

Pathology

- genes
- IL1 cytokines
- amyloidosis

Binge Revision

- Medsynapse by

Dr. Nikita

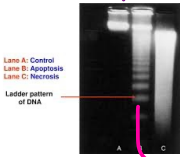
29/4/24

General Pathology

- * B2 Dialysis amyloidosis → β₂ microglobulin
- ↳ prog. for MEN multiple myeloma.
- thyroid tumor → Acal → Medullary
 - ↳ MEN 2
- EE - extracellular, eosinophilic
- starch deposn
- β pleated sheets on xray crystallography
- 1° → AL 2° - AA (2A) - 2° * Biref → Polarising
- AI-1

Necrosis vs apoptosis

- pathological
- inflammt ⊕ → necrosis ⊕
- cell size ↑
- cell memb disrupted
- smear pattern



- CD95
- annexin V
- pop → stepladder

Necroptosis: • Rip1,3 mediated. * Pyroptosis → • IL1
 • acute pancreatitis

- anti apop →
 ↓
 cell lives
 (Cl)

- BCL2
- BCL-XL
- MCL-1

- proap (ai)
- Bax ✓
 - Bax ✓
 - Bad, bin, bid

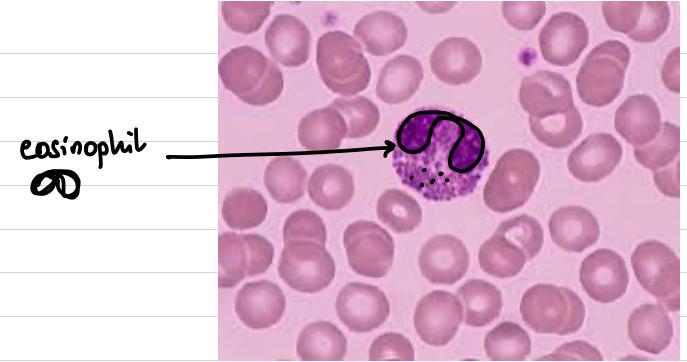
* Cell in cell app:

↓
Entosis
 ↓
same type cell.

Stains

★ Mast cells

— T.B.



★ myelin

— Luxol (~~fast~~) blue

★ ⊕ IHC brown

— DAB (Diaminobenzidine)
Browns

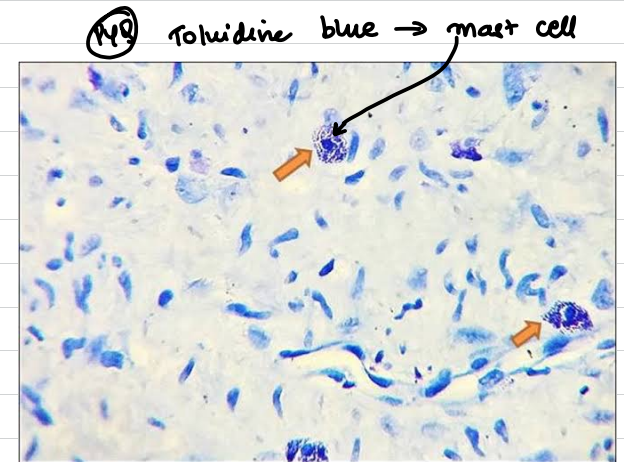
★ Iron

— Perls / Prussian blue

★ elastic fibres

— Verhoeff

^ von Kossa → calcium



cardiac amyloid

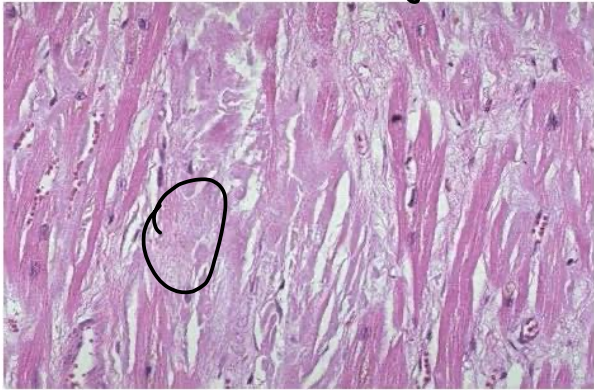
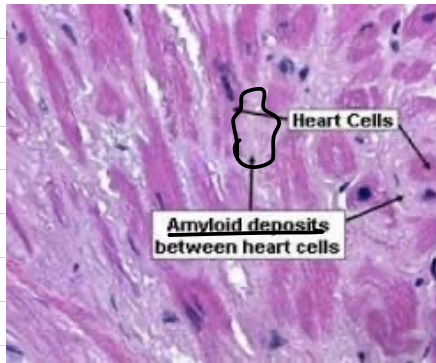


Figure 5: Histologically confirmed amyloid deposits (light pink) between myocardial fibers.



senile amyloid → Heart

• ATTR wild (N) protein

• Restrictive CM

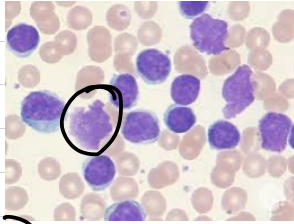
→ Transthyretin

→ Diastole dysfunction

• S4 (S1) of ventricle

Hematology

* **CLL** →



- elderly
- flu
- parachute smudge (autoimmune)

◦ elderly \bar{c} smudge cells

◦ **Flow Cytometry** - CD5 + CD23⁺ (combined⁺)

◦ B cells Mature

◦ m/c - 13q delⁿ - good prog*

◦ 17p delⁿ - poor prognosis

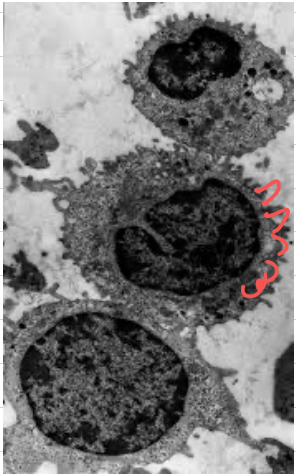
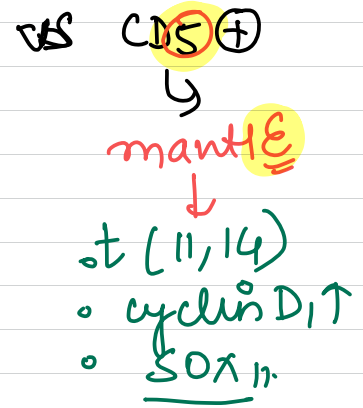
- autoimmune hemolytic anem
- L.N → proliferation centres ⊕

DOC → Fludarabine

◦ **Richter syndrome** → CLL → aggressive lymphoma (DLBCL)

Basophilia → in **CML**

↳ myeloid



- TR acid phosph⁺
- CD103, annexin A1
- Hairy cell
- Memory B
- Red pulp
- No LN
- spleen⁺

Prognostic factors in ALL

Determinants	Favourable	unfavourable
WBC Counts	<10,000	>2,00,000
Age	2-10 years	<1yr, >10yr
Gender	female	male
Ethnicity	white	blac
Node, liver, splenomegaly	absent	massive
Testicular enlargement	absent	present
CNS involvement	absent	Csf blast and pleocytosis
FAB Type	L1	L2
Cytogenetics	t(12;21)(TEL-AML1) Trsomyies 4,10,17	t(9;22)(bcr-abl) t(4;11)(MLL-AF4)
Ploidy	hyperdiploidy	hypodiploidy
Time to remission	<14days	>28days

(un)fav → extremes
 ALL
 • Hypo → (un) diploidy
 square (4,11) (9,22) • male ✓
 • L2 ✓

AML

Subtype	Description	Cytogenetics
M0	Minimally differentiated acute myeloid leukaemia (AML).	
M1	Acute myeloid leukaemia without maturation.	
M2	Acute myeloid leukaemia with maturation.	t(8;21)(q22;q22), t(6;9)
M3	Promyelocytic, or acute promyelocytic leukaemia (APL)	t(15;17)
M4	Acute myelomonocytic leukaemia.	inv(16)(p13q22), del(16q)
M4 Eo	Myelomonocytic together with bone marrow eosinophilia	inv(16), t(16;16)
M5	Acute monoblastic leukaemia (M5a) or acute Monocytic leukaemia (M5b)	del(11q), t(9;11), t(11;19)
M6	Acute erythroid leukemias, including erythroleukemia (M6a) and very rare pure erythroid leukaemia (M6b)	
M7	Acute megakaryoblastic leukaemia	t(1;22)

Arsenic trioxide /
 • ATRA → in Rx of APL (APML)
 tri M3

* Blood components

< -18°C

1 yr

- FFP → multiple coag.
- cryoppt. (-30°C) b. def.

f. 8, vwf, fibrinogen

2-6°C

cool

- whole blood → blood loss

- CPD - 21d
- CPDA - 35d
- SAGM - 42d.

20-24°C

± agitator

• 5 days

- platelets

• 1 unit of PRBC ↑ Hb^g by 1 gm dl. / Hct by 3%

- platelets
 - random donor → 10k ↑
 - single donor → 30k ↑

- Screen for: High malaria screening
 - H M S
 - HIV
 - Hep B/C
 - syphilis

* Massive blood transfusion:

- cin 24 hrs

complicns:

- ↑K → RBC lysis → K out
- ↓Ca → citrate binds to Ca.
- alkalosis > acidosis
- coagulⁿ ↓ (DIC)
- Hypothermia (cold temp)
- citrate toxicity

↓23BP4

- * TRALI
- ~ARDS
- cin 6 hrs
- anti HLA/WBC Ab
- BP

vs

- TACO
- ↑BPC (circulatory overload)

★ m/c genetic hyper-coagulability →

• Leiden V mutation

(resistant to inactiv'n by prot C)

4(N) → anticoagul'n.
• vit K dep.

★ Order of draw

ivf culture → blue → Red → yellow → green

uniform school

drive

green

Grey

← Pink
Pinky

← lavender
love

(hair)
glucose

Draw Order	Tube Color	Description
1		Blood Cultures
2	Blue	Sodium Citrate
3	Red	Clot Activator
4	Yellow	SST
5	Light Green	Lithium Heparin
6	Dark Green	Sodium Heparin
7	Pink	EDTA
8	Grey	Sodium Fluoride
9	Yellow	ACD Solution

city school

→ Red

SST → serum

→ Hara

Sodium Heparin

EDTA → lavender

Sodium Fluoride → grey

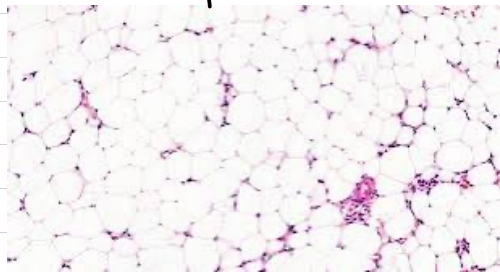
ACD Solution

★ **sickle cells** : ↑ mechanical (small vessel → infarct)
fragility / Thalassemia
 • ↓ osmotic

• ↑ osm. fragility → spherocyte / AHA
 ↳ COombs ⊕

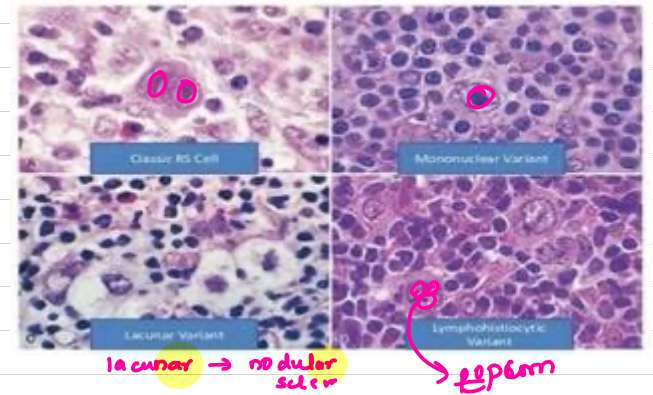
Aplastic anemia (fat)

★



No splenomegaly

- aplastic crisis → parvo (PAg RBCs)
- PRCA → Thymoma
- Benzene → Blood benzidine → bladder



lacunar → no diater selection

↳ popcorn

★ Hodgkins

→

CD1530
classical

Worst → lymphocyte depleted ★

↳ 2045

nonclassical

• LP → popcorn cell / LEK
good prognosis, no EBV
 excellent

* **IDA** →

- TIBC → ↑↑
- Transferrin sat^o → ↓
- **Mentzer** index → ↑ > 13. $\frac{MCV}{RBC\ count}$
↳ Thal: zero
- platelet count ↑↑
- RDW → ↑↑
- (N) is Thal
↳ genetic
all cells =

ACD

- Ferritin ↑
 - Hepcidin ↑
 - Ser: iron ↓
- ↑ve APR
↑ in inflam

* ^{Six:} **B6** def → **Sideroblastic**

* **xLR** → G6PD def

A

Immunology

- ★ Lack of CD40 → Hyper IgM
 - switching IgM → other.
 - ↑ IgM, ↓ IgG
 - recurrent pyogenic/PCP infections

CD40 + CD40 Ligand → XLR-IgM
 B T cells Helper ★ WAS

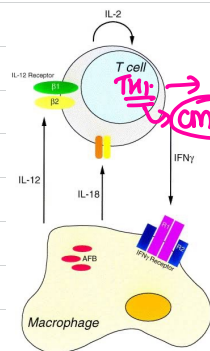
- ★ Central tolerance → No autoimmunity
 - AIRE gene → defect → AiPE
 - autoimmune regulator → Thymus-negative selection.

- ★ BARE lymphocyte:
 - abst class II MHC
 - Combined ID → CD4 cells T_H + B cells ✓

- T-ALL → NOTCH1 gene
 - EgA → Burkitt's lymphoma
- Teen thymus: + child mediastinal mass

vs iPEX → pfor3 → ⊕ on Treg/cells. suppress of T cells.

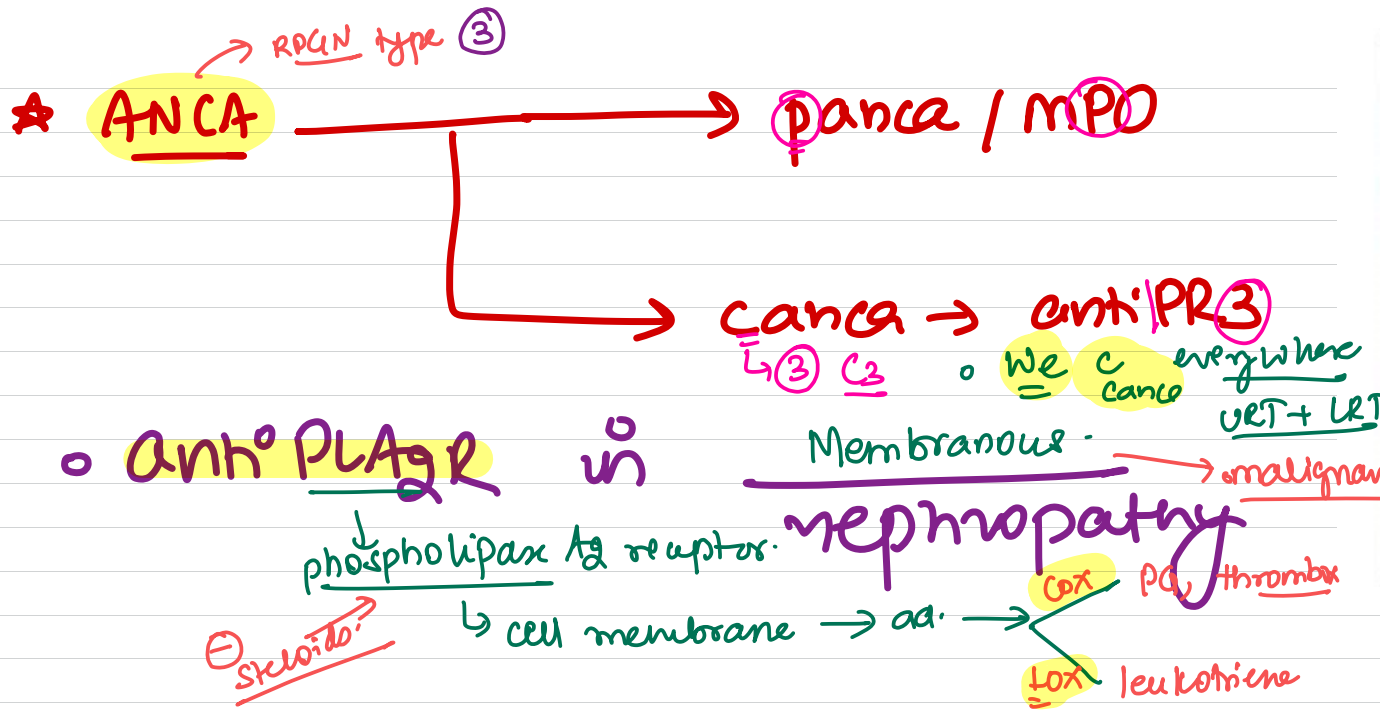
- ★ granuloma (gamma) → IFN-gamma
 - prod. by Th1 cells & Macrophages produce IL12 ⊕
 - ↳ macro



vs Th2 - HH Humoral

• Th1 ↓

Th2



Type I (Anti-GBM Antibody)	1 → GBM → <u>APS</u>
Renal limited Goodpasture syndrome	
Type II (Immune Complex)	2 → <u>IC</u> →
Idiopathic	
Postinfectious glomerulonephritis	✓
Lupus nephritis	✓
Henoch-Schönlein purpura	✓
IgA nephropathy	✓
Others	
Type III (Fauci-Immune)	3 → <u>ANCA</u>
ANCA-associated	
Idiopathic	
Granulomatosis with polyangitis (formerly Wegener granulomatosis)	★ (A)
Microscopic polyangitis	

ANCA, Antineutrophil cytoplasmic antibodies; GBM, glomerular basement membrane.

★ **B-cells:**

- ① ↑ affinity for Ag by somatic hypermutation
 - ② (IgM and IgD) together: due to alternative RNA splicing
 - IgM → μ heavy chain
 - IgD → δ heavy chain
- introns exons

NK cell : - CD 16, 56, 94 P. CD95 Fas: ↓ apoptosis
 body • ADCC → type 2 HSN
 ↓ MHC expression → virus / malignant cells
 • not MHC restricted → perforin

Innate vs adaptive immunity

	Innate immunity	Adaptive immunity (Ab) T+B-
COMPONENTS	Neutrophils, macrophages, monocytes, dendritic cells, <u>natural killer (NK) cells</u> (lymphoid origin), complement, physical epithelial barriers, secreted enzymes	T cells, B cells, circulating antibodies
MECHANISM	Germline encoded <u>gamma delta T cells</u>	Variation through V(D)J recombination during lymphocyte development
RESPONSE TO PATHOGENS	Nonspecific Occurs rapidly (minutes to hours) No memory response	Highly specific, refined over time Develops over long periods; memory response is faster and more robust
SECRETED PROTEINS	Lysozyme, complement, C-reactive protein (CRP), <u>defensins</u> , cytokines epithelial cells	<u>Immunoglobulins</u> , <u>cytokines</u>
KEY FEATURES IN PATHOGEN RECOGNITION	<u>Toll-like receptors (TLRs)</u> : pattern recognition receptors that recognize pathogen-associated molecular patterns (PAMPs) and lead to activation of NF-κB. Examples of PAMPs: <u>LPS</u> (gram ⊖ bacteria), flagellin (bacteria), nucleic acids (viruses) endotoxins	<u>Memory cells</u> : activated B and T cells; subsequent exposure to a previously encountered antigen → stronger, quicker immune response CD14 macrophage

alternative, lectin

gamma delta T cells

epithelial cells

endotoxins

CD14 macrophage

Important cytokines

Acute (IL-1, IL-6, TNF-α), then recruit (IL-8, IL-12).

Secreted by **macrophages** Q

Interleukin-1 Causes fever, acute inflammation. Activates endothelium to express adhesion molecules. Induces chemokine secretion to recruit WBCs. Also called osteoclast-activating factor.

“Hot T-bone stEAK”:
IL-1: fever (**hot**).
IL-2: stimulates **T** cells.
IL-3: stimulates **bone** marrow.
IL-4: stimulates Ig**E** production.
IL-5: stimulates Ig**A** production.
IL-6: stimulates a **K**ute-phase protein production.

Interleukin-6 Causes fever and stimulates production of acute-phase proteins.

Tumor necrosis factor-α Activates endothelium. Causes WBC recruitment, vascular leak.

Causes cachexia in malignancy QQ
Maintains granulomas in TB.
IL-1, IL-6, TNF-α can mediate fever and sepsis.

Interleukin-8 Major chemotactic factor for neutrophils.

“**Clean up on aisle 8.**” Neutrophils are recruited by **IL-8** to **clear** infections.

Interleukin-12 Induces differentiation of T cells into Th1 cells. Activates NK cells. ⊕ IFNγ

Facilitates granuloma formation in TB.

Secreted by **T cells**

Interleukin-2 Stimulates growth of helper, cytotoxic, and regulatory T cells, and NK cells.

Two - T cells
3 - m 3 - Marrow.

Interleukin-3 Supports growth and differentiation of bone

From Th1 cells → TH 1 IL 2 3-γ IFN (granuloma).

IL12
macrophages.

Interferon-γ
Secreted by NK cells and T cells in response to antigen or IL-12 from macrophages; stimulates macrophages to kill phagocytosed pathogens. Inhibits differentiation of Th2 cells. Induces IgG isotype switching in B cells.
Increases MHC expression and antigen presentation by all cells. Activates macrophages to induce granuloma formation.

From Th2 cells → ④ IL4 5 10 13

Interleukin-4
Induces differentiation of T cells into Th (helper) 2 cells. Promotes growth of B cells. Enhances class switching to IgE and IgG.
Ain't too proud 2 BEG 4 help. class switching

◦ Eosinophil
◦ IgA

Interleukin-5
Promotes growth and differentiation of B cells. Enhances class switching to IgA. Stimulates growth and differentiation of Eosinophils.
I have 5 BAEs.

Bas
anti

Interleukin-10
Attenuates inflammatory response. Decreases expression of MHC class II and Th1 cytokines. Inhibits activated macrophages and dendritic cells. Also secreted by regulatory T cells.
TGF-β and IL-10 both attenuate the immune response.

Interleukin-13
Promotes IgE production by B cells. Induces alternative macrophage activation.
Interleukin thir③ promotes IgE.

IL 1 → pyrogen

2 → Two - T cells

3 → Marrow

4 → IL-4 → switching

5 → S BAE IgA

6 → aPK

8 → \emptyset → chemokine

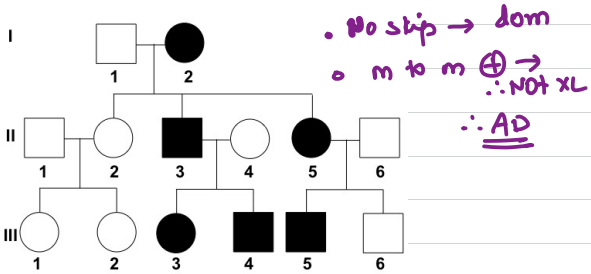
10 → bas - antiinflamm | Treg

12 → ~~macro~~ macro → \oplus Th → IFN γ

13 → Ig E

\emptyset myeloid → ^M 123
lymphoid → ^L 17
T

Genetics



★ **Patau** → 13 → P
 • **Edwards** → 18
 • **proencephalic**
 • **palate**
 • **cutis aplasia**
 • **polydactyly**

• every dec
 • early death
 • 5 fingers/teeth

• **sickle cell** → AR - point
 • **Huntington** → AD. **Hunter XL**
 (3M) ↓ **gaba** / **Ach.** **CAG**

★ **CF** → AR ΔFSDB
 • **leber** → mitoch.
 • **DMD** → XL

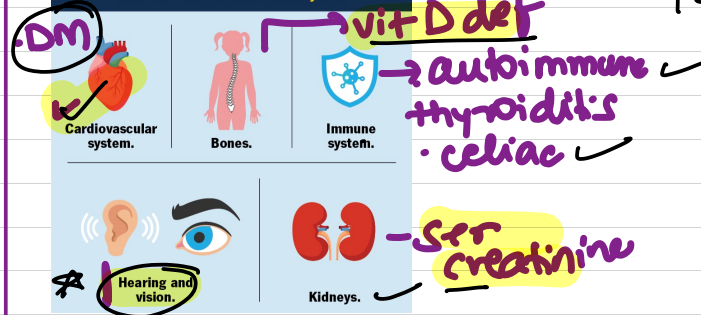
• **myotonic dystrophy** → AD chrom 19 CTG

★ **Turner** : lymphatic

fetal hydrops ✓
 • cystic hygroma ✓
 • hands edema.

Mosaic ↓
 ↑ gonadoblastoma

Turner syndrome is associated with certain medical conditions that affect your:

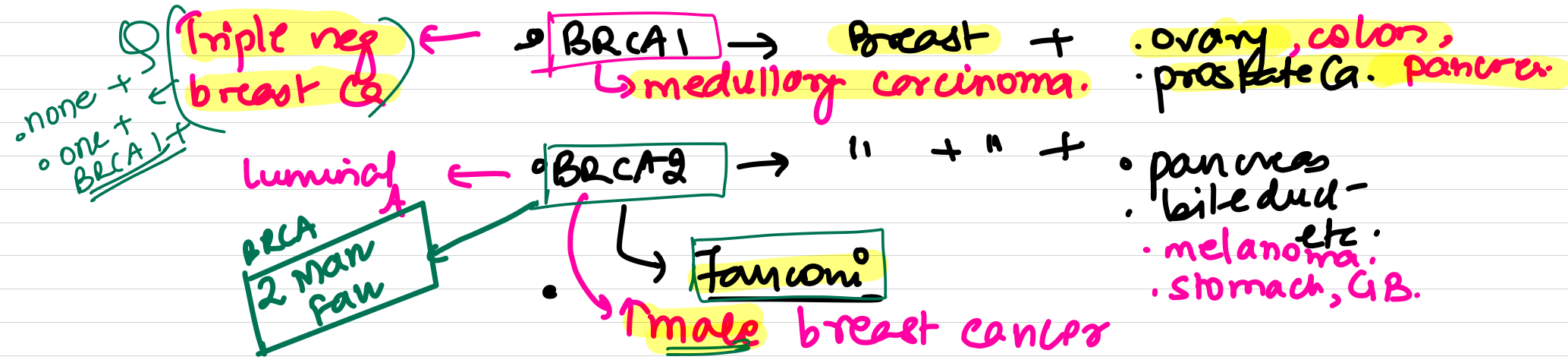


• **Protop Av**
 • **COA**
 • **HSK**
 • **streak gonads**
sec abst
 • NO MR

★ **Rett** :
 • females dom.
 • XLD.
 • **MECP gene**
 • **Troferitide**

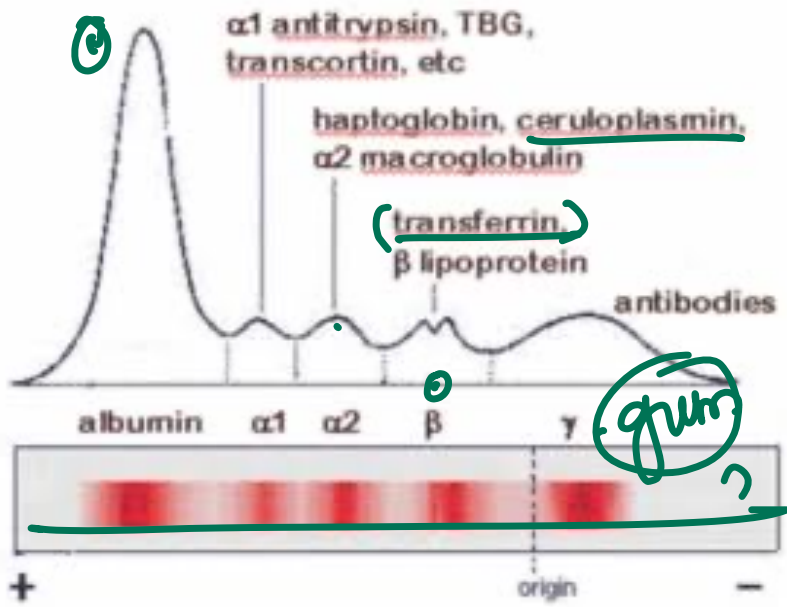
★ BRCA_{1,2} → 17q ← 13q →

- Tumor suppressor genes ✓
- dsDNA repair ✓



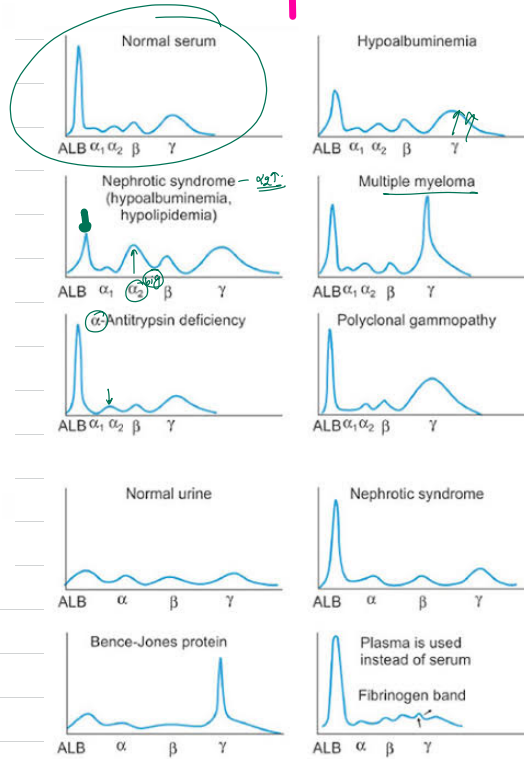
★ luminal (A) breast Ca: → ER/PR +
• HER2 -ve
• prolif ↓, ki67 ↓

BRCA2
ER/PR
|
favourable
good



↑ in nephrotic :

2
 4 big proteins
 not filtered



GIT

* alcohol liver dysfunction → GGT ↑
AST/ALT > 1.5
 ↓
less.

* FAP → CRPE

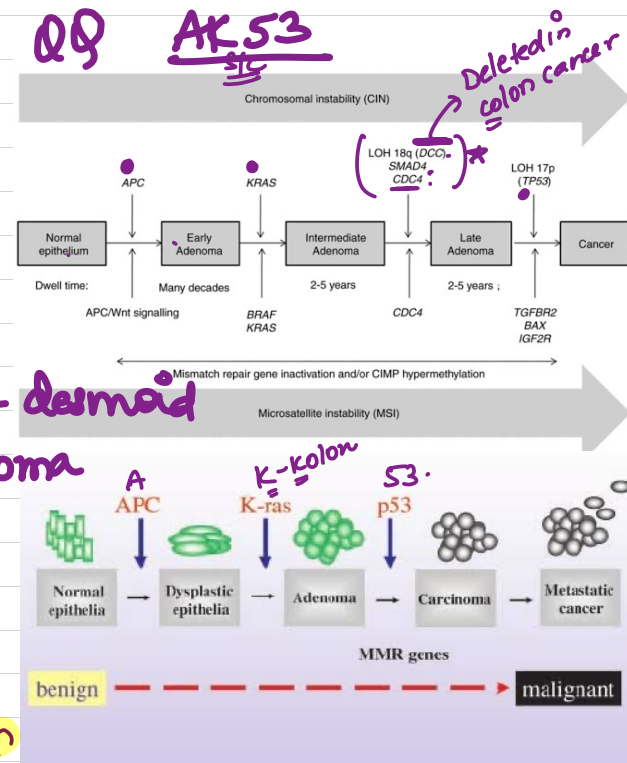
- sq
- Turcot → Turban → Brain tumor
- Gardners → prick → skin
 • sc. fibrous - dermoid
 • bones - osteoma

* myc

- C → Burkitt
- L - small-intest
- N - neuroblastoma

* RAS

- K → pancreas, adenolung, colon
- N → melanoma, AML
- H → Bladder, kidney



* GIST →
IF / cajal

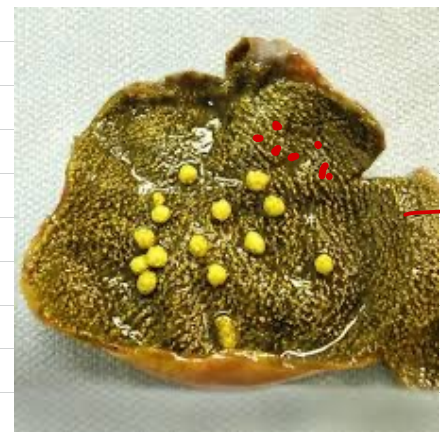
- cKit ✓
- CD117
- DOG1


* ^{chrom 2} ALK :: Anaplastic large cell
Lymph → lung · Non-SCLC

* Jak2 → myeloprolif.
(PCV)

* NO acid in pernicious anemia (after pentagastrin inject)

↓
anti parietal
↓
IF / acid ↓

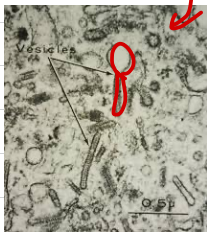


→ Strawberry UB
• cholesterolosis
• USG → 
comet tail

CNS

beveled lytic skull.

★ LCH → Birbeck granules



- CD207 ✓
- CD1a ✓
- S100 → • NCC
 - melanoma
 - schwannoma
- HLA-DR ⊕

HSC → $\left(\begin{array}{l} \text{Di} \\ \text{-calvarial} \\ \text{-exophthalmos} \end{array} \right)$

★ TB meningitis : \rightarrow MRS: lipid peak.
• ↑ lymphocytes, glucose ↓, basal exudates (gluc ⊕ viral)
• cobbles

★ { perineural invasion : adenoid cystic
Nerve

★ Hot spot : Warthin / (on a war hot)
Tescan adenolymphoma

★ pleomorphic
↳ parotid.
• epith + mesenchymal
• chondroid
• PLAG1 ⊕

CVS

★ Infective endocarditis:

3 culture samples:
gap of 30min bet each.

2 - peripheral

1 → valve

Coxiella
Bartonella
H/quit

chordae ⊕
biviable

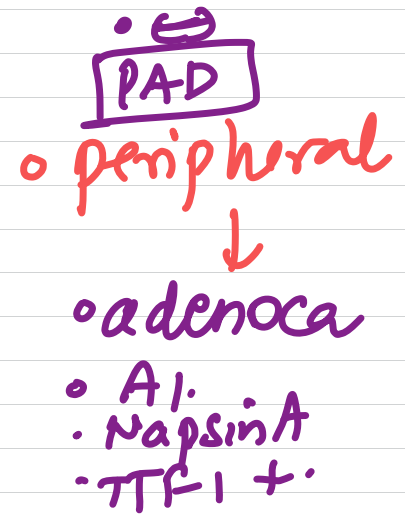
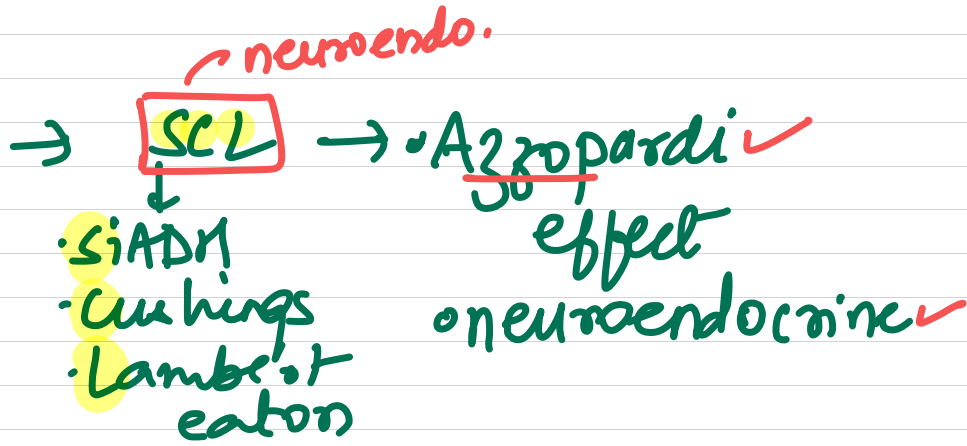
• Immunologic

→ GORi
(GN, Osler, Roth)
(ouch ouch) immunol.

Lungs

- ★ ° Asbestosis ^{box} → LL / mesothelioma → calretinin ⊕
- ° silicosis → crazy paving (crasi) | PMF prog. massive fibrosis ~TB.
- ° coal miners → Caplan syndrome → (RA)
- ° fibrothorax → asbestosis → (RA)

★ chromogranin + synaptophysin

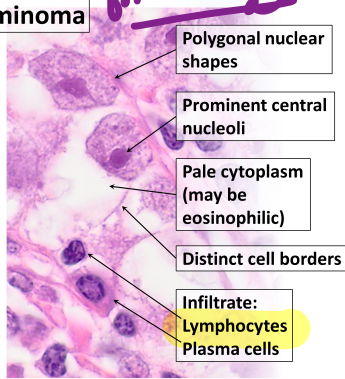
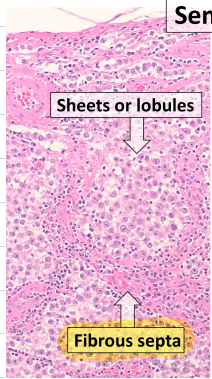


★ Hypercalcemia → squamous - (Ca) mous

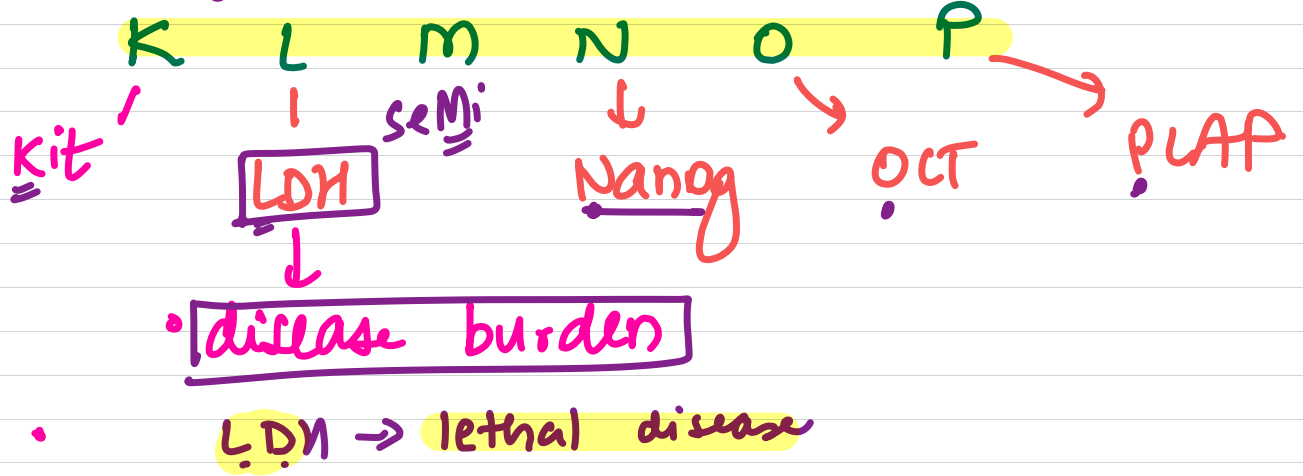
• lepidic → BAC ~ consolidation

Reproductive

dysgerminoma
 ↳ DPL → lymphocytic
 ★ **Seminoma** →



bird egg



- ★ Reinke crystals : Leydig
- Schiller dual : YES - G
- signet ring : Kruken.
- call exner bodies : granulosa corp.

or highly radiosensitive



Schiller glomerulus

Renal

* m/c adrenal @ incidentaloma :

Q fat → chemical shift

o adenoma non functional

Q lipid rich → HU on CT < 10 → ΔStic
o > 10 → CECT → rapid wash in, washout

* clear cell carcinoma Renal:

• m/c sporadic ✓

o (3p) - VHL ✓ → 3. → clear.

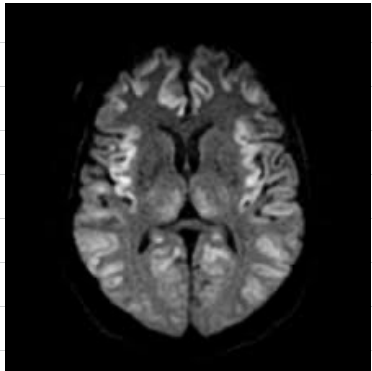
o PCT x DCT

PVC
PCT VHL clear cell
3p.



Infections

* CJD

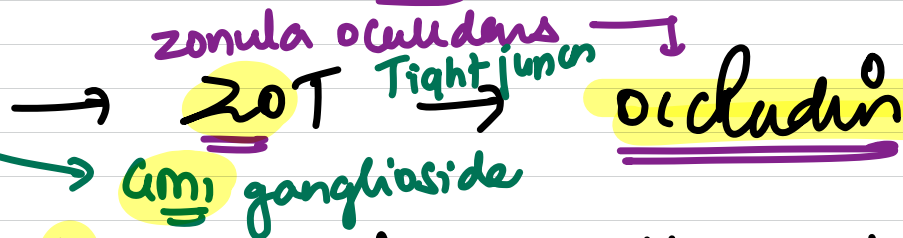


-
- abn protein folding
 - myoclonus & dementia
 - EEG - periodic bursts
 - MRI - cortical ribboning
 - HIP - spongiform degeneration
 - CSF → SA14143 (number).
SA 14-3-3

- AiD
- ataxia
- incont
- dementia

NPH

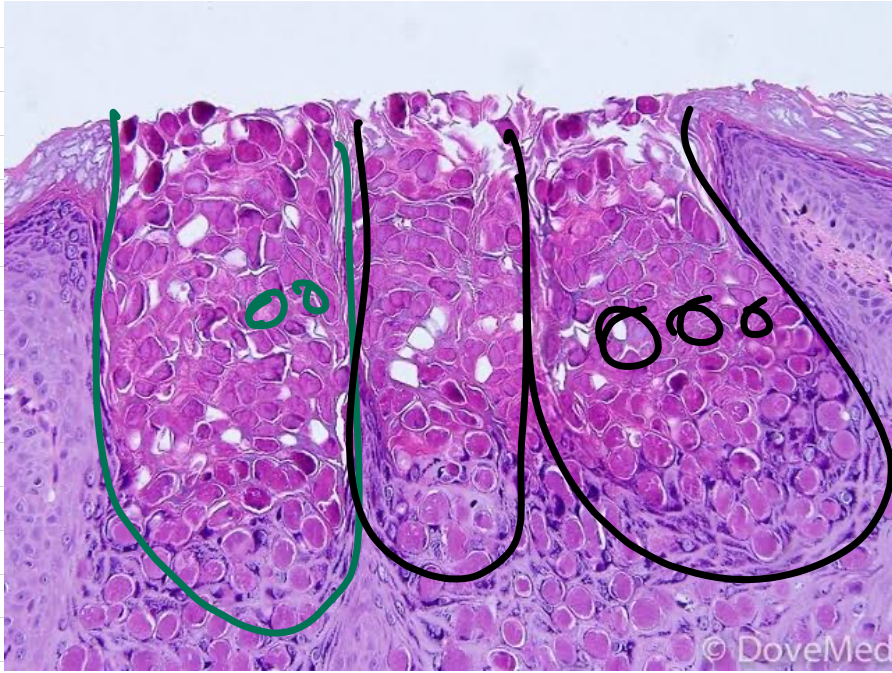
* COT → colera toxin



* metastasis → ↓ E-cadherin adhesion.

* HPV → • laryngeal papillomatosis - HPV 6, 11

↳ low risk HPV



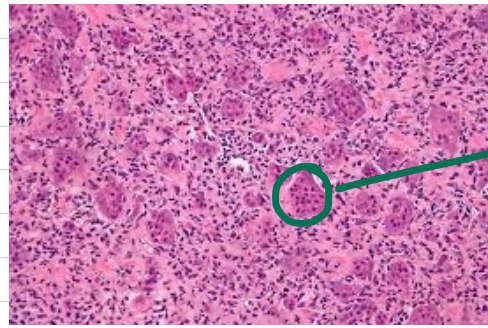
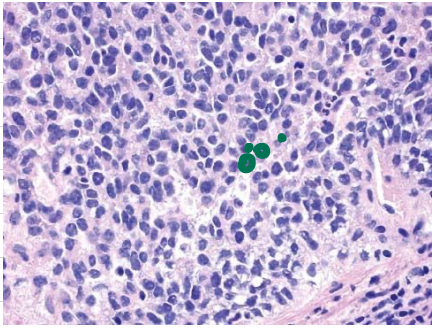
FAQ ini

HP bodies in MC
mollus.

HP MC

- pox
- umbilicated skin

Bones



giant cell tumor / osteoclastoma
↓
TRANK

hypoth → p. pit
◦ Heming bodies
↓
⊕ post pituitary

Ewing → small round blue cells. CD99 (+11, 22)
• child fever ⊕
• diphysis

Ewing's sarcoma/peripheral neuroectodermal tumor

Table 1 Small Round Blue Cell Tumors

Hepatoblastoma
Lymphoblastic Lymphoma
Medulloblastoma
Merkel Cell Carcinoma → MERCD 20
Nephroblastoma
Neuroblastoma
Non-Hodgkin Lymphoma
Primitive Neuroectodermal Tumor/Ewing Sarcoma ✓
Retinoblastoma
Rhabdomyosarcoma
Small-Cell Anaplastic Carcinoma
Wilms Tumor

- Neuroblastoma
- Rhabdomyosarcoma → **Desmin ⊕ s. muscle**
- Wilm's tumor
- Non-Hodgkin's lymphoma
- Synovial sarcoma
- Desmoplastic small round cell tumor
- Small cell carcinoma
- Retinoblastoma
- Hepatoblastoma
- Nephroblastoma
- Small cell osteogenic sarcoma
- Granulocytic sarcoma

• Neurosecretory bodies fin

① pheochromo (medulla)

② prolactinoma

③ medullary thyroid Ca