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August 2015 Session

Dr. Thammem

MEDICINE

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To Study From Book:

GIT
LIVER

Jain Stationery
F-69/5 Gautam Nagar
New Delhi - 110049
Mob.: 9811982449
Endocrinology

Suppress → Hormone → Gland → N → ↓

Stimulate

Diagnosis of Endocrine disorders

PITUITARY GLAND

All anterior pituitary hormones are under stimulatory control of hypothalamus except Prolactin (inverse influence of Dopamine)

Prolactin → Undu → influence of Dopamine

Hypothalamus

Pituitary stalk damage

Vascular mode of ANT POST N\nNeurogenic mode

ADH → DI initially (transient) → SIADH (constant) due to obstruction

Finally of vessels in pituitary

Recovery of Permanent lesion

↓ ADH ↓ ADH ↓ DI

SIADH

ADH → Receptors → Aquaporin → Active reabsorption of H₂O

↓

(Mostly in the medullary OS)

H₂O → plasma volume ↑ ANP → Renal → Aldosterone → Na⁺, H₂O ↓

↓ MG ↓
Patients of SIADH generally do not have edema

\[ \text{SIADH} \rightarrow * \text{Euvolemic} \]
\[ * \text{True hypovolemia (due to AVP)} \]
\[ * \text{Urine Na}^+ < 20 \text{ mEq/L} \text{ (Should be above } 20) \]
\[ * \text{Urine osm > Plasma osm} \]

Single most important parameter for plasma osmolality \( \rightarrow [\text{Na}^+] \]

\[
\text{PLASMA OSM} = \frac{2(\text{Na}^+) + \text{Glu} + \text{BUN}}{18} + 2.8
\]

\[
\text{or} \quad \frac{2(\text{Na}^+) + \text{Glu} + \text{BUN}}{18} \]

(4) Testing for SIADH:

Folstein loading test \( \rightarrow \) AVP remains high (normally AVP \( \downarrow \))

Confirm diagnosis of SIADH.

True about SIADH are NE:

1) Vaptans are new class of drugs approved for it
2) Urine Na is \( \uparrow \) to \( \downarrow \)
3) The plasma Na can be as low as 125 mEq.
4) Water loading test can be used for diagnosis

CF:

1) Headache
2) Somnolence
3) Altered sensorium
4) Seizures

\( R \) - Fluid restriction \( \downarrow \) order
\( N\text{a}^+ \) Correction \( \downarrow \) of \( R \)
Vaptans

Convulsion selective V receptor
Telmisartan \( \downarrow \) blockers

depolarization

Rapid correction of sodium may cause "Central Pontine Myelinolysis"
Polyuria: > 40 - 50 ml/kg/day

> 3 litres/day

Urine osmolality

< 300 mOsm/l ↓

Free water loss

> 300 mOsm/l ↓

Actual loss

Primary polydipsia

Diabetes Insipidus

Psychogenic polydipsia

Central

Nephrogenic

* Plasma Na⁺ conc ↓

may be @ but never Na⁷

or @ but never Na⁷

* Plasma Na⁺ conc ↑

* When deprivation test

(4 hr & 8 hr after water deprivation)

[Urine osm ↓]

(should decrease by at least

50% to say primary polydipsia)

[Urine osm ↔]

[Urine osm ↓]

[Cortisol Depressin ↓]

[Urine Osm ↑]

[Prospressin ↓]

[Fludiazepine]

[Na⁺ Absorb ep]

[Na⁺ lost in urine]

After Na⁺ absorption in ADH

[Na⁺ Absorb all others]

[Na⁺ Absorb all others]
Polyuria
urine < 300 mosm/L

ADH ↑
Nephrogenic DI

Primary polydipsia

MRO of pituitary Tumor
(post-pituitary normally appears bright)

Bright spot

Primary polydipsia
Central DI

Trauma +
Polyuria (> 3 L/day)
Cerebral salt wasting synd.

Diabetes insipidus

* Urine Sodium ↑
\( \text{Chlorine} \leq \text{20 mEq/L} \)
* Urine Na+
\( \text{Chlorine} \geq \text{20 mEq/L} \)

\( S \text{ Na}\downarrow \text{/N} \)
\( S \text{ Na} \uparrow \)

Eboth urine Na+ ↑& S Na+ ↑ → m.o. cause → Saline infusion
Prolactinoma:

- Macroadenoma of pituitary: Prolactinoma

\[ \text{GnRH} \downarrow \]

\[ \text{LH} \downarrow \quad \text{FSH} \downarrow \]

\[ \text{Placenta} \downarrow \quad \text{Steroids} \downarrow \]

- Prolactin levels (>1000 ng/mL) 
- Physiological state
- Dopamine blockers 
- Drug history
- Common
- Hypothyroidism 
- TSH levels 
- Cause of \( \uparrow \) PRL

Prolactinoma

Gynaecomastia

\[ \text{Erectile dysfunction} \]

- Prolactinoma doesn't cause gynaecomastia

- Gynaecomastia (5%)
Macroadenoma

Visual symptoms +


cABeropalladine

(cess after four months)

Visual symptoms persist

Surgery

Trans-sphenoidal resection

Pregnancy

Prolactin levels rise up. pregnancy don't correlate to severity

Prolactinoma

Microadenoma


Growth Hormone

Liver → TGF →

Epiphyseal growth → Bone size/length ↑

↑ protein synthesis
Growth hormone

No ↑ insulin ↓ sensitivity

Anemia Arthritis Synthesis Metabolic process

↑ FSH

Insulin Antibiotic Proteins Enzyme

Like activity Activity Synthesis Growth

Arginine → ↑ GH → Muscle mass ↑

↑ Fat

↑ Skull size → Mandible growth ↑ → gape □ for speech

Finger ↑

Foot ↑

English man's changing hat disease

Enlarged skull size → Paget's disease → Enlarged sphenoid (??)

Hematoma Enlarged sphenoid

Hair part thickness ↑ 20 cm

Fleshy palate

↑ Glucose + Insulin resistance → Diabetes Mellitus

↑ No ↑ Systemic vascular resistance ↑ → Hypertension

Liver → Cardiomyopathy → Ischemic heart disease

Colon polype ↑ → ↑ risk of a Colon

Mist stuffy handshake
1. Growth hormone levels are not useful in assessment.

Screening test → TGF-1 levels →

N →

Rule out disease

Confirmatory test

(Not usual overnight fasting)

75 gm glucose

After 1 hr

GTT is suppressed
→

Compared to baseline
Compared to baseline

Acromegaly

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

Rx: B.O.C is Surgery

Drugs: Somatostatin analogues (Octreotide, Lanreotide)

MR

Reresetable → Non Reresetable

Trans-Sphenoidal Resection → Gamma Knife Surgery

(No benefits)

GHR receptor blocker (Regrowth)
Cushing disease: Cortisoloid excess due to pituitary adenoma
Cushing syndrome: Entire spectrum of Cortisoloid excess disorders.

M.C. cause of Cushing syndrome: Pathogenesis

ACTH ↑
* Pituitary adenoma
  * Adrenocorticotrophic hormone ↑
  * Ectopic ACTH syndrome
  * Pigmentation
  * No pigmentation

Pituitary adenoma Ectopic ACTH

* Insidious
  * Rapid onset

ACTH ↑ Cortisol ↑ → Mineralocorticoid

* Hypokalemic
  * Hypokalemic
  * Metabolic alkalosis
  * Metabolic acidosis

<50% → 90%

* Insidious course leads to rapid onset → No induction of 11β-hydroxylase

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 = 1:1

* Obesity
  * Obesity
  * Obesity

(If obesity is absent it is due to malignant tumors)
Early manifestation of Cushing's → lab → loss of diurnal variation of cortisol levels.

Next manifestation/earliest clue → site pain (after constitutional features)

Cushing's

- Thin skin
- Moon face
- Bruised abdomen, Easy bruisingability
- Thin extremities
- buffalo hump
- Atherosclerosis arterio-lysis

Investigation

Cushing Supressed

Overnight / low dose Drosa Supression test

↓

1 mg Dexamethasone 11 pm

↓

exam cortisol

Cortisol ↓

Rule out Cushing

ACTH

↑ ACTH

↓ ACTH

Pituitary adenoma

Adrenal cause

Ectopic ACTH

NCCI - abdomen

High dose Drosa Supression test

↓

Early Drosa 48 hrs

<6 cm

↑

Benign

Metastasis

Pituitary

↑

Ectopic

17 metastatic ↑
* (Ambiguous)

Petrous vein → ACⅡ

Peripheral vein → ACⅡ

Petrous: Peripheral > 2:1 → Pituitary

< 1:4:1 → Ectopic

* Pancreatic → acts through Somatostatin receptors

* Ketone bodies

* Methylobene → 14Hydroxylase inhibitors

R.O.C → Surgery

DISORDERS OF SEXUAL DIFFERENTIATION (DSD)

XX DSD

XY DSD

XY DSD: SRY gene on Y chromosome → development of testis

Testosterone

→ Mullerian inhibiting factor

5 α Testosterone reductase

Dihydroxy Testosterone

Androgen receptors (X-chr. codes for androgen receptors)
Internal Genitalia → Mullerian duct → female structures

→ Wolffian duct → male structures

External Genitalia → develops from common indifferent structures

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

* MIF → blocks the Mullerian development.
* Testosterone → promotes development of Wolffian duct.

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

5\(\alpha\) reductase deficiency

\(\text{MIF} + \rightarrow \text{No mullerian development} \ \} \ \ \text{\(\alpha\)-internal genitalia} \)

Testosterone → Wolffian development

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

Androgen Receptor In Sensitivity

Testosterone + → No action on receptor → Wolffian Duct absent

MIF + → Mullerian duct \(\phi\) → No mullerian system

DHT + → No action on receptor → \(\phi\) external genitalia

Testes are present in the abdomen / undescended
* Will 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 testis are either undescended or even a indirect inguinal hernia and have a 30 fold higher risk of malignancy (Seminoma)

Testicular feminization syndrome  MRKH Syndrome  Mullerian agenesis  XX

- T.G → Absent
- Axial genitilia → Absent
- Erect genitalia → f
- Breast → M
- Breast → M
- Axillary/pubic hair → Absent
- Axillary/pubic hair → (N)
- Inguinal hernia → Int

Gonadal Dysgenesis:  → Pure gonadal dysgenesis  → Mixed gonadal dysgenesis

Pure gonadal dysgenesis:  → Breast development

No testosterone, No AR

Breasts Int., sex genitalia are female by default

* Breast development → absent

* Axial/pubic hair growth → N (due to androgen from adrenal)
Mixed Gonadal Dysgenesis

* One testis (genital) is streak, one gonad is normal

* General masculine picture, not proper masculinization because just one gonad is present (ovariation is not complete)

* Hypoplasia or anovaros

Range: Normal female $\rightarrow$ Male

any phenotype in between

XX DSD

* Maternal cause: Androgen-producing tumor $\rightarrow$ during pregnancy androgenic drugs

* Fetal cause: Congenital Adrenal Hyperplasia

  1. 21α-0H deficiency
  2. 11 α-0H deficiency $\rightarrow$ Androgen
  3. 3β-0H deficiency

Cytochrome p450 oxidoreductase

* Arinmalese defect: Glucocorticoid receptor gene mutation

* Anti-4 Mutation

\[ \text{FSH} \rightarrow \text{Estrogen} \]

\[ \text{TH} \rightarrow \text{Theca cells} \rightarrow \text{Testosterone} \]

\[ \text{CYP17A1} \rightarrow \text{Cell} \]

CHSL

Cholesterol $\rightarrow$ 17 hydroxy corticosteroids

\[ \text{Pregnenolone} \rightarrow \text{17-0H pregnenolone} \rightarrow \text{DHEA} \]

\[ \text{11b-hydroxylase} \rightarrow \text{Pregnanolone} \rightarrow \text{17-0H pregnanolone} \rightarrow \text{Androstenedione} \]

\[ \text{21b-hydroxylase} \rightarrow \text{Deoxytestosterone} \rightarrow \text{Deoxy cortisol} \rightarrow \text{Testosterone} \]
Medulla Reticularis
Fasciculata
Glomerulosa

Most common enz. defect → 21α hydroxylase deficiency

Autosomal recessive

Any defect of horizontal enz. will ↓ formation of Cortisol

A courageous will constantly stimulate adrenal cortex

Cortisol

21αOH / 11βOH deficiency → 17α H androgen levels will ↑

Can be used for evaluation in case of
ambiguous genitalia

(17-OH progesterone more preferred than 17α-hydroxylase)

Deoxy cortisolone (DOC) has mineralocorticoid action.

21αOH

- Aldosterone ↑
- xx → Ambiguous genitalia
- xx - ambiguous genitalia
- xy - premature puberty
- Metabolic acidosis
- Hyperkalemia
- Hypertension

11βOH

- Aldosterone ↑
- xx - Ambiguous genitalia
- xx - Ambiguous genitalia
- xy - premature puberty
- Metabolic acidosis
- Hyperkalemia
- HTN +
Phaeochromocytoma / Paraganglioma

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

95% Abdominal
5% Extra-abdominal

90% Nodal
10% Extra-nodal

- Organ of Zuckerkandl
- Wall of urinary bladder (Split of AP during catheterism)
- Ovary

Rule of 10: 10% Extra-abdominal
10% Bilateral
10% Children
10% are malignant at the time of diagnosis

Tyrosine

\[ \text{DOPA} \]

\[ \text{Dopamine} \]

\[ \text{Nor Adrenaline} \]

\[ \text{Porphobilinogen} \]

Not present in extra-adrenal tissue, so in such tumor, adrenaline is not present.

Porphobilinogen\( \rightarrow \)Methyltransferase (PMMT)

Adrenaline

Phenylethylamine \( \rightarrow \) Methyltransferase (PMMT)
Extra-adrenal
Nor epinephrine

Adrenal Phase
Epinephrine
Nor epinephrine

If MEN syndrome, then one adrenal -> no adrenal is produced

Malignant Phase:
N/C ratio
Miotic spiracles
Do not help to differentiate
Capsular invasion
Metastasis = only way to differentiate

Production of catechol / primitive metabolites

\[ \text{QF:} - \text{headache (no symptom)} \]
\[ \text{diaphoresis} \rightarrow \text{diaphoresis} \]

Taste loss (differential for cat. loss)

Phaeochromocytoma

* Catechols ↑
→ 18
→ T\text{\textsubscript{1}} \rightarrow R\text{\textsubscript{1}}

* Hyperadrenergic features
  * ↑ BMR
  * C.N. loss
  * Tachycardia (SUT + AF)

Thyrotoxicosis

* Hyperadrenergic features
  * ↑ BMR
  * C.N. loss
  * Tachycardia (SUT + AF)

HTN: sustained

Tremor: occasional

Tremor
Phaeochromocytoma

* Orthostatic hypotension ☑️
* absent

(due to volume contraction)

* ☐
* ARR deposition ☑️

↓

Tens ↓ 24 hr urine → catecholamines & Metanephrine assay → T.O.C. (fractionated)

* Plasma → catecholamine & free metanephrine assay

* Chromogranin A levels ↑ in plasma.

↓

Optimal siv. for phaeochromocytoma → abdominal MRI (sensitivity)
localization if +ve ↓ if -ve.

MIBG MIBG (sensitivity 81%)

(to look for meta)

↓

Best investigation ↑ DOPA PET.

↓

Alpha blockers

Phenoxybenzamine (route to achieve full effect)

Arginin

Phenolamine

Alpha blockers

Beta blockers → surgery

Conn's - primary hyperaldosteronism

Aldosterone ↑

→ Na⁺ ↑ + H₂O → ANP ↑ → Na⁺ + H₂O ↓

→ K⁺ ↓

→ H⁺ ↓ (metabolic alkaloïd)

→ HTN Renin ↓
Primary hyperaldosteronism (Conn) do not have oedema.

**Spironolactone, Eplerenone (Aldo receptor blocker)**

Primary hyperaldosteronism (*Aldo, Kreula*)

Abdominal imaging

AFL - adrenal enlargement (70%)

Conn's should only be used for Adrenal adenoma (30%)

not for adrenal hyperplasia.

**Autoimmune Polyglandular Syndrome**

**AEG 1**

- *Early Childhood, Infant*  
  
- *Hypo parathyroidism*  
  *Hypoparathyroidism, Celiac Spine, Dermatite herpet.*

- *Hypoparathyroidism*  
  *Graves disease*

- *Musocutaneous candidiasis*  
  *Hyperparathyroid, do-

- *Addison ane hypothyroid*  
  - do -

- *Atopy*  
  - do -

- *Hyperparathyroid*  
  - do -

- *Type I diabetes*  
  - do -

- *Addison's disease*  
  - do -

- *Vitiligo*  
  - do -
MEN-1  MEN-2A  MEN-2B  MEN-4
Werner syndrome  Liddle syndrome

* Parathyroid adenoma (i.e.)  * MTC  * MTC  * PTH adenoma
  Multiple
  * Phaeochromocytoma  * Phaeochromocytoma  * Phyllary adenoma
  * Entero-pancreatic problem  * PTH adenoma  * Magafoid  * Gastric Anal.
  Gastrinoma
  * Lichen-angitoid  * Pancreatitis  * Pancreas
  Visceral
  Tumor
  entero-Neuroendocrine  lesion
  neuroroma  * Py
  * Retinoblastoma  * Hirschspring's  -  * Adrenal
  * Carcinoid
  * Phaeochromocytoma (i.e.)

Mc. entero-pancreatic tumor in MEN1 \( \Rightarrow \) Gastrinoma
Mc. pancreatic tumor in MEN1 \( \Rightarrow \) Insulinoma
Mc. tumor in MEN1 \( \Rightarrow \) Parathyroid adenoma

Gastrinoma \( \Rightarrow \) Gastrin

\( \downarrow \) Basal acid output

\( \downarrow \) Peptic ulcer disease

3. Severe Gastrin can be due to:
   1) PCT
   2) Pernicious anemia
   3) Atrophic gastritis

If Stomach \( pH < 2.0 \) Serum Gastrin is \( > 1000 \mu g/mL \)

\( \downarrow \)

* Mc. site for Gastrinoma  Gastrinoma
  Duodenum 8 1st Process

[\( \downarrow \)] - PCT, Surgery
Insulinoma: Episodes of hypoglycaemia

72 hr fasting (i.v.c.)

Insulin: Glucose < 0.3. (Check insulin:glucose ratio every hour)

possibility of insulinoma

Insulinoma → Fasting hypoglycaemia

β-cells

Sulphonylurea → Insulin

pro-insulin

β-cell

C-peptide

insulin

Gastropid ↓

> 0.9 mg/l (fast) < 0.9 mg/l
> 200 pmol/l < 200 pmol/l

[Q]: *Diazenide + Carbohydrate diet*

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

* Metastatic: Streptozocin + 5FU

Surgery → Localisation of tumour in pancreas

ELIS

CT (Contrast CT) → I.V.C.

Intra-operative Ultrasound

* Gold Standard: Angiography
CARCINOID

Location: ⅔ → GIT
  ileum ③
  rectum ③
  colon ④

⅓ → lung ①
appendix ⑤

ovary

(Carcinoid syndrome is rare in rectal carcinoids.)

* M.e. complaint of Carcinoid tumor: Abdominal pain
* M.e. complaint of Carcinoid syndrome: Flushing & diarrhea

Carcinoid Syndrome

QFE: * Diarrhea

* Flushing
* Asthma-like wheezing episodes
* Endocardial Fibrosis - RV

TR > TS > PR > PS - Serotonin

Iow: Best: PET scan

T.O.C: Scintigraphy

Niacin ↓

Surgery

Diarrhea
Dermatitis
Dementia

Tryptophan
Carcinomatoma

Diarrhea

Gall stones

Ulcers

* Werner-Morrison Syndrome
* WDHA Syndrome
  - Watery diarrhea
  - Hypokalemia
  - Hypochloremic
  * Stool osmotic gap < 50 mosm/L
  * Stool sodium output > 90 meq/L

(Case of secretory diarrhea → Stool osmotic gap > 50 mosm/L)

Calcium Disorders

Calcium

\[ \text{Ionised } Ca^{++} \quad Ca(perox) \quad Ca \text{ bound to Albumin} \]

\[ \begin{align*}
50\% & \\
10\% & \\
40\% & 
\end{align*} \]

\[ \text{Ca}^{++} \xrightarrow{\text{alkalosis}} \text{Ca} \text{ bound to albumin.} \]

(in case of hyperventilation → CO₂ washout → alkalosis → Ca⁺⁺ → Carpopedal spasm)

Hypocalcemia → cells become hyper excitable → Exaggerated jerks
  → Spasms, Tetany
  → Tetralogy
**Pseudo Hypoparathyroidism**

- Defect in Gsa receptor.
- PTH ↑
- Loss of function mutation → Albright Osteodystrophy

**Pseudo Pseudo hypoparathyroidism**

- Defect in bone forming protein or cAMP control.
- Osteoclastic activity (O) cAMP is unaffected.
- Gsa activity (N)

**McCune Albright Syndrome**

- Gain of function.
- Gsa overactivity.
- Polyostotic fibrous dysplasia.
- Precocious puberty.
\[ \text{Ca}^{++} \xrightarrow{\text{PTH}} \text{Bone} \xrightarrow{\text{PTH}} \text{Ca}^{++} \xrightarrow{\text{Vit D}} \text{Phosphate} \]

- If there is \text{Vit D} toxicity \( \rightarrow \text{Ca}^{++}, \text{PO}_4^{--} \)
- If there is hypoparathyroidism \( \rightarrow \text{Ca}^{++}, \text{PO}_4^{--} \)

\text{Hypoparathyroidism} \quad \text{Vit D dependent:}

- \[ \text{Ca} + \text{PO}_4 \]

\text{Chronic Renal Failure} \:\text{Vit D is not formed; Ca}^{++} \quad \text{phosphate is not excreted; PO}_4^{--} \]

\text{Normal values:}
- \text{Ca} = 9 - 11 \text{ mg/dl}
- \text{PO}_4 = 2.5 - 4.5 \text{ mg/dl}

\text{Cre} = \geq 1.3 \text{ mg/dl} \quad \text{is indicative of ERF.}

\text{PBP, osteocalcin are osteoblastic / bone forming markers.}

\text{Proline, hydroxyproline are osteoclastic / bone resorption markers.}

\text{Granulomas have 1,25OH activity \rightarrow formation of vit D.}
Ca  P<sub>3</sub>  PTH  ALP

Primary hyperparathyroidism  ↑  ↓  ↑  ↑

Hypercarnicaemia  ↓  ↑  ↓  N/↓

Rickets/ostemalacia  ↓/N  ↓  ↑  N/↑

Lactose  ↑  ↑  ↓  N

Malignancy/PTHrP  ↑  ↓  ↓  ↑

Ca, cell Ca, lung

Osteoporosis  N  N  N  N  N

Paget's  N  N  N  N  ↑

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

↑Ca / ↑Mg → PTH↑ or  ↓Ca / ↓Mg → PTH↑

Small cell Carcinoma can cause hypoCalcemia but generally doesn't cause hyperCalcemia unless there is metastasis to osteoclastic activity

Paget's disease coupled hyperactivity

osteoclastic ↑

osteoblastic ↑

Multiple myeloma  ↑  ↑/N  ↓  N

osteolast activating factor

Pickoff gene ↓ silenced

Feedback of osteoblastic activity is suppressed.
Pseudohypoparathyroidism

- Due to deficiency of receptor activity

- N/N

- Short stature

- Osteoporosis

- Hyperphosphatemia

PTH is defective, mainly due to dominant inheritance

Ca++ is low

Osteoclasts

Bone forming protein

Ca++ is low

Osteoporosis

Ca++ is low

Pseudohypoparathyroidism

- Short stature

- Hyperphosphatemia

- Osteoporosis

- PTH is defective, mainly due to dominant inheritance

- Ca++ is low

- Osteoporosis

- Pseudohypoparathyroidism

- Short stature

- Hyperphosphatemia

- Osteoporosis
Familial hypocalcemic hypercalcemia

Hyperparathyroidism

Familial hypocalcemic hypercalcemia

+ 2nd decade

+ Adrenal Dominant
  1st/2nd decade

+ Renal Stones

+ Urine Ca ↓

+ Urine Ca ++ ↓

- Urine Ca ++ → 2%
- Urine Ca ++ < 2%

In hyperparathyroidism, the Ca++ sensing receptors on the vascular endothelium of the kidneys stop Ca++ absorption after a certain level of hypocalcemia, ie Ca++ secretion leading to renal stones.

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

* Thiazide diuretics help unmask the diagnosis of hyperparathyroidism due to their Ca retaining action as a long term effect.
Vitamin D Dependent Rickets

Type I: 25-OH cholecalciferol (100) \rightarrow 1,25(OH)\_2 COF
\[\text{deficiency} \]
\[\text{Ca, \text{P}_4} \text{ (due to low absorption from G1T)}\]

Q: Vitamin D supplementation life long

Type II: 25-OH COF \rightarrow 1,25(OH)\_2 COF \rightarrow Receptor \rightarrow unresponsive
\[\text{responds} \]
\[\text{Ca on the receptor} \]

very high dose of vit D

Q: Vitamin D supplementation life long

Vitamin D resistant Rickets:

Hypophosphatemic Rickets \rightarrow P}_{4} \_4\_4\_4

Inheritance \rightarrow XLP

\[\text{vit D supplementation + P}_{4} \_4\_4\_4 \text{ supplementation} \]
\[\text{Only vit D won't help}\]
Hypothalamus → 3° hypothyroidism → T_{3}, T_{4}, TSH, T_{4} → Pituitary → 2° hypothyroidism → T_{3}, T_{4}, TSH, T_{4} → Thyroid → Primary hypothyroidism → T_{3}, T_{4}, TSH

If TSH is ↑ then it is Central hypothyroidism.

In 1° hypothyroidism → ↑ TRH → causes ↑ Pituitary (due to direct and biophyl stimulation)

Normal TSH → 0.5 - 5 IU

Radio iodine uptake is dependent on TSH.

↑ for RAIU → TSH has to be high → Stop thyroxine (T_{4})

RAIU ? Tissue deficiency

Hypothyroidism

Toxic → Exogenous administration of thyroxine

RAIU + Thyroiditis

Thyotoxic → a) Hashimoto's Thyroiditis

RAIU + b) Subacute Thyroiditis

c) Gravida
* Graves Disease
* Toxic Adenoma

* Toxic
* Toxic

* Autoimmune Abs.
* Adenomatous part of thyroid producing excess thyroxine

* TSH receptor Ab → most specific ↓ (anti-TSHR)

\[ \text{Goiter} \xrightarrow{I_{2}} I_{3} \xrightarrow{T_{3}, T_{4}} \]

(Anti TPO Ab also seen)

* TSH ↓
* TSH ↓

* GAG ↓ +
* Absent
* Propranol +
* Thyroid acropathy (finger tips)
* Acroparesthesia
* Hypothyroid Myxedema

* RAIU = heterogeneous
* Nodular uptake

* \[ ^{131}I \text{ Scintigraphy} \]
  * Anti thyroid drugs
  - Antithyroglobulin
  - Baptythiouracil

* Surgery
  * RF ablation

[ Surgery has to be done in Retrosternal goitre ]

because if RF ablation is given Retrosternal goitre → Bleed may happen
  Compress the airway
Thyroiditis > RAIU is low (except in recovery phase)

- Hashimoto's
- Subacute
- Riedel's

- Autoimmune
- DeQuervain's
- Thyroiditis

- Antinuclear Abs
  - Fever, Cold
  - Nausea
  - Acute TPO Abs
  - Sore throat
  - Hypothyroid (becomes hyper after steroid)

- Wilms Tumor
  - Pain in neck
  - Tenderness thyroid
  - Dysphagia
  - Hard mass [most pt.]

- Type I DM
  - Pernicious anemia
  - May have silent hypothyroid (w/p.)

- Lymphocyte infiltration
  - Lymphocytic thyroiditis

  - Fibrosis can also happen

  - Adams-Darkwater's contracture
  - Retroperitoneum - Osmond's
  - Buzel - Payrane's [ED]
  - Mediastinal fibrosis

- Sc and toxic > β blockers
  - MSARR
  - Ty[-]
  - Antithyroid
  - Steroids
  - Tamoxifen (to reduce fibrosis)

Thyroiditis → T4

[It is not given due to upregulated receptors]

Kombigoril, if given in 1st trimester may cause Cerebral Palsy

Acute thyrotoxicosis is caused by Bacteria → subcapsular abscess

Thyroid function is Normal

[Subthyroid]
Wolff-Chaikoff's Phenomena: $T_2 \rightarrow T_3, T_4$

Hashimoto Phenomena: $T_2 \rightarrow T_3, T_4$

Endemic Tissue Deficiency → Thyroid to adjust

↓ $T_3$ given

↓ $T_3$ is not preserved

↓ Hashimoto effect $→ T_3$ is produced

Excess iodine

Radioiodine $\rightarrow T_4$ (crosses blood-brain barrier better)

β Blockers $\rightarrow T_3$ (active moiety)

Adrenalectomy

DIABETES MELLITUS

>/', Pre-Diabetes: * FBS = 100 - 125 mg/dl

Impaired Fasting Glucose

* PPBS = 140 - 199 mg/dl

Impaired Glucose Tolerance

HbA1c = 5.7 - 6.4

Overworked β cells $→$ Insulin

慢性 course $→$ Insulin $↑$

Hyperglycemia

Glucose $↑$

Receptor resistance

↓ Insulin $→$ Pathways of Glucose entry

↓ glucose
Drug of Choice: Metformin (to increase glucose receptor sensibility to work hard on the β cells)

if not controlled, Metformin

Metformin + OHA
(prefered in older patients)

Metformin + Basal Insulin
(prefered in pts ≤ age 70)

↓ Life expectancy

to preserve the β-cells for later years

 גestroational Diabetes Mellitus

- 50% loss of β-cell mass is required to be lost to develop type II DM

(if ≥ at threshold level before pregnancy)

(during 2nd trimester → glucose ↑ due to HCG)

( gastroational DM) → high risk of development of type II DM

(No congenital malformation) by 2nd trimester

Pre-gestational DM → organogenesis has happened

Canciter

NTD

VSD >>> TGA

Spina bifida >>> Sacral agenesis
TYPE I DM:

- Autoimmune
- Viral infection - Cytomegalovirus
- Exogenous - Insulins

- MCA P2/P2-Q

Type I

∂ > 45 yrs

- Autoimmune
- Non-obese
- T cell Abs

- Glucokinase Deficiency

- GADA

- CMI
  - Apoptosis

TH2
  - Nitric oxide metabolites

- T cell destruction
  - Aneurysm deposition in blood vessels

Insulin

@ the time of diagnosis almost 80% of adults are lost

Ketoadicidosis +

- Family history: + > 3-fold increase

MODY

Autosomal Dominant

Type I → MNE - Ax
Type II → Glucokinase - Most frequent
Type III → MNE - Ia - Most Common
Type IV → IPF
Type V → MNE - IB
β-cell mass is normal
No peripheral resistance to insulin
Non-obese patients
Defect - Glucose sensing Defect

[?]: low dose of Sulphonylureas.

Type I DM

- < 25 yrs.
- Non-obese

Type II DM

- < 25 yrs.
- Non-obese

- Family history in 3 generations
- AD-penetrance > 80%
- Ketones:
  - Non-ketotic (KA is rare)
  - No OHAs (SUR)
  - Abs ++

+ LADA (latent autoimmune Diabetes of adult)

* Abs+ - TCA, GRADA
* HLA - DR3/DR4.
* > 25 yrs.
* Initially OHAs can be administered but rapidly become unresponsive to OHAs and require insulin.
* Non-obese.

[?]: Treat as with Type I DM.
* Immunosuppressants.
* Steroids.
DIABETIC COMPLICATIONS

<table>
<thead>
<tr>
<th>Microvascular</th>
<th>Macrovacular</th>
<th>Non vascular</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Retinopathy</td>
<td>- IHD</td>
<td>- Infections</td>
</tr>
<tr>
<td></td>
<td>- Stroke</td>
<td>- Glaucoma</td>
</tr>
<tr>
<td></td>
<td></td>
<td>- Cataract</td>
</tr>
<tr>
<td></td>
<td>- Neuropathy</td>
<td>- Gastroptly</td>
</tr>
<tr>
<td></td>
<td>- PVD</td>
<td></td>
</tr>
</tbody>
</table>

- Tightly control of blood sugar → 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 diabetes than non-diabetics

- HbA1c → controlled: 4.5 → twice a year
- Uncontrolled: 4 times a year

- Metformin
  - GFR < 45 ml/min → Reduce the dose
  - < 30 ml/min → Stop metformin

- GFR > 1.4 → Stop metformin
- GFR > 1.5 → Stop metformin

- Thiazolidinediones → PPAR agonists
  - Can be used in renal failure
  - Need to be stopped in heart failure (NYHA 3, 4)
  - Can cause weight gain
**Pioglitazone**

- LDL ↑
- HDL ↑
- TG ↑
- Possible complications
- May be implicated in Ca Bladder

**Saxagliptin**

Dual PPAR agonist against PPARγ

↑ insulin resistance

**SGLT-2**

- Required for reabsorption of glucose from PCT
- Blocks, no glucose reabsorption
- Glucosuria
- Better control of HbA1c

*E.g.*: Canagliptin, Dapagliptin

assoc. with risk of vaginal infections, UTI

**Insulin**

- A-cells
- Amylin → ↓ Glucagon

**Glucose**

- Ramlimtid
  - ↓ Glucagon
  - Increased satiety
  - wt. loss
  - Can be used in both Type 1 & 2
Incretins

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

**INCRETIN EFFECT**

GLP-1 \{ incretin released by the L-cells of duodenum.
GLP-2 \rightarrow \text{ in Type II DM patients}

GLP-1 may cause \( 
\text{ in} \ \text{insulin release from \( \beta \text{-cells} \) (Glucose dependence of GLP-1)}\)

\( \text{GLP-2} \) inactivation by \( \text{DPP-IV} \)

Exantide \( \rightarrow \) modified GLP-1 \( \rightarrow \) not inactivated by DPP-IV

GLP-2 \( \rightarrow \) derived from Gila Monster analogues

Liraglutide

Dulaglutide

\( \text{DPP-IV inhibitors} \)

\{ Liraglutide \}
\{ Exenatide \}
\{ Older generation \}

\{ Alogliptin \}
\{ Vildagliptin \}

S/F: Pancreatitis / NIC adults

Lanaglaptin

GLP-1 analogues are more efficacious, cause wt loss, Route - SC.

DPP-IV inhibitors are less efficacious, Route - oral.

Dose should be modified in renal failure for both.
LIPIDS

Formula for calculating LDL:

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

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:

✓ MCRP + TC:HDL
✓ MCRP (best single parameter for future risk of MI)
✓ TC:HDL
✓ Non-HDL (TC:HDL)
✓ Apo B/Apo A1
✓ LDL
✓ Lp(a)
Type I → Familial Hypercholesterolemia → ↑ Cholesterol (Lipoprotein Lipase deficiency)

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

Type III → IDL (Receptor defect) → ↑ ApoB100 (defect)

Type IV → Diabetes Hypercholesterolemia → ↑ LDL

Type V → Combined → LDL, TG, VLDL ↑

Type IIb and IIr are the most common.

Xanthomas are not seen in IIb and IIr.

Tendon Xanthoma → IIa

Palmar + Superoceptive Xanthoma → III

Superoceptive Xanthomas are seen in type II (rare)

Re: LDL HDL TG

Statin ↑↑ (max) ↑ ↓

Fibrin acid ↓ ↑ ↓↓ (max)

Niacin ↓ ↑↑ (max) ↓
ApoA₁ - Associated with HDL (lecithin)

ApoB₄₈ - Derived from ApoB₁₀₀ by RNA editing
→ associated with chylomicrons

Chemical change
↓

Glycosyl is replaced by glycine (glycol)

absent: ApoB₄₈ → Abetalipoproteinemia

present: like Friedrich's Ataxia

lipid instability → irregular membrane

Acanthoblasts

Spur cells

[R] - large dose of 1% F

{Type IIa: has the highest risk of CAD/HD}

Type IIa type 1 → homozygous → death in 1st/2nd decade

heterozygous → death in 3rd/4th decade

SAME: Syndrome of Apparent Mineralocorticoid Excess

Cortisol → Cortisol (has mineralocorticoid activity)

↓ RAAS

11β-HSD dehydrogenase

Aldosterone → Cortisol deficiency due to mutation

↓

Cortisol level ↑

↓

↓ mineralocorticoid activity

Aldosterone levels are low
Cardiology

JVP

- a-wave - atrial contraction
- c-wave - bulging of tricuspid valve - in diastole, atrial contraction
- x-descent - atrial relaxation
- x'-descent - ventricle contraction → wall of atria & ventricle is sucked by the ventricle - atrial expansion
- v-wave - venous return into RA
- y-descent - early diastolic filling (70-80% of filling occurs by this)

v-wave is taller in LV atrium due to compliance of LV atrium

- Giant a' wave: TS, PS, PAH, RV diastolic dysfunction
- Cannon a' wave: AV dissociation, V ectopic (misc. cause) irregular
  VT, Complete heart block (very frequently) coronary
  Functional mitral - regular cannon a' wave
'C' waves - TR (normal 'r' descent is missing)

Premature 'u' wave - 'u' wave taller than 'a' wave

Rapid 'x' descent - Tamponade

Rapid 'y' descent - Constrictive pericarditis

Square root sign \ Constrictive pericarditis

U-pattern JVP

Equalization of pressures in heart (RA, RV indistinguishable, pulm. art. pressure)

seen in Cardiac tamponade & pericarditis

Cardiac Tamponade

Constrictive pericarditis

* Rapid 'x' descent

* Absent 'y' descent

Kussmaul's sign

* No Kussmaul sign

* JVP decreases on inspiration

* present

* Absent paradoxus

* 1/2 of pts = present

VSD, papillary muscle will

not allow a pulsus paradoxus

in Tamponade
Pulmonary edema 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% to 80% of arm circumference.
* Cuff should be deflated at 3 to 4 mmHg per second.
* Column or dial should be read nearest to 0.5 mmHg.
* First audible Korotkoff sound -- SBP, last audible -- DBP.

**Blood Pressure Measurement**

- Systolic:
  - Arterial higher
  - Automated
  - Manual

- Diastolic:
  - Manual / Automated higher
  - Arterial

Manual measurement underestimates the SBP while it overestimates the Diastolic AP, compared to intra-arterial measurement.
HEART SOUNDS

S₁  S₂  S₃  S₄  S₁

DIASTOLE  SYSTOLE

Conditions for loud S₁:

1) The valve leaflets shut more quickly.
2) The valve leaflets are wide open.

Seen in:
- Tachycardia
- Tachyarrhythmia
- Mitral stenosis
- Short PR interval
- Calcified valve annulus

In pts. of soft S₁, MS → don't do Balloon Mitral valvulotomy
- because MS will worsen
and calcified commissures won't yield

S₂:

A₂ occurs earlier than P₂.

P₂ is delayed in inspiration. Inspiration splitting is more
A₂ is early in inspiration

During expiration: S₂ appears as a single sound due
do close splitting (<20 msec)
- Usually early and late
A_2 P_2
So split

\[ \text{Severe MR} \rightarrow \text{atrial} \]

\[ \text{AR} \rightarrow \text{Narrow} \]

\[ \text{AS} \rightarrow \text{Narrow, reverse} \]

\[ \text{LBBB} \rightarrow \text{Narrow, reverse} \]

\[ \text{PS} \rightarrow \text{wide} \]

\[ \text{Pulm HTN} \rightarrow \text{Narrow} \]

\[ \text{PDA} \rightarrow \text{Narrow} \]

\[ \text{HTN} \rightarrow \text{Narrow} \]

\[ \text{ASD} \rightarrow \text{Wide fixed} \]

In [PDA] \rightarrow The blood flowing from Aorta to PA doesn't go to RV

- It goes to lungs and then to LA 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 pressure in PA will be

- Pulmonary valve early overcoming the pressure in RV

In [A2 HTN] \rightarrow P_2 occurs last because aortic pressure can't close the valve

- Over RV and LV, it takes a longer time to pump the

- Blood against against P pressure.
* auscult. I \* pre load  ausc. = \* after load

* early diastolic filling = atrial contraction
S3 will not be seen in MS.
S4 will not be seen in R.fib.

H. s2  R.h.s2  H. s4
→ Atr. MR, PR  → TR, PR  → HTH
→ PDA, VSD  → ASD  → AS.

→ Hyperdynamic condition  → G.A.
\* exercise, anaemia,  → MI
\* pregnancy.

→ Physiological < 30 yrs of age
→ THD = MR

**cyanotic Congenital Heart Disease**

cyanosis  \* Pulmonary Blood Flow  cyanosis + pulmonary

\[\begin{array}{l}
\downarrow \\
\text{ToF}
\end{array}\]

\[\begin{array}{l}
\uparrow \\
\text{TAPVC}
\end{array}\]

\* Patent's

\* Tricuspid

\* Truncus arteriosus

M.C. cyanotic HD : TOF
M.C. cyanotic HD at birth : TAV.
M.C. cyanotic HD in children : TOF
TETRALOGY OF FALLOT

- Pulmonary stenosis
- RVH
- VSD
- Overriding of Aorta

25% of TOF have a Rt-sided aortic arch

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

Blue TOF → Silent Chest
Pink TOF → Murmur is present

Pulmonary stenosis is inversely related to Murmurs.

Blue TOF → Cyanosis → Catecholamines ↑

Infundibular contraction

↓

Less blood flow → No Murmurs.

Genetic Null: RVOT ↑

O₂ ↓

Squinting → falls due femoral artery → ↑ pressure in Aorta.

RV starts pushing blood into PA
[A] of cyanotic spell:  
* β blockers
  
* Humidified Oxygen
  
* Morphine (depress the respiratory centre)
  
* α agonists (vaso-constrictors)
  
Features not occurring in TOF:
  
Y-Ray:  
- Boot shaped heart
  
  
→ Cardiomegaly
  
  
→ CCF
  
  
→ Newborn Gynoid
  
  
R. 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)
  
Potts Shunt:  
→ PA - Desc. aorta

(Robinson's Shunt:  
→ PA - Asc. aorta)

Ebstein's anomaly:

* Atrialization of the RT ventricle.
  
  The septal height is present inferior to its normal location leading to atrial enlargement.

Sail like septum:  ECHO finding
There is no pulmonary stenosis

Functional pulmonary blockade is present.

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

At Triuspid Regurgitation is int.  x-ray: box-shaped
Thrice is huge cardiomegaly in children.  Massive Circulo mega.

FCG = tall P waves (due to RA enlargement).

Tricuspid Atresia

ASD is a must in Tricuspid Atresia and TAPVC.

Left axis deviation in the ECG & Gyneotic Heart Disease → TA
(because the LV dominates the TA)

Total Anomalous Pulmonary Venous Drainage:

→ Supracardiac → SVC  33% have a right-sided aortic arch.

→ Cardiac → Right atrium.  Not a ductus dependent condition

→ Inf-supracardiac → IVC  S - white fixed.

Portal vein (worst prognosis)

X-ray: Snowman’s appearance

Figure of 8 appearance.
Transposition of Great Arteries:

The baby will present with cyanosis at birth.

Partial procedure → Atrial Septostomy

Later → Switch procedures

* X-ray: Egg on side/string appearance (only for uncorrected transposition)
* Systemic circulation

Corrected transposition

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

* D-transposition is corrected.
* L-transposition is uncorrected.

ISCHEMIC HEART DISEASE

Chest pain → Chest pain varying [a sensation → pericardial disease]
   [2 position → pericardial disease]
   [Upine → 1, erect → 1]
   [2 palpation → Musculo-skeletal]

Cardiac chest pain:  
   * Compressive [Posterior cervical sin is damaged]
   * Radiating → jaw, neck pain
   
   Epigastric (never below umbilicus)
Serum troponin should be reported → Treatment/prognosis depends on troponin level

New Onset Regional Wall Motion Abnormality (RWMA)

* Akinetic segment due to defense mechanism preventing further damage to the ischemic area.
* RWMA is detected earlier than ECG on ECHO

NO RWMA (new onset) → Myocardial infarction is excluded.

New onset RWMA → not specific but sensitive for MI.

**Classification of MI**

<table>
<thead>
<tr>
<th>Type</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Sudden Cardiac death</td>
</tr>
<tr>
<td>IIa</td>
<td>1. Ischemic pain.</td>
</tr>
<tr>
<td>IIb</td>
<td>2. ECG changes (ST changes or New QRS)</td>
</tr>
<tr>
<td>III</td>
<td>3. Echo - RWMA (new onset)</td>
</tr>
<tr>
<td>IV</td>
<td>4. Angiography - Coronary thrombosis</td>
</tr>
<tr>
<td>V</td>
<td>CABG → Troponin &gt; 10 times above N</td>
</tr>
</tbody>
</table>

**Treatment**

1) Best
2) Oxygen therapy
3) Aspirin - 325 mg (can be given before any procedure like ECG, thrombolysis) → Reduce mortality
4) NSAIDs - don't reduce mortality
5) Morphine - IV (control of pain)
6) IV β blockers → with modified dose. CCB are not to be used.
7) Heparin (Nitroprusside worsens mortality)
Thrombolytic therapy

Primary percutaneous coronary intervention

- Thrombolytic therapy is faster
- and requires less facilities
- Earlier the procedure
- More muscle can be saved
- Ballooning with permanent stent placement can be done

* If it is not possible to do
  PCI in 2hrs, then do
  Thrombolytic therapy

* Door to needle time < 30min: goal
* Door to balloon time < 90min: goal

STEMI - 2013

PCI non capable hospital

if it is possible to transfer to PCI capable hospital

No

Yes

do PCI in 2hrs

Thrombolytic therapy

(3-24 hrs angiogram)

After 12 hrs, 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 pt. is hemodynamically stable 
PCI after 24 hrs is of no benefit

hemodynamically unstable -> PCI always has a benefit
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.

\[
\begin{align*}
\text{AWMI} & \rightarrow \text{LADCA} \\
\text{LWMI} & \rightarrow \text{LCXCA} \\
\text{ALWMI} & \rightarrow \text{LMCA} \\
\text{TWMI} & \rightarrow \text{RCA}
\end{align*}
\]

Hypotension

Ant/Anti:

- Bradycardia
- Inotropic Balloon pump (IABP)
- Atropine
- TEE should be done after

RV Failure

- No pulm. Press
- TEE just provides symptomatic benefit
- IABP

Avoid nitro

No mortality benefit of IABP
- Left Main Coronary >50% blocked → CABG (better than PCI)
  Triple vessel disease
  Restenosis rate
  CABG: Saphenous graft → 60-70% / 10 yrs.
  Internal Mammary Artery → 30-30% / 10 yrs.

  PTCA: - Only clot removal Septal Wall → 40% / 1 yr.
  - Bare metal stent → 20% / 1 yr.
  Drug Eluting Stent + → 10-15% / 1 yr.
  - Dual anti-plt therapy

  Restenosis: PTCA > CABG.

  CABG is not done due to: 1) Stenotomy/scan on chest
  (not preferred) 2) Hospital stay/ Mortality surgical vs

  - Bare Metal Stent
  - Drug Eluting Stent

  * Endothelialization of stent (not complete)
  → Paclitaxel
  → Sirolimus
  * indication pts: intolerant to
  → Everolimus

  Anti-plt. sthld drugs.

  Endothelialization of stent is not complete

  for min 1 yr [2 anti-plt. drugs
  should be given]

  Regional wall motion abnormality: post mi:

  Viable tissue Scan tissue
  (angiogram doesn't help in differentiating the above/normal tissue)
Viability indicated by:

- Stress ECHO ( Dobutamine scan)

- Nuclear perfusion studies
  - Tc-99
  - Th-201 / Sesta MIBI

- MRI - T.0.c

- PET scan - Best investigation

MRI to T.ost:
- Scar -> Bright (late enhancement)

Viable Myocardium

Skewed Myocardium

- Alternating myocardium

Coronary flow - good

- Hypoperfusion of myocardium

Reperfusion is beneficial.

- In Technetium pyrophosphate scan -> Scar is bright

In pyrophosphate, calcium = Ca++

Ca++ in dead / scar tissue

- Scan is bright
ARRHYTHMIAS

Speed of current across:
1) Muscle: 0.5 m/s
2) Bundle of His: 1 m/s
3) Purkinje fibres: 40 m/s

AVN is the slowest conducting tissue of the heart.

1st part of septum to be excited: LV, lower RV septum.
Last part to be activated LV → posterior basal part of LV. (last)
RV → pulmonary conus

If QRS width < 0.125 sec → current is entering the ventricles through the bundle of His and the left and right bundles.

Endocardial cell → longer refractory period → direction of depolarization is...
Myocardial cell: shorter refractory period → repolarization is...
Poor progression of Ranaw - if the Ranaw doesn't progressively increase in height from $V_1$ to $V_6$

Arrhythmias: → automaticity → re-entry

(Defibrillation shock will not work if there is no re-entry)

will not work in case of a flat line → because defib homogenizes the current in the heart into the same phase

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

Atrial Fibrillation → idiopathic

Hypertension

Aortic Heart Disease

Mitra Stenosis

Hypoatricosis:

Alcohol (Holiday heart syndrome)

Electrolyte Imbalance

Rate: 350 - 550/min - due to multiple re-entry currents around the pulmonary openings or in the RV
**ECG:**
- No p-wave or irregular p-wave (very baseline)
- qrs wave is normal (narrow)
- R-R interval fluctuates (due to erratic conduction by AV)

**R:**
- Rate control
  - n/a
  - safer and easier
  - Thrombotic
    - Close to anti-aggregants
  - Defiboloids + d-c for rhythm
- Slow AV node conduction
  - Adenosine (1, 2, 9 sec)
    - → β-blocker
    - used for AF
    - Verapamil, Dilatazem
    - Digoxin

**A-fib:**
- > 48 hrs → lyse atrial clot

**Rate control**

**Anticoagulation:**
- Do not do rhythm reversal
- min 3 wks anticoagulat
  - changes of embolism

**Rhythm reversal**
- Confirm anti-coag for 4-6 wks

(ANTI-CEGULATION IS GIVEN BECAUSE ELECTRICAL ACTIVITY MIGHT BE RECOVERED BUT
- MACH ACTIVITY IS NOT RESTORED - ELECTRO-MECHANICAL DISSOCIATION)

**CHADS vascular score**
- Cardiac failure → 1
- HTN → 1
- Age > 75 → 2
- DM → 1
- Stroke/TIA → 2
- Vascular - Cardiac → 1
- Age 65 - 75 → 1
- Sex female → 1
* Conventional anticoagulants &
  
  Prostacyclin \rightarrow \text{Direct thrombin inhibitors}

  - Rivaroxaban \text{ Factor IIa antagonist}
  - Apixaban

  For any arrhythmia \rightarrow \text{Electro-physiological study}

  \downarrow

  Radiofrequency ablation

  Cox Maze technique: to prevent recurrence after radiofrequency ablation

  **ATRIAL FLUTTER**: Single or Macro Re-entry Circuit

  Usually in the 8th atrium.

  ECG \rightarrow \text{Multiple P-waves \rightarrow Slab Tooth appearance}

  QRS complex is narrow

  R-R interval is fluctuant

  [IR]: Some atrial fibrillation

  except Radiofrequency ablation is quite easily done

  compared to Atrial fibrillation.

  **PSVT**: mechanism:

  AVNRT (Atrioventricular nodal re-entrant tachycardia) 60-70%.

  AVRT (Atrioventricular re-entrant tachycardia) 20-30%.

  Atria & ventricles are not contracting simultaneously \rightarrow \text{no cannon o' 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-waves may be there - buried in the QRS complex
- Rate > 150/min
- R-R interval is regular (not fluctuant)

WPW: Torsade de Pointes

P-waves are always present (never absent)
always occur after the QRS complex

a. Carotid massage

- iv: Adenosine (long) - D.e.c. fails → Dobutamine + AV node blocker
  - β-blocker
  - CCB to prevent further episodes
- Diginin
  - Cardiopulmonary

Type A: Accessory pathway via His to RV (m.c.) → Radiofrequency Ablation

Type B: Accessory pathway via RA to AV

WPW syndrome: - Most pts. are hemodynamically stable
- Impulses generated by SAN (40-60/minute)

ECG: QRS is broad > 0.12 sec.

PR interval is same as P-wave

Delta wave is present (due to conduction by the band of muscle)

If AV-blockers are used → Only conduction through muscle band

Hence avoided I, II, III, aVF

- Adenosine
- β-blockers
- CCB
- Diginin → worst
Best treatment is radio-frequency ablation.

After RF ablation → A → A

Drug: Class Ia, Ic, III

Mild symptoms → Severe Symptoms

Ventricular Ectopic

Unilocal Ectopic → localized pathology

Multilocal Ectopic → Electrolyte imbalance

- Drugs
- Alcohol
- Inflammatory processes
- Diuretics
- Diffuse irritation of myocardium

Compensatory pause is seen in ventricular ectopic.

Run of vent. Ectopics → VT

Rate > 100/min.

Run > 30/sec → Sustained VT ≤ 30/sec → Non Sustained VT

Ventricular Ectopic → VT / VFib

- β Blockers
- Catecholamines

Risk of > 10 Ectopics/min.

Conversion of shorts Ectopics

VT / VF → R-on-T phenomena (Ectopic in presence where T-wave should be).
* Synchronized Defibrillation → Cardioversion
  - Shock should be given at Raven.

* Non-Synchronized Shock may be given in:
  → Palpable VT
  → Ventricular Fibrillation

[Box]:
*(Only β-blockers have benefit in Ventricular Ectopic)*

* Intra-Cardiocellular Defibrillation
  - Indications → Multiple Vent Ectopic
    → Ejection fraction < 30% (< 25%)
    → Congenital heart blocks

Ventricular Tachycardia

- Monomorphic VT
- Polymorphic VT

Morphology of QRS complexes are different
- Identical

Broad QRS is seen in:
- Bundle Branch blocks
- P-wave before every QRS
  (> 0.125)
- VT → no p-wave before QRS
- Wolff-Parkson syndrome
- Idioventricular → Automotility

No p-wave before QRS

VT → Rate > 120/min

Atrial → Idioventricular 40 → 120/min

Idioventricular < 40/min.

M. C. cause is reperfusion arrhythmia.

If persist...

Avoided agent
VT

Long QT syndrome

Congenital LQTS

Acquired LQTS

LQTS → Emotional

β blockers

Torsades du pointes

LQTS → Emotional stress

Cyclical polymorphic VT → long QT

LQTS → Sleep

ICD

80-90% of LQTS is 1 & 2.

Failed β blocker or dancel ed pt: ICD.

R → Acute VT → β blockers.

VT + Stable → B procainamide

+ ECHO normal

VT + ECHO Abnormal → Amiodarone.

Polymorphic VT: Magnesium sulfate.

Ventricular fibrillation.

Multiple and numerous re-entry currents

Most of the QRS complexes are similar.

Compression rate

Shock → 1 min → 90%

10 min → 30%
AED: Automatic Electrical Defibrillator.

Cardio-Pulmonary Resuscitation:
- Not 15:1, Multiple pad giving CPR: 15:2.
  - Chest Compression: 30:2 (Chest compression first then ventilation).
  - Airway: Reli - 100% humid.
  - Breathing: Depth: Sternum should go down by 2-3 cm.
    (1/3 of A-P diameter in all age groups)

Heart Blocks:

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

Type II: Mobility I → Wanderbeach → Progressive prolongation of PR
  - Mobility II → Fixed PR interval.

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

- Palpitations
- Dizziness
- Syncope
- Pain

Parasomatic implantation: Mobility II & Type III.

Beemaker implantation is not done in Type II.
Current towards the Electrode - positive deflection

Current towards -ve Electrode - negative deflection.

Current 90° to the Electrode axis - Biphasic (near base line).

Axis determination of ECG.

PR interval: 2.5 small boxes
PR segment: 2.5 small boxes
QRS: 2 small boxes
Safety interval: 7.5 small boxes.

QT interval: 10 small boxes
σ: 0.94 sec upper limit
ψ: 0.96 sec upper limit.

Heart rate = \frac{1300}{n(small)} or \frac{1500}{n(large)}

15 large boxes = 3 sec

No. of R waves in 3 sec \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 1st lead of the most biphasic wave.

If the 1st lead is mostly +ve then the axis is in the axis of the 1st lead.

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

Atrial Enlargement:

- If the P-wave is >2.5 small boxes → indicates atrial enlargement

Lead I, aVF → upright P-wave → source is from S-A node.

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

Height of P-wave ↑ → >2.5 small boxes (2-3 small boxes) (Lead II)

Rt. Atrial Enlargement.

Width of P-wave ↑ → >2.5 small waves (Lead II)

Width > 1 small box.

>1 small box

left atrial enlargement

V1 → P wave → Rt. atrial Enlargement
$V_1 \rightarrow$ Lt atrial enlargement

$V_1 \rightarrow$ bi-atrial enlargement

$V_1 \rightarrow$ bi-atrial enlargement

$2 \times$ small boxes

Rt atrial enlargement - P pulmonale (stenosis in cor pulmonale)

Himalayan S wave

Left Ventricular Hypertrophy:

$V_1$ Normal $\rightarrow$ LVH

$V_6$ Normal $\rightarrow$ LVH

Criteria: $S_1 + R_{(V5/V6)} > 35$ 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 ↑ afterload, HTN, Aortic stenosis

Proper criteria for Ventricular Enlargement / Hypertrophy: ESTES
AVL \rightarrow \text{fallen than 12 small boxes} \rightarrow \text{LVH.}

Voltage criteria is useful for pts \(\geq 35\) yrs old.

\text{a.k.a. Sokolow Lyon Criteria}

\text{Right Ventricular Hypertrophy:}

\text{Normal}

\begin{align*}
V_1 & \rightarrow \text{RVH} \\
V_6 & \rightarrow \text{RVH}.
\end{align*}

\text{R}_{V_1} + \text{S}_{V_6} > 10 \text{ mv} \text{ in male} \rightarrow \text{indicative of RVH.}

\text{Rt. ventricular strain} \rightarrow \text{Bimodal T-wave in V_1, a_V, V_6.}

\text{Rt. vent. enlargement + Strain = Rt. vent. Hypertrophy}

\text{MYOCARDIAL INFARCTION ECG:}

\text{\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{myocardial-infarction-ecg.png}
\end{figure}}
In pericarditis there is Pan - ST elevation.

Concavity of ST elevation is suggestive of pericarditis

Concavity upward \( \rightarrow \) Pericarditis

Saddle type ST elevation

Concavity downward \( \rightarrow \) Myocardial infarction.

Acute pericarditis:
- PR S (PR segment depression)
- Widespread concave (saddle shaped) ST elevation
- Reciprocal ST depression \( \& \) PR elevation in other x
- Absence of reciprocal ST depression elsewhere

Evolution of STEMI

Before infarction
Min - Hrs
Hrs \( \rightarrow \) 1 day
1 week
1 month

1st change in MI: Hyperacute tall T wave

In ST elevation MI \( \rightarrow \) Reciprocal changes should be seen in the opposite leads

(for pericarditis reciprocal changes are absent)
Bundle Branch Block

Normal

V1 RRBB. M pattern in V1 (RBBB case)

V6 RRBB
W pattern in V6

V1 LBBB
R ventricular activity
Septal activity
L ventricular activity

V6 LBBB
Septal activity
R ventricular activity
M pattern in V6

WILLIAM
MARROW

RBBB → last part of QRS in V6 → R ventricle.
last part of QRS in V6 → R ventricle

LBBB: last part of QRS in V6 → R ventricle.
last part of QRS in V6 → R ventricle.
Fascicular Block

In fascicular block - no lead should have broad QRS (slow)

Fascicular block is decided only by limb leads (not chest leads)

I

Left anterior fascicular block (left ant. hemiblock)

III

will always have left axis deviation

usually beyond -45°

Small Q in leads I, II, AVL
Small R in leads II, III, AVL

Tastricusoid deflection in all > 45°"s

Left posterior fascicular block (left post. hemiblock)

(will always show RBBB)

Pulmonary Embolism:

M. e. present in Short Gillon.

S1 QRS S wave in lead I

I wave in lead III

Twisted T waves in lead III

May also have RBBB along with features of pulmonary embolism

T wave inversion may be present in V1, V2, V3
Osborn wave: seen often in GBS at the J-junction.
seen in hypothermia
seen in the lateral chest leads

Brugada Syndrome
RBBB & ST elevation in V1-3
RBBB & ST elevation in V1-3

Sudden death is a possibility
Lupus, Channelopathy
SCN5A gene mutation
- Carvedilol ST elevation in V1, V6
- J point elevation
- Inverted T wave
- Broad P wave & some QRS prolongation

Functional Right: Rate 40-60, no p wave, normal QRS complexes.

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

SUT & conduction defects
- VT

- Cannon a waves
- Paroxysmal tachycardia
- GBS concordance
- Capture beats
- Fusion beats

Electrical artifact is seen in effusion
Cardiomyopathy:

MC type of Cardiomyopathy is Dilated.

DCM: Idiopathic

- Toxic
- Viral infections
- Alcohol
- Drugs - Dopaminergic, Dopaminergic
- Endocarditis Cardiomyopathy
- Connective tissue disorders

Heart failure = reduced ejection fraction.

\[
\text{EF} = \frac{\text{SV}}{\text{EDV}}
\]

Systolic dysfunction

- Diuretics.
  - A \\
  - \( \beta \) Blockers (low dose)
  - \\
  - Tiothepine - Dopramine
  - Digoxin

Synchronization \( \rightarrow \) Dual Chamber Pacing

ICD \( (23.5\% \ EF) \)
Correct the underlying cause.

Rem: Amyloidosis

- Paranit (Chagas)
- Marfanoid
- Connective tissue disease... RA
  - SLE
- Hemochromatosis (both DCM & Rem)
$\text{EF} = \frac{SV}{EDV} = 75\% \text{ EF}$

Diastolic dysfunction.

Heart failure & preserved ejection fraction.

Rx:
- Diuretics
- $\beta$ Blockers
- ACEi

Correcting the underlying condition

Hypertrophic CM

\[ \begin{array}{c}
\text{Systolic} \\
\text{Athlete}
\end{array} \quad \begin{array}{c}
\text{Asymmetric} \\
\text{Obstruction}
\end{array} \quad \begin{array}{c}
\text{HCM (Idiopathic hypertrophic cardiomyopathy)} \\
\text{Familial HCM} \\
\text{Sporadic HCM}
\end{array} \]

Incidence of sudden death is higher.

HCM:
- S4m: Systolic anterior portion of mitral valve
- Mild mitral regurgitation

HCM: Arrhythmogenic RV Cardiomyopathy
- Irregular muscle fibers
- Fat (adipose) in muscle biopsy
- Muscle fiber disarray
- Fibrosis (pockets of scar)
Murmur HOCM:

- Less blood, ↑ the murmur (peculiar to HOCM)
- Lower EDV, the louder will be the murmur.
- Louder murmur: ↑ EDV, ↑ FOR.

In standing: pooling of blood in lower extremities → ↓ venous return → ↓ LV filling → ↓ murmur increases.

Valsalva → the pressure in thorax ↑ → ↓ LV filling → ↑ murmur.

Squatting → femoral is reversed, gastrocnemius contracts → ↑ LV filling → ↓ murmur.

Handgrip: ↓ murmur.

Nitrites: ↑ murmur (contraindicated).

Digoxin: ↑ murmur (caused).
HCM - Both diastolic & systolic dysfunction

- Survival benefit is improved by β-blocker, e.g.
  - protected against sudden death
  - CCB (Diltiazem, Verapamil)
  - Disopyramide
  - Septal Myectomy / Myotomy
  - ICD

Mitraal valve prolapse

LV EDV → TMurmur

Physiology of loudness of murmur
- less blood → lax chordae
  - more prolapse
- more blood → tight chordae
  - less prolapse

will be similar to HCM...
arthritiS

炎性

- R.A.
- Spondylitis
- Gout
- Connective tissue d.
- Post viral

- X-ray: Bone loss
  - Osteopenia
  - Osteoporosis
  - Erosions

滑液:
  - TLC > 20 000/μl
  - TLC < 20 000/μl
  - >50 000/μl (acute)

  - ESR ↑ > 50
  - CRP ↑

晨僵 >1 hr.
(M.S. <1 hr. can be either inflammatory or degenerative.

类风湿:

① No. of joints
② Duration (weeks)
③ Anti-CCP
④ ESR, CRP

① No. of joints: ② Duration (weeks): ③ Anti-CCP: ④ ESR, CRP: RA, OA
Erosions, subcutaneous nodules, morning stiffness are not included in new criteria.

* PIP, MCP, Wrist (i.e., MCP) spared. Wrist
  Base of thumb - most common
  MCP spared.
  DIP spared.

* PIP and DIP are involved.

* Inflammatory Conditions
  Involving the DIP Joint
    Post viral
    Pauciarticular
    Reiter's

* Elbow, knee, MTP... is involved in RA.
  PIP - Bechterew's
  DIP - Heberden's

* Shoulder joint is involved
  in elderly.
  Hip
  Knee

* Ankle is involved.
  Ankylosis-Chronical
  Connalextends (lower Q, lumbar vertebrae.

* ↑ IHD

Pectoral: Rheumatoid arthritis
  Synovitis (synovial fluid)
  Synovitis in spiroplasmosis

Lung:
  Pleuritis
  Pleural Effusion (gum broth)

Liver:
  Cholesterol + RA
  Regressia fibrosis

Heart:
  Restrictive cardiopathy.
Splenomegaly
Anemia of Chv. disease
DMACC
Neutropenia + Splenomegaly + RA - Felty Syndrome

Nervous syndrome: Compressive neuropathy
Mononeuropathy multiplex in 50%.

Kidneys: Membranous nephropathy
Intestinal nephropathy (due to drugs for RA)

Rx: DMARD

- H.98
- Anti TNFa
- Ancotara IL-1

Cats.: [MTX]
- Infliximab
- Infliximab IL-6
- 
- Etanercept
- Adalimumab - E.R. Blockers

Sulfasalazine - L-Tc, DC

Sulfonamide - Dihydro-orotate dehydrogenase inhibitors

- Oligospermia is seen in Sulfasalazine, MTX
   (Reversible)

TNFa antagonists S/F:
- Reactivation of TB (TB should be ruled out
  before starting Rx)
- Neurophil
- Lupus-like rashes
- Avoided in HIV (Given in HIV & CD4 > 200)
Spondyloarthropathy:

- Ankylosing Spondylitis
  - M > F
  - Sacroiliac (low backache)
- Reiter's (Reactive arthritis)
  - Enthesitis - bursitis, longitudinal ligaments, vertebral
- Psoriatic arthritis
  - Assoc. with HLA B27
  - Assoc. with HLA
- IBD associated arthritis
  - Sera negative (no RA factor)
    - Psoriatic may have RAP 5-10%
  - Syndesmophytes are present in all

Ankylosing Spondylitis

- Ankylosing hyperostosis (Garson)
  - Male < 40 yrs
  - > 50 yrs
  - Low backache > 3 months
  - Backache (lumber)
  - Sacroiliitis + (symmetric)
    - Sacroiliac spared
    - In the morning
  - HLA B27 > 90% pts.
  - No HLA assoc. assoc. to DM.
  - Not specific, very sensitive
  - Sclerosis test:
    - Syndesmophyte formation
  - X-ray:
    - Bony, sym. sacroiliitis, PLL spared
    - Bamboo spine
    - Dagger sign
    - Trolley track
* Neuro deficit because
  Both L.H. & R.H. involved.
  Candle draping appearance
* Marginal syndromes formation
* Bamboo spine - due to marginal involvement
* Digger sign - ossification of enthesinous ligaments

Reiter's / Reactive Arthritis:
* Low back ache (asymmetric sacroiliitis)

\[
\text{Conjunctivitis} \quad \triangledown \quad \text{Arthritis} \quad \text{(Knee, Pulled, DIP)}
\]

* Vesicles \rightarrow Gouty or psoriasis
  Infections causing
  \text{Keratoconjunctivitisคับ}
  Chlamydia (\text{Cook})
* Penile vesicles
  \text{Gonorrhea genitalia}
  \text{Syphilis}
  \text{Gonorrhea}

\[\text{Rx: NSAIID, Steroid, Mtx (common for all)}\]
\[\text{Ureaplasma urealyticum}\]
\[\text{Doxycycline only for Reiter}\]
\[\text{Mycoplasma genitalium}\]
HIV
Psoriatic Arthritis

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

  → Oligoarticular (<4 joints)  ➔ Asymmetric/Gymnastic
  
  → Polyarticular (>4 joints)

* Arthritis mutilans (destructive arthritis)

* DIP sw. is classical, asymmetric sacro-iliitis

* Nails: pitting → Splitting (Chrysanthropy)

  → Ray: Pencil-in-cup deformity

  → Mouse ear appearance

Rx: Psoriasis + Arthritis = Mix (D-o-c)
  
  Arthritis = Etanercept (D-o-c)

GOUT

M.c.: 1st MTP involvement = Podagra

  → More colder the joint = more chance of being gouty.
  
  → Serum uric acid has no relationship with acute gout

Synovial: * TEC > 2000/mil (may be as high as 5000)

  | Negative BE 
  | Needle Shaped 
  | Sodium urate 

  | Crystalllopathy 
  | Yellow when parallel to polarized light
Rhomboid shaped CPPD crystals are seen in pseudo-gout.

**Acute**: Don't use in acute:
* Intra-articular steroids: Allopurinol
* Colchicine: Probeneed
  * Chelsea does not affect uric acid: Aspirin
  * Reduces inflammation
  * Life dose dependent → diarrhea.

**Chronic**: Uric acid ≥ 7 mg/dl.

X-ray findings in chronic gout:
* Marginal erosions → sharp spikes (Marty's sign)
  * Tophi (hard joint) → G sign

Uric acid > 7 mg/dl:

- Over producer
- Under excreter

10%: Uric acid > 800 mg/day
90%: Uric acid < 800 mg/day

- Allopurinol
- Probeneed
- Feurosad
- Benzibamide, etc.

New drugs:
- Canakinumab
- TLR-1 blocker
- Pegloticase
- Uric acid oxidizers
- Fibrinolytic Raspucinase

- Atlanta

Pseudogout: Synovial fluid
TLC > 2000

Rhomboidal CPPD crystals:
X-ray: Knee joint effusion

R.: NSAIDs, Intra-articular Steroids

VASCULITIS

<table>
<thead>
<tr>
<th>Large</th>
<th>Medium</th>
<th>Small</th>
</tr>
</thead>
<tbody>
<tr>
<td>Takayasu</td>
<td>PAN</td>
<td>Microscopic panniculitis</td>
</tr>
<tr>
<td>Temporal arteritis</td>
<td>Kawasaki</td>
<td>Wegener's (GPA)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Churg-Strauss (EGPA)</td>
</tr>
</tbody>
</table>

Granuloma: Takayasu arteritis

Temporal arteritis

Wegener's (GPA)

Churg-Strauss (EGPA)

Immunee Complex: Polyarteritis Nodosa

Henoch-Schönlein purpura

Takayasu

Temporal

- Large + medium
- Granuloma
- Arterial
- Skip lesions
- Age < 40 yrs
- E:M = 3:1
- Extracranial vessels are not involved
- Aorta vessel: Subclavian
- M.C. vessel: Temporal artery
- L.C. vessel: Coronary

Asymptomatic pulse.
- Difference in BP > 10mmHg
- Headache, scalp tenderness
- Abd. pain, bowel ischaemia
- Polyangiolus Rheumatism
- I: CRF, HTN (Renal vessels inv.)
- Diffuse pain = proximal mus.
- Classification
- Art. ischaemia = optic neuropathy
- I: Arch of aorta I - Arch of aorta
- II: Asc. aorta II - Asc. aorta (Irreversible)
- III: Rad. aorta III - Thoracic aorta
- IV: Aortic arch IV - Aortic arch
- Q: Overlapping
- (Paraaorta)
- Q: High dose steroids
- Q: Initially steroids
- IV: Use of the temporal artery
- After rheuma. steroids don't work
- Rx: 4cm segment of temporal artery
- Surgery: Stenting or
- Re-anastomosis

Polyarteritis Nodosa  Microscopic Polyangiitis  Wegener's Granulomatosis

| -ve | p - ANEA | c - ANEA (70%) |
| MBs Ag tue (20%) |

Medium vessels + capillary  Capillaries + Venules  Capillaries + Venules
never vessels

Lung - spared  ILD  ILD

Bronchial artery  Alveolar b/lage - hemoptysis  Alveolar b/lage - hemoptysis
may be involved  No cavity  Cavity + + (Enfiedal lung, lobe

Muscle Skeletal pain)  Glomerulonephritis +  GN +

Arthritis / Arthralgia  Focal necrotizing GN  - do -

M.S. organ - Renal  Crescentic GN  Crescentic GN

No GN.
<table>
<thead>
<tr>
<th>Condition</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polyarteritis nodosa</td>
<td></td>
</tr>
<tr>
<td>Microscopic Polyangiitis</td>
<td></td>
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<tr>
<td>Wegener's Granulomatosis</td>
<td></td>
</tr>
<tr>
<td>RBC casts in urine</td>
<td>RBC casts in urine</td>
</tr>
<tr>
<td>Mononeuritis Multiplex</td>
<td>+ (not common)</td>
</tr>
<tr>
<td>+ (not common)</td>
<td></td>
</tr>
<tr>
<td>Mesenteric - Abd pain</td>
<td>-</td>
</tr>
<tr>
<td>Malena</td>
<td></td>
</tr>
<tr>
<td>Coronary - IHD</td>
<td>-</td>
</tr>
<tr>
<td>Gangrene of digits</td>
<td>very rare</td>
</tr>
<tr>
<td>Granuloma</td>
<td></td>
</tr>
<tr>
<td>Atherosclerotic</td>
<td>✓</td>
</tr>
<tr>
<td>Cyclophosphamide</td>
<td></td>
</tr>
<tr>
<td>Should not be given for more than 6 months (Neuromuscular, Cystine, Bladder)</td>
<td></td>
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<tr>
<td>Maintain: Mtx</td>
<td></td>
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<tr>
<td>Rituximab (anti CD20)</td>
<td></td>
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<tr>
<td>Mycophenolate, Mycophage, Azathioprine (Steroid sparing)</td>
<td></td>
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<tr>
<td>HSP: Usually &lt; 20 yrs</td>
<td></td>
</tr>
<tr>
<td>can occur &gt; 50 yrs</td>
<td></td>
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<tr>
<td>Tired: Palpable purpura (Essential feature), mc feature</td>
<td></td>
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<tr>
<td>Stand in buttocks</td>
<td></td>
</tr>
<tr>
<td>trunk</td>
<td></td>
</tr>
<tr>
<td>Arthralgia</td>
<td></td>
</tr>
<tr>
<td>Loose joints, knee, ankle</td>
<td></td>
</tr>
<tr>
<td>Mesenteric - Abd pain, Malena</td>
<td></td>
</tr>
<tr>
<td>Hematuria + Proteinuria (Glomerulonephritis) 20-40% pts</td>
<td></td>
</tr>
</tbody>
</table>
Biopsy: Neutrophilic infiltrate
  * Luepoldhotic vasculitis
  * Anaphylactoid purpura

Immunofluorescence → IgA

Rx: Steroids

Mc. vasculitis in children HSP (Bums, Urine)

Kawasaki Disease

* Exclusively Children
* Peak: 1 to 5 yrs (3 to 2 yrs old children mc.)
* Coronary involvement - Myocardial dysfunction
* Fever x 5 days (unexplained)

Four out of 5 criteria:
1) Conjunctivitis (peri-lateral sparing)
2) LN + (Cl: n > 1.5 cm in size)
3) Polycyclic Rash (on trunk)
4) Peripheral Sign → Swelling
   → Dequamation
5) Mucosal Sign → Strawberry tongue
   → Dry Cracked lips

Rx: IV immunoglobulin + Aspirin
Steroids can be given after 3 wks of IVIG

M. c. primary vasculitis - Cutaneous Vasculitis

Hypersensitivity Vasculitis
   (Post capillary Venule)
SLF

F:M = 9:1

New criteria

* Skin → Immunological

* Alopecia → AntA

* Synovitis (arthritis) → Anti-Sm

* Oral ulcers → Anti DsDNA

* Renal → Anti phospholipid

* Neurological → Complement

Blood → Coombs test two

Old criteria

* Malar rash → Blood Ab

* Discoid rash → Renal

* Arthritis → ANA → Anti-Sm

* Oral ulcers → Thrombosis → Anti DsDNA

* Arthritis

* Photosensitivity

Malar rash: Butterfly pattern. Malar area should be spared.

Discoid rash: Scarring + Alopecia.

Oral ulcers: Hard palate, generally painless.
Neurological: Behavioural

Seizures

Parkinson's

Cerebral

Blood:

Anaemia, neutropenia, pancytopenia, thrombocytopenia

Pancytopenia

Sensitivity

Specificity

Anti-SSA: 90% 10% - 15%

Anti-SSB: 20% 98% - 100%

Anti-DSDNA: 60% 95% Most accurate

Anti-DSDNA titre correlates to disease severity

Rx:

SLE

Non-threatening

Conservative: less dose

High dose steroids:

Azathioprine

Mycophenolate

Cyclophosphamide

 Rituximab

Belimumab

M.e. presenting complaints of SLE:

Systemic/constitutional

Arthritic/Musculoskeletal

Haematological
APLA Syndrome

Lupus Anticoagulant
↓
50% Thrombosis

β2-glycoprotein Ab in the most imp. Ab.

Anti-Cardiolipin Ab.

Antec. is seen in 50% of the cases.

Thrombogenic state (don't present a bleeding)

Pregnancy: Thrombosis in placental bed

- Abortions (10%)
- IUDE
- Stillbirth
- Ultrasound placental insufficiency

Warfarin (2nd trimester)

Stretch are not to be given in APLA syndrome

- Heparin (1st trimester)
- Warfarin in 1st trimester: Chondroplasia punctata (common)
- Chondroplasia punctata (rare)

Asymptomatic: PT N

APTT ↑ (m.c. cause of isolated PT)

in an asymptomatic person.

2nd: Factor V deficiency

Mix sample test: PT ↑ (presence inhibitors in the pt. sample)
Thrombosis  Arterial - Stroke / TIAs
Venous - DVT
CVT

Russell viper venom test time - prolonged

+ phospholipids (freeze dried platelets)
Hammed platelets

RVVT becomes normal

Anticardiolipin syndrome

VDR1 tue  FTNs - ve
due to anti-cardiolipin Ab

Rx:  Anti-coagulation

INR:  arterial thrombosis  2.5 - 3.0

venous thrombosis  2.0 - 3.0

Only in AHA, prosthetic valves INR > 3.0
Systemic Sclerosis

Localised CREST

Diffuse es.

Calcinosis

Carotenoid

Raynaud's

Eso. dymoability

Sclerodersty

Telangiectasia

(peri-unual)

Also seen in dermatomyositis

Sclera +

Face, Fingers, Feet

-ve. & Above Elbow Trunk. ++

±

Total, Arthralgia,

Arthritis

4% Renal involvement 15%

1° PAH

Lung involvement ILD

ILD- rare

PAH

M. cause of death in Scleroderma is Lung disease

Anti- Centromere

Abs.

Anti- Scl 70

Anti- DNA poly III
Q: D penicillamine (low dose)

- the thickening of skin

Roynaud: ccb.

AAC

- Bosentan

Sympathetomy

Supportive treatment

Sjogren's Syndrome

F:M = 9:1

- Dry Eye

- Dry Mouth

- Dry vaginal mouth

Hepato-splenomegaly

Interstitial nephritis - Type I RTA

M:O lymphoma - MALTOMA (Marginal B cell low grade)

Secondary Sjogren: Any GID assoc. to Sjogren's

- RA (m.e.)

- SLE

- MTCO

- PBC

Inv: Anti-Ro (SSA)

Anti-La (SSB) - more specific
lobial bipity \- Midi socket gland

R. Superficial

Artificial

Art. Hyp."lop hative

Clinic
directed sale

Breast

Duds- container

Nipple - epidermis

Cortical endocrino - accumulations of cells - ducts, like nec

Pathology

Rceptor - H+ As, H+ B2a

Thrombogenic cardiac
Immunology

Innate immunity / Non specific  Adaptive / Specific / Acquired immunity

- Anatomical barriers
  - T helper cells
- Physiological barriers
  - Humoral → Igs → B cells
- Biochemical barriers
  - CRT → T cells
- Switch on / off
- Anatomical - Skin posts
  - Cilia
  -Lysozyme
  - Lag phase
- pH stomach
  - Neutrophils, NK cells
  - Complement, Macrophages
  - Dendritic cells

"Toll-like receptors"

No memory, no lag phase

Antibody

Antigen binding site

Variable region: binding specificity to antigen

Hyper variable
Ab + papain \rightarrow 2 Fab + 1 Fc

Ab + papain \rightarrow 2 Fab (Fc destroyed)

Isotypes: 
- \( \gamma \) for IgG, IgA, IgM, IgD, IgE
- \( \alpha \) for IgA, IgM
- \( \mu \) for IgM
- \( \delta \) for IgD
- \( \epsilon \) for IgE

Total no. of isotypes: 18

due to \( k \) and \( \lambda \) chain in each.

Isoletype - Specificity of Ab - variations in variable site

Allotype: same antigen

IgG1, IgG2

kind to same antigen

but difference in the heavy chain / structural differences

Allergic polymorphism - between 2 individuals of same species

Ab diversity:

Heavy: [V D J -] [\( \mu \) \( \kappa \)]

Light: [V J]

\( V_1, V_2, V_3, V_4 \) \( D_1, D_2, D_3 \) \( J_1, J_2, J_3 \)

Random pairing and shuffling by RNA enzymes

\( V_5, D_7, J_5 \)
Any sequence of V, D, or J can be joined to each other
leading to a different pattern of VDJ sequence.

It is only present in immature cells.

\[ v_{22}D_{10}J_1, TgM \quad v_{31}J_3D_1 \]

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

If antigen binds:

Clonal selection, Clonal amplification

\[ \text{Mitotic bursts} \]

Plasma cells with the same antibody type

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

Weak binding

\[ \downarrow \]

More proliferation of the same type of cells

Stronger binding than the parent cell

Less/no proliferation

Further mutation/changes in the hyper-variable region

Selection & proliferation of the best antibody forming cells.
Affinity maturation is clear by somatic hypermutation.

* IgM is a poor marker for fetal toxoplasma.
  For fetal toxoplasma, better marker is IgG (but IgM appears late).

To detect Toxoplasma in mother, IgG is used:

- If affinity is very good → remote infection
- If affinity is less → recent infection → 1 chance of fetal toxoplasma.

T cell receptors:

\[ \text{P} \]

- T cell receptor

HLA receptors:

\[ \text{H} \]

- HLA class I (binding site for class I molecules)
  - H1, H2, and H3

- \( \beta_2 \) microglobulin
  - By binding site for class I

Invariant chain:

- Two chains, two domains in cell
- Invariant chain protects against binding of any antigen unless specific antigen is recognized.
<table>
<thead>
<tr>
<th>HLA-I</th>
<th>HLA-II</th>
<th>HLA-III</th>
</tr>
</thead>
<tbody>
<tr>
<td>A</td>
<td>* DP</td>
<td>* C, C</td>
</tr>
<tr>
<td>B</td>
<td>DQ</td>
<td></td>
</tr>
<tr>
<td>C</td>
<td>DR</td>
<td></td>
</tr>
<tr>
<td>150</td>
<td>&gt; 250</td>
<td>100</td>
</tr>
</tbody>
</table>

- **A** and **B** subtypes
- **C** is polymorphic
- **DR** subtype
- HLA-II is more polymorphic than HLA-I

- Inherited in codominant pattern

For individual identification:
2) Fingerprinting
3) DNA fingerprinting
4) HLA typing

- All nucleated cells
- All antigen-presenting cells
- Platelets
- Dendritic cells (most potent helper)
- Macrophages
- B cells
- Activated T lymphocytes

(Plasma cells don't have HLA-II)
(Naive T cells don't have HLA-II)

- Intra-cellular defense
- Extracellular defense

- CD3
- CD4

- B: Microglobulin
- T: T-cell receptor chain
**HLA-I**

- **Virus infects a cell → proliferates**
  - Proteasome breaks the virus into protein particles.
  - Presented to the TAP receptor.
  - Viral particles are presented to MHC-I.
  - MHC-I recognizes particle as foreign.
  - Migrates to surface (via β2-microglobulin).
  - CD8 recognizes the MHC-I and the viral particle.
  - CD8 induces apoptosis of the infected cell.
  - Via perforins and Granzymes → release cytochrome → activate caspase.

M.C. method of evasion of viral particles is blocking of the TAP receptors.
Progressive acidification of the Golgi vesicle degrades the invariant chain to CLIP peptide.

After fusion of the vesicle with the phagosome, MHC II removes the CLIP peptide.

The bacterial particles bind to MHC II.

MHC II migrates to the surface and presents to CD4 cells.
Carbohydrate antigen - weak immune response
because large carbohydrates will not be processed.

No T-cell dependent pathway

No memory
only B-cell dependent response

\[ \text{Pre Th} \rightarrow \text{Th0} \rightarrow \text{Th1, Th2} \]

\[ \text{IL-10} \rightarrow \text{Th1, Th2} \]

\[ \text{IL-4, IL-6} \]

\[ \text{Th1} \rightarrow \text{IL-12, IL-22, IL-26} \]

CMI

- Fungal infection
- Multiple sclerosis
- Rheumatoid arthritis

\[ \text{Granuloma, Humoral immunity, IL-4, IL-6, IL-10} \rightarrow \text{Th}1, \text{Th}2 \]

\[ \text{IL-5} \rightarrow \text{Eosinophils} \]

Max rise in replication: IL-6
HEMATOLOGY:

To pick up iron → Transferrin

1. Ferritin

channels from all tissues.

Transferrin Fe → Serum Iron

Iron packaged in Ferritin is not included in A.I Fe.

Hepcidin: Produced by the liver.

- Blocks the ferroportin channel
- Controls iron absorption of Fe from intestine
- Bilirubin release of Fe from storage sites

Anemia of Chronic Disease: -↓ Fe ↓ - due to ↑ hepcidin.

↓ Ferritin ↑

Anemia with decreased iron levels: the body reduces hepcidin levels, allowing for iron absorption.

Neuer drugs: Hepcidin receptor antagonists
Ferritin is inversely related to transferrin synthesis.

Transferrin receptor assay: Sensitive marker for IDA. (100% BCR in TDA)

- Ferritin levels are ↑ in A transferrinaemia
- In DM, Receptor mutation ferritin levels are ↓

- T. Iron: 80 - 150 mg/dl
- MCV: 80 - 100 fl

- Ferritin: 80 - 300 mg/l
- RDW: 10 - 15

- TIBC: 250 - 400 µg/dl

- Transferrin saturation: 38% (15 - 50%)

Iron deficiency

Thalassemia minor

Anaemia of CHD, Disease

Normal: Normal (80 - 90%)

- Fe < 50 µg/dl
- MCV is not < 60 fl. S & ↑ Hb > 7 gm/100 ml. ↑ Ferritin

TIBC ↑↑

Transferrin saturation < 15%

Tf-R > 10

Transferrin-Ferritin index

TIBC index

3 - Tf-R > 2

Log Ferritin

Most sensitive & specific

Gold Standard: EMR

- MCV ↓

- ↓↓↓ disproportionate

- Micronutrition

- Disproportionale

- UI severity of anaemia

- RBC < 5 million/µm³

- > 5 million/µm³
Methemoglobinemia

- MCV > 13
- MCV ↓ < 13
- RBC (increased)
- RBC (↓)
- RDW ≥ 15
- RDW < 15
- PhD also increase in
- Folate, B12 deficiency
- Max RDW is seen in dimorphic anemia.

Iron-Deficiency Anemia:
- Idiopathic
- Congenital: 3,6,12 defect
- Acquired: Alcoholic
  - Lead
  - Pyridoxine deficiency
- Ringed sideroblast

- S. Fe ↑
- S. Ferritin ↑
- TIBC ↓

- Dimorphic PAS
- Basophilic stippling (C3H, heme porphyrin)

Macrocystic Anemia:
- MCV > 100 fl.
- Dimorphic PAS
- ↓ Reticulocyte count - ineffective erythropoiesis
- Taradice, Gall stones ±
B2 deficiency  Factor deficiency

• Neuropathy +
• SAD +
• Memory loss +

• Hypothyroidism
• Pernicious
• Autoimmune
• Anemia

• Homocysteine ↑

• Methyleneonate ↑↑

• Source: non-veg, green leafy vegetables

Hereditary Spherocytosis

M.C. defect: Gpl:1 defect → Spherocytosis

More severe: Spectrin defect → Chronic fragility ↑

CF: Savonarola, Gall stones

Reactive Spheranogeny (Deletion of ROC causes release of growth factor)

Deletion of platelets doesn't release growth factor

AHA

Warm

* Ag - Rh

* Ab - IgG

Name of complement: Agglutination + Cold Hemolysin

* Ag-1:1
* Ag: IgM
* Ab - IgG

Cold: ↑

Complement activation ↓
Warm
- Spherocytosis
- Splenomegaly
- Osseous fragility
- Jaundice/gallstones

Cold
- Cold agglutinins
- Cold hemagglutin
- Cold hemolytic
- Eclampsia in liver

Intravascular hemolytic

Paroxysmal Cold
- Splenomegaly
- Donath-Landsteiner type

Direct Coomb's Test +
- Direct Coombs +

Causes: TTP
- SLE
- Myeloplasma
- Malaria

* Drugs
- Influenza

* Hepatitis
- Penicillins/Cephalosporins

* Gross hematuria → Ab Methylchol

* Immune complex: Quinine/Quinidine

Ab & Ag → RBC

Paroxysmal Nocturnal Hemoglobinuria:

committee process

Megakaryocyte 
Platelet

Monocyte 
Macrophage

Neutro, Eosin, Eosinophils

Lymphoid

Lymphocytes (B, T)

NK cells

Hbc
PNH - is an acquired stem cell defect.

**PIGA gene** → **GPI anchor**

→ *Decay activating factor (DAF) inhibitor of*
  - Homologous factor (HFA)
  - MIRI

→ in defect

*Complement associated membrane damage*

During sleep → CO₂ is retained → pH ↓ → immune activation ↑

*Early morning ↑ cell destroy*

- **PNH**
- **Pancytopenia**
- **Thrombosis**

**Screening test**: **Hep's test** (best screening test) - mild acid is added

Sucrose Hemolysis Test (Sucrose in an acidic region)

**Confirmatory test**: **Flow cytometry** - Absence of:

- CD55 = DAF
- CD59 = MIRI - more specific

[**Eculizumab**]

**Haptoglobin & in any intravascular hemolysis**

→ **suicide protein**

*Haptoglobin binds to free Hb (if chromium is filtered in plasma)*

→ RBCs ↓ damaged)

Engulfed by Macrophage

*Stationary can't cross endothelium*

Haptoglobin is destroyed → Hb is recycled
Suspected Transfusion Mismatch → Start Mannitol
↓ diuresis
Pushes the Hb through the nephron.

Hemoglobin Abnormalities

\[ \text{HbA} \to \alpha, \beta \]
\[ \text{HbA}_2 \to \alpha_2 \beta_2 \to 96-98\% \]

\[ \text{HbF} \to \alpha_2 \gamma \to <2\% \]

\[ \alpha \text{-thalassemia} \]
\[ \beta \text{-thalassemia} \]

↑ HbF

Hydrops fetalis

Neonatal complications/anemia

Stable

\[ \text{HbH} \cdot \beta \]

\[ \text{Beta} - \gamma \text{, fetus, neonatal} \]

\[ \alpha_4 \text{-unstable } \to \text{hemolysis} \]

Gene deletion

Point mutation

\[ \alpha \text{-thalassemia} \]

↓

\[ \alpha \text{-alleles for } \alpha \]

\[ ++ / ++ \to n \]

\[ ++ / + - \to \text{silent carrier} \]

\[ + - / + - \to \text{Thalassemia minor} \]

\[ + - / + - \to \text{Thalassemia minor, } (\text{HbA is present in small amount not zero}) \]

\[ 0 \to - / - - \to \text{Hydrops fetalis} \]
**β-thalassemia**

- **Point mutation**
  - $\beta^-$ (partial $\beta$ chain)
  - $\beta^0$ (no $\beta$ chain)

- **Genotypes**
  - $\beta^+ / \beta^+$: Thalassemia major
  - $\beta^+ / \beta^0$: Thalassemia intermedia
  - $\beta^0 / \beta^0$: Thalassemia minor
  - $\beta^0 / \beta$: Thalassemia minor

- **Hb Levels**
  1. Thal major: $0-10$, $9-10$, $80-96$
  2. Thal int.: $0-30$, $4-10$, $6-100$
  3. Thal minor: $85-95$, $4-8$, $1-5$

- **Hb F**
  - HP Hb F: $20-40$ in HP Hb F, then in adult, Hb F rises

- **Note:** In all above conditions, Hb F is ↑ in adulthood.

**β-thalassemia** - generally symptomatic.

**HP Hb F** - generally asymptomatic.
NESTROFT: Naked Epo Single tube Red cell Membrane Fragility test

OF ↓ → Thalassaemia

HPHFE

↓ Severe IDA

NESTROFT + → HbA2

↓ in 1st trimester - Thalassaemia

♀ HbA2 ↑↑

♂ HbA2 ↑

↓

25% - T major

50% - T minor

25% -

Sickle Cell Anaemia

Missense Mutation → α-chain → 6th position

Glutamine is replaced by Valine.

SSa

βS/βS

HbA/HbS = 0/100

Hbs > 80%

HBF 2-25%

Sickling - Vaso-occlusive episode

Hand foot Syndrome

Pulmonary infarct

Stroke

Splenectomy crisis

Hepatomegaly

Hypertension

Sickle trait

HbA/HbS = 60:40

HbA > 60%

Hbs < 40%

Sickling doesn't occur

Isolated papillary necrosis
Hydroxyurea → ↑ HbF  
Prevented the polymerization of Hbs. 

Reduction of bleeding episodes 

Myeloproliferative Disorders 

- Polycythemia Vera  
  - Essential Thrombocytosis 
  - CML 
  - Primary Myelofibrosis 

Polycythemia Vera. 

WHO criteria: 
- Major 
- Minor 

- HCT ↑↑ 
- JAK-2V617F mutations 
- BM Biopsy → Trilineage proliferation. 

C/E: 
- Involved Erythrocytosis 
  - Hyperferritinemia → Thrombosis 
  - Eosinophilia 
  - Hyperuricemia → Gout/keratoconjunctivitis 
  - Hypersensitivity reactions 
  - Histamine + → Aquagenic pruritus, post-bathing itching 
  - Hypoglycemia → PVD. 

* Massive Splenomegaly. * No ↑ risk of infection.
Lab: - Serum B<sub>12</sub>↑, B<sub>12</b> binding protein ↓

[ ] → hydration +

→ Phlebotomy → ↓ HCT

*Induce iron deficiency anaemia:

→ TENA

→ Radiolabelled P<sup>32</sup> (not advised) → leukemogenic

→ Roxulitinib → ↓ the spleen size.

**Essential thrombocytosis**

- Ptt. count > 400,000/mm<sup>3</sup> Pct > 400,000 also seen in
- HCT ↓
- JAK-2 mutation 50%

*Proliferation:

**GEE:** Erythromelalgia - Redness + Pain in theDigits

Thrombosis

- Bleeding - Acquired vWF disease (vWD)

Splenomegaly - mild/moderate

[ ] *Aspirin

*Hydroxyurea (D.O.C)

*TENA

*Anagrelide (FDE)**
CML

- Fullness in abdomen - Spleenomegaly
- Bone pain - Splinal tenderness
- URTI, Infections

T.e > 25,000/ul @ diagnosis may be > 50,000/ul

CML
- Low lymphoid cell
- Leukemia
- RPR granules
- 100,000/mm
- @
- B22
- LAP
- 
- Serum < 70
- @
- CML
- @
- PRK

FISH - t[9;22] - 95% cases are detected

PCR - BCR-ABL fusion may be seen in the absence of t[9;22]

- Aplastic
- Herniated

- Hypophosphat

Ph (9;22) → Tyrosine kinase activated

Rearrangement → DNA repair system

2-5 yrs

Leukemia

Chronic phase: % blasti < 10%

Accelerated phase: 10-19% blasti, plt count <1,000,000, >10,000
- Spleen size ↑
- Basophils > 20%
Blast phase: Blasts > 20% (may convert to ALL, AML or AM) 

Prognosis:

Sokal's (American) 

Hasford (better) (Fare)

* Age
* Age

* % Blasts
* % Blasts

* PC
* PC

* Spleen size
* Spleen size

* % eosinophils

* % Basophils

Rx:

CML

Bone Marrow

Chemotherapy (G.O.C)

Transplant

Imatinib

10-20% mortality

Rejection

Graft vs Host Disease

Imatinib: Competitive ABL binding site inhibitor
Primary Myelofibrosis

Iron drop Marrow
Massive Splenomegaly
Bone marrow aspiration - Dry tap

Rx: Roxulitinib. (for reducing spleen size)

CD 1 → Histiocytes * CD 11 - lymphocytes
  { CD 3, CD 4, etc. }
  CD 19
  CD 21 EBV

CD 20
  B cell
  CD 22
  CD 23

CD 10 → CALLA * CD 117
  (Common ALL antigen)

ALL

AML

Biphenotypic leukemia

Undifferentiated

Bone Marrow failure

Anemia - fatigue

WBC - infection

Platelets - bleeding, petechiae

Hematopoietic, ENH

Tumer lysis syndrome - ↑ uricemia

Interstitial nephritis

↑ PO4, ↓ Ca++

↑ K+
ALL

AML

Children usually  
Elderly (peaks age > 65yrs)

M0 - Minimally differentiated
M1 - Myeloblastic 1 diff. 
M2 - Myeloblastic 2 diff.  
M7 - Auer +

70-75% - mature B cell

Null cell  Burkitt's  
M3 - Ery

Pre B cell (m.c. ALL)

T cell
M5 - Monocytic - CD4, CD64

Down's m.c. arise = ALL

Mediastinal mass = ALL
M6 - Erythroleukemia = M60

PAS + 70% of pts.

Stains: MPO, SBB, NSE

CD10 - CALLA

CD19, 20, 22, 23 - B cell markers

CD3 - Non-T cell marker

CD7 - B cell

CD13, 117 - myeloid markers

CD14 - monocytic, macrophage

C3 - leucocyte

Markers of both ALL & AML

Biphenotypic leukemia

Mixed Chimeric Acute Leukemia (MCL)

Undifferentiated: No expression of CD3, MPO, CD22, CD79a,

absence of strong expression of CD10


**Prognosis**

<table>
<thead>
<tr>
<th>All</th>
<th>Good</th>
<th>Bad</th>
</tr>
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</table>

- **Age**
  - $>10$ yrs.
  - $<1$ yr.
- **TLC**
  - $>500$ cells/mm$^3$
  - $<500$ cells/mm$^3$
  - $>50,000$ cells/mm$^3$
  - $>100,000$ cells/mm$^3$
- **Hyperplasticity**
- **Aneuploidy**
- **t(12, 21)**
- **t(8, 14)**
- **t(4, 11)**
- **t(9, 22)**
- **Granule/CNS**
- **Presence of peripheral blasts after 2 weeks of Chemotherapy**
- **Males**
- **Females**

**AML**

<table>
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</table>

- **t(8, 21)**
- **t(15, 17)**
- **t(16, 10)**
- **inv. 16**
**MGUS**  
Multiple Myeloma  
Waldenström's

- Monoclonal gammopathy of uncertain significance
  - (Most common)
- Pre-malignant?
- Bone marrow
  - Plasma cells <10%, Plasma cells >10%
  - IgG↑/IgA↑  
  - (IgG↑/IgA↑)
  - TgM↑
  - Hyperviscosity

- M-spike <3g/dl.
- No M-spike release
- lytic lesions
- Bone pain
- Ca++↑
- No renal failure
- No lytic lesion
- Ca++↑ (Renal failure → Ca++↑)
- Hb levels ↓ (due to ↑Ca++)
- No organomegaly

- Neuropathy
- Anemia
  - HTN

- Treatment
  - C - Calcium
  - R - Renal failure
  - B - Bortezomib

- Neuropathy
  - A - Anemia (most finding)
  - B - Bone pain (rare, presenting complaint)

- M. cause of death: infection

- Amyloidosis - AL

- Prognosis: most imp.
  - Autologous SCT
  - Fludarabine
  - Plasmapheresis

- Very high ESR:
  - ESR is due to
  - Asymmetric changes on RBC
  - CSF → collect Mmm cells

- Polycythemia, BCR-ESR ↑
  - CCF
  - [Linalidomide]
  - [Dexamethasone]
  - [Bortezomib]

- A fibrinogenemia → ESR zero
  - [Trasylol (Recombinal)]
  - [Fibrinogen]
Smoldering MM

\[ \text{Plasma cells} \geq 10\% \quad \text{Plasma cells} < 10\% \]

\[ \text{IgG/IgA} \geq 3\text{g/dl} \quad \text{IgG/IgA} < 3\text{g/dl} \]

\[ \text{CRAB} \quad \text{CRAB} \]

Multiple Myeloma

\[ \rightarrow \text{M-spike} \quad \rightarrow \text{M-spike} \]

\[ \rightarrow \text{Marrow plasma cells} \geq 10\% \quad \rightarrow \text{Plasma cells} \geq 10\% \]

\[ \rightarrow \text{CRAB lesions yes} \quad \rightarrow \text{CRAB lesions no} \]

\[ \rightarrow \text{Peripheral smear} \quad \rightarrow \text{Peripheral smear} \]

\[ \text{Plasma cells} < 20\% \quad \rightarrow \text{Plasma cells} \geq 20\% \]

Melphalan based regimen

- \[ \text{MP} \quad \text{MPT} \]

\[ \begin{align*}
\text{Methanes} & \rightarrow \text{Methanes} \\
\text{Prednisolone} & \rightarrow \text{Prednisolone} \\
\text{Thalidomide} & \rightarrow \text{Thalidomide}
\end{align*} \]

**Heavy Chain Gammopathy:** Very high serum IgA symptoms of 15x G11 (abd masses)
Bleeding Disorder

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

Coagulation
- Path of Blood: Haematoma
  - Thigh
- Haematrhoea
- Delayed umbilical slurry
  - Factor VIII deficiency
  - Factor IX

- Bleeding time ↑
  - PT, PTT ↑

Intrinsic
  - No spontaneous bleeding
  - Factor XII
  - Factor XI

Extrinsic
  - Factor VII

PTT
  - Factor VIII
  - Calcium + Cal.
  - Spontaneous bleeding

Prothrombin → Thrombin

Fibrinogen → Fibrin

Clot Stabilizing factor

Clot deficiency → PT, PTT, RT, TT

detected by "Owen Clot Fix" test.
Fibrinogen → Fibrin → EDP

Stable Clot
- plasmin
- D-dimer

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

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

Factor V mutation, Leiden mutation → M.C. inherited hypercoagulopathy

Protein C can't act → Protein C resistance → Von Willebrand's disease

Hypercoagulopathy

Antithrombin III: Mainly acts on factor X (inhibitor)

Heparin concentrates ART & factor X together

So inhibits the activation of factor X.

Heparin resistance - Antithrombin III deficiency
Platelet disorders:

![Diagram showing VWF, fibrinogen, and platelet aggregation]

- Acquired thrombocytopenia → Renal failure → Uremia → Platelet function defect

<table>
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- Thrombocytopenia
  - Megakaryocytic

- Severe defect
  - abn + vWF = abn
  - abn + vWF = abn

- von Willebrand factor antigen test
  - Failure of aggregation
Congenital Hemophilia

* Inherited, XLR
  * Male = female
  * Factor VIII deficiency
    * Abs against factor VIII
      * 50 - 150 IU/dl
  * Hematoma +
  * Petechiae +
  * Muscle +
  * Hemarthrosis +
    * Joints are usually spared
    * Hemarthrosis is rare
    * In children, ankle joint

* PT (IN)
  * Prolonged

Mixed sample test
1:1 → PT → 1:1
1:1 → PT → 1

* Normal value:
  * PT 7 min
  * Aplastic anemia
  * Asymptomatic patient

  * PT 12.7 - 15.4 sec
  * 1st degree anticoagulant (m-c)
  * PTT 28.3 - 33.4 sec
  * 2nd factor VIII deficiency
  * VIII 50 - 150 IU/dl

1.0. Aplastic anemia: do not have splenomegaly

1.0. ITP
  * Child
  * DIC is a diagnosis of exclusion
  * Fever
  * Petechiae/Purpura
    * Don’t administer platelets (↑ production)
  * «(?)» → Steroids
  * Megakaryocytes → Phagocytosis (80-100nucleoli)
Rhagom → Ab against Rh antigen of RBCs

The Fc receptors are saturated

No Ab reaction against platelets

- Aspirin
  - Prostaglandin
  - Placenta rupture
  - IV Ig
  - Splenectomy (must be vaccinated against encapsulated org. beforehand)

(Pt can only be given before Splenectomy)

TTP

\[ \text{vWF multimers} \rightarrow \text{vWF} \text{m} \rightarrow \text{vWFm} \text{ in TTP} \rightarrow \text{platelet plug formation} \]

- ADAMTS13
  - Defect

PENTAD of TTP

- Thrombocytopenia
- Microangiopathic HA.
- IL-1, TNF
- Pyrogens → fever
- Neurological deficits
- Renal involvement (minimal)

- Coombs' -ve anemia
- PT / aPTT / T - IN

- Complement is unaffected → C3 levels

HUS:
- Diarrhea 
  - Shigella
- Drugs (Erythromycin, Penicillin)
  - Vasocytotoxin damages Endothelium
  - Multiple Ab → plug formation
* Thrombocytopenia
  * Maha
  * Ca levels & Complement are involved
  * Renal disease +++
  * Neuro deficits minimal
  * Fever is absent
  * Coomb's test is -ve
  * PT/PTT/TT - (x)

R.: HUS, TTP
  - Plasmapheresis
  - Exchange transfusion R.o.c.
  - Platelet transfusion can be given
  - Treat the underlying cause in HUS

Microangiopathic Hemolytic Anemia - RBC destruction in small vessels

Not seen in heart valves (prosthetic)
NEUROLOGY

Headache

\[ \text{Migraine} \quad \text{Tension} \quad \text{Cluster} \]

\[ \checkmark \text{F > M} \quad \checkmark \text{F > M} \quad \checkmark \text{M > F} \]

\[ \checkmark \text{Up - usually} \quad \checkmark \text{Band-like, compressive} \quad \checkmark \text{Up} \]

\[ \checkmark \text{Throbbing} \quad \checkmark \text{Bifrontal} \quad \checkmark \text{Deep piercing pain} \]

\[ \checkmark \text{Migraine Headache} \quad \checkmark \text{Excruciating pain} \quad \checkmark \text{Petro-orbital} \]

\[ \text{Nausea, vomiting} \quad \text{Febrile, less headache} \quad \pm \]

\[ \text{Photophobia} \quad \pm \]

\[ \text{Photophobia} \quad \pm \]

\[ \text{Osmophobia} \quad \pm \]

\[ \text{Movement worsens} \quad \text{Restless, head banging} \quad \text{Pacing} \]

\[ \text{Age:} \quad \text{Local neuro defects} \quad \text{Normal} \quad \checkmark \text{Up irritability} \quad \checkmark \text{Up frequency} \quad \checkmark \text{Up cerebration} \]

\[ \text{\checkmark 2 episodes/day} \quad \text{\checkmark 1-2 episodes/day} \]

\[ \text{\checkmark No neck stiffness} \quad \checkmark \text{Bupivacaine} \quad \checkmark \text{Triptans (P.O.)} \]

\[ \text{\checkmark Pseudomeningeal pain} \quad \checkmark \text{NSAIDS} \quad \text{100% O₂} \]

\[ \text{\checkmark Triptans} \quad \text{\checkmark TCA} \]

\[ \text{\checkmark Migraine attacks} \quad \text{\checkmark Bupivacaine} \quad \text{Bupivacaine - Verapamil} \]

\[ \text{\checkmark Ergotamine} \quad \text{Better lifestyle} \quad \text{Steroids} \]

\[ \text{\checkmark Caffeine} \quad \text{Biofeedback} \quad \text{Methylprednisolone} \]

\[ \text{\checkmark Severe headache in chronic migraine} \quad \text{Relaxation techniques} \quad \text{Lithium} \]

\[ \text{\checkmark Neuro-infusion} \quad \text{\checkmark Baclofen (Gabapentin, Methadone)} \quad \text{\checkmark Valproate} \]

\[ \text{\checkmark Fluoxetine} \quad \text{\checkmark Gabapentin} \quad \text{\checkmark Chlordiazepoxide (hypotesis internal)} \]
Frequent/migraine - Botox or Xeomin injection

Should not be used in migraine:
- Verapamil
- SSRIs
- Clonidine

Cluster headache
- Chronic parasympathetic
- Tenderness
- Shoulder lasting yrs. Neurography
- associated congestion & itching
- U+ U+ 10%
- Autonomic features +
- Deep piercing retro-orbital +
- Responds to Toradol ++
- Toradol
- Dexamethasone ++
- Lamotrigine +
- Valproate +

Caloric stimulation test

Water temperature 37°C ± 1°C vs. 30°C ± 44°C

Vertebrobasilar paroxysmal stimulation pulls 1st eye in opposite direction
- Cold: opposite
  - R  →  0  →  0  →  L
  - blocks  →  vestibular  →  cortical (fast)
- Warm: same
  - R  →  0  →  0  →  L
  - stimulates  →  cortical (slow)
Direction of nystagmus is according to the fast component

If cold water stimulation → Up beating nystagmus
If warm water → Down beating nystagmus

Vertigo

BPPV → Meniere's → Vestibular neuritis/labynghiitis
Benign Paroxysmal Positional Vertigo → Long lasting vertigo: m/o.
Viral infection
Post-8C Canal
SNHL
Tinnitus
Vestigo - noise - hours
Nystagmus, rotatory upbeat
Diplopia
Nystagmus: Horizontal
Vertigo: minutes
Pain in the ear
Triggered by change in position, Fuller in the ear
↓ Head Impulse Test

RX: Diuretics
RX: Betahistine
RX: Tizanidine + Trizacida

Spleen's Manoeuvre
Inj. Gentamicin
Inj. Steroids
Inj. Steroids
In decompression of Endolymphatic sac

Aphasia

Naming is the first thing to be affected.

Comprehension → Repetition → Speech fluency

Wernicke's → O → O → ↑
Broca's → N → O → ↓
Conduction → O → O → N
TCS. → O → N → N
TCH. → N → N → ↓
Isolation → O → N → ↓
1. Wernicke's aphasia:

- Repetition: 
- Comprehension: 
- Word output: 
- Speech fluency: 

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

Neologism: 
Tangentialism: 
Naming is affected (anomia).

- Repetition: O
- Comprehension: O
- Word output: ↓
- Speech fluency: ↓
- Echolalia: He can only repeat, can't understand

7. Global aphasia
   - Seen in: Infants
   - Post-concussion
   - Post-trauma

- Repetition: ()
- Comprehension: O
- Word output: ↓
- Speech fluency: ↓
- Repetition: ()
- Comprehension: O
- Word output: ()
- Speech fluency: ()
- Paraphasia
- M.C. aphasia

* In pure word deafness or/and pure alexia → Naming is preserved

[Diagram of neural pathways and structures]
Deep tendon reflexes: Muscle spindle 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.

- Tone ↑
  Spastic
- DTR ↑
- No wasting - due to trophic effect
- Fasciculation (visible)
- Fasciculation (only recordable)

Flaccid weakness

- AHC disease
- Neuropathy
- Myopathy

Proximal > Distal
Distal weakness > Proximal
Proximal weakness > Distal

- Buttoning of shirt
  "Hair, chair, chair."
- Mixing of food

Sensory --> Sensory effects
  No sensory effects

DTR - Ab
DTR - Ab
DTR - N/A

CK - N/U
CK - N/U
CK ↑ x 5 times

Normal is < 3.00 (uL/L)
Dystrophinopathies

\(\checkmark\) DMD  \(\checkmark\) Becker's

(xLR)  (xLR)

\(\checkmark\) Males are affected  \(\checkmark\) do-

\(\checkmark\) Dystrophin - Absent  ↓

\(\checkmark\) Hypertrophy of Calp  -do-

\(\checkmark\) Axial > Dermal  -do-

\(\checkmark\) Gower's sign +

Childhood disease  Peak -> 2nd/3rd decade

peak -> 3-5 yrs

1st decade

\(\checkmark\) ok peak 3-8 yrs

\(\checkmark\) >8 yrs ok decline

\(\checkmark\) ok decline in 3rd decade

\(\checkmark\) Unable to walk beyond 12 yrs

\(\checkmark\) Able to walk beyond 15 yrs

\(\checkmark\) Cardiomyopathy +

\(\times\) Mental impairment +

\(\checkmark\) Cause of death is weakness of chest muscles + weakness of cough reflex injection

A: Steroids  E: Steroids
- Fascia - Scapula Humeral
- Myotonic Dystrophy

- AD
- AD

- Anticipation - Intragenetic repeat

- Face muscles involved
  - Shoulder
  - Denigfactors
  - Of foot
  - Winging of scapula
  - Distal > Proximal

- Myotonic ++

- No cardiac involvement

- Cardiac involvement
  - Temporal - Surfing wasting
  - Facial - Tenderness

- Cataracts → for blue appearance
- Hypogonadism
- Gynecomastia
- Mental Retardation

- Duodenal pyloric MD - Autonomic muscle inn.

- Pharyngeal muscle inn.

- Facial hypoactivity

- Empty Dreifus Syndrome: CR proximal

- Distal - Proximal is spared in lower limb

- Contractures present

- Flexion → Elbow, ankle, knee
**Mitochondrial myopathy:** Only maternal inheritance.

**Bx:** Trichrome stain - Ragged Red fibres.

**M.c. manifestation:** CHN progressive external ophthalmoplegia.

No diplopia (despite ECM involvement)

** Kearns-Sayre Syndrome:**

- Chronic progressive Ext. ophthalmoplegia
- Triad:
  - Retinitis pigmentosa (atypical)
  - Variable: 1) Conduction abnormalities of heart
  2) Ataxia
  3) CSF ↑ protein

→ in typical RP, peripheral vision is affected first - tunnel vision.
→ in atypical RP, central vision (fovea) is affected first.

**MELAS:** M.e. mitochondrial encephalopathy.

**MERFF:** Mitochondrial Epilepsy & Ragged red fibres.

**Periodic Paralysis** → Muscle○→○, CK↑, transient problem

- Hypokalemic
- Hyperkalemic

Frequency ↓

- Hypokalemic
- Hyperkalemic

- Hypokalemic
- Hyperkalemic

- Channel affected ○

- Na

- Associated with hypokalaemia.
NMJ disease

+ Transient / intermittent weakness
+ FOM weakness
+ Biopsy ⊙, OK ⊙

Myasthenia Gravis × Lambert Eaton Myasthenic Syndrome (LEMS)

Pre-synaptic
At → Ab receptor → any
At's → fast Ca Channels
At → Muscle kinase (one)

Erection = weakness?

DTR = (⊙)

SF. EMG → jitter
Repetitive nerve stimulation
RNS → decremental

(Incremental (due to mining of bliss Ca channels)

(because only posts postsynaptic cretina are affected)

Thymic hyperplasia / thymoma
(Thymus is not involved when
As against Muscle specific kinase
is present)

♀ - Occurrence abduction♀
♀ prolonged abduction
♀ arm drop (Fasanen phenomenon)

Acidosis, Nodules, INH
Hyperplasia, Hypothyroid
Thymectomy should not be done in:
- Child < 13 yrs
- Adult > 50 yrs
- Ab and Malign.

- Breast Ab: Add R
- Occular M.G.
- EVC +

Myasthenia Gravis
Botulinum tox.

EOM +
TOM spared

EOM +
TOM spared

7OM + Papil abnormality
Accomodation
Blurred of vision

Autonous +

Neuropathy

Axonal
- B12 deficiency
- DM
- AIP
- Alcohol
- Lead poisoning
- HIV
- Lyme's disease

{AIDP = acute IgG demyel. polyradiculoneuropathy
coped wth "
- AIDP --> GBS
- Cope --> Onion bulb appearance
- in peripheral nerve

"Length rule" should be
fulfilled for axonal pattern:
Longest arm is affected first
Shorter arms are affected later

0 (not followed)
GBS - Guillain-Barré Syndrome

- Autoimmune: IgG against Myelin \( \rightarrow \) Anti-GM antibodies
- Trigger: Campylobacter jejuni \( \rightarrow \) molecular mimicry

- Ascending acute flaccid paralysis
- Descending GBS - Miller Fisher Variant
- Symmetric weakness
  - Bladder is rarely involved (if at all it is transient)

- CSF \( \rightarrow \) Cell count is normal, albumin is ?
- Abnormal - cytological dissociation (no pleocytosis)

- NCV: F wave \( \rightarrow \) indicates the integrity of the entire nerve and the AHC.
  - G-F gap \( \rightarrow \) F wave latency
    - Indicates slow conduction
    - Degeneration disorder

- H-wave / H-reflex \( \rightarrow \) is done to assess S, integrity
  - Equivalent to ankle jerk
  - Absent in: neuropathy
  - AHC disease

- Other features - Autonomic disorders \( \rightarrow \) HTN \( \rightarrow \) 5-CCB
- Peripheral \( \rightarrow \) D- Dibutamine

- Do not use Steroids.
- Ligation & Manoeuvre (Both not at the same time)
- DVT prophylaxis
- Protection from infections.
Posterior (joint position, vibrations, fine touch, 2 point)

10% control of aut.

Lateral CS tract

Lat. Spinthalamic (pain, temp)

Spinothalamus

Extra-pyramidal

Ant. CS tract

Ant. Spinthalamic - crude touch, pressure

Minimal yrs.

Posterior Column: - Thickest myelinated fibres

Faster conducting

Escape Compressive lesions.

Lat. Spinthalamic - Connect at the same level.

Lesion - fast on the opposite side

Only post. column b/c involvement - (Faber disease)

Romberg's test TOO

Closed eyes swaying = L problem

Can't get his feet together = cerebellar

Pain is common.

Minor stimuli produces pain.

UMN b/c + Posterior Column finding: - SACE

En. deficiency

Only progressive UMN b/c = Motor neuron disease - primary lateral sclerosis

Mixed UMN + LMN = Amyotrophic lateral sclerosis: ALS
Only LMN + muscle atrophy $\rightarrow$ Spinal muscular atrophy

Half 2/3 of Spinal cord lost, 1/3 sensory + CS fiber $\rightarrow$ Anterior spinal artery syndrome

Central cord syndrome: - Trauma

Syringomyelia: M.C. site of Syrinx formation - Cervical cord

Cape like distribution Post column is normal.

Crossing fibers of lateral spinobulbar are compressed

Dissociative anesthesia of arm (present in burn of the hand)

- Involvement of lateral horn $\rightarrow$ Horner's syndrome
- Involvement of ATC $\rightarrow$ Flaccidity, LMN weakness of arm
  Lower limb spasticity due to compression of caudal ATC

Syringomyelia is commonly associated with Arnold Chiari Malformation

Half of Spinal Cord Involved - Brown Sequard Syndrome

- Proprioceptive loss $\rightarrow$ loss ipsilateral
- Weakness ipsilateral
- Pain + Temperature loss contralateral
Intramedullary tumors:
- Ependymoma
- Astrocytoma

in children:
- Astrocytoma

Intramedullary tumors:
- Metastasis (Most of the cells go to the thoracic vertebrae except proximal & caudal)

Site for primary vertebral tumor:
- Thoracic

Intradural extramedullary:
- Schwannoma
- Meningioma
- MP
- F > M
- AO
- Juxta-tumoral osteoporosis
- Enlargement of tumor
- Pumpkin shaped tumor
- Contrast CT
- Absent homogeneous uptake
- Hyperdense uptake

Intramedullary:
- Diffuse pain
- Sensory sparing
- Early & late tract involvement
- Spinal sensory loss
- Early spastic weakness
- Asymmetric
- CSE usually normal
- CSE abnormal
Cauda Equina

- Loss of sacral sensory elements
- Back ache
- Loss of superficial reflexes (Babinski)
- Asymmetric muscle weakness
- Loss of Bowel & Bladder
- Relative sparing of bowel, bladder.
- Saddle anaesthesia

Brain Stem

Rule of 4:

1. Structures \(\rightarrow\) Medial \(\rightarrow\) MLF \(\rightarrow\) Medial lemniscus

2. Structures \(\rightarrow\) Midbrain

4. Structures \(\rightarrow\) Midbrain

4 CN \(\rightarrow\) Medulla

4 CN \(\rightarrow\) Pons

4 CN \(\rightarrow\) above pons

4 CN \(\rightarrow\) Medial \(\rightarrow\) 3, 4, 6, 10

Lateral 
- 5, 7, 8, 9, 10, 11
- Deep around 6
- Can be inn in both medial &

Brainstem - CS tract lesion - all weakness

Medial lemniscus lesion - all proprioceptive loss

MLF lesion - Internuclear ophthalmoplegia

Spinothalamic lesion - all hemianaesthesia

Spinocerebellar lesion - all ataxia

Sympathetic lesion - Horner's Syndrome

Sensory nerve lesion - facial all hemianaesthesia
9. Sensory - PPW - gag reflex

Medulla -
10. Palatal muscles - unilateral deviation to the opposite side of the lesion

11. Trapezius - SCM

12. Muscles of tongue, deviation to same side in paralysis

Face - 5. Sensory face

6. Lateral rectus

7. Facial muscles

8. Assess hearing.

Vth - 3. Ophthalmoplegia

4. Superior oblique

III - 5th nerve palsy - down and out eye + ophthalmoplegia

VI - 12th nerve palsy - head is turned to the same side of the lesion

IVth - 11th nerve palsy - head is tilted (because so also rotates the eye)

PERF = para pontine reticular formation

Malignant tumor in brain:
- Metastasis
- Astrocytoma
- Glioma
- Oligodendroglioma
- Meningioma
- Ependymoma

Primary in skull:
- Glioma

2nd Meningioma

3rd Schwannoma
PPRF is connected to the nucleus through MLF.

In lesions of MLF → the affected side → no adduction.

The normal side → abduction

Adduction of the abducted
(normal side)

If convergence reflex is (N): MR is normal.

If nerve nucleus is (N)

If nerve is normal:

Davies' restriction syndrome - muscle disease.

One & Half Syndrome: PPRF and MLP loss on one side.

Adduction and abduction are lost on the ill side.

Adduction is lost on this side.

Convergence reflex is (P)

B/F MLF Loss: All adduction loss on both sides.

Abduction normal on both sides.

Seen in Multiple Sclerosis.
1/4th n para + 1/4th syndrome = 8 and half Syndrome

Medial Medullary Synd.: M.C. vessel → Vertebrobasilar artery > Anti-spinal (Medullary Branch)

Lateral Medullary Synd.: M.C. vessel → PICA Vertebrobasilar > PICA

Vertebrobasilar → Vertigo names

Inf. cerebellar peduncles → Horner's VI

Sympathetic fibres → Acopia VI

Spinothalamic → Pain, Deep CS

Sensory tract of 5th → Sensory of face CS

Nucleus ambiguous → Dysarthria

Dysphagia

CN Proprioception → Medial - Dizziness

CNs cranial → Taste

Tongue - 12th CS

Lateral Medullary/Wallenburg/PICA Syndrome

Medial Medullary Syndrome

4th n with para + weakness (c.s.) → Medial ponsite - Midline Gasser Syndrome

6th n + 7th n + CS + Sensory → Forllo Syndrome

Medial Midbrain Syndrome → Weber Syndrome
Nethargel + Benedict's - Claude

Lateral Nethargel Syndrome - 3rd and 6th

Benedict's syndrome - 3rd
Red nucleus
Chorea acuta
ML - propriocep
Pt part of medial midbrain
Mild weakness, left nerve lesion

Lup. collineus - integrates visual + motor pathways
Red nucleus - Chorea acuta

Weber

Benedict

Malter CS tract ML
Corticobulbar Red nucleus
Medial Midbrain Medial Midbrain

M.S. Intracranial tumor in children: Astrocytoma - Supratentorial 80%
Infratentorial 20%

M.S. Malignant i.e. Tumor - Medulloblastoma (80% infratentorial)

M.S. Infratentorial tumor in children: Medulloblastoma
M.S. Supratentorial tumor in children: Craniopharyngioma
Dystonia

Repetitive cycles of:

- Tremor
- Myokimia - slow

Non-repetitive:

- Voluntary → tic
- Gilles de la Tourette disease

Distal segment: animal

- Fast, jerky, involuntary movements - Choreo, Hypokinesia, Ballismus

Gilles de la Tourette - M/F, Childhood

Motor:

- Echopraxia - copying the acts
- Aprosoprania - obscene gestures

R.: Guajofesia / Agoraphobia

Hypokinesia

- STN lesions → Hemiballismus → proximal wild flinging movements
- Hypoclastic yields → CPD / SSPE

Parkinson's:

- Tremor → 1/4 of diagnosis, 5/1 peak / terminal disease
- Rigidly
- Akinesia / Hypokinesia
- Poor palmar reflex

Micrographia

Hypophonia.
Musk like factor
Freezing episodes
Festination/Parkinsonian gait
Orthostatic hypotension

Parkinson's

- Parkinson's Plus Syndromes
  - Progressive Supranuclear Palsy
  - Multiple System Atrophy
  - Corticobasal Degeneration

1. Rigidity +
2. Hypokinesia +
3. Postural reflexes Abn
4. Parkinsonian gait +

Response to levodopa +++ Poor response to levodopa

Tremor ++ absent

PSP: Vertical gaze palsy (ocular problems)
- Squint away from gaze - may be rarely seen in MSA, PD
- Downgaze affected first > upward gaze later
- Dopamine doesn't work
- Pramipexole, Amantadine (Dopamine agonists) are used

MSA: Cerebellar + Basal Ganglia
  ↓
  Ataxia + Parkinson's

- Orthostatic Hypotension + Fludrocortisone
Rx of Parkinson's
- Dopamine agonists
  - Amantadine
  - Aprindine
  - Amipropidine/ropinirole
  - Rotigotine

✓ ComT inhibitors
✓ MAO-B inhibitors
  - Selegiline/Rasagiline (1st Rx in Parkinson's)
  - Levodopa + Carbidopa.

DBS: SMT + GPT.
↓

* Dementia

* Reversible
  ✓ B12 deficiency
  ✓ Hypothyroidism
  ✓ Hypogonadism
  ✓ Subdural bleed (trauma)
  ✓ Normal pressure hydrocephalus

* Irreversible
  ✓ AD (Alzheimer's)
  ✓ Vascular (MID) - Multi-infarct dementia
  ✓ Lewy body dementia
  ✓ Frontal-temporal dementia
  ✓ Huntington chorea
  ✓ CAD

✓ Normal pressure hydrocephalus: CT = enlarged ventricles.

Dementia (weak)

**TRIAD**

- Incontinence
- Ataxia (wobbly)

Rx: Trouble the CSF out → Ventriculo-peritoneal Shunt
↓

Normalizes the CSF volume.
Alzheimer Disease

\[ \text{Ab\textsubscript{4}} \downarrow \]
Neuritic plaque \hspace{1cm} \text{Tau} \uparrow \hspace{1cm} \text{Neurofibrillary Tangles}

\[ \downarrow \hspace{1cm} \text{Neuronal destruction} \]

\[ \text{Dementia} \]

Temporal lobe first involved \to neocortex \to frontal \to occipital lobe.

Temporal - hippocampus - nuclei of Meynert.

\text{c/f: - }
- Prosopagnosia (loss of memory)
- Amaurosis (loss of learned skills) - despite intact power
- Apraxia (loss of knowledge) - object agnosia
- Aphasias

Acalculia is a very late feature. Anosognosia (loss of awareness of deficit).

\checkmark \text{Prosopagnosia - occipito-temporal circuit lesion - inability to recognize face.}

\checkmark \text{Rimutagnosia - occipital lobe lesion.}

Component of Balint's syndrome.

Simultaneous evaluation of multiple things in - ve

\text{Paragnosia - occipital lobe lesion.}

\text{after image}

Image persists despite change in stimulus.
AD
Vascular (MID)

Gradually progressive
Step-ladder decline in patient functioning

DIR - 
Plantar -

Re: Donepezil → Ach ↑
Rivastigmine
Memantine → NMDA

Fronto Temporal
Lentil body

Apathy
Dissociation
Poor judgment
Hyppersonality
Hyper sexuality
Hyper phagia

Huntington's Chorea - Chr. 4

Autosomal Dominant
Tri nucleotide repeat → CAG

Dementia, Chorea, Athetosis
Imaging - Caudati lesion

R: Tetrabenazine
Physical anti-epileptics
CTD

- Park disease
  - $\alpha$-helix $\rightarrow$ $\beta$-helix
  - $\beta P^c \rightarrow \beta P^{2c}$ (non-folding)

- Rapidly progressive dementia
  - (Protein mutation)
  - Another protein (non-folding)

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

- EEG $\rightarrow$ # Slow waves $\rightarrow$ background
  - Low amplitude
  - Sudden sharp bisphasic waves

- CSF: -14.3-3 protein

- $R$: No cure

- Multiple Sclerosis
  - Subclassification $-\text{other}$

- Pathology: Inflammation
  - Demyelination
    - Oligodendrocytes
      - Remyelination
        - Astrocytes
          - Gliosis
            - Retaining remalinging type of cells (m.e.)

- Secondary progressive
- primary progressive type of MS

- Age: >50 yrs.

- Optic neuritis

- Periventricular bands of sclerosis

- Cerebellum

- Brain stem

- Spinal Cord

- Optic neuritis + Transverse myelitis

- Multiple sclerosis

- Devic's Neuromyelitis Optica

- Usually U.H. O.N.

- TM incomplete

- TM incomplete

- Bands of sclerosis (MRI)

- Periventricular grey

- MRT - @

- Hypothalamic Oedema

- Abs against Aquaporin + channel

- CSF - Atypical bands

- Rare

- Rare

- Rare

- Relapsing remitting pattern

progressive
indicators of MS:

- Warmness
- Sensation in warm
- Limb in demyelinated track
- Hoff's phenomena
- All intranuclear ophthalmoplegia
- Trigeminal neuropathy deficit
- Burdick's sign - Eclusion of neck, shock-like sensation down the spine

- Cold: Sensory "pin and  needles" (first)
- Optic neuritis
- Motor deficit: above the level - UMN, below the level - LMN
- Bladder
- Sexual dysfunction

I.O.C.: MRI

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

Disease Modifying drugs

- Tysabri (2.0 mg) Oral
- Glatiramer
- Fingolimod
- Mitoxantrone
- Dimethyldiumetrae
- Natalizumab
- Teriflunomide

(Continued on (Progressive Multifocal Leuкоencephalopathy)
(18 months) White matter pathology)
Natalizumab: Can be given at the start of the disease course and checking of JC virus at every 6 months (or ed)

- Efficacy of drugs:
  - Mitoxantrone (max) → poor tolerance
  - Natalizumab
    - Dimethylfumarate
    - TEN-A

Drugs for Progressive Multiple Sclerosis:
- Mitoxantrone
- Beclomethasone
- Mix
  - Pulse Cyclophosphamide
  - IV g
  - Pulse Methylprednisolone

Seizures

ATCS: Valproate
- Lamotrigine

Absence: Valproate
- Ethosuximide (better; not available)

Focal:
- Oxcarbazepine
- Valdenpr; levetiracetam
- Falez
- Lamotrigine

Myoclonic/AEE/Atonie: Valproate

Neonatal seizures: Phenobarbital
Feverile seizure: Diazepam (seizure happens when temp falls so paroxysmal or anti-epileptic can’t be used as prophylaxis)

Infantile spasms: ACTH

Tuberous sclerosis: Vigabatrin

Pregnancy: If seizure is controlled - don’t change the drug. Administer felbamate and continued monitoring

New seizure in pregnancy: cat A: Lamotrigine

Oxcarbazepine
Levetiracetam
Ethosuximide
Zonisamide

Cat C: Topiramate
Phenobarbital
Carbamazepine - CZ. - or. in pregnancy

Phacomatosis

Tuberous sclerosis: (ventriculocapillary schistocytes)

Vogt’s triad - Epilepsy

Adenoma Sebaceum

Ash leaf macules (hypo-pigmented)

Cafe au lait macules (coffee coloured)

Blue-green patches (raised)

Meningo-fibroma - phagocytosis

 LPARAM  


delta
Subependymal Giant Cell Astrocytoma (SEGA)

- Location: foramen of Monro

- Heart - Rhabdomyosarcoma

- Kidney - Angiomyolipoma

- Neurofibromatosis

- Type 2
  - Von Recklinghausen's Disease

- Chr - 17
- Eye - <i>few nodules (1cm)</i>
- Cafe-au-lait - >6 in number, each >1 cm in diameter
- Axillary/inguinal freckling
- Tibial/epicondylar dysplasia - 'Bone rod' sign
- Perf temporal neurofibromas - >2 in number
- Optic nerve glioma

- Usually assoc. with phaeochromocytoma

- NF - 2.
- Chr - 22
- Acoustic neuroma (inf. division of vestibular nerve)

- Sturge-Weber Syndrome

- Degeneration - (CPL) (even cross the midline)
  - Track appearance of calcification
  - Portrait stain
  - MRI: seizures, hemisensory hemiparesis
**VHL Syndrome**

Chr. 3

- Cerebellar Hemangioblastoma (in 98% of cases only hemangioblastoma is seen, otherwise other tumors are also seen, e.g., hemangioma)
- Ataxia
- Polydactyly

- All Renal Carcinoma

- Epididymal cysts

**NEPHROLOGY**

- Proteinuria: 150 mg/day
- Albuminuria: 30 mg/day

**Urine albumin:**
- < 10 - 300 mg/day: Microalbuminuria
- > 300 mg/day: Macroalbuminuria

- > 3.5 gm/day: Nephrotic range ≥ 3.5
- < 3.5 gm/day: Nephrotic range
- Upto 1 gm/day: Interstitial nephritis

**Dipstick**
- Normal differential: Glu, albumin, γ-globulin
- In multiple myeloma, dipstick may be positive

**Dipstick:**
- Positive

- Leucocyturia
- Ketone
- Urobilinogen
- (++) Glucose
- (++) Protein

**Hb, PCV**
If nitrite is picked up by Dipstick - it is also most specific test
from Gram-ve ULC.

- RBC in urine
  - Isomorphic
  - Shape is maintained
  - Source is distantISTORY
    - urinary bladder
    - uterus
    - urethra

- Eosinophiluria

- RIN
  - RBCs Emboli in kidney
  - Allergic interstitial nephritis
    - hotel procedure
    - no drug intake
    - RBC
    - sterile pyuria
    - Eosinophiluria
    - Contrast induced nephropathy
      - Complement is not affected.
      - Creat
      - No embolic phenomena
      - Prevention: hydration + NaHCO3
      - Choice of contrast - iso-osmolar contrast (best)
      - N-acetyl cysteine
Red:

WBC → pyelonephritis, interstitial nephritis

RBC → G.N.

Beady, brown → ATN (most specific/reliable)

Granular

Hyaline → Normal

Kidney disease

Glomerular

Tubular

Glomerular Disease:

- Nephrotic / Nephritic

* Cause

- 3. Complement (Nephritic)

Path findings:

Nephrotic

Nephritic

Proteinuria > 3.5 g/day

< 3.5 g/day

Hematuria ++

Hyperlipidemia

↑ S. Cholesterol

Severe edema +++
Nephrotic

- HTN +

- IgG - infection
  - Consolidated organ
  - Pneumococcal (Common)

- Protein C, AT III + thrombosis
  - Membranous nephropathy

Causes:
  - Minimal Change Disease
  - FSGS
  - Membranous nephropathy
  - Diabetic
  - Amyloidosis

Nephrotic Syndrome

MCN: cause - idiopathic
  - Infectious, allergy
  - NSARD
  - Hodgkin's lymphoma

Patho: Light light microscopy: +

Electron microscopy: loss of podocytes

Membranous:
  - Causes: infection - HBV, Malaria, syphilis, leprosy, filariasis, endocarditis
  - Cancer
  - Drug, breast, colon

Autoimmune - RA, SLE

Drugs - MSARDs, penicillin, penicillamine
Patho: Sub-epithelial deposits

IF: Spike and dome pattern immunofluorescence.

Marker: M-PAP ++ (Membranous phospholipase A2)

**ESAS**

* Causes:
  - HTN
  - Obesity
  - HIV (reflex nephropathy in HIV)
  - VUR
  - SCA (ickle cell)
  - Heroin abuse
  - Aplastic (when it presents as nephrotic)

Marker: S-PCR ++

Patho: Vascular Epithelial proliferation

Focal Sclerosis

Glomerular foot collapse (Collapsing nephropathy)

\[ \text{seen in HIV} \]

**Amyloidosis**

Screening test: Abdominal fat pad biopsy

\[ \text{if no result specific organ bx} \]

Attaining = Congo red + polarized light - Apple green birefringence

**Diabetic Nephropathy**

Diffuse Glomerulosclerosis

Focal Nodular Glomerulosclerosis (More specific)

[LD noduli]
Fibrin cap

Papillary drops

Tubules $\rightarrow$ Glycogen deposits $\rightarrow$ Arteriolar sclerosis

**ANCA**

**APS**

**IgA nephropathy, Berger's**

Systemic/polyarthritis, Pharyngitis (Bacterial) $\rightarrow$ Pharyngitis (viral) $\rightarrow$ 2 days

4-12 weeks $\rightarrow$ 7-14 days

Hematuria

Hematuria

(Pharyngitic Hematuria)

**GN - Type III**

Acute glomerular cause of hematuria in adults

Associated with Henoch-Schönlein Purpura

Potter's/ Subepithelial deposits

Epithelial bumps

(Lumpy-bumpy deposits)

> 95% recovery rate

Excellent prognosis

End stage renal disease

**ANCA - assoc. glomerular disease**: in 40%

- ANCA: c-ANCA: PR3 +, p-ANCA: MPO +

Good Pasture's - linear deposits

Churg Strauss

**Churg Strauss**: Asthma-like episodes, Renal involvement

- Arthralgia
- Eosinophilia
- 2nd most cause of Monoclonal Multiple
- B. u. - Granuloma
**MEGAN-1**

**Causes:**
- Hereditry cryoglobulinemia
- Should have joint or skin involvement
- Partial lipodystrophy
- Patchy loss of subcutaneous fat

**SLE**
- Concor (lung, breast, kidney)

**Path:**
- Spikelike splitting of GM
- Hematoxylin deposits
- Perinuclear deposits
- Ribbons-like deposits
- C3 nephritic factor

**Classical pathway of Complement**
- Alternate pathway

**Henoch-Schönlein Syndrome**

**Hereditary Nephritis**

- Collagen IV
- Collagen VI
- (autosomal dominant)

**Ocular:**
- Anterior lens cataract, keratoconus, megacornea, Retinal degeneration

**Depression (SNHL)**

- Presenting complaint of Alport

**Renal:**
- Hematuria + Proteinuria


Classical pathway
Alternate pathway

\[ \text{Fluffy deposits: IgAN} \]

- capillary

Endothelium

\[ \text{Complement:} \ C_1 \rightarrow C_2 \rightarrow C_3 \rightarrow \text{alternate} \]

\[ \text{IgAN II:} \ C_1 \rightarrow C_2 \rightarrow \text{alternate} \]

Classical
Alternate

Received an \[ C_2 \]

Type \[ C_2 \]

Factor B

Bipazixin

Classical
Alternate

Intrarenal nephropathy

Papillary epithelial proliferation

Tubular atrophy

Gross nephropathy

Papillary epithelial proliferation

\[ \text{Fluffy deposits: IgAN} \]

\[ \text{Intrarenal nephropathy} \]

\[ \text{Papillary epithelial proliferation} \]

\[ \text{Gross nephropathy} \]
Tubular Disorders

Pre Renal

- ATN
- \( \frac{\text{BUN}}{\text{Cr}} > 20 \)
- \( \frac{\text{Urine No}^-}{\text{Cr}} < 20 \text{meq/l} \)
- \( \text{Fena} > 2\% \)

Fractional No + < 1%

\[
\text{Fena} = \frac{\text{Urea} \times \text{Per} \times 100}{\text{Urea} \times \text{Per}}
\]

Urine osm > 450 mOsm/l

Hydrine Cast

Muddy brown / Granular Cast

GFR

1. > 90 ml/min
2. 60-90 ml/min
3. 30-60 ml/min
4. 15-30 ml/min
5. 0-15 ml/min

Drug dose modification

Rapidly convert to ESRD
Cystatin-C → New marker for CRF
Better marker than Creatinine
Not dependent on muscle mass.

Renal Failure: → Acidosis, ↑ Ca, ↑ PTH

ARF → CRF

PO₄ ↑
Ca ↓
K⁺ acute, K⁺ ↓
CRF K⁺ ↑

↓ PO₄
Ca ↓
K⁺ ↓
Anemia

↓ PTH

M. acidosis

↑ Renal osteodystrophy

Bound Ca → ionised Ca²⁺

So signs of hypocalcaemia are NOT apparent despite ↓ serum Ca²⁺

RATTER'S

NSAIDS.

Na⁺ 65%

↑ Na⁺

↓ Na⁺/K⁺/Cl⁻ 25%
**LIDDLE'S SYNDROME** (pseudo-hyperaldosteronism)

- **Apical Channel Defect**
  - The apical channels are not secretory/regulated as replaced.
  - Loss of K+ and Tg-Na+

**Renin** ↓ (due to feedback)

- Hypokalemia
- Metabolic alkalosis
- HYN
- Normal stones

**Re:** (Hardware to block apical Na+ Channels)
Bartter's Syndrome vs. Gittleman's Syndrome.

like furosemide
like thiazide.

Defect: loop of Henle
Defect: Na-Cl Distal tubule

MAP vs. MAP

$\frac{K^+}{\text{Met. alkalosis}}$ vs. $\frac{\text{K}^+}{\text{Met. alkalosis}}$

Urea ↑ → stones.

Urea ↓ → No stones.

Ung → N

RTA 1, 2

- Hypokalemia
- Metabolic acidosis (normal anion gap)

RTA 1

- Distal tubule defect
- Acid excretion defect

Urine pH > 5.5

RTA 2

- Proximal tubule defect
- Bicarb reabsorption defect

Urine pH < 5.5 (due to KCO3 depletion)

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

Associated with stones

- Glycosuria, aminoaciduria, phosphaturia.

Inflammatory - urine acidification test
Sodium + Nitrite

Give acidic substance → Fractional $\text{HCO}_3^-$ reabsorption $> 15%$

Urine pH 7.5 (normal)
Causes: Sjogren's
- Hyperparathyroidism
- Multiple Myeloma
- Amphotericin B

Causes: Fanconi's
- Metabolic disease (6 ATP)
- Gastrectomy
- Multiple myeloma

Type 4 RTA

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

Anion gap is ↑ in Renal failure
\[ AG = Na^+ - (Cl^- + CO_3^{2-}) = 12+4 \]

Metabolic acidosis

\( \text{AG} \) \[ \text{↑ AG} \]

Ketoneacidosis - Starvation

- Alcohol
- Diabetic

Diabetes
- Acetazolamide

Hydrogen ion
- Drugs: ACE, ARB
- Toxic

- VC \( \text{Na}^+ + \text{K}^+ - 	ext{Cl}^- \) \[ \text{↑ VC} \]

Alcohol

Uremia
INH overload, Trans

DNA

Lactic acidosis

Ethylene glycol
Sodium
\[ \text{AG gap} = \frac{\text{AG} - 18}{24 - \text{HCO}_3^-} \]

\[ \Delta \text{gap} < 0.4 \rightarrow \text{NAGMA} \]

\[ 0.4 - 1 \rightarrow \text{NAGMA} \text{ Mixed metabolic acidosis} \]

\[ 1 - 2 \rightarrow \text{HAGMA} \]

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

**ABG**

\[ \text{pH} = 7.35 - 7.45 \quad 7.40 \]

\[ \text{CO}_2 = 35 - 45 \quad 40 \quad \text{Venous blood - 45 is} \]

\[ \text{HCO}_3^- = 22 - 26 \quad 24. \]

*Normal Compensation → Both CO\(_2\) and HCO\(_3^-\) move in the same direction*

\[ \begin{align*}
\text{CO}_2 & \uparrow \\
\text{HCO}_3^- & \uparrow \rightarrow \text{Normal compensation} \\
\uparrow & \rightarrow \text{may be simple or mixed} \\
\downarrow & \\
\uparrow & \rightarrow \text{mixed} \\
\downarrow &
\end{align*} \]

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

*In respiratory acidosis/alkalosis, the kidney may compensate partially*
ROMEO:  
\[ \text{pH} \quad \text{CO}_2 \]
\[ \uparrow \quad \downarrow \quad \uparrow \quad \downarrow \]
\[ \text{Respiratory} \quad \text{alkalosis} \]
\[ \text{Metabolic} \quad \text{acidosis} \]
\[ \text{Metabolic} \quad \text{alkalosis} \]

CO₂ should not be in the normal range to apply ROMEO rule.

\[ \begin{align*}
\text{pH} & \quad \text{CO}_2 \\
7.20 & \quad 24 \\
\text{Gap} < 15 & \quad \text{Metabolic}
\end{align*} \]

\[ \begin{align*}
7.20 & \quad 7.4 \quad 40 \\
\text{Gap} > 15 & \quad \text{Respiratory}
\end{align*} \]

Compensation formula:

Met. acidosis: \[ \text{CO}_2 = 1.5 \left( \text{HCO}_3^- \right) + 2 \pm 2 \]

Met. alkalosis: Every 10° in \[ \text{HCO}_3^- \], CO₂ should rise by 7.

Respiratory:

\[ \begin{align*}
\text{Acidosis Acute} & \quad 1 \quad 10 \\
\text{Chronic} & \quad 4 \quad 10 \\
\text{Alkalosis Acute} & \quad 2 \quad 10 \\
\text{Chronic} & \quad 5 \quad 10 \quad \text{m}^+ \\
\end{align*} \]

Henderson's Equation:

\[ \text{H}^+ = \frac{24 \times \text{CO}_2}{\text{pH}} \]

\[ \begin{align*}
\text{pH} & \quad \text{CO}_2 \\
7.60 & \quad 60 \\
7.50 & \quad 60 \\
7.30 & \quad 50 \\
7.20 & \quad 60
\end{align*} \]
Respiratory

\[ \text{CO}_2 \quad \text{pH} \]

acute $\rightarrow$ \[ 10 \quad 0.08 \]

chronic $\rightarrow$ \[ 10 \quad 0.03 \]

\[ \begin{align*}
\text{Na}^+ & \quad 140 \\
\text{K}^+ & \quad 4.0 \\
\text{Cl}^- & \quad 106 \\
\text{HCO}_3^- & \quad 14 \\
\text{CO}_2 & \quad 24 \\
\text{pH} & \quad 7.39 \\
AG & \quad 20
\end{align*} \]

\[ \text{pH} < 7.4 \rightarrow \text{acidosis} \]
\[ \text{CO}_2 > 24 \rightarrow \text{not resp. acidosis} \]
\[ \text{HCO}_3^- < 14 \rightarrow \text{met. acidosis} \]

\[ \text{AG} = 20 \]

\[ \begin{align*}
\text{CO}_3 & = \frac{3}{2}(14) + 8 \pm 2 \\
& = 29 \pm 2 = 27 - 31
\end{align*} \]

\[ \text{CO}_2 \text{ in below 27, caution of CO}_2 \text{ Resp. alk} . \]

\[ \text{met. acidosis + Resp. alk} . \]

\[ \text{AG ap} = \frac{20 - 12 - 8}{10} = 0.8 \rightarrow \text{mixed metabolic acidosis} \]

\[ \begin{align*}
\text{pH} & \quad 7.30 + \text{acidosis} \quad \text{metabolic acidosis} \\
\text{CO}_2 & \quad 28 \\
\text{HCO}_3^- & \quad 16 \\
\text{AG} & \quad 20
\end{align*} \]

\[ \text{CO}_2 = \frac{3}{2}(16) + 8 \pm 2 \]

\[ \text{AG} = 20 \]

\[ \begin{align*}
& = 29 \pm 2 = 28 - 31
\end{align*} \]

\[ \text{CO}_2 \text{ is above 24, retention of CO}_2 \text{ Resp. acidosis} \]

\[ \text{AG ap} = \frac{20 - 12 - 8}{8} = \frac{0.8}{8} \rightarrow \text{Mixed MA + Resp. acidosis} \]
RESPIRATORY

FEV - Spirometry
RV - Body plethysmography
○ FVC - TLC: No washout
○ FVC - TLC: He dilution test

<table>
<thead>
<tr>
<th>Obstructive</th>
<th>Restrictive</th>
</tr>
</thead>
<tbody>
<tr>
<td>FEV₁ ↓/↓ ✓</td>
<td>↓</td>
</tr>
<tr>
<td>FVC N/↓</td>
<td>↓/↓</td>
</tr>
<tr>
<td>FEV₁/FVC ↓</td>
<td>N/↑</td>
</tr>
</tbody>
</table>

FEV₁, FVC above 80% is considered (✓)
FEV₁/FVC > 70% (0.7) is considered (✓)

Gold criteria: FEV₁/FVC should be < 0.7 to be called a "Obstructive COPD"

A FEV₁/FVC > 70% → FVC > 80% → Normal
       FVC < 80% → Restrictive lung disease

DLCO: CO and O₂ have the same diffusing capacity
      but CO binds to Hb 250x more strongly than O₂, so it doesn't
      diffuse back into the alveoli unlike O₂.

DLCO = Surface × k̄
      Thickness

√DLCO - Bronchići → N
√ COPD → ↓
√ Emphysema → ↓
√ Asthma → N
√ ILD → ↓
R-L (Joe) → ↓
L-R (MSP) → ↑
Anatomic Age → ↑ (falsely ↑ in TLC)
Pulm. Emphysema → ↓ FEV₁, -1/4 EVC - Δ Ratio ↑
At. Pulm. HTN → ↓ Isolated ↓ in DLCO
Polyglobulia → ↑ DLCO should be corrected for Hb
Anemia → ↓

DLCO → 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

↑ VEP → Variable intrathoracic obstruction
PULMONARY EMBOLISM:

- Dyspnea on Exertion
  - **CXR** → normal in initial stage
  - non-specific infiltrates
    - Atoll sign: wedge shaped
    - subpulmonic consolidation
  - Weber's sign: oliguria
  - pleural effusion: haemorrhagic → trauma
    - tumour
  - Kerley B lines
  - Fleur de lis opacity
  - Shift sign: prominence of RI pulmona artery
  - **ECHO** → pulm hypertension (mean pressure >25 mmHg at rest
    - pulm regurgitation
    - RV hypokinesia

DVT in common in:
- joint replacements (hip, knee)
- ICU patients
- Flight travel
- Thoracentesis
Thrombotic Therapy

- High risk - CT angiogram
- Low risk - D-dimer

Rule out PE: Investigate for high risk

Gold standard: Invasive Catheter angiogram

Unstable
- Thrombotic Therapy

Stable
- Heparin

Contraindication of TI

Mechanical dissolution of clot

C.T. to thrombolysis

Absolute:
- History hemorrhagic stroke
- Active intracranial neoplasm
- Recent (<6 months) intracranial surgery or trauma
- Active or recent gastrointestinal bleeding in prior 6 months

Relative:
- Bleeding diathesis
- Uncontrolled severe HTN

Off
- Non-therapeutic INR ≥ 2 months
- Surgery ≥ 48 hours prior 10 days

Platelets ≥ 100,000
Hypersensitivity Pneumonitis

DOC: Hypersensitivity to organic dust matter

Restrictive pattern

CR - Apical fibrosis, groundglass appearance
MZ thin infiltrates, alveolitis

Type III + Type IV hypersensitivity

BAK - lymphocytes CD<sub>8</sub> > CD<sub>4</sub>

Fasciitis, IP of ad seen
Potato - Granuloma

Rx: Avoid the allergen
1) Steroids
2) Cyclophosphamide / Azathioprine

Sarcoidosis:

TLD

Restrictive pattern

CR - Apical fibrosis + hilar lymphadenopathy
MZ thin infiltrates

plural effusion is very rare (<5%)

Hemophili's Syndrome: 1) Hepatoplenomegaly, lymphadenopathy
2) Ca (due to hypervitaminosis D)

ACE 1
ABPA  

Fever, neutropenia  

Rx: Antipseudomonal penicillin  

Allergy to Aspergillus  

Hypersensitivity - Vancomycin  

Catheter  

Type 1 + Type III  

Antifungal: Amphotericin  

Wheeze - D.O.E., Hemoptysis  

CXR - Central bronchiectasis  

Eosinophilia, Tg↑  

I.C.: Skin test - Reagin Tine to Aspergillus  

Bal: Eosinophilia  

Rx: Glucocorticoid + Antifungal cover (itraconazole)  

Rx in invasive aspergillosis - Flucanazole  

Prophylaxis of aspergillosis: Amphotericin  

GERD  

Breathlessness  

Coughing  

Strong odor & Smoking  

Velcro crack (terminal inspiratory crepe)  

HRCT: Lower lobe fibrosis (honeycomb appearance)  

Rx: Pleurodesis  

WP - usual infective pneumonitis  

Bal: Neutrophilia
Rx: Oxygen
Steroids (minimal role)
IV Lung vasoconstrictor

Asthma: GOOD
Stage: >2 yrs
Smoker:

Family History: Asthma
Allergy:

Airway hyperresponsiveness:
- Histamine: Fev, ↑ >10%
- Methacholine: Fev, ↑ >20%

OXR: Normal initially
- Minimal air trapping
- Pneumonia

DLCO: ↑
DLCO: ↓

AGA: Respiratory acidosis
Metabolic acidosis

Rx: Inhalational steroids
Rx: Inhalational anticholinergics
Acute HBV - no. 95% recover. 5% chronic

Chronic HBe: Monotherapy: Entecavir
- Tenofovir
- Peginterferon
- Lamivudine
- Adefovir

Peg IFN: no induction of resistance

Cannot be used in
- Decompensated liver disease
- Immunosuppressed
- Pregnancy, children

HAV

PEG IFN, Ribavirin
+ 

Enzyme protease inhibitors
- Bospreva
- Telzirae

now, 24 weeks of IFN is adequate, indicate 48 weeks.