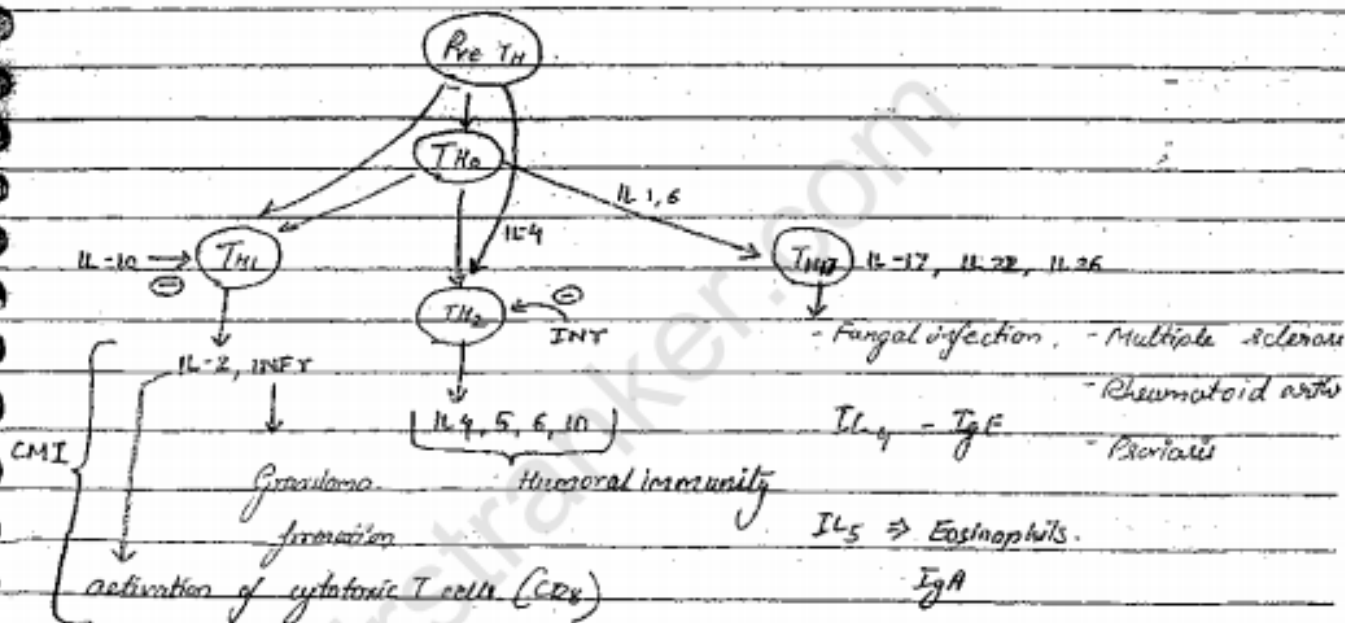


↓ because large carbohydrates will not be processed.

1

1

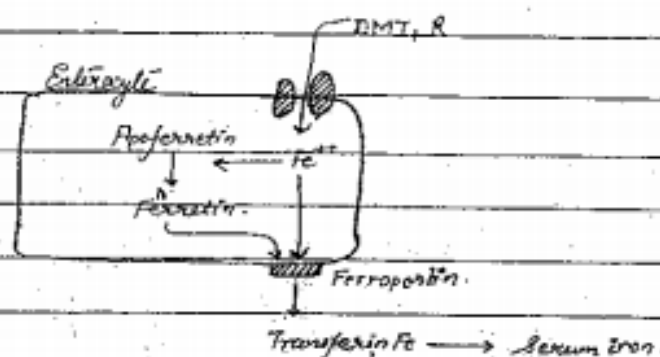
Only B-cell dependent response



Max rise in repair: 11-6.

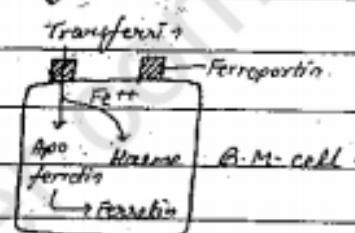


## HEMATOLOGY:



To pick up iron  $\rightarrow$  Transferrin

uses **Ferroportin**  
channels from all tissues.



Iron packaged in **Ferritin** is not included in S-Fe.

**Hepcidin**: Produced by the liver.

Blocks the **ferroportin** channels.

Controls the absorption of  $Fe^{++}$  from intestine  $\downarrow$

$\downarrow$  the release of  $Fe^{++}$  from storage sites

**Anemia of Chr. Disease**:- S-Fe  $\downarrow$       :- due to  $\uparrow$  hepcidin  
S-Ferritin  $\uparrow$

**Thalassemia**  $\rightarrow$   $O_2$  levels are low.

Hepcidin levels are low.

Absorption of iron is  $\uparrow$  from the  
intestine despite iron overload.

Newer drugs: **Hepcidin receptor agonists**

✓ Ferritin is inversely related to transferrin synthesis

✓ Transferrin receptor assay: Sensitive marker for IDA (Can RBC in IDA)

✓ Ferritin levels are ↑ in Atransferrinemia

✓ In DMF, Receptor mutation ferritin levels are ↓

⊗ S. Iron 50 - 150 µg/dl

⊗ MCV 80 - 100 fl

⊗ S. Ferritin 30 - 300 µg/L

⊗ RDW 10 - 15

⊗ TIBC 250 - 400 µg/dl

⊗ Transferrin saturation (33%) (15 - 50%)

⊗ Iron deficiency

⊗ Thalassemia minor

⊗ Anaemia of chr. Disease

S. Fe < 50 µg/dl

(N) / ↑

Normo Normo (80 - 90%)

S. Ferritin < 30 µg/L

(N) / ↑

MCV is not < 60 fl. S. Fe ↓

TIBC ↑↑

(N)

Hb > 7 gm/dl. S. Ferritin ↑

Transferrin sat: < 15%

(N)

↓ (also in sidero, Hemochrom)

Tf-Rs - ↑↑

(N)

N / ↓

Transferrin-Ferritin  
or  
TfR index

(N)

< 1

$\frac{S. Tf-Rs}{log Ferritin} > 2$

Most sensitive & specific

Gold Standard: BMF

✓ MCV ↓

✓ ↓↓↓ disproportionate

microcytosis

disproportionate

the severity of anaemia

✓ RBC < 5 million/mm<sup>3</sup>

✓ > 5 million/mm<sup>3</sup>

IDA

T. Minat

www.FirstRanker.com

www.FirstRanker.com

Meitzner's index

MCV  $> 13$

MCV  $< 13$

RBC (in million)

RBC (in million)

RDW  $> 15$

$< 15$

RDW also increases in

Folate, B<sub>12</sub> deficiency

Max RDW is seen in dimorphic anaemias

Idiopathic Anaemia:

Idiopathic

- Congenital: BHA defect

- Acquired: Alcohol

- Lead

- pyridoxine deficiency

Ringed sideroblasts

S. Fe  $\uparrow$

PBS - Dimorphic

S. Ferritin N/↑

Basophilic stippling (Chr. Porphyruria)

TIBC  $\downarrow$

Macrocytic Anaemias

→ MCV  $> 100$  fl.

→ Dimorphic PBS

→ ↓ Reticulocyte count - ineffective erythropoiesis

→ Jaundice, Gall stones  $\pm$



### B12 deficiency

- Neuropathy +
- SACD. +
- Memory loss +
- Hypochromic } Pernicious  
Anisocytosis } anaemia

Homocysteine ↑

Methylmalonate ↑↑

Source - non-veg

### Folate deficiency

-

-

-

-

↑

M

green leafy vegetables

### Hereditary Spherocytosis

M.C. defect :- osmotic defect

more severe - spectrin defect

PBS

↳ Spherocytes

MCHC ↑

Osmotic fragility ↑

CF: Jaundice, Gall stones

Reactive Splenomegaly (destruction of RBC causes release of growth factors)  
(destruction of platelets doesn't release growth factors)

### AIHA

Warm

\* Ag - Rh

\* Ab - IgG

Role of complement

Cold

Complement activation

Agglutination

\* Ag - 'I'

\* Ab - IgM

Cold Hemolysis

\* Ag - P

\* Ab - IgG

### Warm

- Spherocytosis
- Splenomegaly +
- osmotic fragility ↑
- jaundice/gallstones

Direct Coombs test (+)

### Cold

#### Cold agglutinin

- ↑ destruction in liver
- pain, cyanosis
- no significant splenomegaly
- Direct coombs (+)

#### Cold hemolysin

- Intravascular hemolysis
- Paroxysmal Cold Hemoglobinuria (PCH)
- Donath Landsteiner type
- Direct Coombs (+)

Causes: \* Idiopathic

\* SLE

\* Leukemia/lymphoma

\* Drugs:

\* Haptens: Penicillin / Cephalosporins

\* Cross reactivity → Ab → Methylgluta RBC

\* Immune complex: Quinidine, Quinine

Ab → Ag → RBC

Causes: lymphoma

Myeloplasma

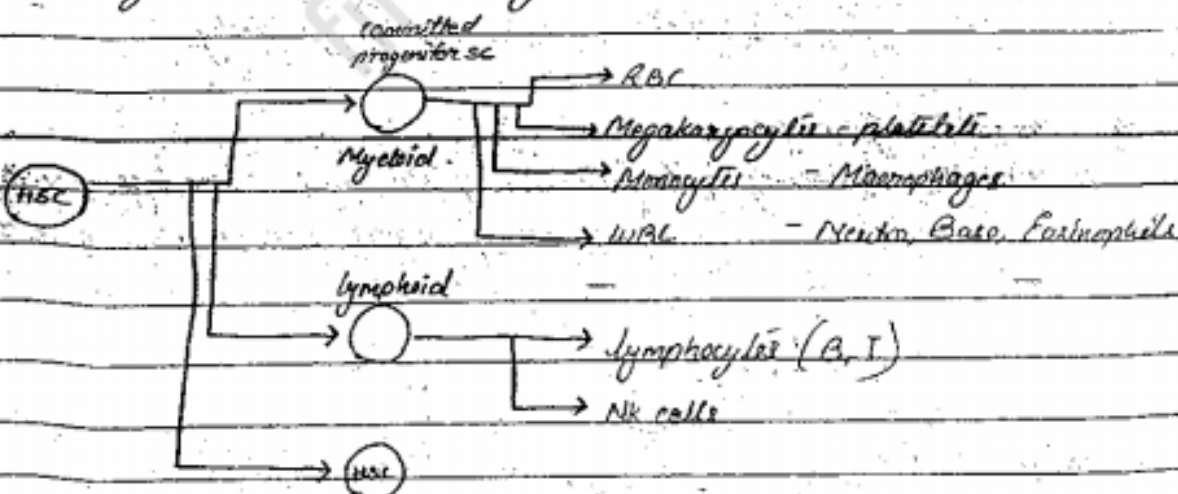
Causes: Measles

Mumps

Malaria

Influenza

### Paroxysmal Nocturnal Hemoglobinuria:



PNH - is an acquired stem cell defect.

PIGA gene → GPI anchor  
↓ defect

↓ binds to

{  
• Decay activating factor DAF  
• Homologous factor HFA  
• MIRL  
} inhibitor of Complement activation

↓ in defect

Complement mediated membrane damage

During sleep →  $CO_2$  is retained → ↓ pH →  $H_2O$  activation ↑  
Early morning ↑ cell destruction

PNH

- Pancytopenia
- Thrombosis

Screening test :- acid test (best screening test) - mild acid is added  
Sucrose Hemolysis Test (sucrose is an osmotic agent)

Confirmatory test :- Flow cytometry - Absence of

{  
CD55 - DAF  
CD59 - MIRL - more specific  
}

[R] :- C5 inhibitor :- Eculizumab

Haptoglobin ↓ in any intravascular hemolysis

↳ Suicide protein

Haptoglobin → binds to free Hb (if disemic Hb is filtered in glomerulus  
↓  
PCT is damaged)

Engulfed by Macrophage. (Iron can't cross membrane)

Haptoglobin is destroyed. Hb is recycled.



Suspected Transfusion Mismatch → Start Mannitol

↓ diuresis

Pushes the Hb through the nephron.

Haemoglobin Abnormalities

Chr. 16 →  $\alpha$

Chr. 11 →  $\beta$

HbA<sub>1</sub> -  $\alpha_2\beta_2$  - 96-98%

HbA<sub>2</sub> -  $\alpha_2\beta_2$  - 1-3%

HbF -  $\alpha_2\gamma_2$  - <2%

$\alpha$ -thalassaemia

$\beta$ -thalassaemia

↑ HbF

Hydrops fetalis

Neonatal complications/anaemia

stable { HbH -  $\beta_4$   
Bart's -  $\gamma_4$  (fetus, neonates)

$\alpha_4$  - unstable → hemolyse

Gene deletion

Point mutation

$\alpha$ -thalassaemia

↓

4 alleles for  $\alpha$ .

4 → ++ / ++ →  $\alpha$

3 → ++ / +- → silent carrier

2 → +- / +- → Thalassaemia minor

1 → +- / -- → Thal major (HbA is present in small amt., not zero)

0 → -- / -- → Hydrops fetalis



$\alpha$ -thal major  $\therefore$  • Neonatal anaemia

- Transfusion dependant
- Thal. facies
- Splenomegaly
- Target cells
- $HbH^{++}$

$\beta$ -thalassaemia:- Point mutation

$\beta$  ————— ( $\beta$  chain)  
 $\beta^+$  ————— (partial  $\beta$  chain)  
 $\beta^0$  ————— (no  $\beta$  chain)

$\left\{ \begin{array}{l} \beta^0/\beta^0 \\ \beta^+/ \beta^0 \end{array} \right\}$  Thalassaemia major  $\left\{ \begin{array}{l} \beta^+/ \beta^+ \rightarrow \text{Thalassaemia intermedia} \\ \beta^0/\beta \end{array} \right\}$  Thalassaemia minor

|                              | HbA                                     | HbA <sub>2</sub> | HbF          |
|------------------------------|-----------------------------------------|------------------|--------------|
| 1. Thal major. $\rightarrow$ | 0-10                                    | 4-10             | 80-96        |
| 2. Thal int. $\rightarrow$   | 0-30                                    | 4-10             | 6-100        |
| 3. Thal minor. $\rightarrow$ | 85-95                                   | 4-8              | 1-5          |
| 4. HP HF                     | $\uparrow$ HbA <sub>2</sub> is not seen | 20-40            | $\downarrow$ |

$\gamma$ - $\beta$  switch is @ 30w  
 $\downarrow$   
 in HP HF there is defective switch

in all the above 4 conditions HbF is  $\uparrow$  in adulthood.

$\beta$ thalassaemia - generally symptomatic.

HP HF - generally asymptomatic.

NESTROET: Naked Eye Single tube Red cell Osmotic Fragility test

OE ↓ → Thalassemia

HPHbF

Severe IDA

NESTROET +  $\xrightarrow{HbA_2}$  (N) in HPHbF  
↑ in 1st trimester - Thalassemia

♂  $HbA_2 \uparrow \uparrow$       ♀  $HbA_2 \uparrow \uparrow$

25% - T. major

50% - T. minor

25% - (N)

### Sickle Cell Anaemia

Mis. sense Mutation →  $\beta$ -chain → 6<sup>th</sup> position

↓  
Glutamine is replaced by Valine

SCA

$\beta_0/\beta_0$

SCT

$\beta_0/\beta$

$HbA/HbS = 0/100$

$HbA/HbS = 60:40$

$HbS > 80\%$

$HbA > 60\%$

$HbF 2-25\%$

$HbS < 40\%$

- Sickling - Vaso-occlusive episode

Sickling doesn't occur

Hand foot Syndrome

(HbA prevents sickling - prevents polymer)

Pulm Infarct

Isolated papillary necrosis

Stroke

Hematuria

Spleen Sequestration crisis

Apoptosis



[R]: Hydranurea  $\rightarrow$   $\uparrow$  HbF



prevents the polymerisation  
of Hbs.

Reduction of sickling episodes.

Protected against *P. falciparum*

SCT ♀

SCT ♂

25% SCT  $\rightarrow$  terminal preg

50% SCT

25% (M)

### Myeloproliferative Disorders

- Polycythemia Vera
- Essential Thrombocythemia
- CMV
- Primary Myelofibrosis

Acute leukemia

Splenomegaly  $\uparrow$  (ET - mild to moderate)

### Polycythemia Vera

WHO criteria

Major

Minor

- HCT  $\uparrow\uparrow$
- JAK-2B mutations

• Erythropoietin  $\downarrow$

• BM Bx  $\rightarrow$  Trilineage proliferation

C/Fs:

- \* 4H
  - $\rightarrow$  Hyperviscosity  $\rightarrow$  thrombosis
  - $\rightarrow$  Hypertension  $\rightarrow$  renal acid stones
  - $\rightarrow$  Histamine  $\uparrow$   $\rightarrow$  Aquagenic pruritis  $\rightarrow$  post bathing itching
  - $\rightarrow$  Hypergastrinemia  $\rightarrow$  PUD

• Intra - Erythrocytosis

- \* Massive Splenomegaly
- \* No  $\uparrow$  risk of infection

Lab :- Serum  $B_{12}$  ↑↑,  $B_{12}$  binding proteins ↑

[Rx] :- → Hydration +

→ Phlebotomy → ↓ Hct  
Induce iron deficiency anaemia.

→ IFN  $\alpha$

→ Radiolabelled  $P^{32}$  (not advised) → leukaemogenic

→ Roxithinib → ↓ the spleen size

### Essential thrombocythosis

- Plt. count  $> 400,000 / mm^3$

PC  $> 400,000$  also seen in

- HCT (H)

Iron def<sup>n</sup>

- JAK-2 mutation 50%

Polycythemia Vera.

S/E :- Erythromelalgia - Redness + Pain in the digits  
Thrombosis

Bleeding - Acquired vWF disease (vWD)

Splenomegaly - mild/moderate

[Rx]

• Aspirin

• Hydroxyurea (D.O.C)

• IFN  $\alpha$

• Anagrelide (PDEI)

## CML

- Fullness in abdomen - Splenomegaly
- Bone pain - sternal tenderness
- WBC infections

TLC  $> 25,000/\mu\text{l}$  @ diagnosis may be  $> 50,000/\mu\text{l}$

## CML

## for leukemoid rxn

## LAL score

Eosinophilia

-

ALP granule

100/100 norm

Basophilia

-

↓

①

$B_{12} \uparrow \uparrow$

-

score  $\leq 70$

LAP ↓

-

↓

• CML

• PMN

FISH - t(9,22) - 95% cases are detected

• Apathic

PCR - BCR-ABL fusion may be seen in the absence of t(9,22)

• Hereditary

lymphoprol

t(9,22) → Tyrosine kinase activated

abl

bcr

Proliferation ↑

DNA repair system ↓

2-5 yrs

Leukemia

Chronic phase: % blasts  $< 10\%$

Accelerated phase: 10-19% blasts, plt count  $< 1 \text{ lakh}$ ,  $> 10 \text{ lakh}$   
Spleen size ↑  
Basophilia  $> 20\%$



Blast phase :- Blasts  $\geq 20\%$  (may convert to ALL or AML)

Prognosis :-

Sokal's  
(American)

HASEFORD (better)  
(Euro)

\* Age

\* Age

\* % Blasts

\* % Blasts

\* PC

\* PC

\* Spleen size

\* Spleen size

\* % eosinophils

\* % Basophils

Rx :-

CML

Bone Marrow

Chemotherapy (R.O.C)

Transplant

Tyrosine Kinase inhibitors

- Curative

10-20% mortality

→ rejection

→ GVH disease

Imatinib

Nilotinib

Dasatinib

→ Ponatinib → Omacetarone

Imatinib :- Competitive ATP binding site inhibitor

## Primary Myelofibrosis

Teardrop Macrocytosis

Massive Splenomegaly

Bone marrow aspiration - Dry tap

[R] :- Rosalitinib (for reducing spleen size)

|                   |   |                      |             |   |                          |
|-------------------|---|----------------------|-------------|---|--------------------------|
| CD 1              | → | Histiocytes          | * CD 11     | - | Leucocyte                |
| CD 3 ✓ pan T cell |   |                      |             |   |                          |
| CD 4              |   | [T cell]             | * CD 15, 30 | - | Reed Sternberg           |
| CD 5              |   | CD 2, 7, 9           | * CD 34     | - | Haematopoietic Stem cell |
| CD 19             |   | immature T cells     | * CD 38     |   | Plasma cell              |
| CD 20             |   |                      | * CD 45 RO  |   | Memory cell              |
| CD 21 EBV         |   | [B cell]             | * CD 16/56  |   | NK cell                  |
| CD 22             |   |                      | * CD 95     |   | Apoptosis                |
| CD 23             |   |                      | * CD 19     |   | Monocyte                 |
| CD 10             | → | Calla                | * CD 117    |   | Myeloid CD 33            |
|                   |   | (Common ALL antigen) |             |   | GIST → Best DOG-1        |

|                       |   |                                       |
|-----------------------|---|---------------------------------------|
| ALL                   | } | Bone Marrow failure                   |
| AML                   |   | Anaemia - fatigue                     |
| Biphenotypic leukemia |   | WBC - infections                      |
| Undifferentiated      |   | Platelets - Bleeding, petechiae       |
|                       |   | Leucostasis - vaso-occlusive episodes |
|                       |   | Hepatosplenomegaly, LND               |
|                       |   | Tumor lysis syndrome - ↑ uricemia     |

Interstitial nephritis

↑  $PO_4$  ↓  $Ca^{++}$

↑  $K^+$

## ALL

## AML

Children usually

Elderly (peak age > 65yrs)

L<sub>1</sub> L<sub>2</sub> L<sub>3</sub>  
70-25% L<sub>2</sub> Mature B cell  
Null cell Burkitt's  
Pre B cell (muc. ALL)  
T cell

M<sub>0</sub> - Minimally differentiated  
M<sub>1</sub> Myeloblastic (not diff)  
M<sub>2</sub> Myeloblastic (diff)  
M<sub>3</sub> PMN  
M<sub>4</sub> Myelomonocytic  
M<sub>5</sub> Monocytic  
M<sub>6</sub> Erythroleukemia → MEO+  
M<sub>7</sub> Megakaryocytic → PAS+

Down's m-c assoc. - ALL  
Mediastinal mass - ALL

PAS ⊕ 70% of pts  
TdT ⊕ L<sub>1</sub>, L<sub>2</sub>  
⊖ L<sub>3</sub>

Soft tissue Chloasma: M<sub>2</sub>, M<sub>4</sub>, M<sub>5</sub>  
DIC: M<sub>3</sub>  
Gum involvement: M<sub>4</sub>, M<sub>5</sub>  
Down's: M<sub>7</sub>

CD<sub>10</sub> - CALLA

CD<sub>19</sub>, 20, 22, 23 - B cell markers

CD<sub>3</sub> - T cell marker

CD<sub>79</sub> - B cell

Stains: MPO, SBA, NSE

Leukemia: M<sub>2</sub>-4 M<sub>5</sub>-5

CD<sub>33</sub>, 117 - myeloid markers

CD<sub>13</sub>, 14 - monocyte, macrophage

C<sub>8</sub> - leucocyte

Markers of both AML & ALL

Biphenotypic Leukemia

Mixed Phenotypic Acute Leukemia (MPAL)

Undifferentiated: No expression of CD<sub>3</sub>, MPO, CD<sub>22</sub>, CD<sub>79a</sub>,  
absence of strong exp. of CD<sub>19</sub>



# Prognosis

ALL

Good



- Age  $\geq 2$  < 8 yrs.
- TLC  $\geq 500$   
 $< 50,000$

• Hyperploidy

• t(12, 21)

• females

Bad



- < 1 yr > 10 yrs.
- $< 500$   
 $> 50,000$   
 $> 100,000$  (B cell)

• Aneuploidy

• t(8, 14)

t(4, 11)

t(9, 22)

• Genotype / CNS tr.

• Presence of peripheral blasts after 2 wks of chemo.

• males

## AML

Good

- t(8, 21) } t these translocations
- t(15, 17) } ever 2 blasts < 20%
- t(16, 10) } A is AML
- inv. 16

Bad

- Monosomy 5
- Monosomy 7
- trisomy 8

### MGUS

### Multiple Myeloma

### Waldenström's

Monoclonal gammopathy of uncertain significance  
(Most common)

- Pre malignant
- Bone marrow

Plasma cells <10%

IgG $\uparrow$ /IgA $\uparrow$

• Plasma cells >10%

(IgG $\uparrow$ /IgA $\uparrow$ )

Plasma cells

IgM $\uparrow$

Hyperviscosity

Sluggish blood flow in aorta

Blurring of vision

• M-spike <3g/dl.

• No OAF release

• No Bone lytic lesion

• Ca $^{++}$  (N)

• No Renal failure

• Hb levels (N)

• Neuropathy

• OAF $\uparrow$   $\rightarrow$  RANK-L

lytic lesions

Bone pains

$\uparrow$  Ca $^{++}$

$\rightarrow$  Renal failure  $\rightarrow$   $\uparrow$  Ca $^{++}$

(due to  $\uparrow$  Ca $^{++}$ )

• Anaemia

• HTN

No OAF, No lytic lesion

Ca $^{++}$  (N)

No organomegaly

[R] - no treatment

except for

neuropathy

C - Calcium $\uparrow$

R - Renal failure

A - Anaemia (m.c. finding)

B - Bone pain (case presenting complaint)

[R]: Fludarabine } Plasmapheresis  
Rituximab }  
Bendamustine }  $\downarrow$  1st

• M.c. cause of death - infections

\* Amyloidosis - AL

\* Prognosis - most imp.

$\downarrow$   
A $_2$  microglobulin

\* Very high ESR

$\downarrow$   
ESR is due to

asymmetric charges on RBC

(recessive charges)

Polythemia, BCR  $\rightarrow$  ESR  $\downarrow$

CCF

Afibrinogenemia  $\rightarrow$  ESR - zero

[R]: Autologous Stem cell therapy

or

• Melphalan Based regimen  
(70yrs)

Autologous SCT

CBF  $\rightarrow$  collect stem cells

{ lenalidomide  
Dexamethasone  
Bortezomib }

Immunosuppressants - Thalidomide  
Carfilzomib

### Smoldering MM

Plasma cells  $> 10\%$



$IgG/IgA > 3gm/dl$

CRAB  $\ominus$

### MGUS

Plasma cells  $< 10\%$



$IgG/IgA < 3gm/dl$

CRAB  $\ominus$

### Multiple Myeloma

→ M-spike

→ Monoclonal plasma cells  $> 10\%$

→ CRAB lesions +ve

→ Peripheral smears

↓  
Plasma cells  $< 20\%$

### Plasma Cell Leukemia

→ M-spike

→ plasma cells  $> 10\%$

→ CRAB lesions +ve

→ Plasma cells  $> 20\%$

### Melphalan based regimens

MP

Melphalan

Prednisolone

MPT

Melphalan

Prednisolone

Thalidomide

Heavy chain gammopathy:- Very high serum IgA  
Lymphomas of the GIT (abd. mass)



## Bleeding Disorder

### Platelets

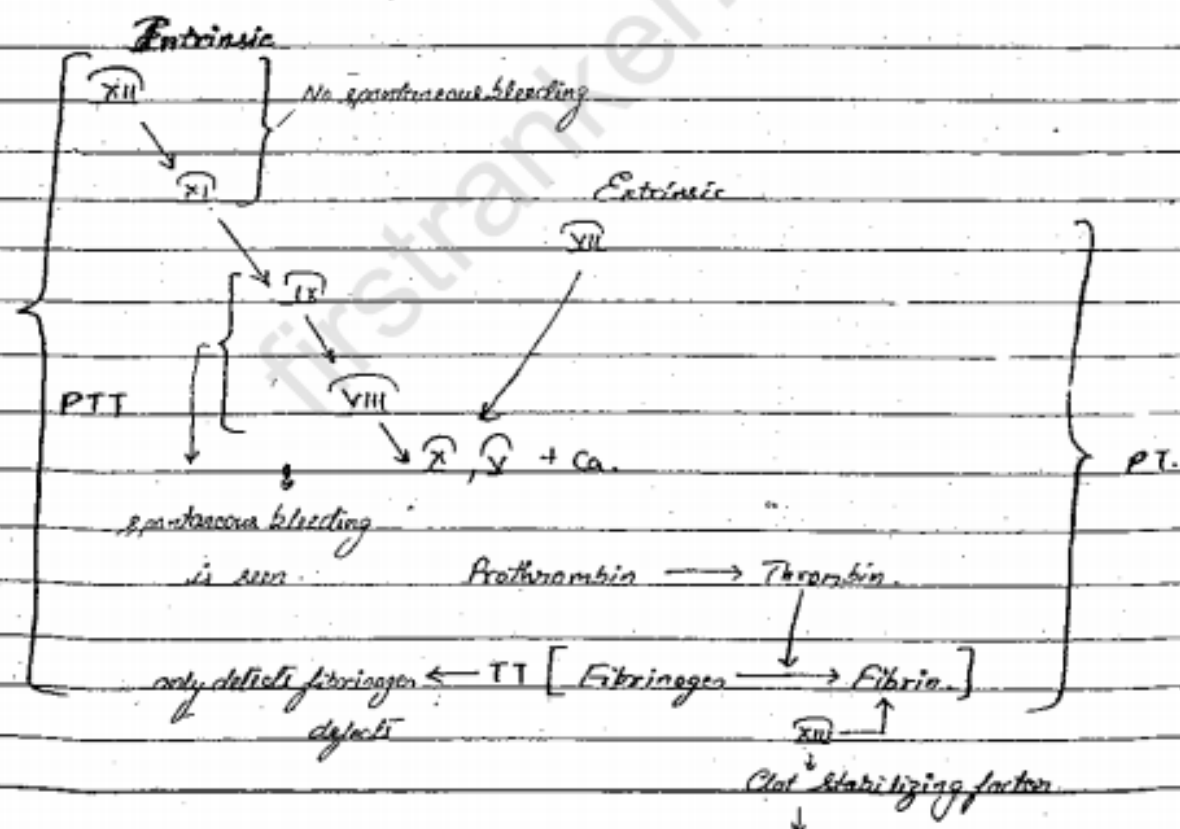
- Petechiae
- Purpura
- Mucosal bleeding
  - Gum bleeding
  - Menorrhagia

• Bleeding time ↑

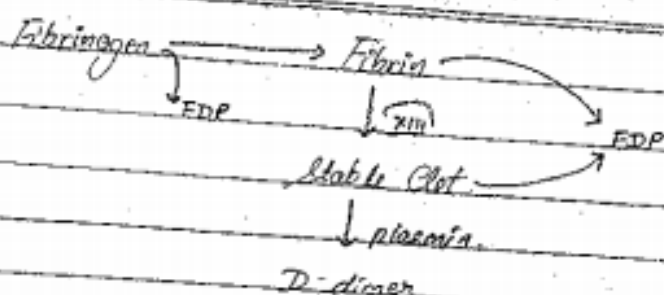
### Coagulation

- Patch of Blood - Haematoma  
↓  
Tough
- Haemarthrosis
- Delayed umbilical stump
  - Factor XII deficiency (m.c.)
  - Fibrinogen
  - Factor V

• PT, PTT ↑



deficiency → PT (M) PTT (M) BT (M) TT (M)  
detected by → Urea Clot lysis test



EDP is the most sensitive } for hypercoagulopathy  
D-dimer is most specific }

Protein C : Doesn't allow the activation of factor V.

factor V mutation leads to mutations in protein C inherited hypercoagulopathy  
↓  
protein C can't act (protein C resistance) \* m.c. inherited bleeding disorder is VWD.  
↓  
hypercoagulopathy

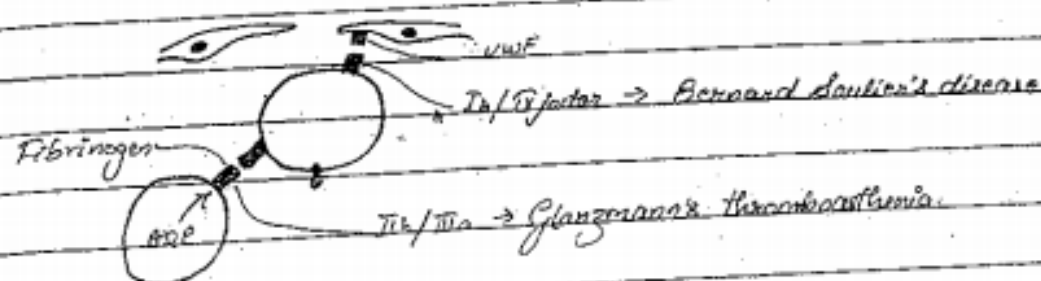
Antithrombin III :- mainly acts on factor X (inhibits)

Heparin concentrates ATIII & factor X together

↓  
So inhibits the activation of factor X.

Heparin resistance - Antithrombin III deficiency

# Platelet disorders :-



Acq thrombasthenia → Renal failure - Uremia.

↓  
platelet function defect

VWD

BS

GA

Bernard Soulier's

Glanzmann's

AD

AR

AR

PT - N

PT (N)

PT (N)

PTT - N/t

(N)

(N)

vWf ↓

(N)

(N)

(-)

Thrombocytopenia

Megakaryocytosis

(-)

## Ristocetin test

abn, + vWF → (N)

abn, + vWF - abn

(N)

## ADP fibrinogen test

(N) aggregation of plt

(N)

failure of aggregation



## Congenital Hemophilia

\* Inherited XLR

Males

\* Factor VIII deficiency

(N) 50-150 u/dl

\* Hematoma +

Bone +

Muscle +

\* Hemarthrosis +

(in c. joint knee joint)

in children ankle joint

\* PT (N)

PTT prolonged

Mixed sample test

1:1 → PTT → (N)

\* Normal values :- AT 7 min

PT 12.7 - 15.4 sec

PTT 26.3 - 39.4 sec

VIII 50-150 u/dl

## Acquired Hemophilia

\* Males = females

\* Abs against factor VIII

+

+

+

\*

joints are usually spared  
hemarthrosis is rare

\*

PT (N)

PTT ↑

1:1 → PTT → ↑

Asymptomatic patient? ↑ PTT

1<sup>st</sup> lupus anticoagulant (m.c)

2<sup>nd</sup> factor VIII deficiency

TTP, Aplastic anemia → do not have Splenomegaly

TTP

Child

Fever

TTP is a diagnosis of exclusion

Petechiae / Purpura

PCV ↓

Megakaryocytosis

q: → Don't administer platelets (↑ Ab production)

→ Steroids

→ Plazmas (or IgG antibodies)

Rhogam  $\rightarrow$  Abs against Rh antigens of RBCs

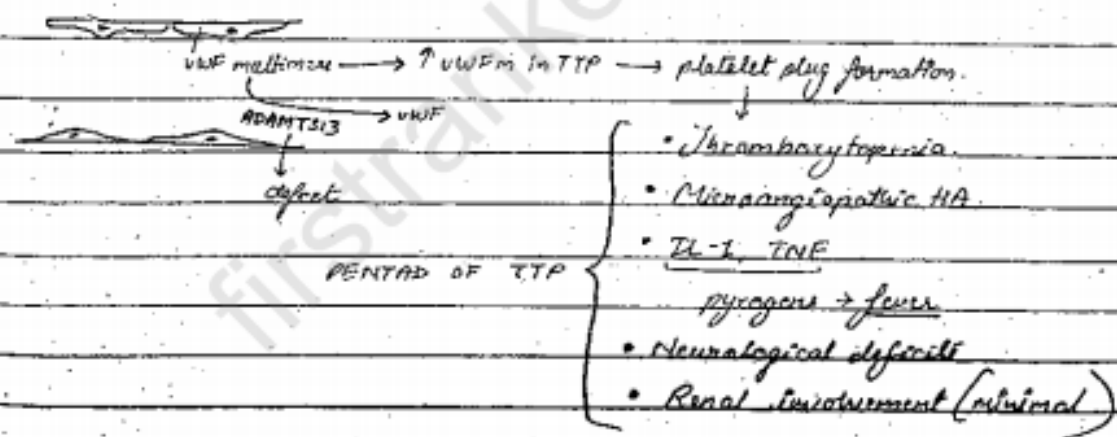
The Fc receptors are solubilised

No Ab reaction against platelets

- Azathioprine / Mycophenolate
- Plasmapheresis
- IV IgG
- Splenectomy (must be vaccinated against capsulated org. before hand)

(RBC can only be given before Splenectomy)

## TTP



• Coombs' -ve anaemia

• PT / PTT / TT = (N)

• Complement is unaffected  $\rightarrow$  C3 levels (N)

HUS: • Diarrhoea  $\rightarrow$  E. coli  $\rightarrow$  m.c. cause (Shiga like toxin)

• Drugs (Bleomycin / Mitomycin)

Venocytotoxin  
 $\downarrow$   
damages Endothelium

Multiple plt. plug formation

- Thrombocytopenia
- MAHA
- $\text{Ca}$  levels  $\downarrow$  Complement is involved
- Renal disease  $++$
- Neuro deficits minimal
- Fever is absent
- Coomb's test is -ve
- PT/APTT/TT - (N)

Rx: HUS, TTP

- Plasma pheresis
- Exchange transfusion R.c.c.
- Platelet transfusion can be given
- Treat the underlying cause in HUS

Micro-angiopathic Hemolytic Anemia - RBC destruction in small vessels

- Not seen in heart valves (prosthetic)



## NEUROLOGY

### Headache

**✱ Tension headache**

**✱ Migraine**

**✱ Cluster**

✓ E > M

✓ E > M

✓ M > F

✓ up - usually

✓ Band like, compressive

✓ up

✓ Throbbing

✓ Bifrontal

✓ Deep piercing pain

✓ m.c. primary headache

✓ Excruciating pain

✓ Retro-orbital

Nausea, vomiting

Feature less headache

Photophobia

Phonophobia

Osmophobia

Movement worsens

1 hr headache

Normal

✓ up exacerbation

may be present

✓ up exacerbation

✓ up congestion of conjunctiva

✓ 1 episode/day

✓ No neck stiffness

✓ Aura + (classical)

✱ Paracetamol

✱ Triptans (p.o.)

✓ NSAIDs (starting of headache)

✓ NSAIDs

✓ 100% o

✓ Triptans

✓ TCA

5HT<sub>1A</sub> agonists

✱ Propranolol

Prophylaxis - Verapamil

✓ Ergotamine

Better lifestyle

Steroids

✓ Caffeine

Biofeedback

Methysergide

✓ Severe headache in chronic migraine

Relaxation technique

Lithium

✓ Intranasal infusion

Prophylaxis → β-blockers (Apropranolol, Metoprolol)

✓ Valproate

✓ Gabapentin

✓ Amitriptyline

✓ Clonidine (intranasal)

✓ Intermittent / infrequent migraine - Botulinum toxin injection

(68)

✗ Should not be used in migraine:-

- Verapamil
- SSRI
- Clonidine

Cluster headache

Chronic paroxysmal  
Hemicrania

SUNCT

Short lasting w/o Neurologic  
assoc & Congestion & tearing

✓ w/o  
✓ Autonomic features

✓ w/o  
✓ +

(w/o)  
+

✓ Deep piercing retro orbital

✓ +

+

✓ Responds to Triptans (++)

⊖

⊖

⊖

✓ Indomethacin (++)

⊖

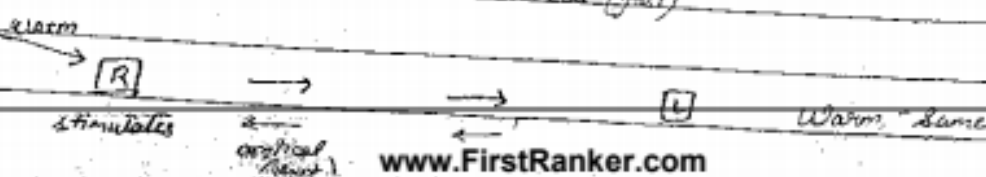
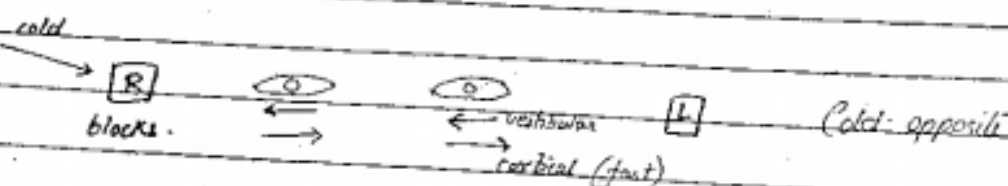
✓ Lamotrigine ⊕

✓ Valproate ⊕

Caloric Stimulation Test

Water Temperature  $\rightarrow 37^{\circ}\text{C} \pm 2^{\circ}\text{C}$  i.e.  $30^{\circ}\text{C}$  &  $44^{\circ}\text{C}$

Vestibular apparatus stimulation pushes the eye in opposite direction



Direction of nystagmus is according to the fast component

✓ B/L: cold water stimulation → Upbeating nystagmus  
 ✓ R/L: warm water → Downbeating nystagmus

### Vertigo



#### BPPV

Benign Paroxysmal Positional Vertigo → long lasting vertigo  
 mine-house

- Post-L.C. Canal
- Nystagmus - rotatory upbeat
- Vertigo - minutes
- Triggered by change in position

#### Meniere's

→ long lasting vertigo  
 mine-house

- SNHL
- Tinnitus
- Diplopia
- Pain in the ear
- Fullness in the ear

[Rx]: Diuretics

Triamterene + Thiazide

- inj. Gentamicin
- inj. Steroids
- In decompression of Endolymphatic sac

#### Vestibular neuritis/labyrinthitis

- m.c. -
- Viral infection
- Fever, cold, sore throat
- Vertigo - mine-house
- Nystagmus - Horizontal

[Rx]: Head impulse test

[Rx]: Antihistamines

(useful long term)

[Rx]: Dix Hallpike Test

[Rx]: Epley's Manoeuvres

### Aphasia

Naming is the first thing to be affected. -

Comprehension

Repetition

Speech fluency

Wernicke's →

⊖

⊖

↑

Broca's →

N

⊖

↓

Conduction →

⊕

⊖

(N)

TCS →

⊖

(H)

(N)

TCA →

(N)

(N)

↓

Isolation →

⊖

(N)

↓

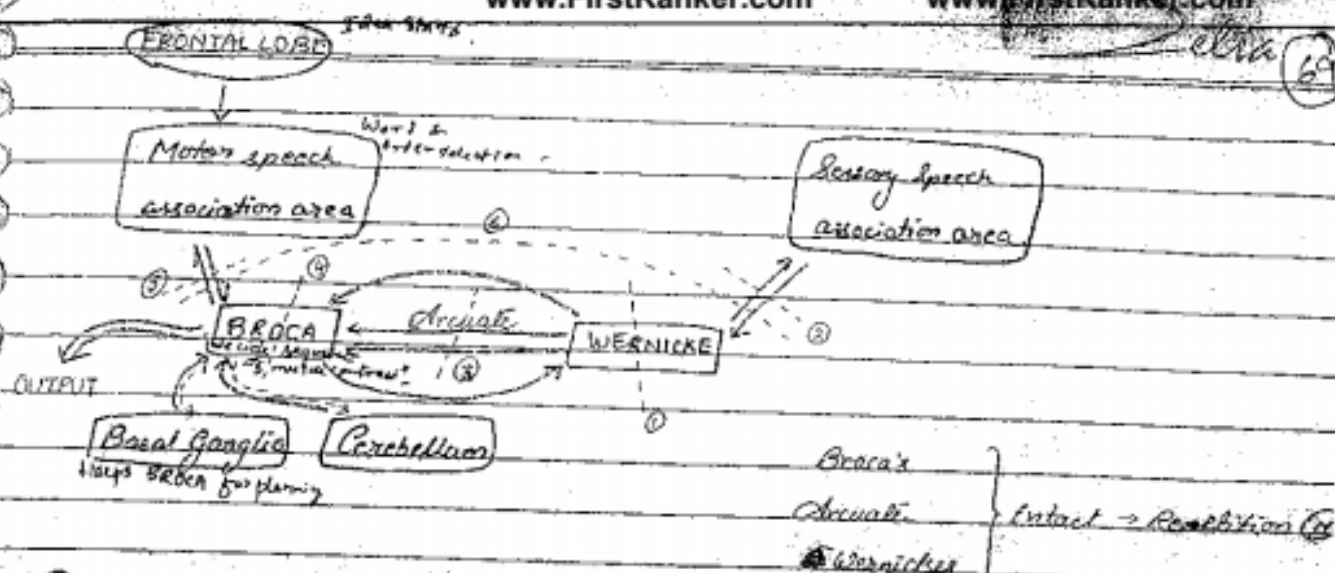
Global →

⊖

⊖

↓





# ① Wernicke's aphasia:-

Repetition ⊖

Comprehension ⊖

Word output ↑

Speech fluency ↑

Neologism ⊕

Tangential aphasia

Meaning is affected (paraphasia)

Wernicke's has some inhibitory control on Broca's. In lesion of Wernicke's, that control is lost.

# ② Trans cortical sensory aphasia

# ③ Conduction aphasia

Repetition = N

Comprehension = ⊖

Word output ⊖

Speech fluency ⊖

Repetition ⊖

Comprehension ⊖

Word output ⊖

Speech fluency ⊖

# ④ Broca's

Repetition = ⊖

Comprehension = N

Word output ↓

Speech fluency ↓

# ⑤ Trans cortical Motor

Repetition = N

Comprehension = N

Word output ↓

Speech fluency ↓

⑥ Mixed transcortical / Isolation Aphasia.

Repetition (N)

Comprehension (-)

Word output ↓

Speech fluency ↓

Echolalia → He can only repeat, can't understand

⑦ Global aphasia <sup>Broca Wernicke.</sup>

Seen in MCA infarct -

Repetition (-)

Comprehension (-)

Word output ↓

Speech fluency ↓

⑧ Anomalous aphasia (m.c. aphasia)

→ Post concussion.

→ Post trauma.

→ Stroke.

Repetition (+)

Comprehension (+)

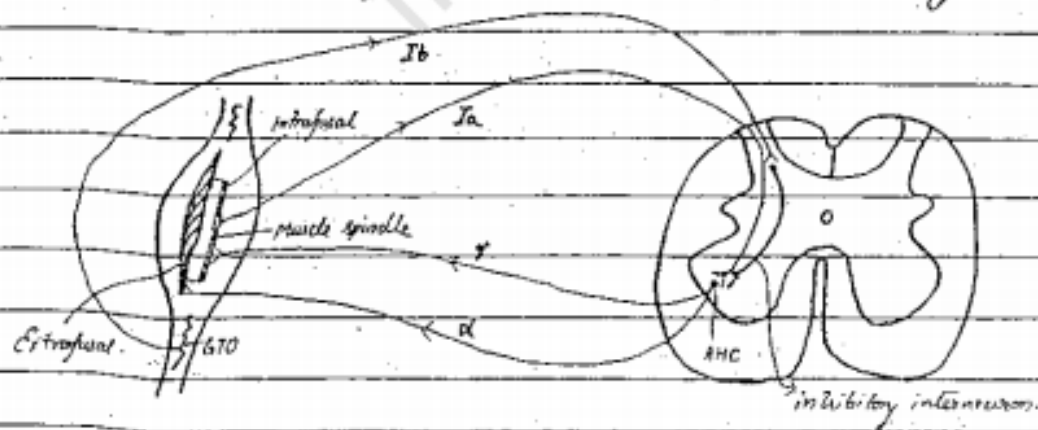
Word output (N)

Speech fluency (N)

Paraphasia

M.C. aphasia

\* In pure word deafness or /and pure alexia → Hearing is preserved.



Deep tendon reflexes :- Muscle spindles are involved.  
GTO is not involved.  
Monosynaptic reflex.

Golgi tendon organ - protective in nature.  
if there is impending risk of muscle/locomotor damage  
the GTO inhibits the AHC via the inhibitory interneuron  
which relaxes the muscle.

| LMN                                                                                                                                          | LMN                                                                                                                                                                                                    |
|----------------------------------------------------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| <ul style="list-style-type: none"> <li>• Tone ↑</li> <li>• Spastic</li> <li>• DTR ↑</li> <li>• No wasting - due to trophic effect</li> </ul> | <ul style="list-style-type: none"> <li>• Tone ↓, flaccid</li> <li>• DTR ↓/absent</li> <li>• Wasting is present</li> <li>• Fasciculation (visible)</li> <li>• Fibrillation (only recordable)</li> </ul> |

Flaccid weakness

| AHC disease       | Neuropathy                 | Myopathy                                   |
|-------------------|----------------------------|--------------------------------------------|
| Proximal > Distal | Distal weakness > Proximal | Proximal weakness > Distal                 |
|                   | Buttoning of shirt         | "Hair chair, stair"                        |
|                   | Mixing of food             |                                            |
| Sensory ⊖         | Sensory effects ⊕          | No sensory effects                         |
| DTR - Abs         | DTR - Abs                  | DTR - N/A                                  |
| CK - N/A          | CK - N/A                   | CK ↑↑ 25 times ⊕<br>Normal is <300 (units) |



**(\*) Dystrophinopathies**

✓ **DMD**

(XLR)

✓ Males are affected

✓ Dystrophin - Absent

✓ Hypertrophy of Calp

✓ Proximal > Distal

✓ Gower's sign (+)

✓ **Becker's**

(XLR)

-do-

↓

-do-

-do-

(+)

✓ Childhood disease

peak - 3-5 yrs

1st decade

Peak - 2nd/3rd decade

✓ Peak 3-8 yrs

> 8 yrs - Ck declines

✓ Peaks in 2nd decade

Ck declines in 3rd decade

✓ Unable to walk beyond 12 yrs

✓ Able to walk beyond 15 yrs

✓ Cardiomyopathy (+)

(+)

✓ Mental impairment (+)

(-)

✓ Cause of death is weakness of chest muscles → weakness of cough reflex → infection

✓ Rx - steroids

steroids

# Fascia Scapula Humeral

\* AD

- \* Fore muscles involved
- \* Shoulder "
- \* Dorsiflexors
- \* of foot "
- \* Winging of scapula

✓ ⊖

✓ No cardiac involvement

✓ Degener +

✓ Coat's disease +

# Myotonic Dystrophy

\* (AD)

Anticipation - Trinucleotide repeat

involved

?

✓ Distal > Proximal

✓ Myotonia ++

✓ Cardiac involvement

✓ Temporalis atrophy wasting } Hatched

✓ Frontal baldness } Jones

✓ Cataracts → fir tree appearance

✓ Hypogonadism

✓ Gynecomastia

✓ Mental Retardation

# Oculo-pharyngeal MD ∴

ocular muscle inv.

pharyngeal muscle inv.

axial myopathy

# Emery Dreifuss Syndrome ∴

UL - proximal

DL - Distal (proximal is spared in lower limb)

Contractures present

flexion → Elbow, ankle, knee

④ Mitochondrial myopathy: Only maternal inheritance.

B<sub>2</sub>: Trichome stain - Ragged bed fibres

✓ M.c. manifestation: Char. progressive external ophthalmoplegia

No diplopia (despite EOM involvement)

★ Kern's Sayre's Syndrome :-

Triad {

- Chronic progressive Ext. ophthalmoplegia
- Retinitis pigmentosa (atypical)
- Variable - 1) Conduction abn. of heart
- 2) Ataxia
- 3) CSF  $\rightarrow$   $\uparrow$  protein

→ In typical RP → peripheral vision is affected first - tunnel vision.

→ in atypical RP → central vision (fovea) is affected first

④ MELAS :- M.e. mitochondrial encephalopathy.

⑤ MERRE :- Mitochondrial Epilepsy & Ragged red fibres

★ Periostic Paralysis → Muscle B<sub>1</sub> ↓, CK ↑, transient problem  
↓  
Channelopathies.

Hypokalemia

Hyperkalemic

Frequency

### Cooling of muscles      ②

Myotonia ⊕

Channel affected (Ca)

Na

associated - thyrotoxicosis



## NMJ disease

- ✓ Transient / intermittent weakness
- ✓ EDM weakness
- ✓ Biopsy (H), CK (H)

### ⊗ Myasthenia Gravis

Post synaptic

Ab → Ach receptors } any  
Ab → Muscle kinase } one

Excretion - weakness ↑

DTR - (H)

Sf. EMG → jitter

Repetitive nerve stimulation

RNS - decremental

(because only post-synaptic nicotinic receptors are affected)

Thyroid hyperplasia / Thyroidoma

(Thyroid is not involved where

Ab against Muscle specific kinase is present)

### ⊗ Lambert Eaton Myasthenic Syndrome (LEMS)

Pre synaptic

Ab's → fast Ca channels

Plg type voltage gated

weakness ↓

Absent

-ve

incremental (due to priming of slow Ca channels)

Autonomic problems +

Small Cell Carcinoma lung

Ty Co

### Δ - Forearm abduction test

after prolonged abduction

axoi drops (Rivachon phenomena)

Pyridostigmine, steroids, IVIg

Plasmapheresis, Thymectomy

Thymectomy should not be done in • Child < 3yrs • Adult > 50yrs • Ab and MuSK

• Absent Ab-AChR

• Ocular MG

• EVE ↓

Myasthenia Gravis

Botulinum toxin

EOM +

IOM spread

-ve

EOM +

IOM + Pupil abnormality

Accommodation "

Blurring of vision

Autonomic ++

Neuropathy

Axonal

• B<sub>12</sub> deficiency

• DM • AIP

• Alcohol • Lead poisoning

• HIV

• Lyme's disease

Demyelination

• AIDP acute, i.e. demyelination polyradiculopathy

• CIDP chronic

AIDP → GBS

CIDP → Onset bulb appearance

in peripheral n/s

(also seen in Refsum's disease)

⊙ (not followed)

"Length rule" should be

fulfilled for axonal problem

↓  
Longest axon is affected first

Shorter axons are affected later

ABS Guillian Barre Syndrome

! Autoimmune. Abs against Myelin  $\rightarrow$  Anti-GM antibodies

Triggers :- *Campylobacter jejuni* → molecular mimicry

"Ascending acute flaccid paralysis"

Descending AOs - Miller Fischer Variant

Symmetric weakness

- Bladder is rarely involved (if at all it is transient)

CBF → Cell count is increased, albumin is 1

dehumus: cytological dissociation (no pleocytosis)

NCV :- F wave - indicates the integrity of the entire nerve and the AHC.

I-F gap  $\rightarrow$  I-F wave latency

↓ indicates slow conduction

demyelination disorder

H-wave / H-reflex  $\rightarrow$  is done to assess S<sub>1</sub> integrity

equivalent to axle jerk

absent in :- neuropathy.

BHC disease

Other features - Autonomic disorders  $\rightarrow$  HTN  $\rightarrow$   $\beta$ -CCB

Hypotension  $\rightarrow \beta$ -Dolbutamine

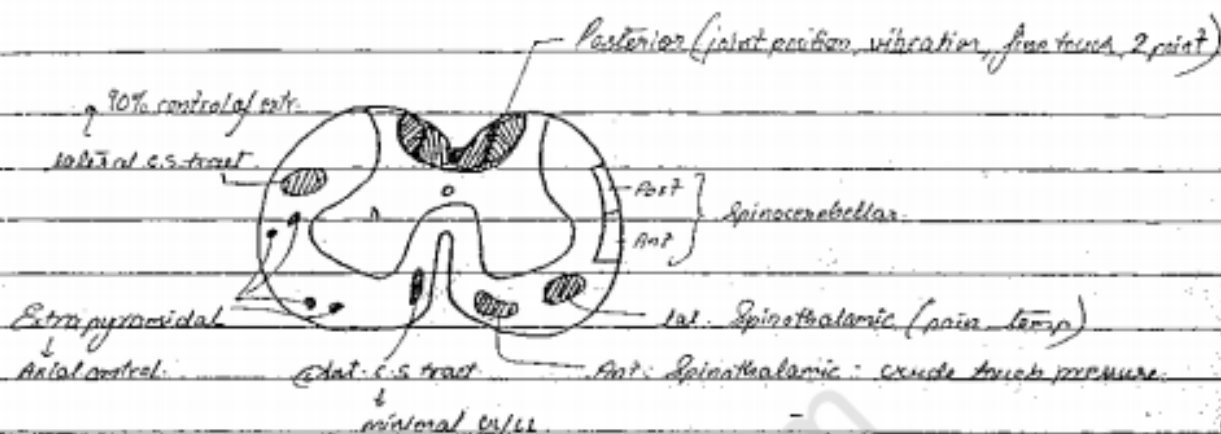
R :- Do not use Steroids

Typh & Plasmodiosis (Both not at the same time)

DNI prophylaxis

Protection from infections





Posterior Column :: Thickest myelinated fibres  
Fastest conducting  
Escape compressive lesions

Lat. Spinothalamic :: Crosses at the same level.  
lesion - loss on the opposite side

Only post. column h/l involvement - (Takes dorsals)

• Romberg's Test -

(Closed eyes swaying → PC problem)

Can't get his feet together → Cerebellar problem

• Pain is common.

• minor stimuli produce pain

UMN h/l + Posterior Column finding :: SACD  
B<sub>12</sub> deficiency

Only progressive UMN h/l → Motor neurone disease - primary lateral sclerosis

Mixed UMN + LMN → Amphotrophic lateral sclerosis ALS

(\*) Only LMN + muscle atrophy → Spina muscular atrophy  
(Kugel's atrophy)

(74)

(\*) Ant 2/3 of spinal cord lost,  $\frac{1}{2}$  sensory + CS loss → Ant. Spinal artery syndrome  
RC is normal

(\*) Cervical cord syndrome :- Trauma.  
Syringomyelia

(\*) Syringomyelia : M.C. site of syrinx formation - Cervical cord.

Cape like distribution Post. column is normal.

Crossing fibres of lat. Spinothalamic are compressed.

↓  
Dissociative anaesthesia of U/L  
(present 2/3 of the hand)

- Involvement of lateral horn → Homer's syndrome
- Involvement of ANS → flaccidity, LMN weakness of U/L
- Lower limb spasticity due to compression of cervical cord tract is rare

/ Syringomyelia is commonly associated 2 Arnold Chiari Malformation

(\*) Half of spinal cord involved - Brown Sequard Syndrome

- ↓
- Proprioceptive loss  $\frac{1}{2}$  U/L
  - Weakness ipsilateral
  - Pain + Temp. loss contralateral

IMC intramedullary tumor - Ependymoma (1<sup>st</sup>)  
Astrocytoma (2<sup>nd</sup>)

in children - Pilocytic astrocytoma (1<sup>st</sup>)

Mc extramedullary tumor - Metastasis (Most of the mets go to the thoracic vertebrae except prostate & ovary)

Mc site for primary vertebral tumor - thoracic

⊛ Extramedullary intradural - Neurofibroma - Meningioma  
• M>F • F > 90yrs  
• RD • juxta-tumoral osteosclerosis  
• Enlargement of foramina  
• Dumbbell shaped tumor  
• Contrast CT  
→ non-homogenous uptake → homogenous uptake

⊛ Intramedullary  
✓ Diffuse pain  
✓ Spinal spurring  
✓ late CSF tract involvement  
✓ CSF usually Normal

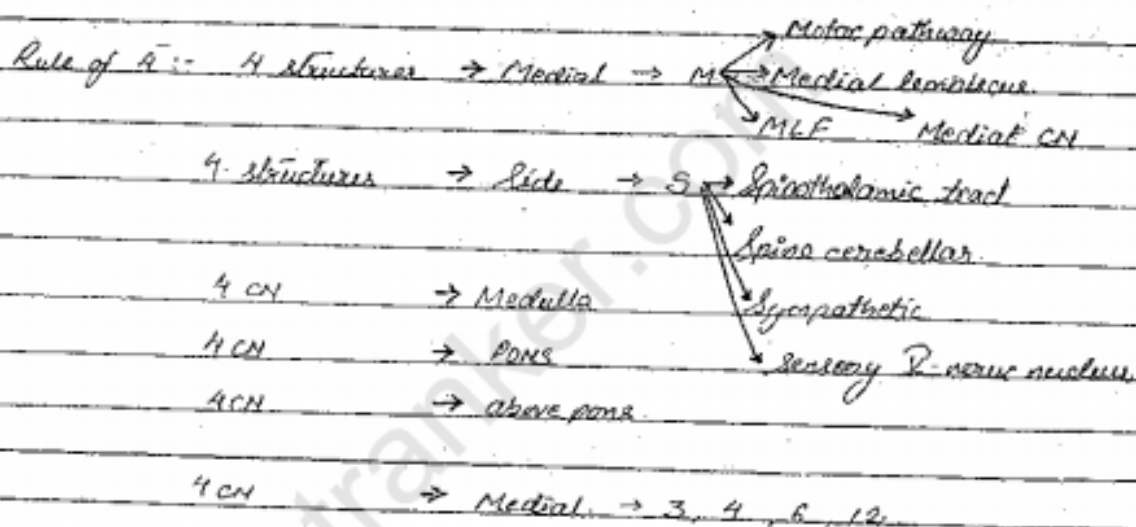
⊛ Extramedullary  
✓ Radiculopathy  
✓ Local sensory loss  
✓ Early spastic weakness  
✓ up. neuronostic  
✓ CSF at(N)



Cauda MedullarisCauda Equina

75

- B/L loss of sacral sensory elements
- loss of superficial reflexes (Ankle)
- loss of Bowel & Bladder
- Saddle anaesthesia
- Bowel ache
- Asymmetric muscle weakness
- Relative sparing of bowel & bladder

Brain Stem

lateral w/c :- 5, 7, 8, 9, 10, 11

↓  
loop around 6↓  
can be inv. in both medial &

lateral syndrome

Brainstem - C-S tract lesion - c/l weakness

Medial lemniscus lesion - c/l proprioceptive loss

MLF lesion - Internuclear ophthalmoplegia

Spinothalamic lesion :- c/l hemianaesthesia

Spino cerebellar lesion :- c/l ataxia

Sympathetic lesion :- Horner's Syndrome

Sensory V nerve lesion :- facial c/l hemianaesthesia

- Medulla -
- 9 → Sensory - PPW - gag reflex
  - 10 → palatal muscles - uvula is deviated to the opp side of the lesion
  - 11 → trapezius - SCM
  - 12 → muscles of tongue, deviated to same side in paralysis

- Pons → 5 → Sensory face
- 6 → lateral rectus
  - 7 → Face muscles
  - 8 → Assess hearing

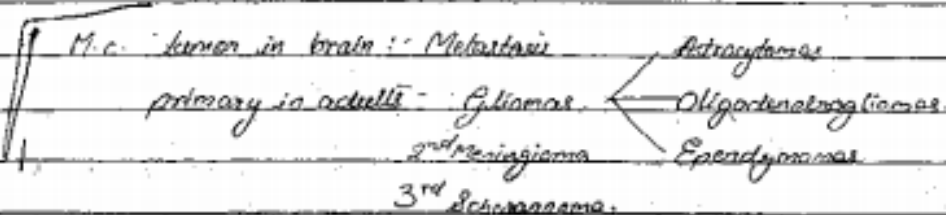
- Midbrain → 3 → ophthalmoplegia
- 4 → Superior oblique

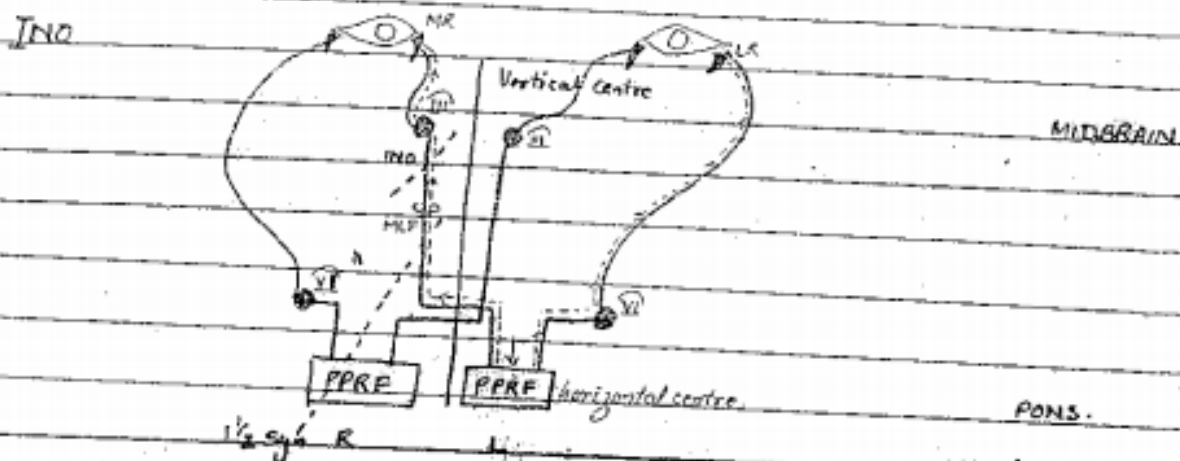
III<sup>rd</sup> n/c palsy - down and out eye + mydriasis

VI<sup>th</sup> n/c palsy - head is turned to the same side of the lesion

IV<sup>th</sup> n/c palsy - head is tilted (because so also rotates the eye)

PPRF → para pontine reticular formation





PPRF is connected to the nucleus through the

In lesions of MLF  $\rightarrow$  the affected side  $\rightarrow$  no adduction

The narrow side  $\rightarrow$  abduction

to normalise

myelogram of the abducted  
(normal side)

If convergence reflex is (+) :- MR is normal.

III Nerve nucleus is (N)

III nerve is normal.

Dancer's retraction Syndrome - muscle disease.

One and half Syndrome :- PPRF and MLF loss on one side.

Both adduction and abduction are lost on the i/l side.

Adduction is lost on the c/l side.

Convergence refers in (14)

B/P MCF loss :- A/P adduction loss on both sides

Abduction normal on both sides

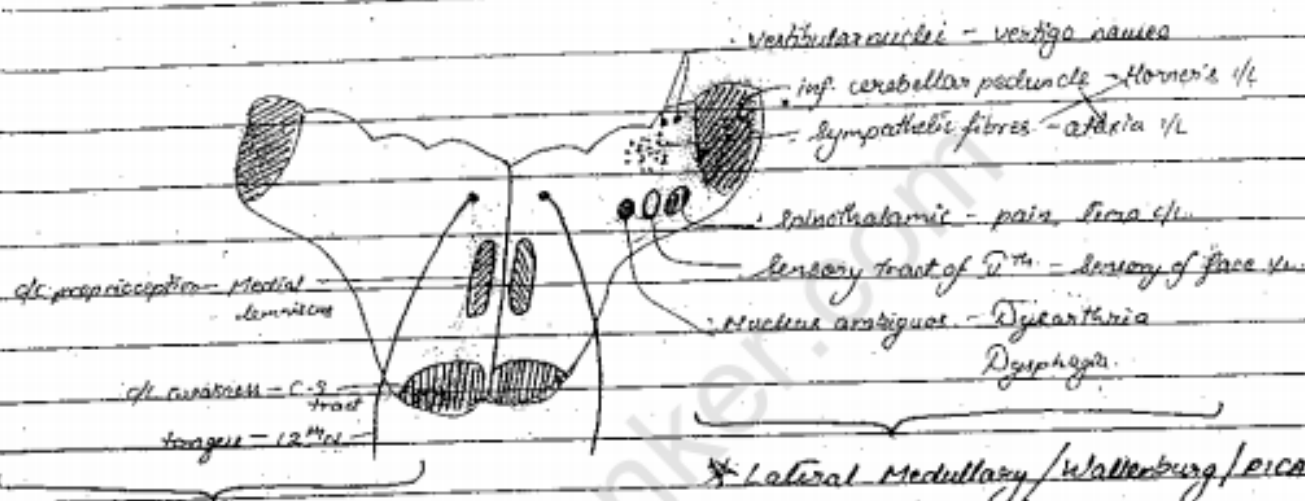
Seen In Multiple Sclerosis



$7^{th}$  nerve palsy +  $1\frac{1}{2}$  syndrome = 8 and half Syndrome

Medial Medullary Synd:- M.C. vessel  $\rightarrow$  Vertebral artery  $\rightarrow$  Ant. spinal (Medullary Branch)

Lateral Medullary Synd:- M.C. vessel  $\rightarrow$  PICA Vertebral  $\rightarrow$  PICA



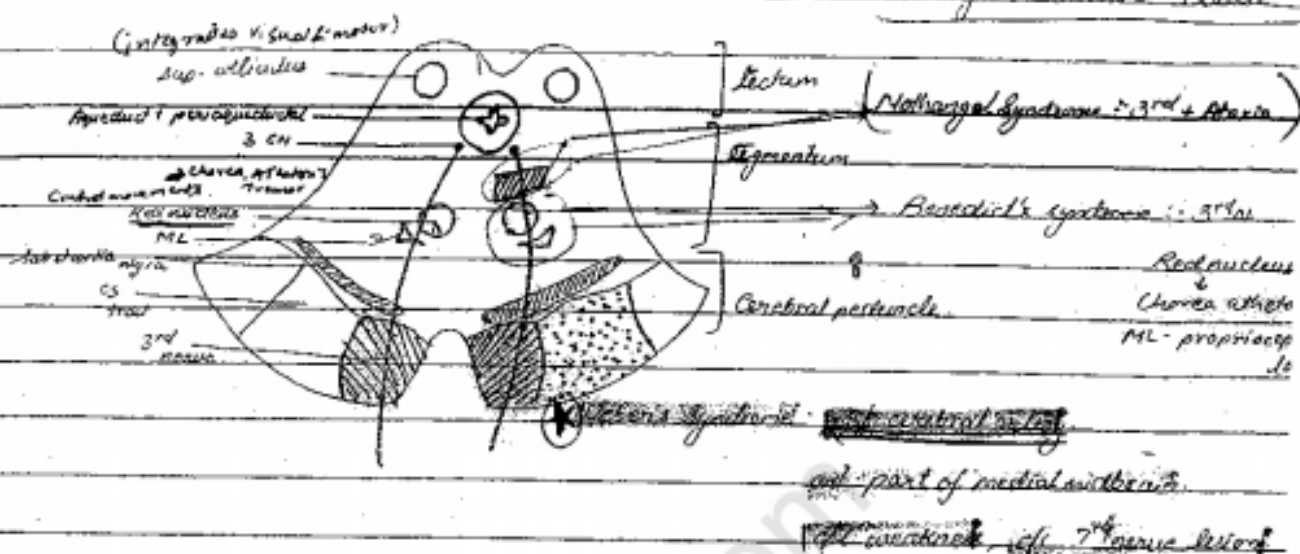
\* Medial Medullary Syndrome

\* Lateral Medullary/Wallerburg/PICA Syndrome

\*  $V^{th}$  with palsy + weakness (C.S.)  $\rightarrow$  Medial palsy - Millard Gubler Syndrome

\*  $V^{th}$  +  $VI^{th}$  + C.S. + sensory  $\rightarrow$  Foville Syndrome

Medial Midbrain Syndrome  $\rightarrow$  Weber Syndrome

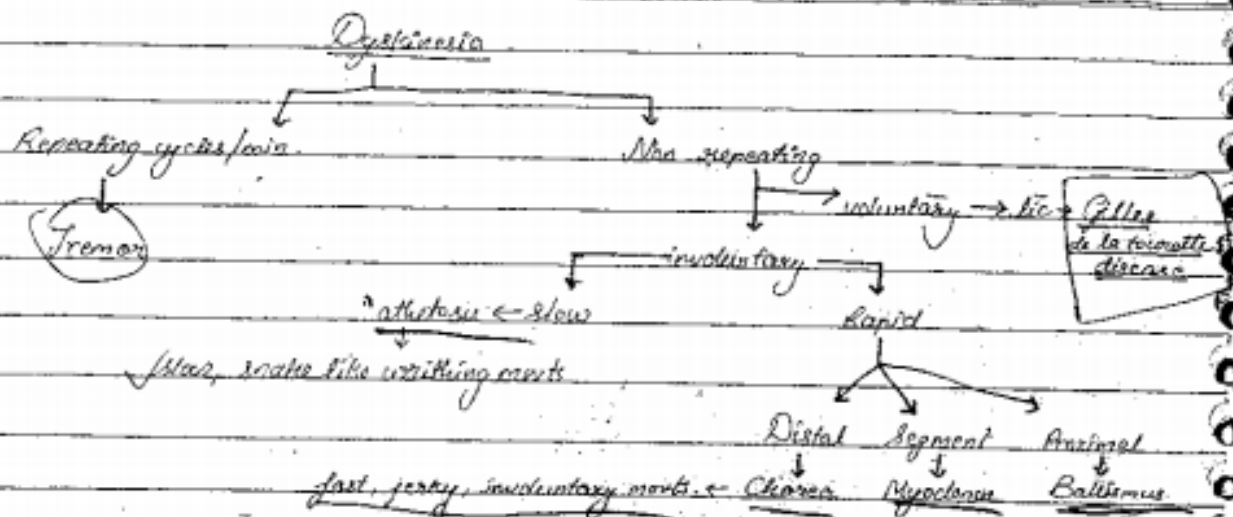


- ✓ Sup. colliculus - integrates visual + motor pathways
- ✓ Red nucleus - Chorea athetosis

Webber  
CN III  
Motor CS tract  
Corticobulbar  
Medial Midbrain

Benedict  
CN III  
ML  
Red nucleus  
Medial Midbrain

- ✓ m.c. Intracranial tumor in children: Astrocytoma
  - Supratentorial 80%
  - Infratentorial 20%
- ✓ m.c. malignant i.e. tumor: Medulloblastoma (95% infratentorial)
- ✓ m.c. infratentorial tumor in children: Medulloblastoma
- ✓ m.c. supratentorial tumor in children: Craniopharyngioma



⊗ Gilles de la Tourette :- MDE, Children

- ⊗ Vocal tics
  - Palilalia - repeating random picked up words
  - Echolalia - echoing the words of the speaker
  - Coprolalia - bad/foul words

Motor

- Echopraxia - copying the acts
- Copropaxia - obscene gestures

R:- Quarofarin } agonists  
Clonidine }

Subthalamic nucleus

- ⊗ STN lesion → Hemiballismus → prolateral wild flinging movements
- ⊗ Myoclonic jerks → CJD  
SSPE

- ⊗ PARKINSONS :- → Tremor → up at diagnosis, b/l - peak/terminal disease
- Rigidity
- Akinesia/Hypokinesia
- Poor postural reflexes

Micrographia

Hypophonia



Mask like face  
Freezing episodes  
Festination / Parkinsonian gait  
Orthostatic hypotension

Parkinson's

⊗ Parkinson Plus Syndromes

- Progressive Supranuclear palsy
- Multiple System Atrophy
- Corticobasal degeneration

✓ Rigidity ⊕  
✓ Hypoalgesia ⊕  
✓ Postural reflexes Absent  
Parkinsonian gait ⊕

⊕  
⊕  
B.N.  
⊕

Response to levodopa +++

Poor response to levodopa

Tremor ++

absent

PSP :- Vertical gaze palsy (ocular problems)

Square jaw posture - (may be rarely seen in MSA, PD)

✓ Downgaze affected first. > Upward gaze later

Dopamine doesn't work.

Pramipexole, Amantadine (Dopamine agonists) are used.

MSA :- Cerebellum + Basal Ganglia

Ataxia + Parkinson's

✓ Orthostatic Hypotension → Hydrocortisone

Rx of Parkinson's

- Dopamine agonists
- Amantadine
- Anticholinergics / Antiparkinsonics
- Rotigotine
- ✓ COMT  $\downarrow$   $\rightarrow$  Entacapone
- ✓ MAOB  $\downarrow$   $\rightarrow$  Selegiline / Rasagiline (1<sup>st</sup> Rx in Parkinson's)
- Levodopa + Carbidopa

DAS: STN + GPT

⊗ Dementia

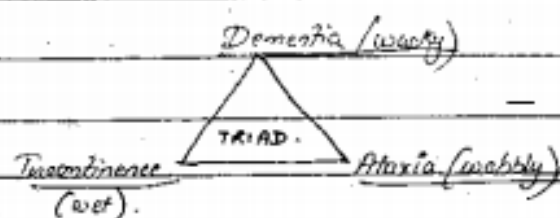
⊗ Reversible

- ✓ B<sub>12</sub> deficiency
- ✓ Hypothyroidism
- ✓ Toxemia
- ✓ Subdural bleed (mic. bleed & trauma)
- ✓ NPH/Idiopathic

⊗ Irreversible

- ✓ AD (Alzheimer's)
- ✓ Vascular (MID) - Multi-infarct dementia
- ✓ Lewy body dementia
- ✓ Frontal-Temporal dementia
- ✓ Huntington chorea
- ✓ CJD

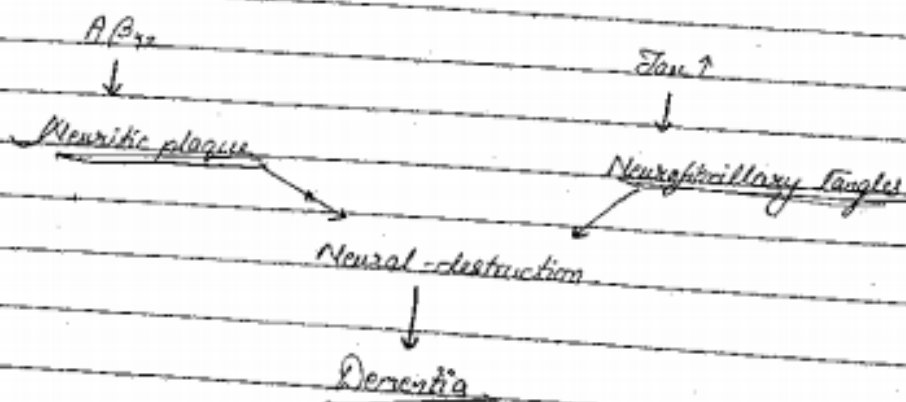
⊗ Normal Pressure Hydrocephalus: CT  $\rightarrow$  enlarged ventricles



Rx: Trickles the CSF out  $\rightarrow$  Ventriculo peritoneal Shunt

$\downarrow$   
Normalizes the CSF volume

## Alzheimer's Disease



✓ Temporal lobe 1st involved → ant. parietal lobe → Frontal → Occipital lobe.

⊗ Temporal - Hippocampus -  
Nucleus of Mayocost

C/E :-

- Anosia (loss of memory)
- Amaria (loss of learned skills) - despite @ motor power
- Agnasia (lack of knowledge) - object agnasia
- Achasia - visual agnasia
- Acalculia is a very late feature.
- Anosognasia (lack of awareness of deficits)

✓ Prosopagnasia - occipito-temporal circ. lesion → inability to recognize faces

✓ Recognition - occipital lobe lesion.

component of Balint's Syndrome.

- Simultaneous evaluation of multiple things is - ve

Palinopsia - occipital lobe lesion.

after image

image persists despite change in stimulus



⊛ AD

✓ Gradually progressive

✓ DTR - (N)

✓ Plantar - (H)

Rx: Donepezil } Ach ↑  
Rivastigmine }  
Memantine → NMDA

⊛ Vascular (MID)

✓ Step-ladder decline in patient functioning

✓ DTR ↑

✓ Plantar ↑

⊛ Fronto Temporal

Apathy

Disinhibition

Poor judgement

Hyperorality

Hypersexuality

Hyperphagia

⊛ Lewy body

✓ Visual hallucinations (Essential)

✓ Capgras Syndrome (delusion of identity)

✓ REM Behavioural AHI

✓ Hoarse Paroxysm

⊛ Huntington's Chorea - Chr-4

Autosomal Dominant

Triaucleotide repeats - (CAG)

✓ Fragile X - CAG

✓ FA - GAA

✓ Fronto-temporal dementia - CTG

Dementia, Chorea, Athetosis

Imaging - Caudate lesion

Rx: Tetrabenazine

Atypical antipsychotics

(\*) CJD

Prion disease

✓  $\alpha$ -helix  $\rightarrow$   $\beta$ -helix

$P_{\alpha P}^c \rightarrow P_{\alpha P}^{sc}$  (non foldable)

↓ touches

another protein (non foldable)

✓ Rapidly progressive dementia  
(Ataxic mutism)

✓ Myoclonic jerks (90% pts)  $\rightarrow$  Startle responses

✓ EEG  $\rightarrow$  slow waves } background  
                                  low amplitude }

Sudden sharp bi/triphasic waves

CSF: - 14-3-3 proteins

R: - No cure

Multiple Sclerosis

✓ Autoimmune - Th17

Pathology: Inflammation

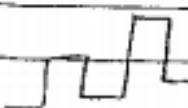
↓  
Demyelination

✓ Oligodendrocytes

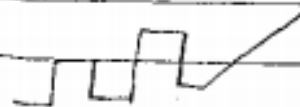
Remyelination

Astrocytes

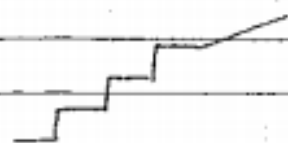
Gliaosis



- Relapsing remitting type of MS (m.c.)



- Secondary progressive



- primary progressive type of MS

C/E: Age:  $\geq 50$  yrs  
 $\leq 50$  yrs

- ✓ Optic neuritis
  - ✓ Periventricular
  - ✓ Cerebellum
  - ✓ Brain stem
  - ✓ Spinal Cord
- } Bands of Sclerosis

⊗ Optic neuritis + Transverse myelitis

Multiple Sclerosis

Devic's Neuromyelitis Optica

- ✓ usually up a.m.
- ✓ TM incomplete
- ✓ Bands of Sclerosis (MRI)
- Periventricular grey

- ✓ B/L O.N.
- ✓ TM complete
- ✓ MRI - (M)
- Hypothalamic involvement

✓ Abs against Aquaporin 4 channels

✓ CSF - oligoclonal bands

- Rare

also seen in (SLE)

• Parvovirus

• Behcet's

Relapsing remitting pattern  
 progressive



\* Indicators of MS:

✓ Schwann → worsen

conduction ↓ in warm

temp. in demyelinated tracts

Uhthoff's phenomena.

✓ Optic intraneural ophthalmoplegia

✓ Trigeminal neuralgia & deficits

✓ Lhermitte's sign - Flexion of neck: Shock-like sensation down the spine.

② C/D:- Sensory "pins & needles" (first)

✓ Optic neuritis

✓ Motor deficits → TM   
 above the level - UMN   
 below the level - LMN.

✓ Bladder

✓ Sexual dysfunction

T.O.C :- MRI

R: Steroids (only in acute episodes, do not improve prognosis)

Disease Modifying drugs.

✓ GA-β (D.O.C.)

Oral:

✓ Glucocorticoids

✓ Fingolimod

✓ Mitoxantrone

✓ Dimethyl fumarate

✓ Natalizumab

✓ Teriflunomide

↓   
 (continuously for < 18 months)   
 ↓   
 PCP (Progressive Multifocal Leukoencephalopathy)   
 (white matter pathology)

Natalizumab: Can be given at the start of the drug course  
 & checking of JC virus Abs every 6 months (19<sup>th</sup> Ed).

④ Efficiency of drugs :-

|  |                                             |
|--|---------------------------------------------|
|  | <u>Mitoxantrone</u> (max.) → poor tolerance |
|  | <u>Natalizumab</u>                          |
|  | <u>Dimethyl fumarate</u>                    |
|  | <u>IFN-β</u>                                |

④ Drugs for Progressive Multiple Sclerosis :-

- Mitoxantrone
- Azathioprine
- MTX
- Pulse Cyclophosphamide
- IVIg
- Pulse Methylprednisolone

### Seizures

④ GTCS : Valproate  
Lamotrigine

④ Absence : Valproate  
Ethosuximide (better, not available)

④ Focal : OxCarbazepine Valden pts - Levetiracetam  
CBZ  
Lamotrigine

④ Myoclonic/JME/etonic : Valproate

④ Neonatal seizure : Phenobarbitone

① Febrile seizure :- Diazepam (seizure happens when temp falls  $\rightarrow$  so parac or anti-pyretics can't be used as properly)

② Infantile spasm :- ACTH

③ Tubercous sclerosis :- Vigabatrin

④ Pregnancy :- if seizure is controlled - don't change the drug  
- administer folic acid and continuous monitoring

⑤ new seizure in pregnancy - cat B :- lamotrigine

oxcarbazepine

levetiracetam

ethosuximide

zonisamide

cat C :- valproate

phenobarbitone

CBZ - ex. in pregnancy

⑥ Phacomatosis

⑦ Tubercous Sclerosis :- AD

✓ Chr - 9, 16

✓ Vogt's triad - Epilepsy

low IQ

Adenoma sebaceum

✓ Ash leaf macules (hypopigmented)

✓ Cafe-au-lait macules (coffee coloured)

✓ Shagreen patches (raised)

✓ Moen's tumor - pathognomonic

(perineural cystic degeneration)



✓ Subependymal Giant Cell Astrocytoma (SEGA)  
m.c. location - foramen of Monro

✓ Heart - Rhabdomyoma

✓ Kidney - Angiomyolipoma

⊗ Neurofibromatosis

⊗ Type - I

Von Recklinghausen's Disease

✓ Chr - 17

✓ Eye - Lisch nodules (iris)

✓ Caffe-au-lait -  $\geq 6$  in number, each  $> 1.5$  cm in diameter

✓ Axillary / inguinal freckling

✓ Tibial / fibular dysplasia - 'Bone island sign'

✓ Piloform neurofibromas  $\geq 2$  in number

✓ Optic n. glioma

✓ usually assoc. w. Phaeochromocytoma

⊗ NF - 2 - Chr - 22

Bilateral acoustic neuroma (1st division of vestibular n.)

⊗ Sturge Weber Syndrome

Degeneration - CPL (never crosses the midline)

- tram-track appearance of Calcification

- Portwine stain

- MR seizures, Hemiparesis, Hemiparesis



If nitrite is picked up by Dipstick - it is the most specific test for Gram -ve IUT

### ⊗ RBC in urine

#### / Isomorphic

Shape of RBC is maintained

Source is before kidney

- urinary bladder

- ureter

- urethra

#### / Dysmorphic

Shape is distorted

- crushed

- Glomerulonephritic - even if 20% cells

(Renal source) are dysmorphic

### ⊗ Eosinophiluria

#### ⊗ AIN

Allergic interstitial nephritis

→ No drug intake

→ Rash

→ Sterile pyuria

→ Eosinophiluria

→ (Clara?)

#### ⊗ Arterio Emboli to kidney

- b/p procedure

→ Creat ↑

→ ↓ C<sub>3</sub>

→ Embolic phenomena - Gangrene - digits

→ Eosinophiluria

### ⊗ Contrast induced Nephropathy

Complement is not affected

Creat ↑

No embolic phenomena

Prevention - Hydration + NAC

Choice of contrast - Iso-osmolar contrast (best)

M-acetyl cysteine



⊗ Casts:

WBC → pyelonephritis, interstitial nephritis

✓ RBC → G.N.

✓ Broad waxy → CRF

✓ Fatty brown/ granular → ATN (most specific/reliable)

✓ Hyaline → Normal

⊗ Kidney disease

Glomerular

Tubular

⊗ Glomerular Disease:

- Nephrotic / Nephritic

\* Cause

- S. Complement (Nephritic)

- Patho findings

Nephrotic

Nephritic

✓ Proteinuria > 3.5 gm/day

✓ < 3.5 gm/day

✓ +

✓ Hematuria ++

✓ Hypertension

↑ S. Cholesterol

✓ Severe edema +++

+

Nephrotic

( $\pm$ )

Nephritic

HTN + +

(\*) Igs  $\downarrow$  - infection

Capculated org.

Pneumococcal (common)

Protein C, AT III  $\downarrow$   $\rightarrow$  thrombosis  
(membranous nephropathy)

(\*) Causes:- • Minimal Change Disease

• ESGS

• Membranous nephropathy

• Diabetic

• Amyloidosis

SPGAN

IgA nephropathy

ANCA assoc. GN

MPGN - I, II

Alport's

Nephritic-Nephritic

conditions

(\*) MCD : cause = idiopathic

insect bite, allergy

NSAIDs

Hodgkin's lymphoma

[m.c. cause of nephrotic syndrome  
in children]

[S-creat is always  $\uparrow$ ]

Patho:- high light microscopy (X)

Electron microscopy loss of podocytes

Plasmodium malarie

(\*) Membranous : causes: infections - HBV, Malaria, Lymphitis, Leprosy, Etiarosis, Schistosomiasis

Cancers - lung, breast, colon

Autoimmune - (RA) (SLE)

Drugs - NSAIDs, probenecid, penicillamine

Patho: Sub-epithelial deposits

IF: Spoke and dome pattern immunofluorescence

Marker → M-PLA<sub>2</sub> IT (Membranous phospholipase A<sub>2</sub>)

⊗ ESGS: causes: • HTN

• Obesity

• HIV (reflux nephropathy in HIV)

• VUR

• SCA (Nodules)

• Heroin abuse

• Alport's (when it presents as nephrotic)

Marker: SuPAR IT

Patho: Visceral Epithelial proliferation

Focal Sclerosis

Glomerular tuft collapse [Collapsing nephropathy]  
seen in HIV

⊗ Amyloidosis:

Screening test :- Abdominal fat pad biopsy

↓ if no result

Specific organ bx

Staining :- Congo red → polarised light - Apple green birefringence

⊗ Diabetic Nephropathy: Diffuse Glomerulosclerosis

Focal Nodular Glomerulosclerosis (More specific)

↓  
(K<sub>1</sub> nodules)



Fibrin caps

Capsular drops

Tubules → Glycogen deposits → Almani Ebrah

(\*) PSAN

Streptococcus/impetigo/Pharyngitis (Bacterial)

4-12 wks. ↓ 7-14 days

Hematuria

(\*) IgA nephropathy / Berger's

Pharyngitis (viral)

2 days ↓

Hematuria

(Lymphangitic Hematuria)

GN - Type III H.S.

M.c. glomerular cause of haematuria in adults

Assoc. E. Henoch Schölein Purpura

Potter's Sub-Epithelial deposits

Epithelial humps

(Curry's hump deposits)

> 95% recovery rate

Excellent prognosis

IgA deposits in mesangium

Mesangioproliferative GN

IgA ← caused by Epitax

80% remission

→ End Stage Renal Disease

(\*) ANCA - assoc. glomerular disease:

→ Serum complement is (H)

R-ANCA: ANCA Mesangio Pharyngitis

C-ANCA - Wegener's

Good Pasture's - linear deposits

Churg Struss

(\*) Churg Struss : Asthma like episodes / Renal involvement

Arthralgia

Eosinophilia

2nd m.c. cause of Mononeuritis Multiplex

B.v. - Granulomas

★ MPGN - I

Causes: Acv 2 or 7 out cryoglobulinemia  
 should have joint or skin involvement

✓ SAGE

✓ BLE

✓ Cancer (lung, breast, ovary)

★ MPGN - II

✓ Inherited

✓ partial lipodystrophy  
 (patchy loss of s.c. fat)

Patho: Spilletti Splitting of GB

- tram track

Sub Endothelial deposits

✓ Dense deposits

Intramembranous deposits

Ribbon like deposits

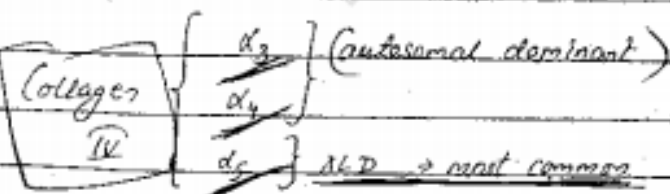
✓ C3 Membrane factor

✓ Classical pathway of Complement  
Alternative

Alternative pathway

★ Alports Syndrome

Hereditary Nephritis



✓ Ocular: Ant. lenticonus, Senataconus, Megalocornea, Retinal defects

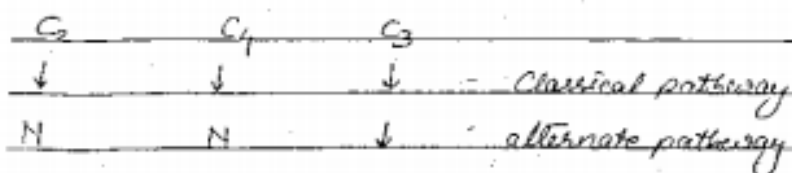
✓ Deafness: (SNHL)

Presenting Complaint of Alports

✓ Renal: Hematuria + Proteinuria



*Delta*

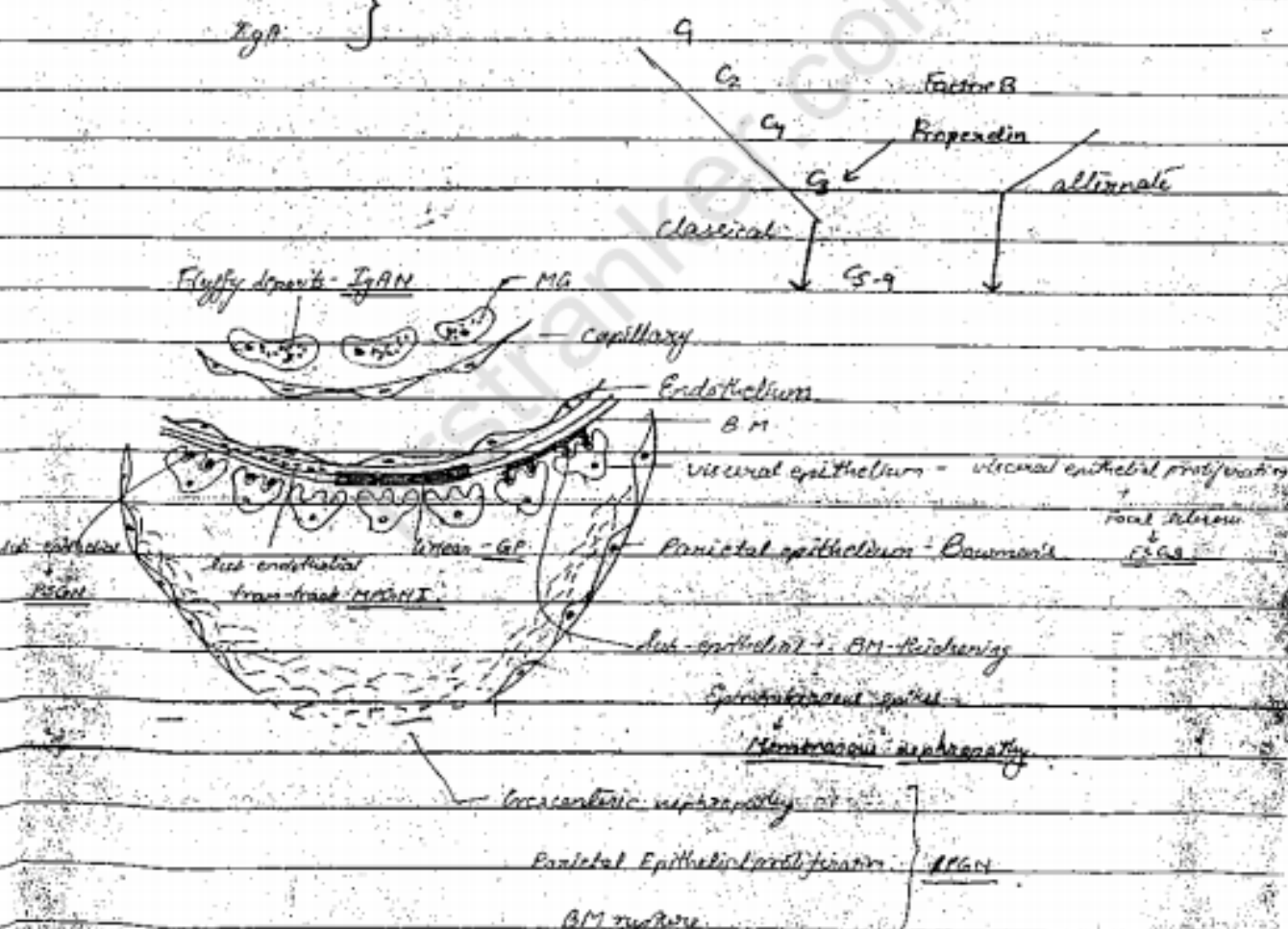


④  $APGN \rightarrow C_1 - \textcircled{N}, C_3 - \downarrow$  - alternate

⑤  $MPGN II \rightarrow C_1 \textcircled{N}, C_3 \downarrow$  - alternate

⑥  $I \rightarrow C_1 \downarrow, C_3 \downarrow$  - classical

$ANCA + AN \rightarrow C_3 \textcircled{N}$   
Eg:  $\downarrow$



Prognosis of RPGN  $\rightarrow$  No. of Crescents



## Tubular Disorders

### Pre Renal

↓ perfusion of kidney

- Acute blood loss - trauma
- Cardiac failure
- RAS

$$\left( \frac{BUN}{Cr} > 20 \right)$$

Urine  $Na^+$   $< 20 \text{ mEq/L}$

Fractional  $Na$   $< 1\%$

$$= \frac{U_{Na} \times P_{Cr} \times 100}{P_{Na} \times U_{Cr}}$$

$$\frac{U_{Cr}}{P_{Cr}} > 40$$

Urine osm  $> 450 \text{ mOsm/L}$

Hyaline Cast

GER

1  $> 90 \text{ ml/min}$

2  $60-90 \text{ ml/min}$

3  $30-60 \text{ ml/min}$

4  $15-30 \text{ ml/min}$

5  $0-15 \text{ ml/min}$

### ATN

Toxin

Drugs

Ischaemic - Pre renal

Glomerular disease

$$\frac{BUN}{Cr} < 20$$

Urine  $> 20 \text{ mEq/L}$

F $Na$   $> 2\%$

$$\frac{U_{Cr}}{P_{Cr}} < 40$$

Urine osm  $< 450 \text{ mOsm/L}$

Muddy brown / Granular Cast

drug dose modifications

Rapidly convert to ESRD

Cystatin-C  $\rightarrow$  New marker for CRF  
 Better marker than Creatinine  
 Not dependent on muscle mass.

Renal Failure.  $\rightarrow$  Anion Gap  $\uparrow$  ed

ARF

$PO_4 \uparrow$

$Ca \downarrow$

$K^+$  acute  $K^+ \downarrow / \uparrow$

CRF  $K^+ \uparrow$

M. acidosis



Bound  $Ca \rightarrow$  Ionised  $Ca^{++}$

so signs of hypocalcaemia are not so apparent despite  $\downarrow$  serum  $Ca^{++}$

CRF

$PO_4 \uparrow$

$Ca \downarrow$

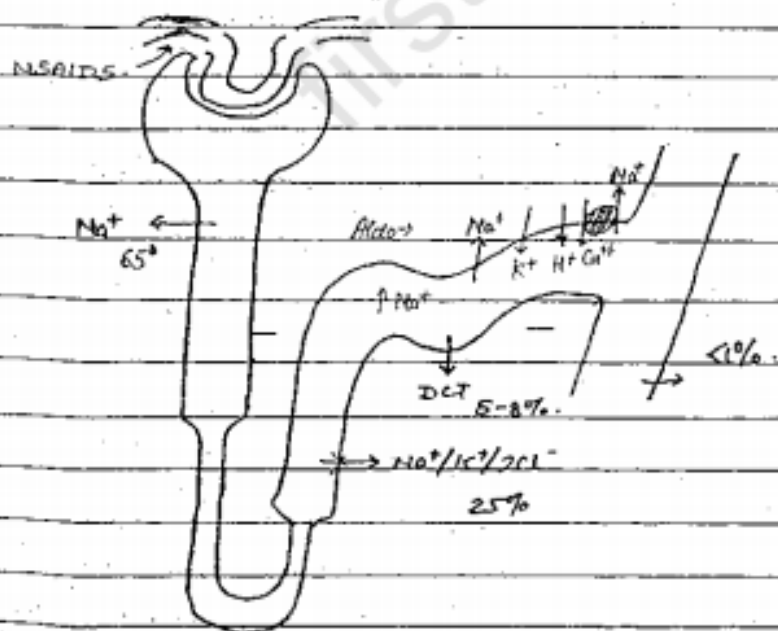
$K^+ \uparrow$

Anaemia

$\uparrow$  PTH

Renal osteodystrophy

BARTER'S



$\text{Na}^+$  is reabsorbed in all parts of nephron.

$\text{Na}^+/\text{K}^+/\text{ATPase}$  transporter is defective

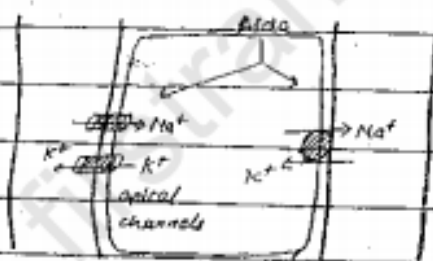
$\uparrow \text{Na}^+$  in DCT

stimulates RAAS  $\rightarrow \uparrow \text{Renin}$

- $\uparrow \text{Aldosterone}$
- Hypokalemia
- Metabolic alkalosis
- Calcium stones
- B.P - N/L

$\boxed{Rx}$  :- NSAIDS.

LIDDLE'S SYNDROME (pseudohypoaldosteronism)



Apical channel defect

- the apical channels are not endocytosed or replaced.
- $\uparrow$  loss of  $\text{K}^+$  and  $\text{Na}^+$

(in Conn's syndrome Aldosterone is  $\uparrow$ )

Renin  $\downarrow$  (due to feedback)

Aldo  $\downarrow$

Hypokalemia

Metabolic alkalosis

HTN

Renal stones

$\boxed{Rx}$  :- Amiloride (to block apical  $\text{Na}^+$  channels)



Bartter's Syndrome

Gittleman's Syndrome

like furosemide

like thiazide

Defect :- loop of henle  
Na<sup>+</sup>/K<sup>+</sup>/2Cl<sup>-</sup>

Defect :- Na-Cl - Distal tubule

(H) BP

(N) BP

↓ K<sup>+</sup> / Met. alkalosis

↓ K<sup>+</sup> / Met. alkalosis

Uca ↑ → stones

Uca ↓ - No stones

Umg → (H)

Umg ↑↑

RTA 1, 2

- Hypokalemia
- Metabolic acidosis (normal anion gap)

RTA-1

RTA-2

Distal tubule defect

Proximal tubule defect

Acid excretion defect

Bicarb reabsorption defect

Urine pH > 5.5

Urine pH < 5.5 (due to HCO<sub>3</sub><sup>-</sup> depletion)

(normal person, urine pH doesn't go below 4.5)

Associated to STONES

Glycosuria, Amino aciduria, Phosphaturia

Inferiatory - Urine acidification test

Saline + NaHCO<sub>3</sub>

↓ glc acidic substance

Fractional HCO<sub>3</sub> excretion > 15%

Urine pH > 5.5

(HCO<sub>3</sub><sup>-</sup>)

www.FirstRanker.com

Causes: Sjogren's  
Hyperparathyroid  
Multiple Myeloma  
Amphotericin B

Causes: Fanconi's  
Metabolic diseases ( $\downarrow$  ATP)  
Cystinuria  
Multiple myeloma

Type 4 RTA

Distal tubule defect  
Diabetes mellitus, obstructive uropathy  
Hyperkalemia, Metabolic acidosis  
Normal anion gap

Anion gap is ↑ in Renal failure

$$AG = Na - (Cl + HCO_3^-) = 12 \pm 4$$

Metabolic acidosis

(NAG)

(TAG)

Hyperchloremic MA

(GI)

(Renal) - RTA

Diarrhea

Addison's

Cholestyramide therapy

Drugs: ACEi

ARB

Ketoadidosis - Starvation

- Alcohol

- Diabetic

✓ Uremia

✓ Lactic acidosis

✓ Toxins

Urine AG

-ve

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

→ +ve

Methanol

Uremia

DKA

Paraldehyde

INH overload, Iron?

Lactic acidosis

Ethylene glycol

Salicylate

$$\Delta \text{Gap} = \frac{\Delta A}{\Delta B} = \frac{\text{Difference in AG}}{\text{Difference in Bicarb}} = \frac{AG - 12}{24 - HCO_3^-}$$

$\Delta \text{Gap} < 0.4 \rightarrow \text{NAGMA}$

$0.4 - 1 \rightarrow \text{NAGMA}$   
 $\text{HAGMA}$  } Mixed metabolic acidosis

$1 - 2 \rightarrow \text{HAGMA}$

$> 2 \rightarrow \text{HAGMA} + \text{Met. alkalosis}$

### ABG

pH - 7.35 - 7.45      7.40

$CO_2$  - 35 - 45      40      Venous blood - 45

$HCO_3^-$  - 22 - 26      24

Normal Compensation  $\rightarrow$  Both  $CO_2$  and  $HCO_3^-$  move in the same direction

| $CO_2$       | $HCO_3^-$                          |                                      |
|--------------|------------------------------------|--------------------------------------|
| $\uparrow$   | $\uparrow$                         | $\rightarrow$ Normal compensation    |
| $\uparrow$   | $\uparrow\uparrow\uparrow\uparrow$ | $\rightarrow$ may be simple or mixed |
| $\downarrow$ | $\uparrow$                         | } $\rightarrow$ mixed                |
| $\uparrow$   | $\downarrow$                       |                                      |

In metabolic acidosis/alkalosis, the compensation by lungs is perfect

In respiratory alkalosis/acidosis, the kidney may compensate partially



| ROME | pH | CO <sub>2</sub> |             |
|------|----|-----------------|-------------|
|      | ↑  | ↓               | Respiratory |
|      | ↓  | ↑               |             |
|      |    |                 | - alkalosis |
|      |    |                 | - acidosis  |
|      | ↓  | ↓               | Metabolic   |
|      | ↑  | ↑               |             |
|      |    |                 | - acidosis  |
|      |    |                 | - alkalosis |

CO<sub>2</sub> should not be in the normal range to apply ROME rule

pH 7.20 CO<sub>2</sub> 24  
Gap < 15 → Metabolic

pH 7.20 PA 74  
Gap > 15 → Respiratory

7.40 40  
7.60 40

### Compensation formula

Met. acidosis CO<sub>2</sub> = 1.5 (HCO<sub>3</sub><sup>-</sup>) + 8 ± 2

Met. alkalosis - Every 10 ↑ in HCO<sub>3</sub><sup>-</sup> CO<sub>2</sub> should ↑ by 7

### Respiratory

|           |         | HCO <sub>3</sub> <sup>-</sup> | CO <sub>2</sub> |
|-----------|---------|-------------------------------|-----------------|
| Acidosis  | Acute   | 1                             | 10              |
|           | Chronic | 4                             | 10              |
| Alkalosis | Acute   | 2                             | 10              |
|           | Chronic | 5                             | 10              |

H<sup>+</sup>

Henderson's Equation =

$$H^+ = \frac{24 \times CO_2}{HCO_3^-}$$

| pH   | CO <sub>2</sub> |
|------|-----------------|
| 7.60 | 20              |
| 7.50 | 30              |
| 7.40 | 40              |
| 7.30 | 50              |
| 7.20 | 60              |

Respiratory

$CO_2$

pH

acute  $\rightarrow 10$

0.08

Chronic  $\rightarrow 10$

0.03

$Na^+$  140

$K^+$  4.0

pH < 7.4  $\rightarrow$  acidosis

$Cl^-$  106

$CO_2$  24  $\rightarrow$  not resp. acidosis

$HCO_3^-$  14

$HCO_3^-$  14  $\rightarrow$  met. acidosis

$CO_2$  24

pH 7.39

$CO_2 = \frac{3}{2}(14) + 8 \pm 2$

AG 20

$$= 29 \pm 2 = 27 - 31$$

$CO_2$  is below  $Cl^-$ , metabolic of  $CO_2$  Resp. alk.

Met. acidosis + Resp. alk.

$$\Delta gap = \frac{20 - 12}{24 - 14} = \frac{8}{10} = 0.8 \rightarrow \text{mixed metabolic acidosis}$$

pH: 7.30  $\rightarrow$  acidosis, metabolic acidosis

$CO_2$ : 28

$HCO_3^-$ : 16

$CO_2 = \frac{3}{2}(16) + 8 \pm 2$

AG: 20

$$= 24 + 8 \pm 2 = 30 - 34$$

$CO_2$  is above 34, metabolic of  $CO_2$  Resp. acidosis

$$\Delta gap = \frac{20 - 12}{24 - 14} = \frac{8}{10} = 0.8 \rightarrow \text{Mixed MA + Resp. acidosis}$$

## RESPIRATORY

PET - Spirometry

$$= EV_i$$

24/11

—EV

For

nc

Body plethysmography

N<sub>2</sub> washout

### The detection test

Obstructive

Fe V

↓ ↓ ↓ ↓

FDC

N/A

Ev.

$$\frac{F_{EV_1}}{F_{VC}}$$

1

Restrictive

Figure 1

1. 1

N/A

N/A

FeV, FVC above 80% is considered (4)

$\frac{f_{FeV}}{f_{PVC}} > 200\% (0.7)$  is considered (ii)

GOLD criteria  $\rightarrow$   $\frac{Fov}{FVC}$  should be  $\leq 0.7$  to be called as Obstructive LPD

\*  $FVC, \frac{FVC}{FVC} \rightarrow 70\%$   
 $\rightarrow FVC > 80\% \rightarrow$  Normal  
 $\rightarrow FVC \leq 80\% \rightarrow$  Restrictive lung disease

⑧ CO: CO and O<sub>2</sub> have the same diffusing capacity but CO binds to Hb 225x more strongly than O<sub>2</sub>, so it doesn't diffuse back into the alveoli unlike O<sub>2</sub>.

$$DLCO = \frac{\text{Surface} \times K_D}{\text{Thickness}}$$

$k_f$  = diffusion coefficient

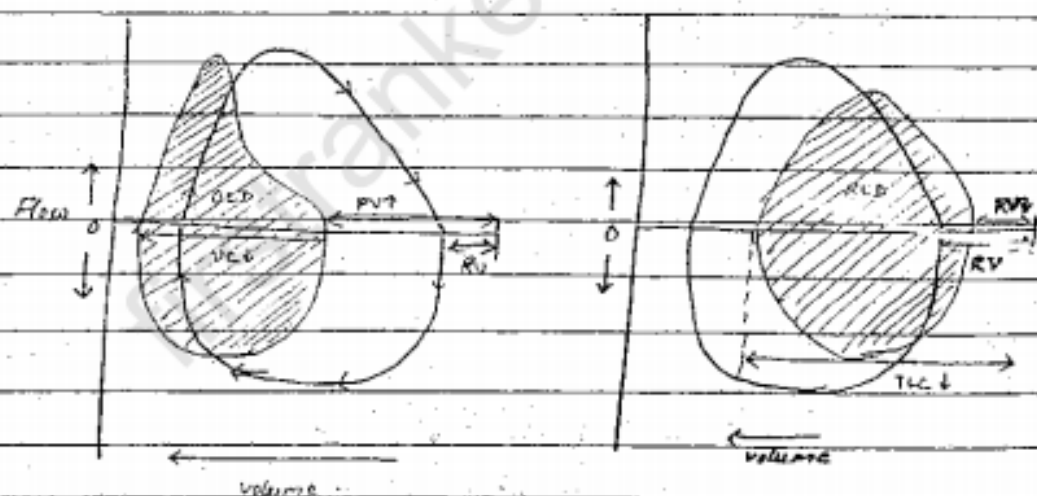
DLCO - Bronchitis  $\rightarrow$  N  
Emphysema  $\rightarrow$   $\downarrow$   
Asthma  $\rightarrow$  N  
ILD  $\rightarrow$   $\downarrow$



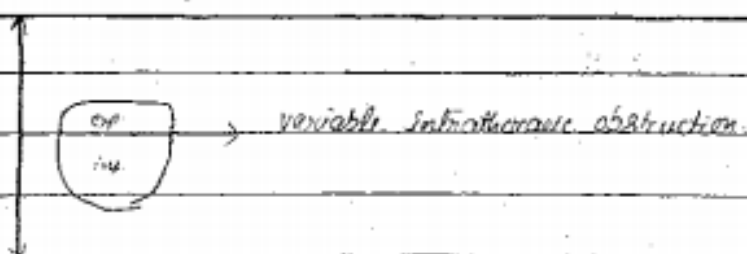
|                |     |                                                        |
|----------------|-----|--------------------------------------------------------|
| R-L (TOF)      | → ↓ |                                                        |
| L-R (VSD)      | → ↑ |                                                        |
| Pulmonary HTN  | → ↑ | (false ↑ in DLCO)                                      |
| Pulm. Embolism | → ↓ | Fav. - (N) FVC - (N) Ratio - (N)<br>isolated ↓ in DLCO |
| Pri. Pulm. HTN | → ↓ |                                                        |
| Polycythemia   | → ↑ | DLCO should be corrected for Hb.                       |
| Anemia         | → ↓ |                                                        |

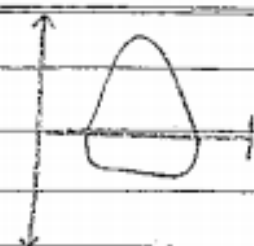
$\frac{DLCO}{TLC}$  → indicates the functionality of the remaining lung after lung resection.

Flow volume Curve:



Intrathoracic narrowing of large airways :- Expiratory stridor.  
Extrathoracic narrowing of large airways :- Inspiratory stridor.





variable extrathoracic obstruction



fixed obstruction. Eg: Tracheal stenosis

### PULMONARY EMBOLISM:

- Dyspnoea on Exertion

\* CXR → normal in initial stage

non-specific infiltrates

Hampton's hump - wedge shaped

subpleural consolidation

Westermark's sign - oligemia

Pleural effusion - haemorrhagic - trauma

tumor

Metting sign

Flecking opacities

PAAG sign - prominence of Rt pulmonary artery

\* ECHO - pulm. hypertension (mean PA pressure  $> 25$  mmHg at rest

pulm. regurgitation

$> 30$  mmHg during exercise)

Rv hypokinesis

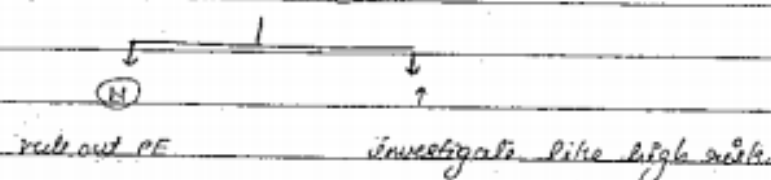
DVT is common in - joint replacements (hip, knee)

ICU patients

Flight travel

thrombosis

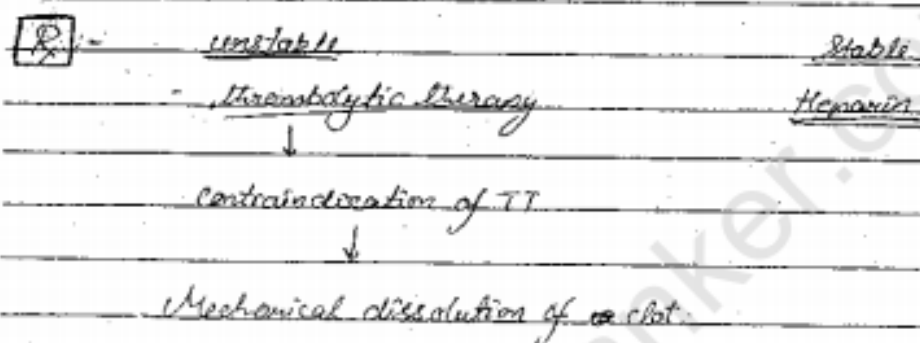
T.O.C. Low risk - D-dimer



High risk - CT angi: T.O.C.

✓ V.P. scan in pt. E renal failure/contrast sensitivity

Gold Standard: Invasive Catheter angiogram.



C.T. to thrombolysis:

- ⊗ Absolute:
- ⊗/haemorrhagic stroke.
  - Active intracranial neoplasm.
  - Recent (< 2 months) intracranial surgery or trauma.
  - Active or recent internal bleeding in prior 6 months.

Relative: Bleeding diathesis

Uncontrolled severe HTN

CPR

Non-haemic stroke < 2 months.

Surgery < 10 days.

PLTs < 100,000.



## ④ Hypersensitivity Pneumonitis

DOE  
Restrictive pattern

Hypersensitivity to organic dust matter  
- Farmer

CR - apical sparing, ground glass appearance

- Bird feather "Bloom" antigen

MZ } infiltrates  
L2 } alveolitis

✓ Type III + Type IV hypersensitivity

BAI - lymphocytes  $CD_8 > CD_4$

✓ Eosinophilia is not seen

Patho - Granuloma

Rx - 1) avoid the allergen

2) Steroids

3) Cyclophosphamide / Azathioprine

## Sarcoidosis:

ILD

Restrictive pattern

CR - Apical fibrosis +

MZ } infiltrates  
L2 }

40 hilar lymphadenopathy

also seen in

✓ TB

✓ Histoplasmosis

✓ Hypersensitivity pneumonitis

pleural effusion is very rare (<5%)

Heerfordt's Syndrome:- (uveoparotitis)

Euthymic Nadarum

BAI -  $CD_4 > CD_8$

Hepatosplenomegaly, lymphadenopathy

↑ Ca (due to hypervitaminosis D)

ACE ↑

ABPA

Febrile neutropenia

Allergy to 'Aspergillus'

[R] : Antipneumococcal penicillin

- Hypotension - Vancomycin  
Catheter

Type I + Type III

- Antifungal : Itraconazole

Wheezes, DOE, Hemoptysis

CXR - Central bronchiectasis

Eosinophilia, IgE ↑

T.O.C : Skin test - Wheat & pure Aspergillus

BAL : Eosinophils

R : Glucocorticoids under Antifungal cover (itraconazole)

R - c in invasive aspergillosis - Itraconazole

Prophylaxis of aspergillosis : Itraconazole

⊗ TRF

GERD

Breathlessness

Clubbing

Strong Assoc. & Smoking

Velcro creps (terminal inspiratory creps)

HRET : - Lower lobe fibrosis (honey comb appearance)

B<sub>2</sub> : Subpleural fibrosis

HR - usual subcutaneous pneumothorax

BAL : Neutrophils



Rx: Oxygen  
Steroids (initial only)  
1/1 lung transplant

Asthma

<40 yrs

COPD

>40 yrs

Smokers?

Family history Atopy  
Allergy

History hyperresponsiveness

A<sub>2</sub>-agonist - FEV<sub>1</sub> ↑ >12%

Methacholine - FEV<sub>1</sub> ↓ >20%

CXR - Normal initially

Minimal air trapping

- Pneumonia

CXR - tubular heart

Barrel shaped chest

lower diaphragm

DLCO: N/T

DLCO: ↓

ABG: Respiratory alkalosis/H

Stable - Resp. acidosis

ABG: Respiratory acidosis

Rx: Inhalational steroids

Rx: Inhalational anticholinergics