Pathology

Binge Revision

- Medsynapse by Dr. Nikita

29/4/24

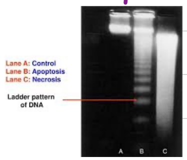
General Pathology

* Dialysis amyloidosis → B2 microglobulin
  - thyroid tumor →

- EE – extracellular, eosinophilic
- starch deposⁿ
- β pleated sheets on xray crystallography
- 1° → AL 2° – AA

* Necrosis vs apoptosis

- pathological
- inflammⁿ
- cell size↑
- cell memb disrupted
- smear pattern



- CD95
- annexin V

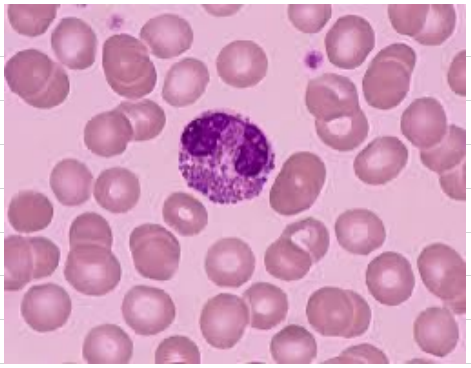
- Necroptosis : · Rip 1,3 mediated.
  · acute pancreatitis

- anti apop → · BCL2
  · BCL-XL
  · MCL-1

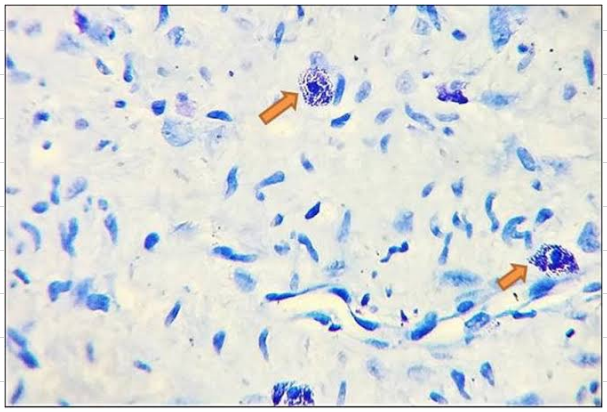
proapo
- Bak
- Bax
- Bad, bim, bid

* Cell in cell app:

Stains



- ★ Mast cells —
- ★ — Luxol fast blue
- ★ IHC brown — DAB (Diaminobenzidine)
- ★ Iron —
- ★ — Verhoeff



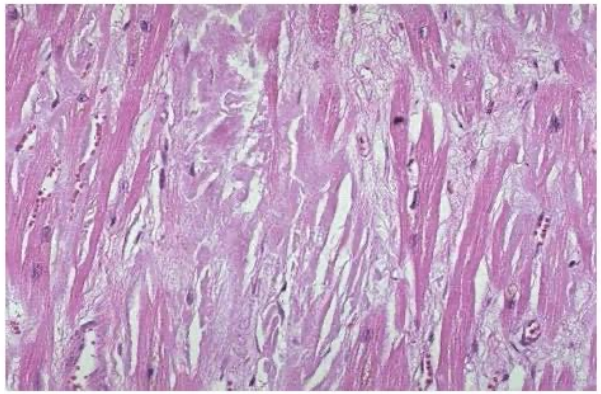
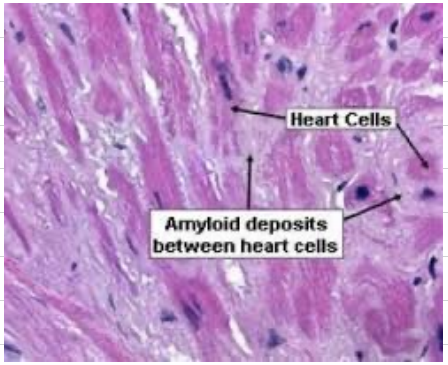


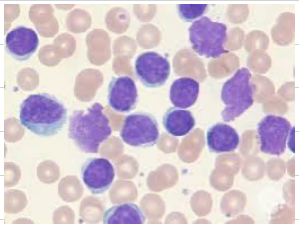
Figure 5: Histologically confirmed amyloid deposits (light pink) between myocardial fibers.



- ATTR
- Restrictive CM

Hemalology

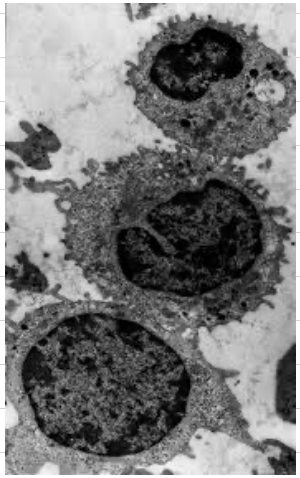
* **CLL** →
  - elderly ♀ smudge cells
  - flow cytometry - CD5 + CD23 +



  - 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.

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) Trsomies 4,10,17	t(9;22)(bcr-abl) t(4;11)(MLL-AF4)
Ploidy	hyperdipoidy	hypodiploidy
Time to remission	<14days	>28days

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)

★ Blood components

< -18°C	2-6°C	20-24°C
↓ 1yr		c̄ agitator ∘ 5days
∘ FFP → multiple coag. f. def.	∘ whole blood → Blood loss	∘ platelets
∘ cryoppt (-30°C) ↓ f. 8, vWF, fibrinogen	• CPD – 21d • CPDA – 35d • SAGM – 42d.	

• 1 unit of PRBCs ↑ Hb by 1 gm% / Hct by 3%

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

∘ Screen for: H M S
- H: HIV, Hep B/C
- M: malaria
- S: syphilis

★ Massive blood transfusion:
- c̄in 24 hrs

complic^ns:
- ∘ ↑K
- ∘ ↓Ca
- ∘ alkalosis > acidosis
- • coagu^n
- • Hypothermia
- • citrate toxicity

★ TRALI	vs	TACO
- ~ ARDS		- ↑BP (circulatory overload)
- c̄in 6 hrs		
- anti HLA / WBC Ab		

* m/c genetic hypercoagulability →
  - leiden V mutation (resistant to inactivn by prot C)

* order of draw

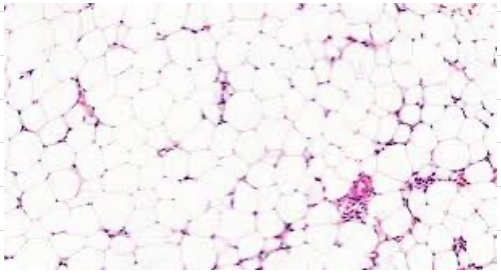
culture → blue → Red → yellow → green → lavend → Pink → Grey

Draw Order	Tube Color	Description
1		Blood Cultures
2		Sodium Citrate
3		Clot Activator
4		SST
5		Lithium Heparin
6		Sodium Heparin
7		EDTA
8		Sodium Flouride
9		ACD Solution

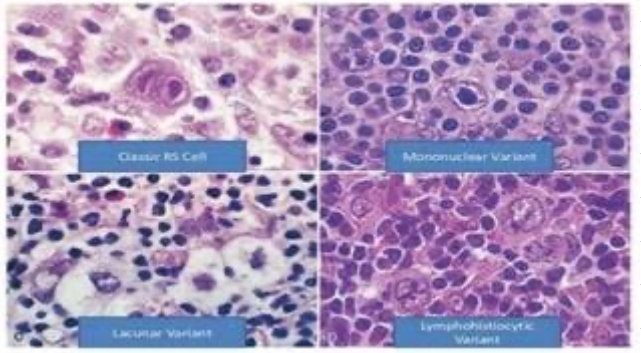
☆ sickle cells : ↑ mechanical fragility / Thalassemia
↓ osmotic

• ↑ osm. fragility → spherocytes / AIHA

*



No splenomegaly



* Hodgkin's → CD1530 classical

CD 2045 Nonclassical

Most → lymphocyte depleted

. LP
. good prognosis, no EBV

* IDA →
  - TIBC
  - Transferrin satu°
  - Mentzer index
  - platelet count
  - RDW

ACD
- ferritin
- Hepcidin

* B6 def ⟶
* XLR ⟶

Immunology

✡ Lack of CD40 → Hyper IgM
- ↑ IgM, ↓ IgG
- recurrent pyogenic/ PCP infecn

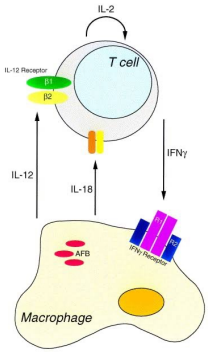
★ WAS

★ Central tolerance → No autoimmunity
- AIRE gene
- autoimmune regulator

★ BARE lymphocyte:
- obst class II MHC
- combined ID

- T-ALL → NOTCH 1 gene
- EgA → Burkitts lymphoma + myc

★ granuloma → . IFN-gamma
- prod by TH_1 cells
- macrophages produce IL12 ⊕



- TH_1 ↓

TH_2

* ANCA → panca / MPO
→ canca → anti PR3

- anti PLA2R in nephropathy

Table 20-6 Rapidly Progressive Glomerulonephritides
Type I (Anti-GBM Antibody)
Renal limited
Goodpasture syndrome
Type II (Immune Complex)
Idiopathic
Postinfectious glomerulonephritis
Lupus nephritis
Henoch-Schönlein purpura
IgA nephropathy
Others
Type III (Pauci-Immune)
ANCA-associated
Idiopathic
Granulomatosis with polyangiitis (formerly Wegener granulomatosis)
Microscopic polyangiitis

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

NK cell : - CD 16, 56, 94

° ADCC

. virus / malignant cells

. not MHC restricted

Innate vs adaptive immunity

	Innate immunity	Adaptive immunity
COMPONENTS	Neutrophils, macrophages, monocytes, dendritic cells, natural killer (NK) cells (lymphoid origin), complement, physical epithelial barriers, secreted enzymes	T cells, B cells, circulating antibodies
MECHANISM	Germline encoded	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), defensins, cytokines	Immunoglobulins, cytokines
KEY FEATURES IN PATHOGEN RECOGNITION	Toll-like receptors (TLRs): pattern recognition receptors that recognize pathogen-associated molecular patterns (PAMPs) and lead to activation of NF-κB. Examples of PAMPs: LPS (gram ⊖ bacteria), flagellin (bacteria), nucleic acids (viruses)	Memory cells: activated B and T cells; subsequent exposure to a previously encountered antigen → stronger, quicker immune response

→ alternative, lectin

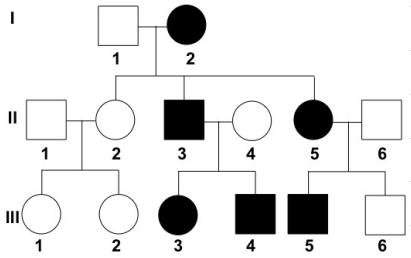
gamma delta T cells.

- by epithelial cells.

Important cytokines	Acute (IL-1, IL-6, TNF-α), then recruit (IL-8, IL-12).	
Secreted by macrophages		
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** st**EAK**": 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. 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.	Facilitates granuloma formation in TB.
Secreted by T cells		
Interleukin-2	Stimulates growth of helper, cytotoxic, and regulatory T cells, and NK cells.	
Interleukin-3	Supports growth and differentiation of bone	

From Th1 cells		
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		
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.
Interleukin-5	Promotes growth and differentiation of B cells. Enhances class switching to IgA. Stimulates growth and differentiation of Eosinophils.	I have 5 BAEs.
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 thirtEEn promotes IgE.

Genetics



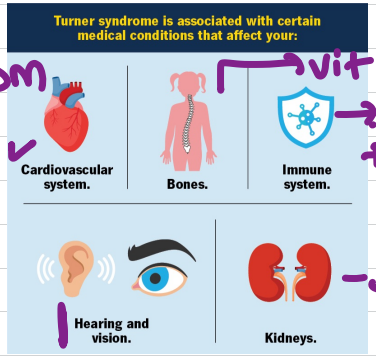
★ · Patau
· Edward
• sickle cell
• Huntington

★ · CF
· leber
· DMD
· myotonic dystrophy

★ Rett :

★ Turner :

fetal hydrops
· cystic hygroma



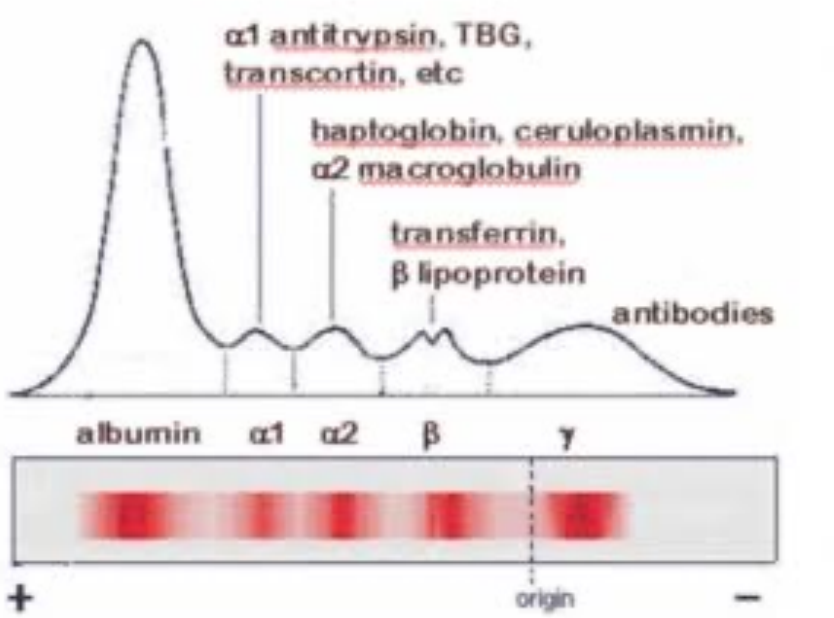
.DM
→ vit D def
→ autoimmune thyroiditis
· celiac
→ ser creatinine

★ BRCA 1, 2 → ∘ Tumor suppressor genes
17q ← 1, 2 → 13q.
• dsDNA repair

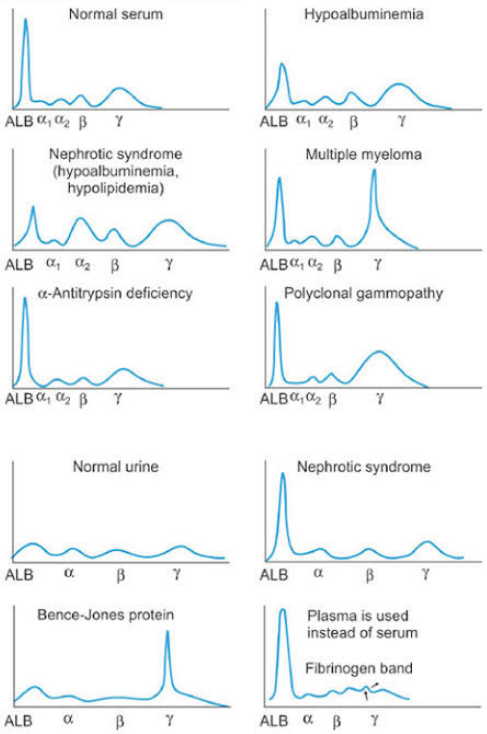
Triple neg breast Ca ← ∘ BRCA1 → Breast + . ovary, colon, prostate Ca. pancreas
↳ medullary carcinoma.

Luminal A ← ∘ BRCA2 → " + " + • pancreas • biliduct etc • melanoma • stomach, GB.
• ↳ Fanconi
↑ male breast cancer

★ luminal A breast Ca: • ER/PR +
• HER2 -ve
• prolif ↓.



↑ in nephrotic : α_2



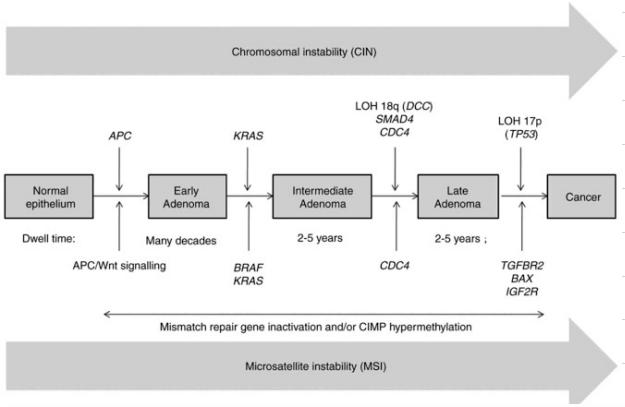
GIT

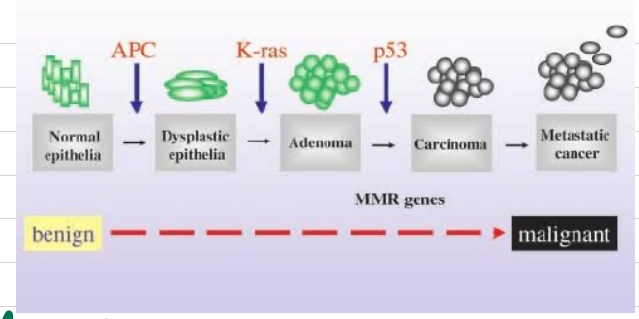
* alcohol liver dysfunc^{n} → · GGT
  · AST/ALT > 1.5

* FAP → · 5q
  · Turcot →
  · Gardners →

* myc
  - c → Burkitt
  - l - small - lung
  - n - neuroblastoma.

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





* GIST → • c kit
• CD117
• DOG 1

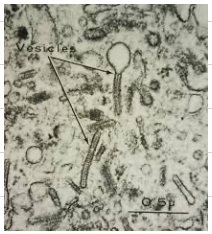
* ALK :: Anaplastic large cell
` NonSCLC

* Jak2 → myeloprolif.

* NO acid in pernicious anemia (after pentagastrin injech)

CNS

☆ LCH → Birbeck granules



- CD207
- CD1a
- S100
- HLA-DR

☆ TB meningitis :

* perineural invasion :

✿ Hot spot :

CVS

* Infective endocarditis :
  - 3 culture samples :
    - 2 - peripheral
    - 1 → valve
  - gap of 30min between each.

Lungs

★ ° Asbestosis → LL
- ° silicosis → crazy pavement | PMF
- ° coal miners → caplan syndrome.
- ° fibrothorax →

★ ° chromogranin + → SCL → ° Azzopardi effect
- ° neuroendocrine
- ° SIADH
- ° cushings
- ° Lambert eaton

★ Hypercalcemia → ° squamous.

Reproductive

* Seminoma → K L M N O P

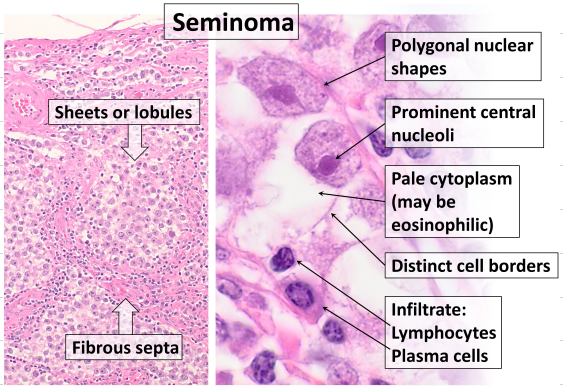
K → Kit

L → LDH → • disease burden

N → Nanog

O → OCT

P → PLAP

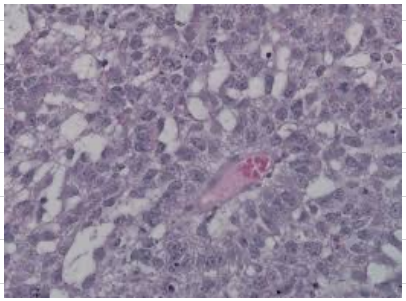


* Reinke crystals :

• Schiller duval :

• signet ring :

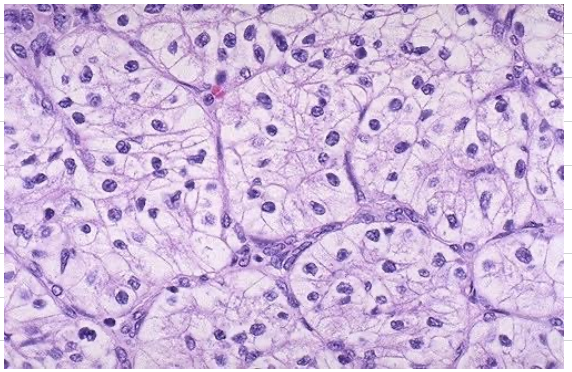
• call exner bodies :



Renal

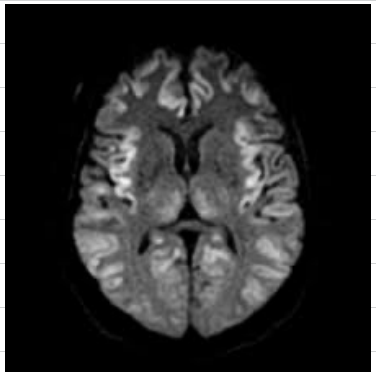
* m/c adrenal incidentaloma :

* clear cell carcinoma Renal:
  - m/c sporadic
  - 3p - VHL
  - PCT



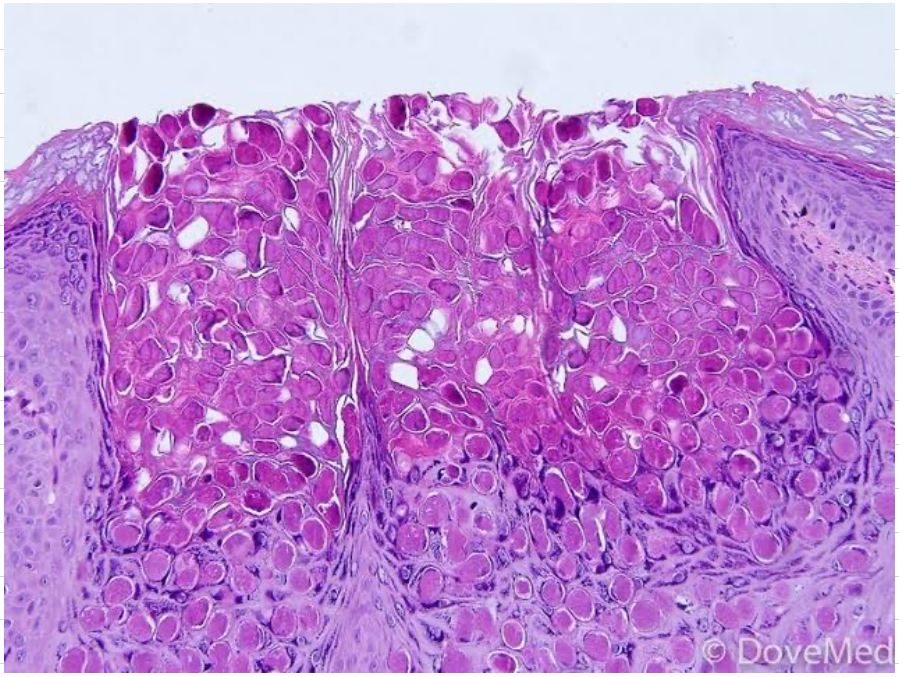
Infections

* CJD → · abn protein folding
  · Myoclonus ± dementia
  · EEG – periodic bursts
  · MRI – cortical ribboning
  · HIP – spongiform degeneration



* COT → 20T → occludin

* HPV → · laryngeal papillomatosis – HPV 6, 11
  ·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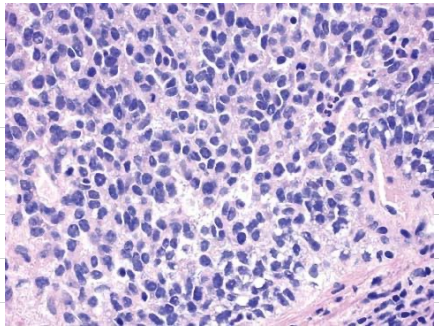
Bones



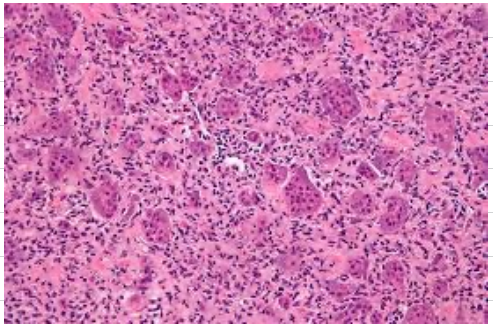


Table 1 Small Round Blue Cell Tumors
Hepatoblastoma
Lymphoblastic Lymphoma
Medulloblastoma
Merkel Cell Carcinoma
Nephroblastoma
Neuroblastoma
Non-Hodgkin Lymphoma
Primitive Neuroectodermal Tumor/Ewing Sarcoma
Retinoblastoma
Rhabdomyosarcoma
Small-Cell Anaplastic Carcinoma
Wilms Tumor

Ewing's sarcoma/peripheral neuroectodermal tumor
Neuroblastoma
Rhabdomyosarcoma
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 + in
- pheochromo
- prolactinoma
- medullary thyroid Ca