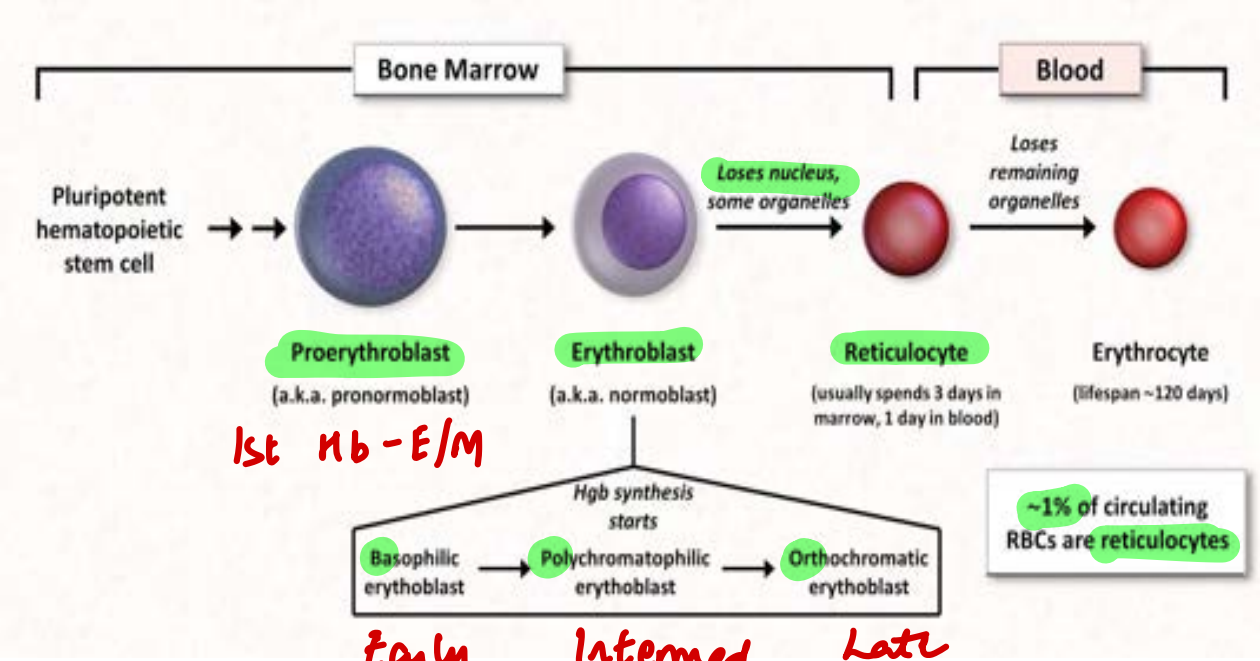
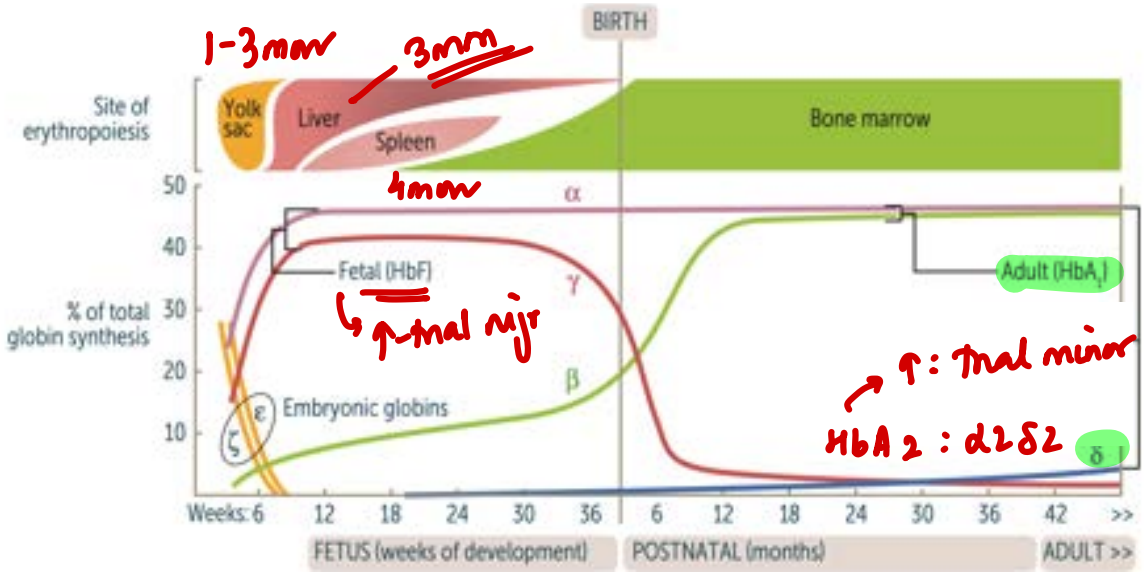
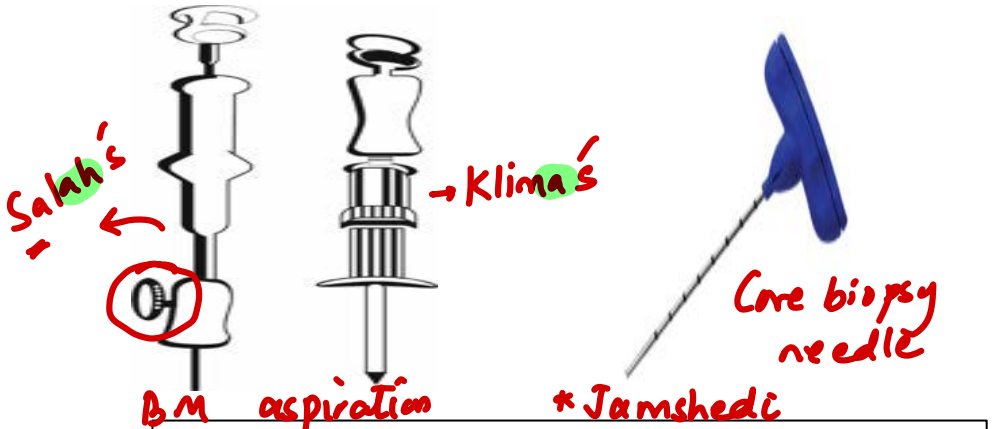
INTEGRATED HEMATOLOGY

Hematology Basics







'RPI'

$$\text{Reticulocyte Production Index (“Retic Index”)} = \frac{(\text{Retic \%}) \times (\text{Hct} / 45)}{\text{Maturation Factor}}$$

Hematocrit (Hct)	Maturation Factor
≥ 40%	1.0
30 – 39.9%	1.5
20 – 29.9%	2.0
< 20%	2.5

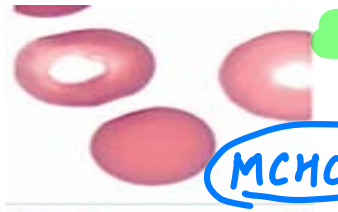
Different references contain slightly different versions of this table.

Preferred site for BMA/ BMB:
Adult- PSIS
Child- Tibia
Low Platelet CI?: No / <20k - precautions *transfuse

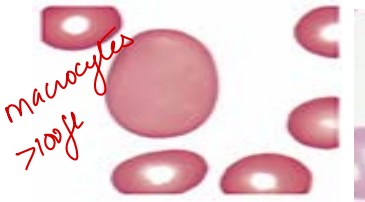
RBC shapes and disorders

Fe list bro

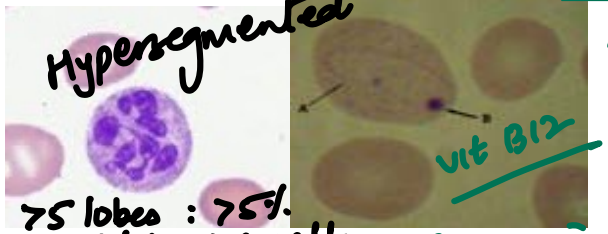
Elliptocytes : HE → mc : Spectrin



Spherocytes : HS → mc : Ankyrin
most severe : Spectrin
↳ AIHA (mc), G6PD
MCHC↑



Macrocytes >100fl



Hypersegmented
>5 lobes : >5%
>6 lobes : 1 cell

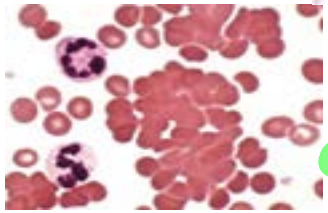
vit B12

Megaloblastic anemia
fine basophilic stippling
Cabot ring

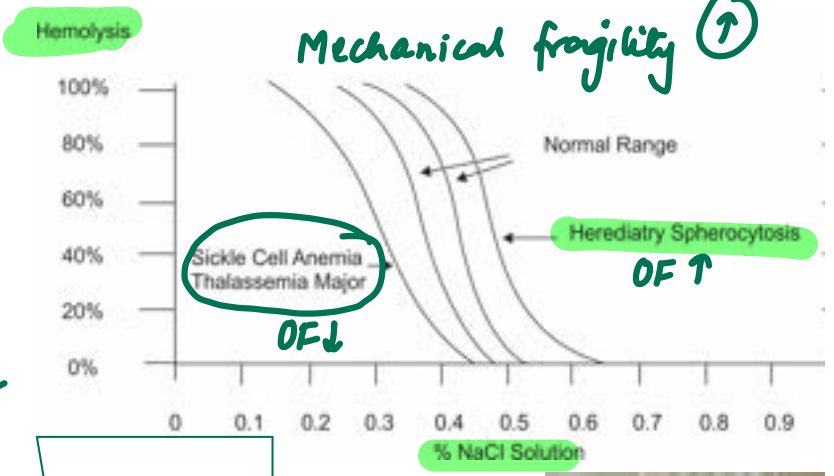
Target : codocyte : Thallasemia

Drepanocyte : SCA
↓
auto-splenectomy
Howell Jolly bodies

agglutination
AIHA
warm (IgG) → CLL, SLE, penicillin, methyldopa
cold (IgM) → Mycoplasma, EBV
DCT ⊕



EYH : jaundice, splenomegaly
↳ HS
BIAM
· EMA binding test
· OF ↑



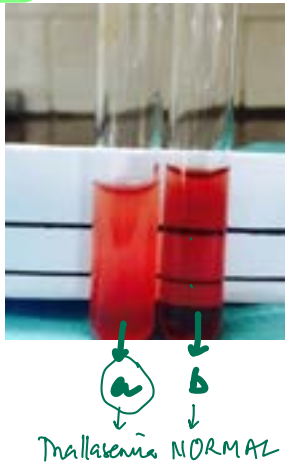
Mechanical fragility ↑

B12 def / folate def / OROTIC ACIDURIA (UMP synthase)

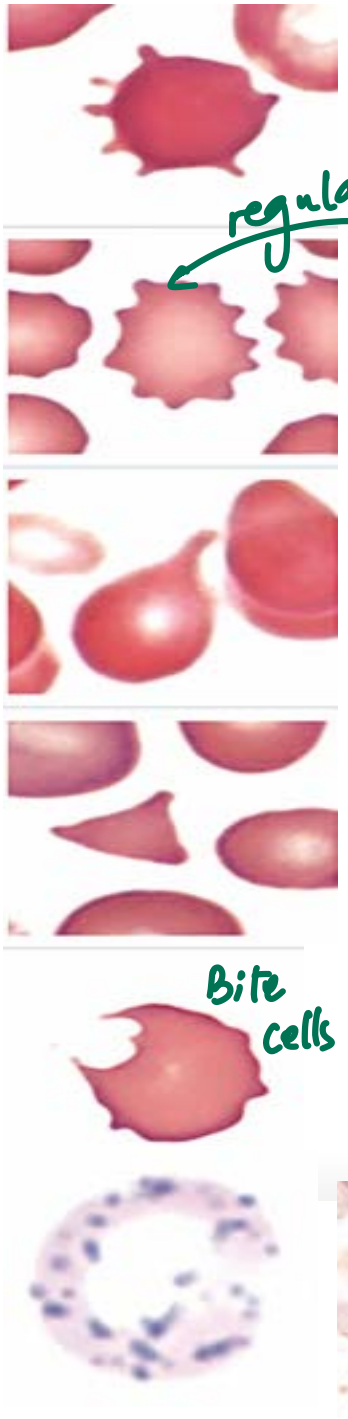
· knuckle ↑pigment
SACD
· ileal D
· Pernicious A
· gastrectomy
· vegans

· junk food
· alcoholics
· pregnancy

NESTROFT



CLL : AIHA + ITP
EVAN'S Sr



Acanthocytes / spur cells → Abetalipoproteinemia (MTTP gene), vit E def

regular

Burr cells / Echinocytes → Burns, Renal failure, Pyr kinase def

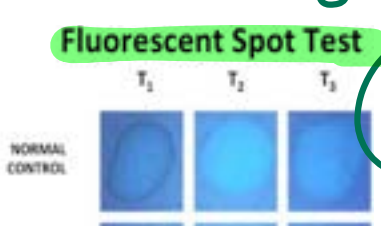
tear drop / dacryocytes → Myelophthisis / Myelofibrosis

schistocytes / Helmet cells → MAHA

- angiopathic HA
- Microangiopathic: HUS / TTP / DIC / HELLP
  - HUS: O157:H7, EHEC
  - TTP: ADAMTS13, neurol sym +
- Macroangiopathic: Prosthetic valves

Bite cells

Heinz body → denatured Hb, crystal violets



G6PD deficiency

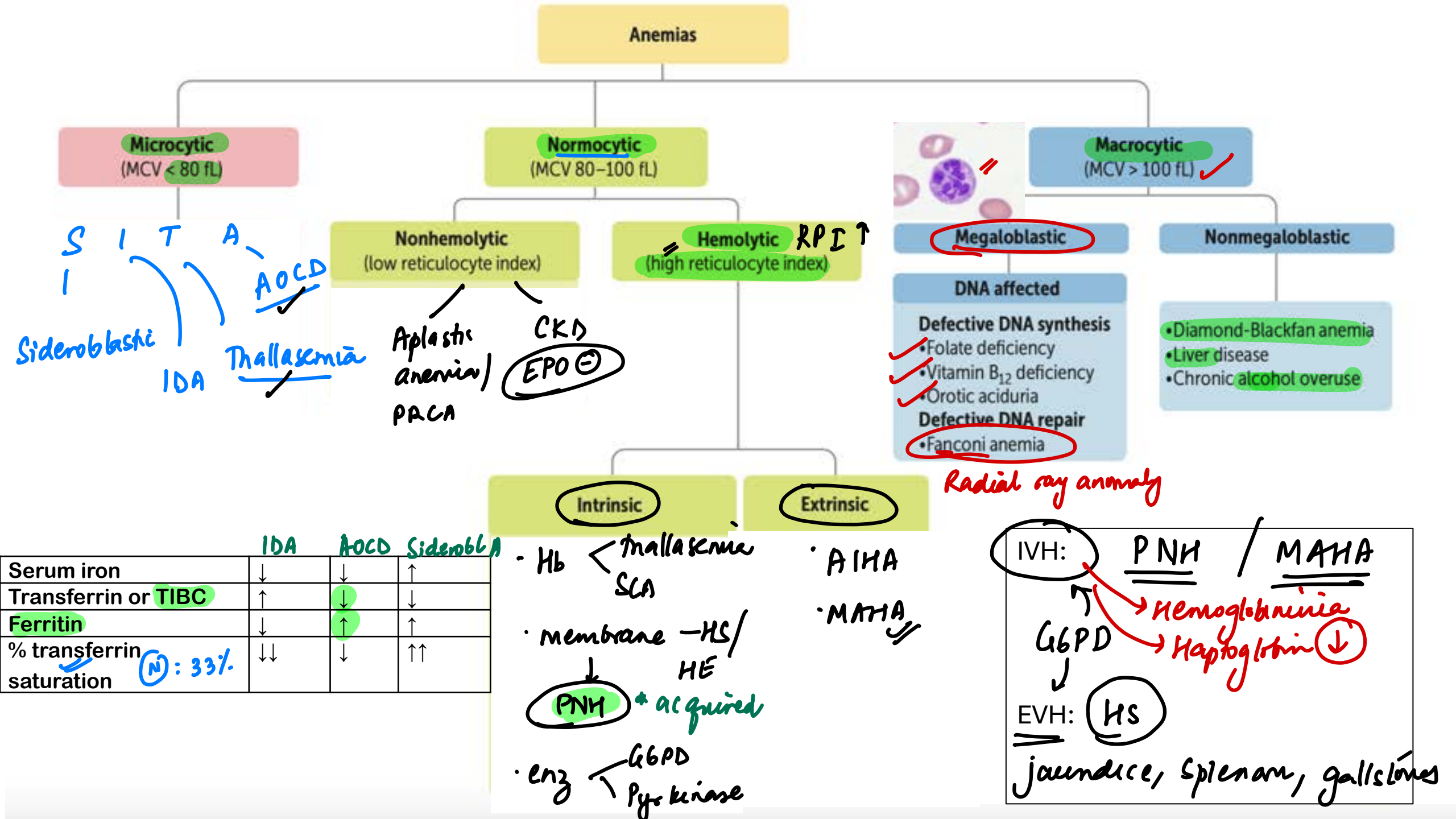
- IVH/EVH
- HMP shunt → NADPH → oxidative stress
  - XLR → auto fluorescence
  - Fava beans, Dapsone, PQ, Sulfa drugs

Basophilic stippling (coarse)

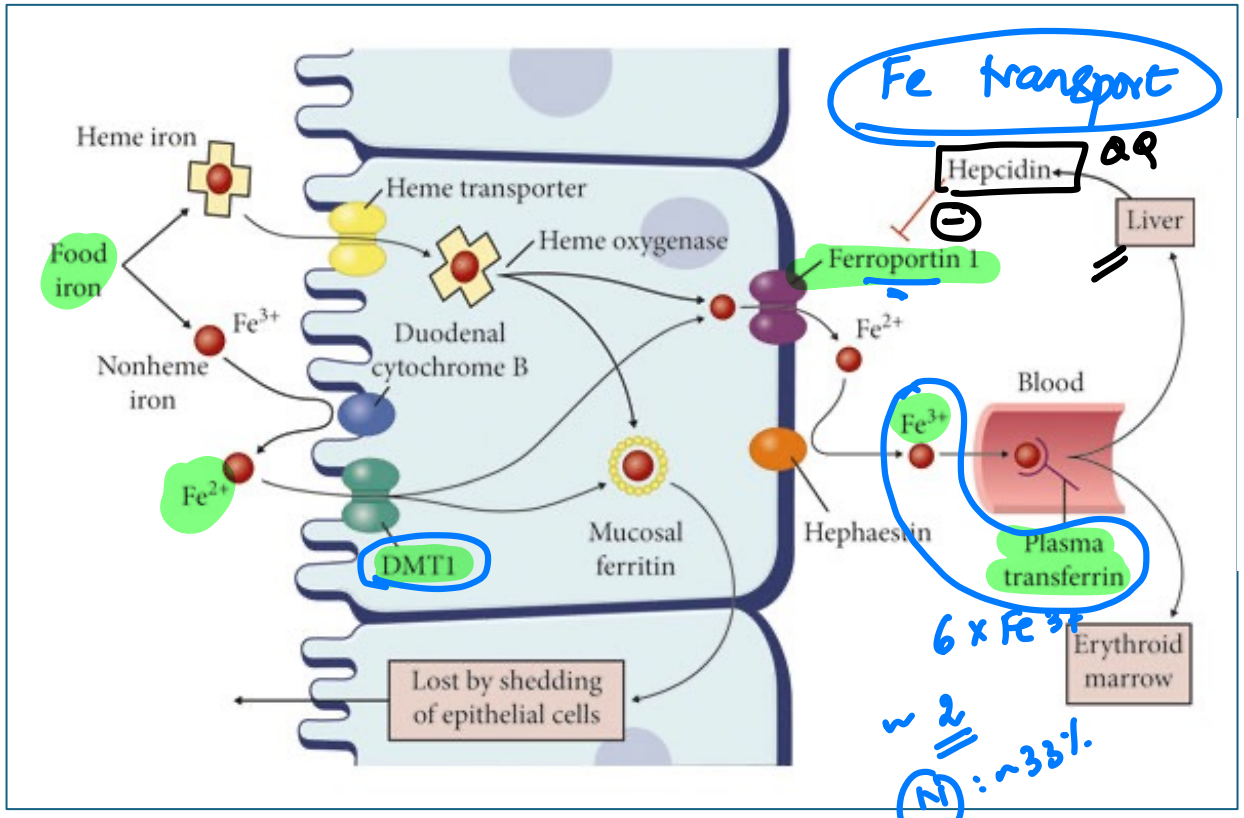
Sideroblastic A → PRUSSIAN BLUE / PERL'S

Ringed Sideroblast

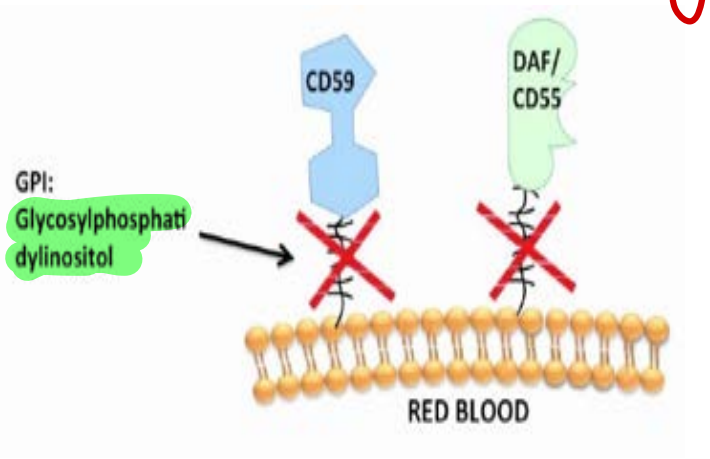
- ALA synthase (XLR) → B6 def (INH)
- Pb → ALA dehydr, Ferrochelat

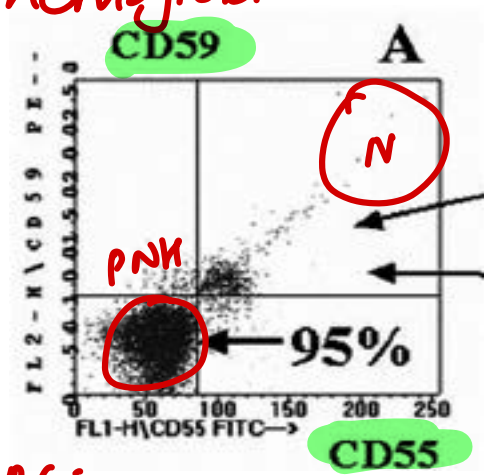


	IDA	AOCD	Sideroblastic
Serum iron	↓	↓	↑
Transferrin or TIBC	↑	↓	↓
Ferritin	↓	↑	↑
% transferrin saturation (N): 33%	↓↓	↓	↑↑



PNH Paroxysmal nocturnal hemoglobinuria





IOC: Flow cytometry

- Intravascular hemolysis
- Pancytopenia
- Thrombosis-Budd Chiari syndrome — mcc of death
- LAP score low
- Aplastic anemia, Leukemia — less
- Ham's acidifed serum test, sucrose lysis test
- GEL CARD TEST — Screening
- Rx-Eculizumab — C5 (-)

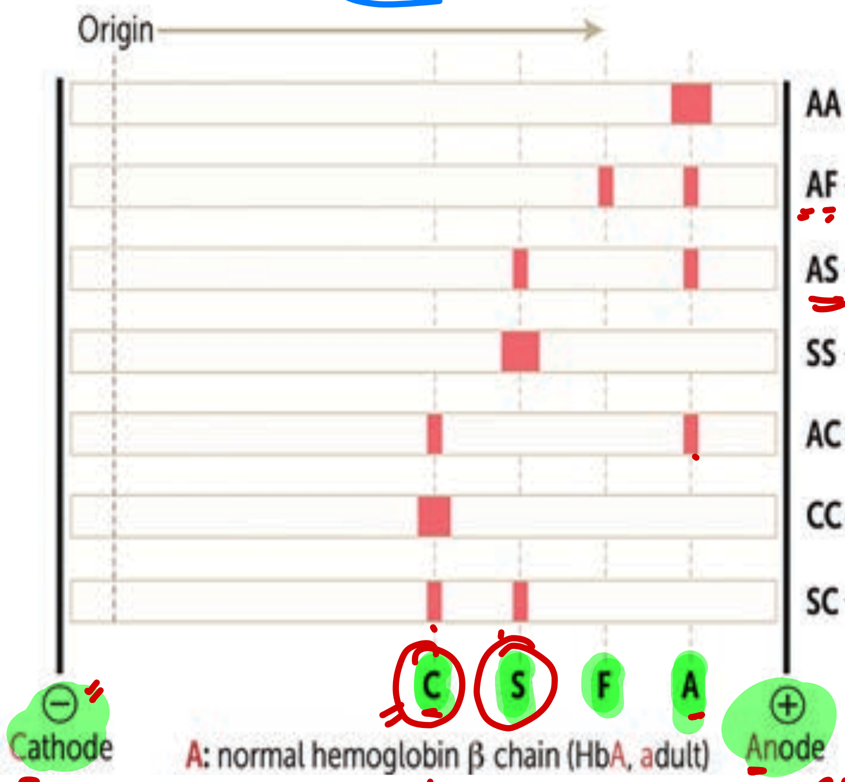
Anemia

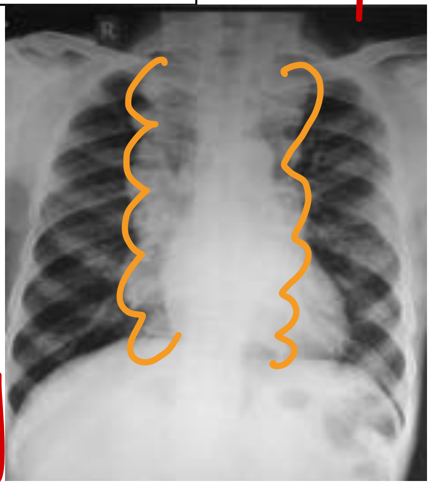
IDA vs Thalassemia minor

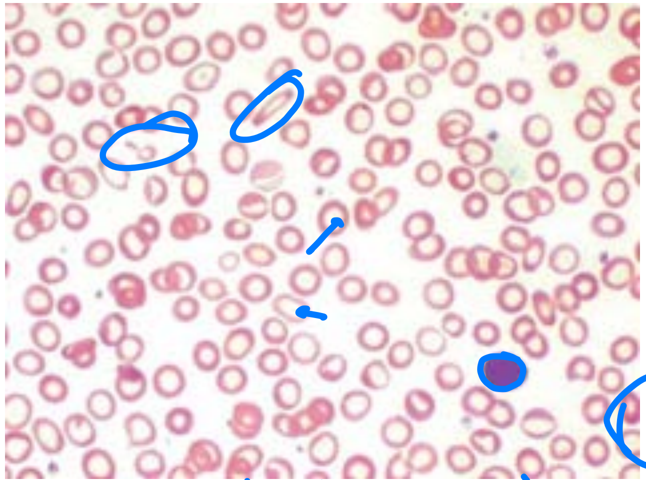
Mentzer index

RDW:

Confirmatory test for thalassemia minor:







Glu -> Valine:

Glu -> Lysine

Chr 16 deletion:

Chr 11 Splicing mutation:

IVS1-5 G->C

SICKLE CELL ANEMIA:

Glutamic acid

Hydroxyurea, Voxelotor

Crizanlizumab

Blood cells

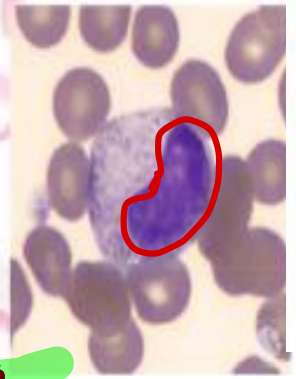
"Lt shift"

Myeloblast

Auer rods

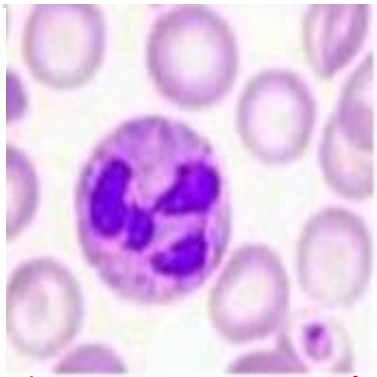
Promyelocyte

Myelocyte

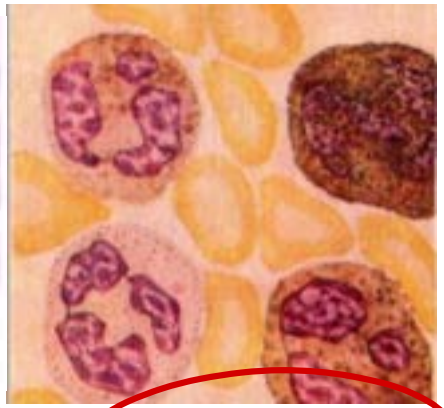


Metamyelocyte

Band / Stab



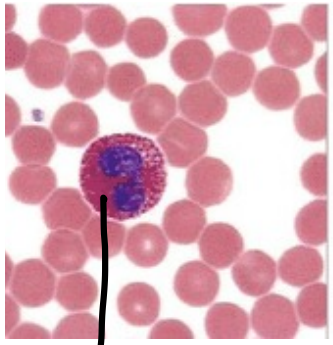
Neutrophil



LAP score

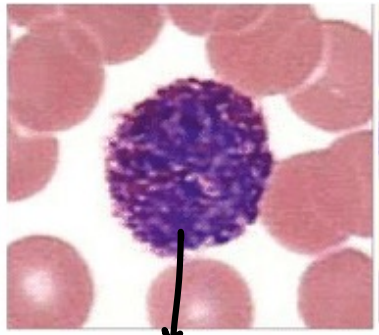
LOW — CML / PNH

HIGH — Leukemoid



E

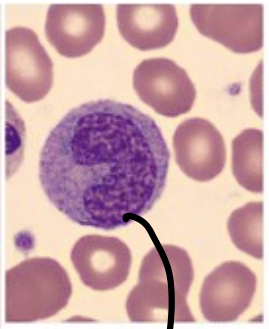
↑ allergy parasitic



Basophil

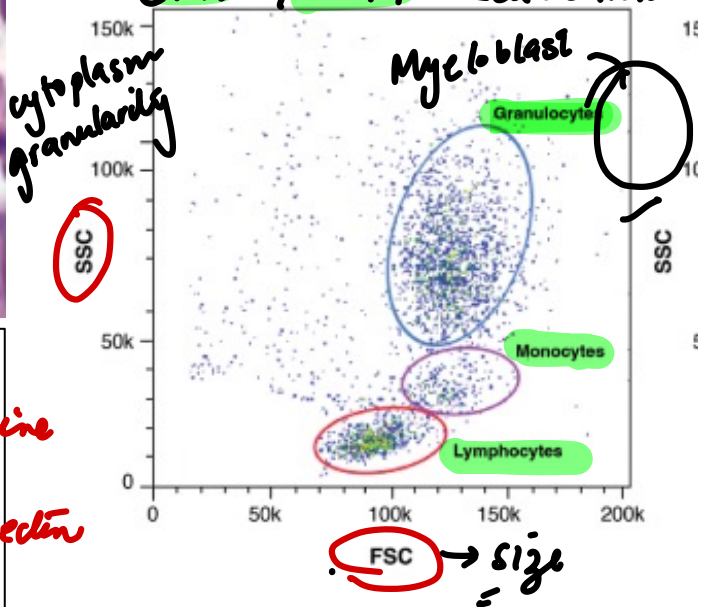
↑→ CML

Tol blue*



monocyte

Lymp #



Dense / delta granules: CASH

Ca^{2+} / ADP / serotonin / histamine

Hermansky Pudlak syndrome

Alfa granules: fibrinogen fibronectin

vWF

⊖ → Pf4

HIT

Grey platelet syndrome

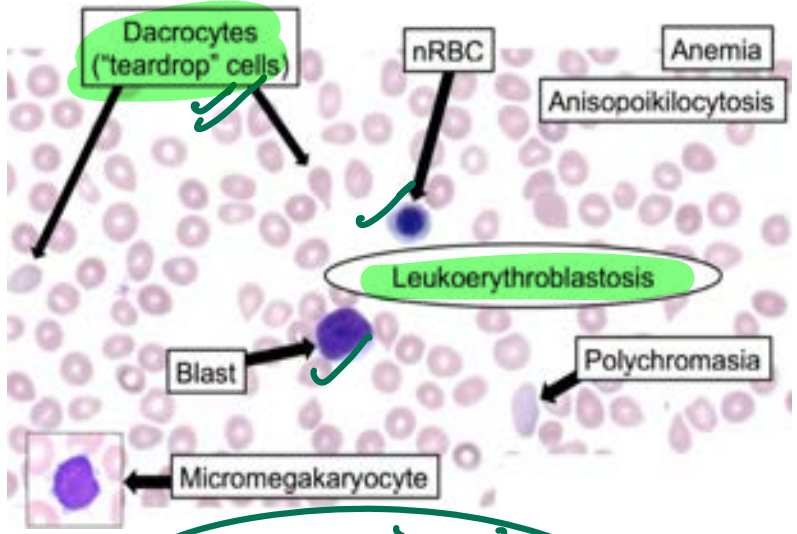
Approach to Pancytopenia

HSM +

HYPERCELLULAR MARROW

Leukemia

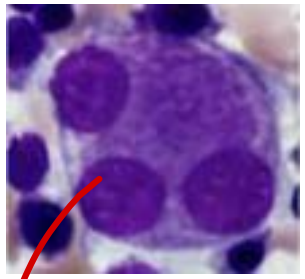
DRY TAP +

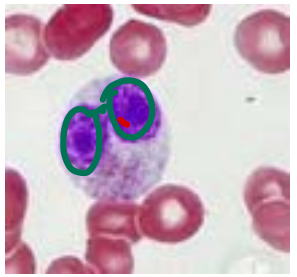


Myelofibrosis

HSM -

HYPERCELLULAR MARROW



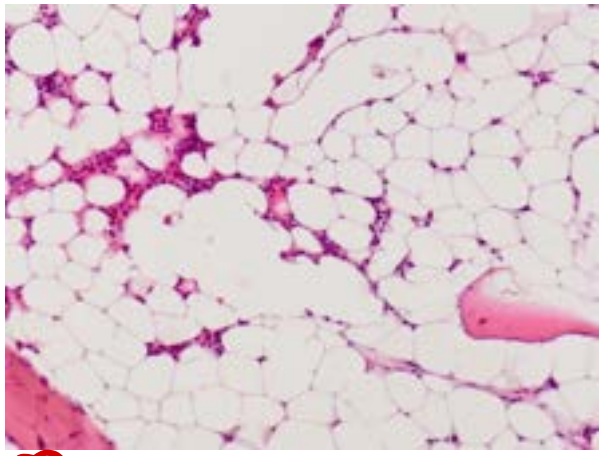


Myelodysplasia

Pawn ball megakaryocyte

Pseudo Pelger-Huet anomaly

DRY TAP +
BMB:



(N) 50% cells 50% fat

APLASTIC anemia

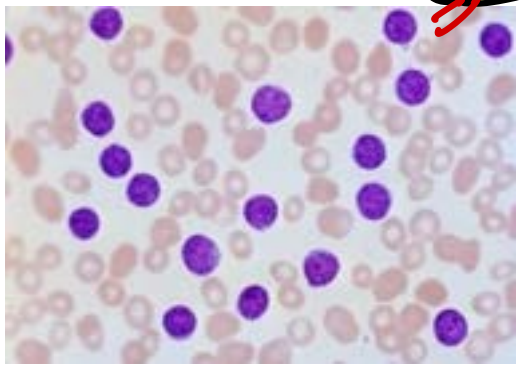
Idiopathic (mcc) / Viral/drugs

Approach to Leukemia

CHRONIC

Lymphocytic

CLL = SLL



Convent school girl

Binet / Rai staging

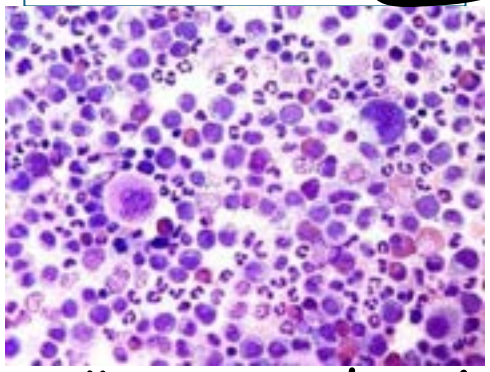
IOC: Flow cytometry

TOC: Fludarabine

Myeloid origin

basophilia ↑

CML



College party / garden party

Chronic : < 10% BL

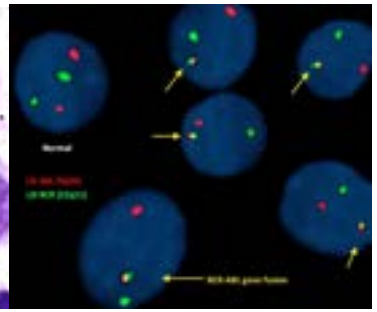
Accelerated : 10-20%

Blastic : > 20% BL

Ph chr - 210KD

t(9;22) ABL BCR

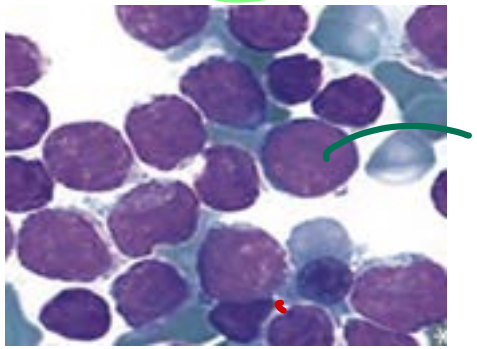
Pseudo-Gaucher cell



IOC: FISH

ACUTE

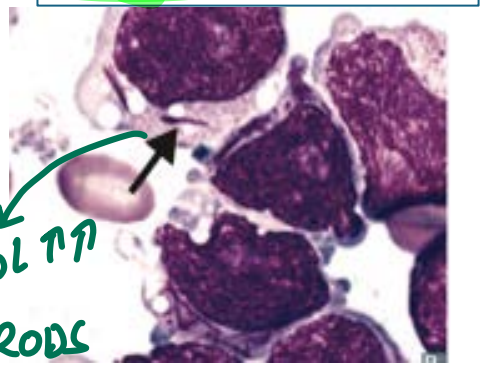
CHILD ALL



Nucleus ↑↑

Lymphoblast

PAS ⊕ - 'dot-blot'



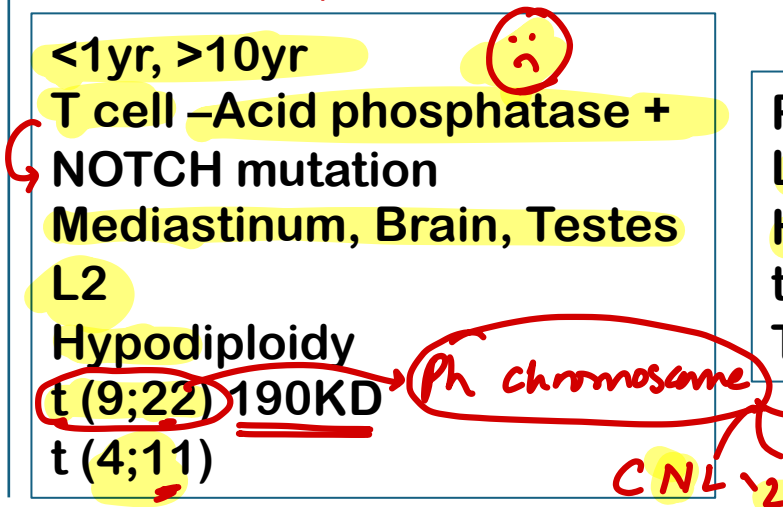
cytopl ↑↑

AUER RODS

Myeloblast

MPO / SBB ⊕

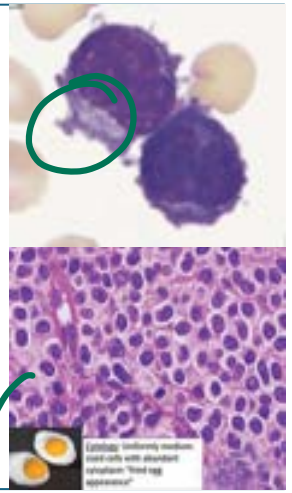
ADULT AML



MC in children: ALL
MC in down syndrome: ALL
MC in downs (<3yr): AML M7
MC in adults: AML
MC with radiation: AML
MC in elderly: CLL
MC in west: CLL
Not associated with radiation: CLL
Associated with deletion-13q: CLL

SPLENOMEGALY + PANCYTOPENIA
DRY TAP +
TRAP+
BRAF mutation
Markers: Annexin A1 (most sp) vs V → apoptosis
CD11c, 25, 103
DOC- Cladribine

Hairy cell leukemia
Red pulp



Fried egg appearance

WHO- FAB → AML

- **M0:** Undifferentiated acute myeloblastic leukemia (5%)
- **M1:** Greater number of myeloblasts with <10% granulocytic differentiation.
- **M2:** Myeloblasts in great number with granulocytic differentiation >10% , NSE <20%. → mc → t(8;21) → mc → chloromas
- **M3:** Promyelocytes that are hyper granular with many Auer rods on CAE or Wright-stain and variant form cells with reniform nuclei, multilobed or bibbed, primeval cells with multiple Auer rods or relative scarcity of Hypergranular promyelocytes.
- **M4:** >20% but <80% NSE-butyrate positivity in Monocytic cells → inv 16
- **M5:** Monocytic cells with >80% NSE positivity. (a) Monocytic differentiated (b) Monocytic, differentiated.
- **M6:** >30% myeloblasts with more than 50% erythroblasts eliminating the erythroid cells.
- **M7:** Acute megakaryoblastic leukemia <5%

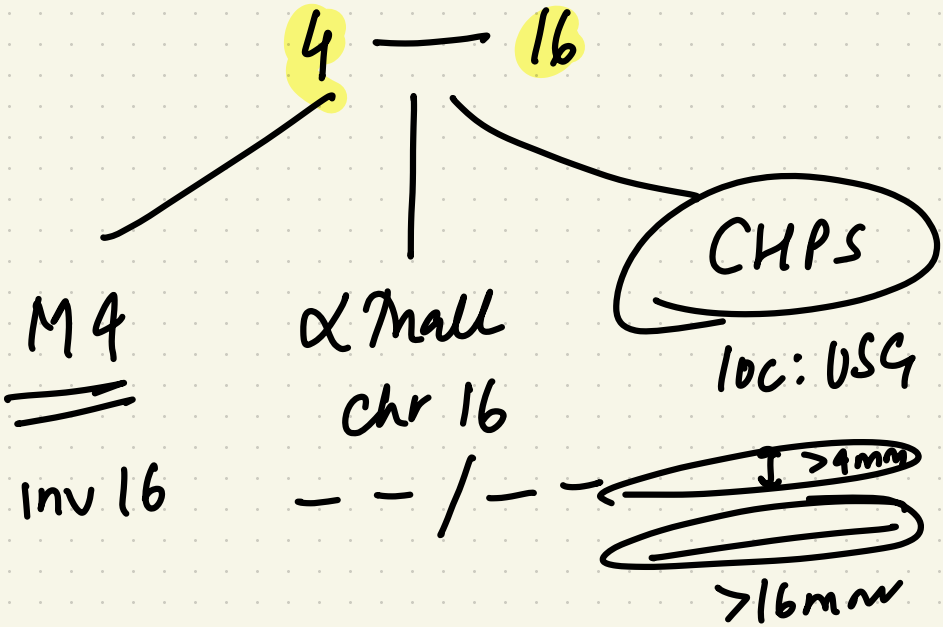
Faggot cells
APML
t(15;17) (APML; RARA)
DIC
Rx: ATRA > As_2O_3

NSE ⊕ "leukemia cutis"

- dry tap
- Down's S

- Mycoplasma
- M.furfur

- Oligodendroglioma : 1p/19q co del
- Seminoma


4
16
CHPS
loc: USG
M4
Inv 16
α Mall
Chr 16
>4mm
>16mm

Approach to NHL

CD 19/20 + : B cell

CD 3+ : T cell

CD 10 +
BCL6 +

MC NHL
MC aggressive
MC extranodal
EBV (+)

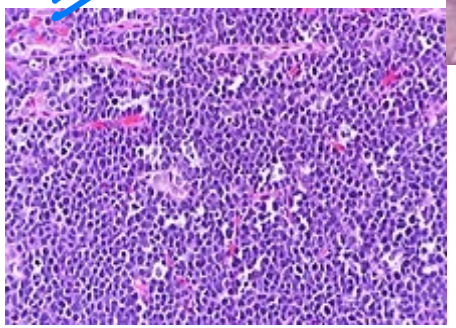
DLBCL

"Richter" transform
SLL/CLL → DLBCL

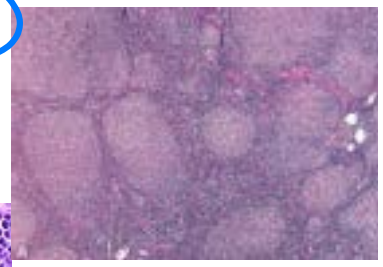
CD 10 +
BCL-2 +

Burkitt

C-myc
Ki 67 100%



starry sky



"waxing and waning" LN QQ

Best prognosis

centrocyte, centroblast

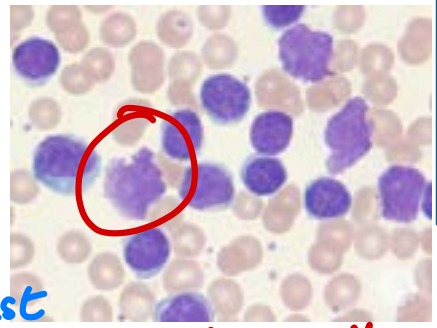
FOLLICULAR

endemic (Jaw)
sporadic (abdomen)

CD 5 +

CD 23+
Cd 200+
DELETION 13q

CLL/SLL



Smudge cells

CD 23-
CYCLIN D1+
SOX 11+
Cleaved/buttock cells
Lymphomatoid polyposis

QQ

Mantle

CD5-
CD 23-
CD 10-

↓

Marginal/MALToma

CLL/SLL

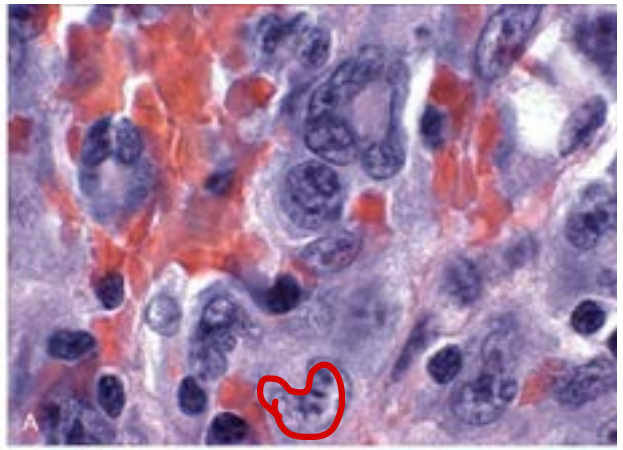
Mantle

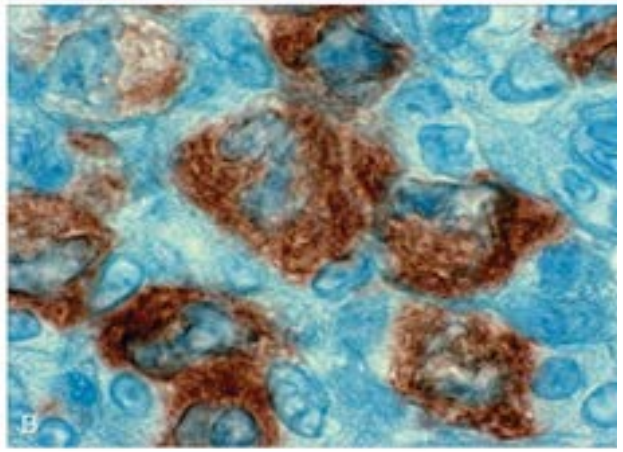
Marginal

MM

- Burkitt
- DLBCL
- Follicular

8 = Burkitt (cmyc)	11 (cyclin D)	14 (IgH)	18 (Bcl 2)
t(8;14)	t(11;18) → Marginal zone		
t(8;22)	t(14;18) → Follicular		
t(2;8)	t(11;14) → Mantle		



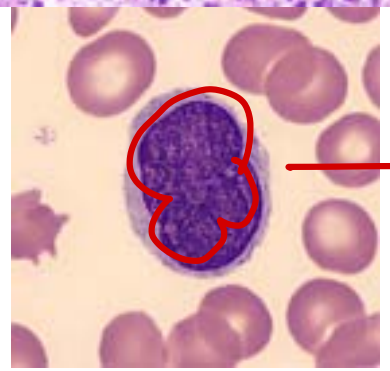


Hallmark cell

Donut cell

Anaplastic large cell

epidermo Tropism



→ cerebriform

↓

Sezary Sx

Mycosis fungoides:
cut T cell lymphoma

↳ Pautrier's microscer

Clover leaf

HTLV I

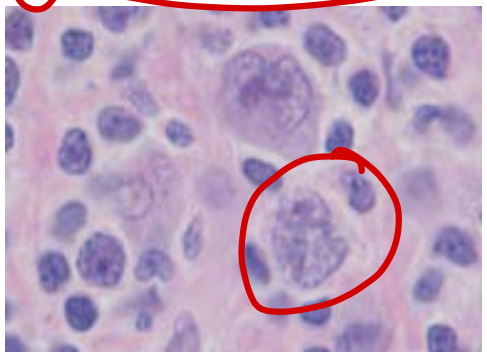
retrovirus

Approach to Hodgkin's lymphoma

REGIONAL LN

CD20 +
CD45+
EMA +
BCL-6 +
EBV LMP -

POPCORN CELL



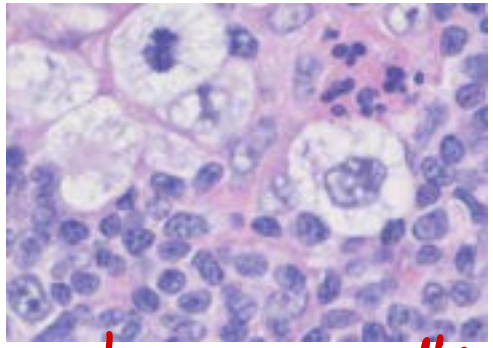
Lymphocyte predominant

Best prognosis

CD 15 +
CD30 + most sensitive
PAX5 most specific
EBV LMP +

Classical RS cell

COLLAGEN NODULES, LACUNAR CELL



Lacunar cells

Nodular sclerosis

BACKGROUND MIXED, CLASSICAL RS

Mixed cellularity

mc India

BACKGROUND LYMPHOCYTE, MONONUCLEAR RS

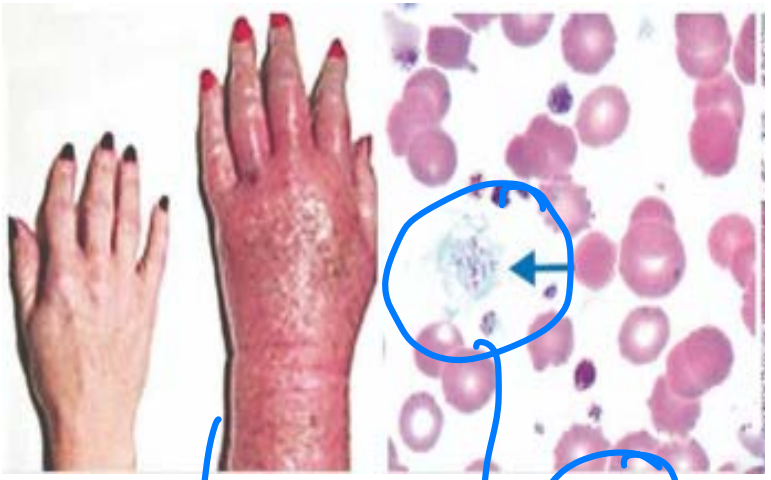
Lymphocyte rich

LOW LYMPHOCYTE, PLEOMORPHIC / MUMMIFIED RS

Lymphocyte depleted

Myeloproliferative disorders

	RBC	WBC	PLATELET	JAK2 MUTATIONS
Polycythemia vera EPO: ↓	↑↑	↑	↑	(+)(+) JAK2 ⊖ Ruxolitinib
Essential Thrombocytosis	–	–	↑↑	30-50%
CML	↓	↑↑	↑	⊖
MYELOFIBROSIS	↓	↓	↓	30-50 %



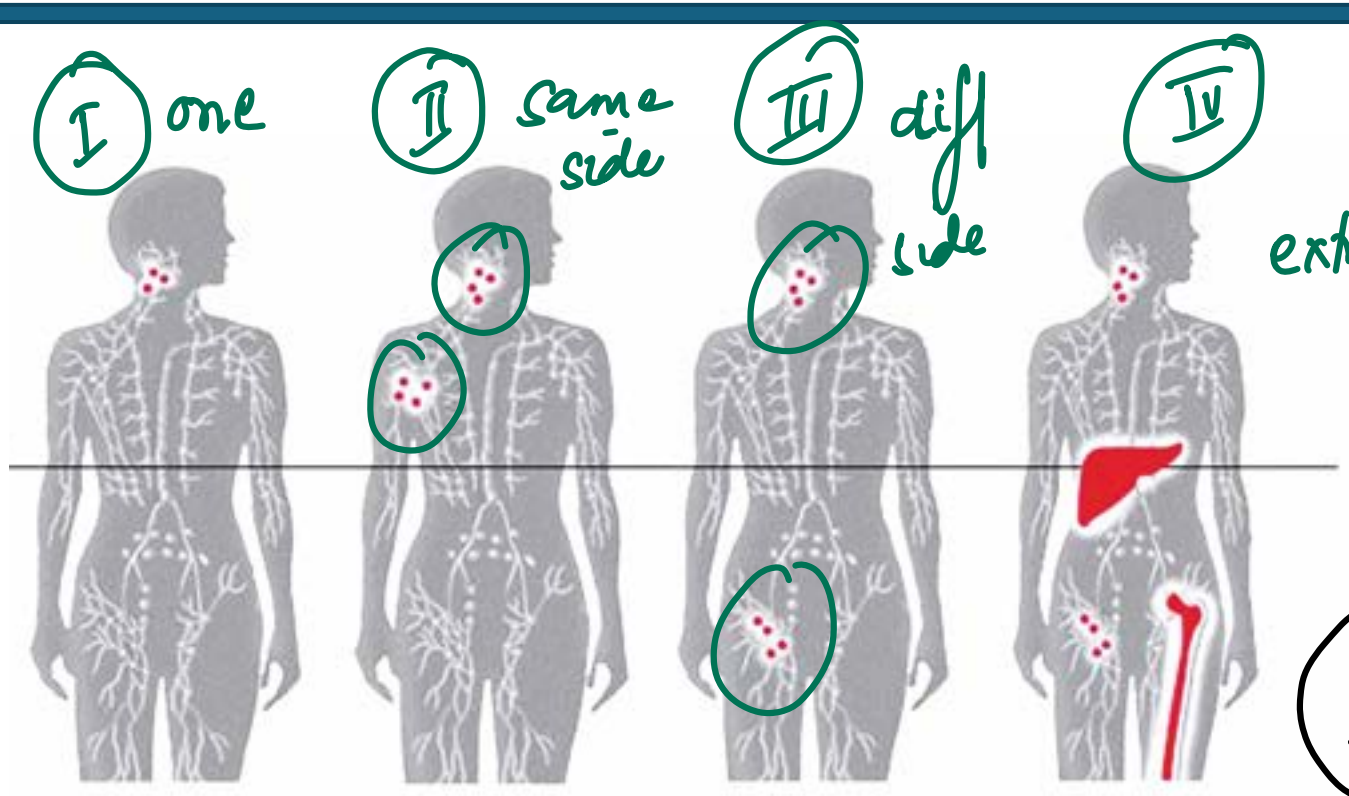
erythromelagia

ET

Stahorn megakaryocyte

PV: aquagenic pruritus

Hodgkin's lymphoma STAGING



Ann-Arbor Staging

extranodal

A / B - symptoms

+ +

℞ : A B V D Regimen

Dacarbazine

Anthracycline

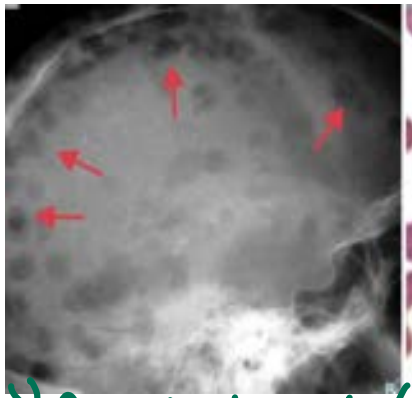
Vincristine / vinblastine

Bleomycin

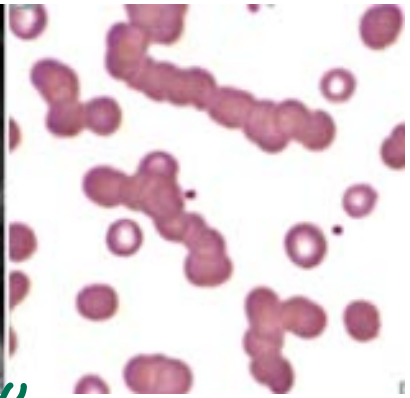
Multiple myeloma

monoclonal

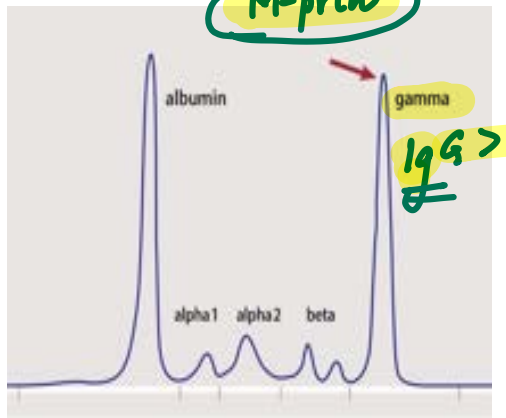
- C = increased calcium levels (greater than 11.5 mg/dL
- R = renal insufficiency (creatinine greater than 2 mg/dL or creatinine clearance less than 40 mL/min
- A = anemia (hemoglobin less than 10 g/dL or 2 g/dL less than normal
- B = presence of bone lesions (presence of one or more osteolytic lesions seen on skeletal radiography, whole-body MRI, or whole-body FDG PET/CT)



"Punched out"



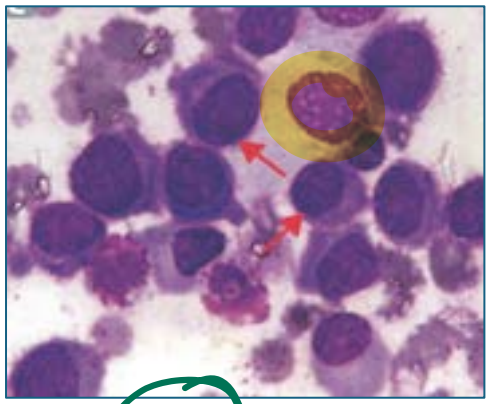
M-prtn



IgG > A > M > D > E

MM DEFINING BIOMARKERS — SLiM

- S = greater than or equal to sixty percent clonal plasma cells in the bone marrow
- Li = involved/uninvolved free light chain ratio of 100 or more with the involved FLC being greater than or equal 100 mg/L → Bence Jones proteinuria
- M = MRI with more than one focal marrow lesion



1° → AL

Mulberry/Mott cells
Flame cells
Russel body- Intracytoplasmic
Dutcher body- Intranuclear

CD38, CD138 → Plasma cell

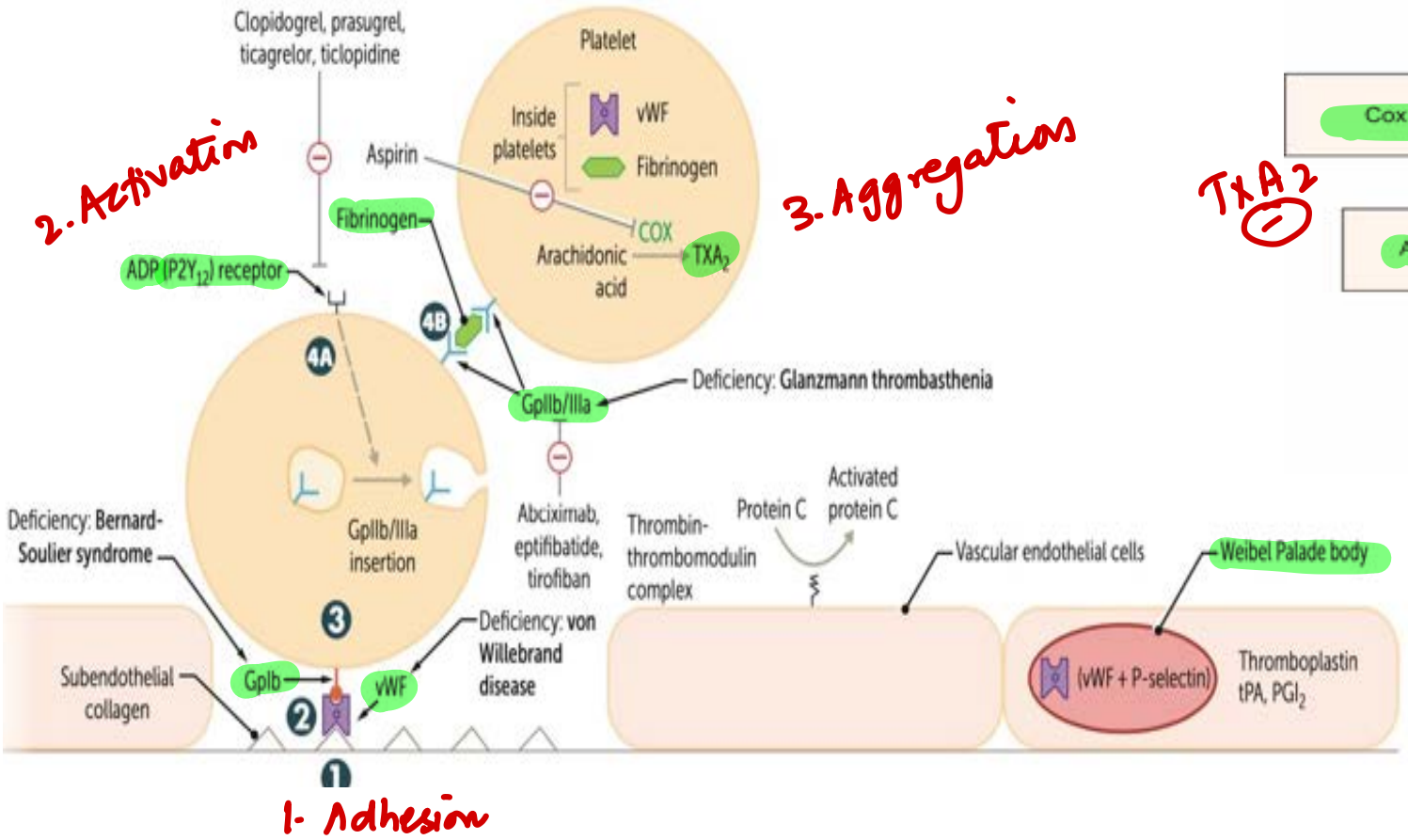
- Lenalidomide
- Dexamethasone
- Bortezomib
- Daratumumab

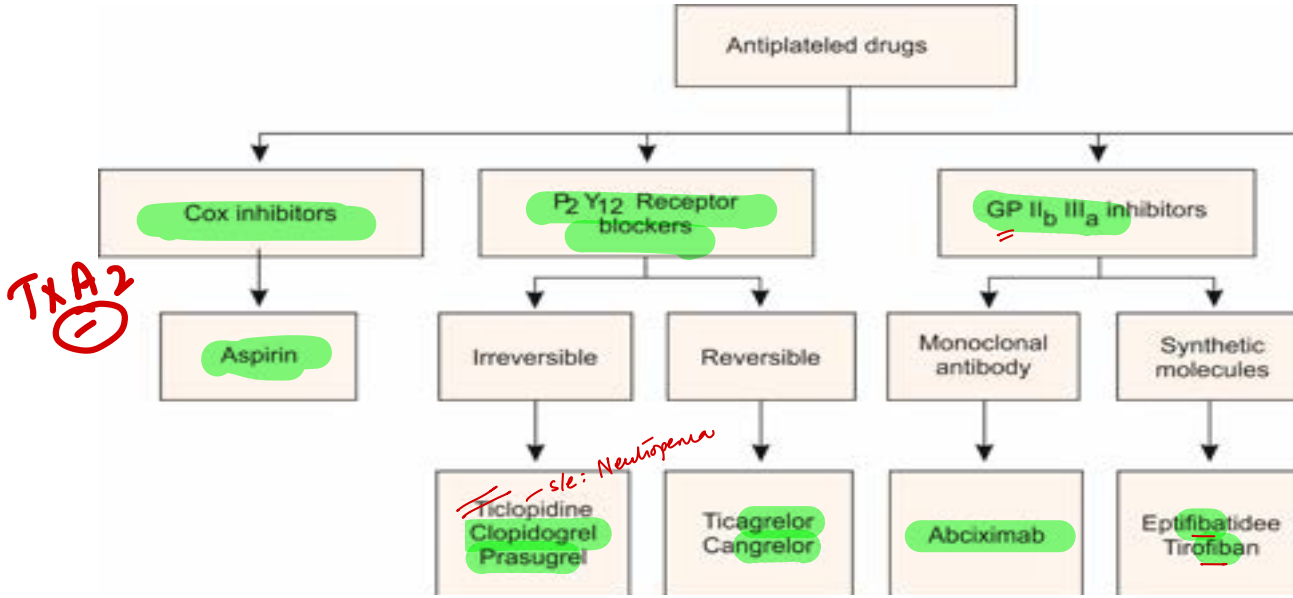
→ CD38 (−)

proteasomes: ubiquitin

MM: Plasma BM >10% + Mprtn >3g/dl + CRAB
MGUS: " <10% + " <3g/dl CRAB (−)
Smouldering MM: Plasma BM >10% + >3g/dl CRAB (−)
Walderstrom's macroglobulinemia: IgM

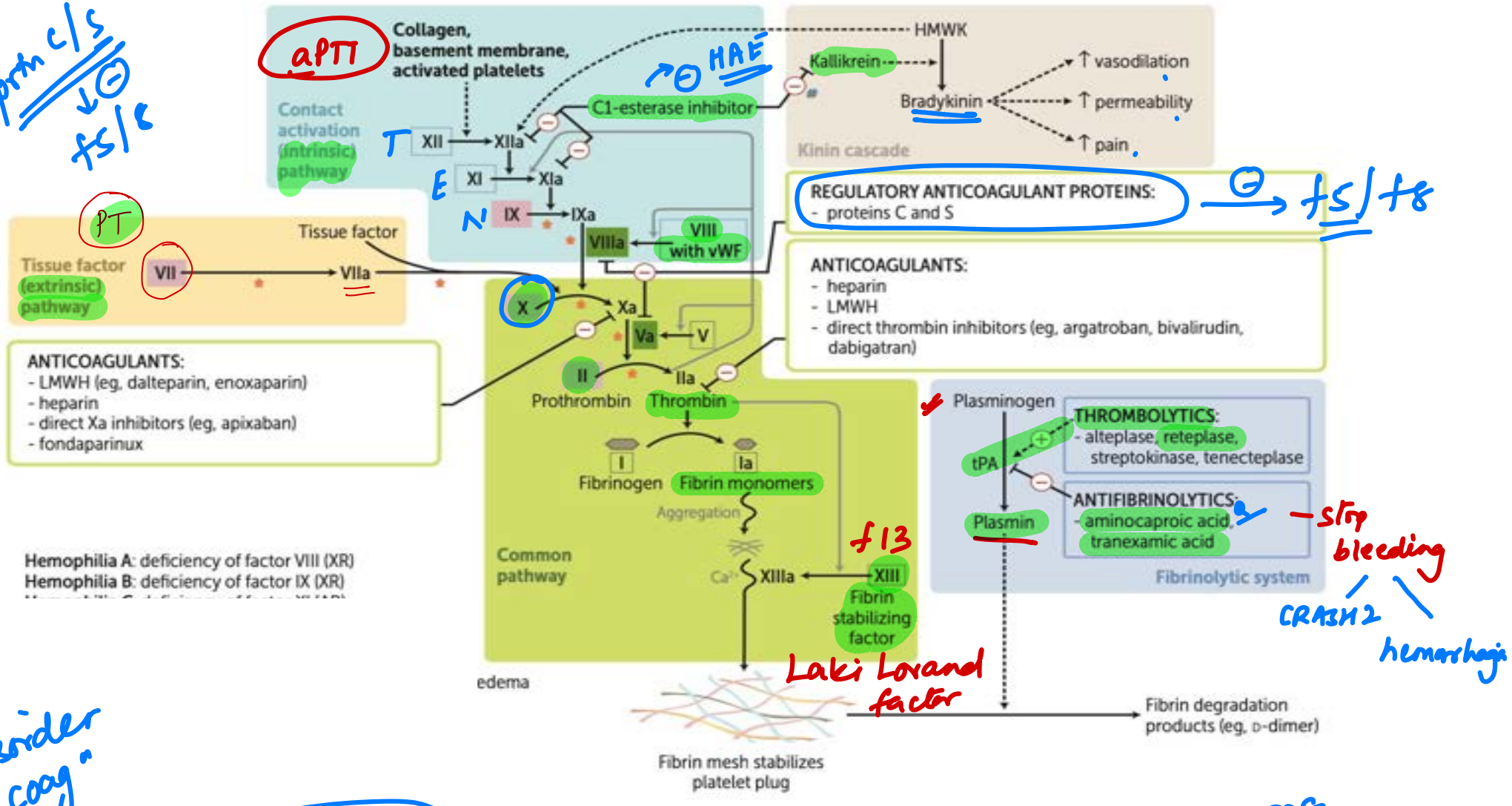
ANTI-PLATELETS: PHARMACOLOY





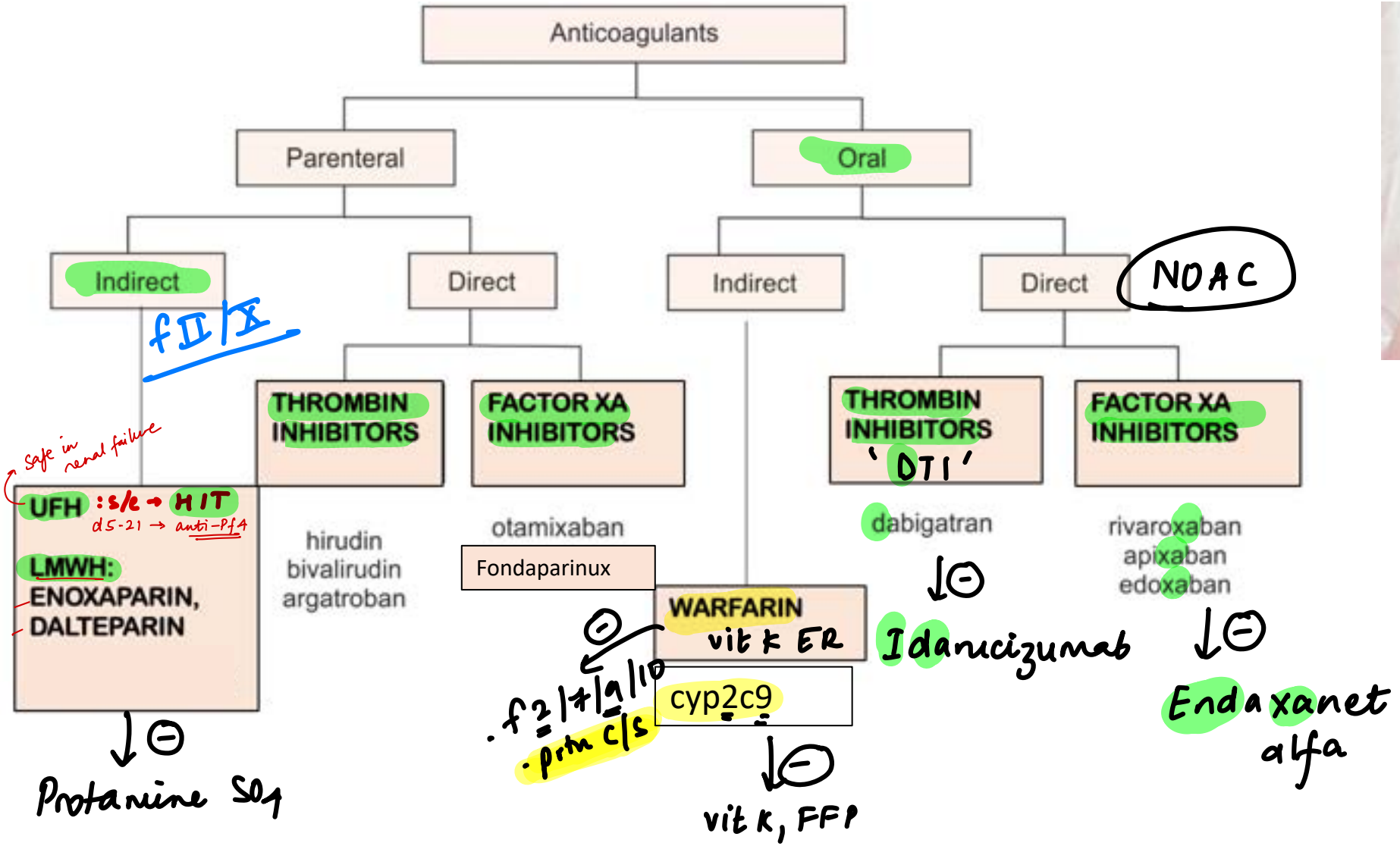
PAR-1 INHIBITOR:
AtoPaxar
VoraPaxar

Coagulation cascade



Factor V Leiden — Production of mutant factor V (guanine → adenine DNA point mutation → Arg506Gln mutation near the cleavage site) that is resistant to degradation by activated protein C. Complications include DVT, cerebral vein thrombosis, recurrent pregnancy loss.

ANTICOAGULANTS-PHARMACOLOGY



Purple toe Sx / dermal skin necrosis

Ciraparantag: antidote —f xa ⊖ / DTI

APPROACH TO BLEEDING DISORDERS

Petechiae
Purpura
BT
(Plt)

PLATELET COUNT

VWD - mc

BT + aPTT prolonged (vWF + f8)
Epistaxis / menorrhagia/ high bleeding after procedures
Chr 12 AD/ Ristocetin aggregation test IOC
TOC: Desmopressin (↑vWF)
Type 1: ↓↓ Quantity
Type 2: ↓ Quality — 2N (f8 release x-AR): RIPA N
Type 3: AR absence qq

Ecchymosis
Hemarthrosis
CT — Coagn factors

PT / aPTT

NORMAL

Abn
ADP/collagen
Aggregation

GpIIb/IIIa ⊖
Glanzmann

REDUCED

GpIb ⊖: Bernard Soulier

Abn Ristocetin
Aggregation,
Giant platelets

anti-GpIIb — ITP qq

Immature
Platelet >6%

1st: Steroids
↓ *
Splenectomy

Oprelevkin IL-11 ⊕ q
Romiplostim, Eltrombopag TPO ⊕
q Fostamatinib tyrosine kinase ⊖

PT RAISED

(extrinsic)
f7 EARLY
vit K def / warfarin toxicity
↓
2/7/9/10

aPTT raised

(intrinsic)
- Hemophilia
  - A - f8
  - B - f9
  ] XLR
  - C - f11 → AR
- APLA

Both normal

f13 / Laki Lorand factor

Both raised

- f10 def
- fibrinogen def
- DIC
  - PT, aPTT, D-Dimer, Thrombocytopenia
  - Oozing from puncture sites
  - D/D - Hemolytic transf rxn

f12 → deficiency
(⊗ bleed in vivo)
Useless

BLOOD GROUPING

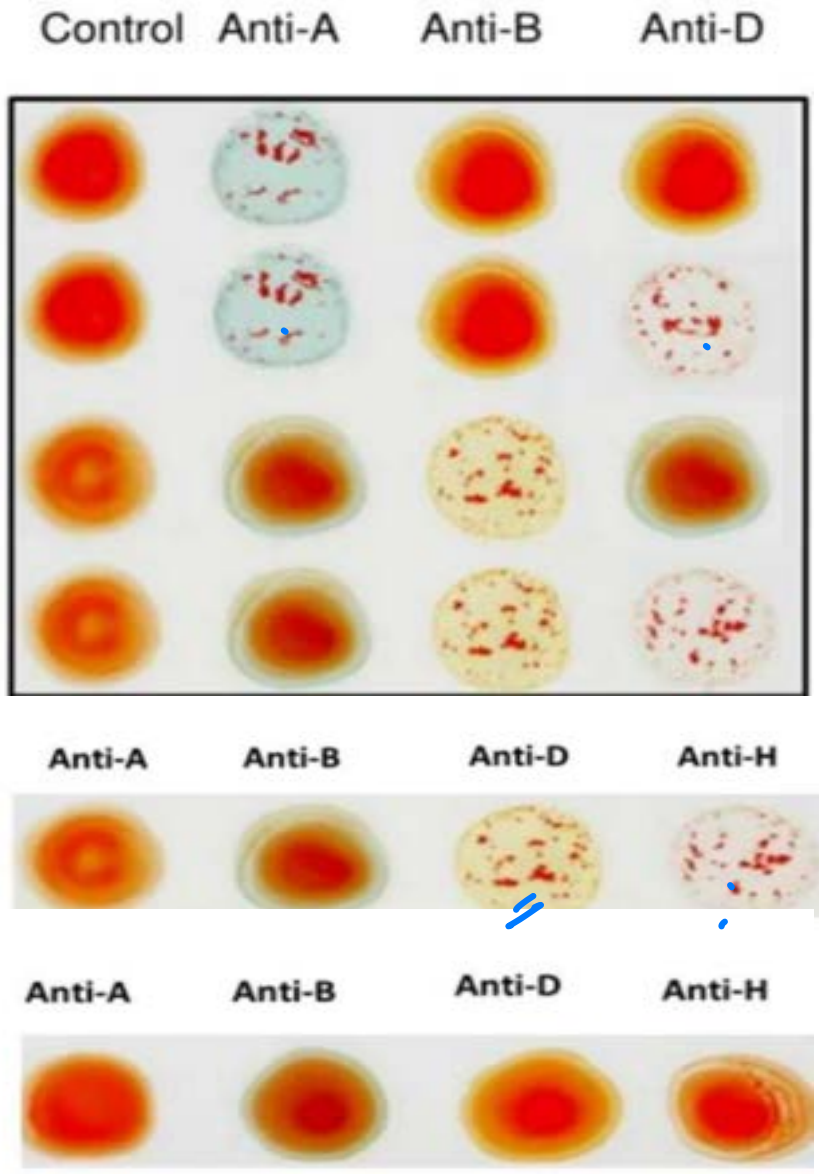
Blood Group	Antigens	Antibodies
A	h, a	anti-b
B	h, b	anti-a
recipient AB	h, a, b	—
donor O	h	anti a, anti-b
Bombay Blood Group	—	anti-h, anti-a, anti-b

Resistance to P.vivax and P.knowlesi : Duffy Ag absent

McLeod syndrome : Kell Ag

Antigens adsorbed from plasma: Lewis Ag

Rh – 1
ABO – 9
h – 19



TRANSFUSION MEDICINE

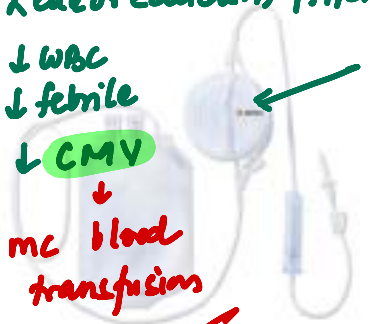
CPD: Citrate Phosphate Dextrose 3wk
CPDA: + Adenine 5w
SAGM: Saline Adenine Glucose Mannitol 6wk

Massive transfusion: >10U/24hrs
Ca: ↓ Mg ↓ (∵ sequestered)
K: ↓ ⟶ ↑K⁺ (∵ RBC lysis)
Acid-base: metab acidosis ⟶ metab alkalosis (∵ HCO_3)
MCC of death: Dilution coagulopathy

	Storage temp	Shelf life	Transfuse within	Increase by
Whole blood / PRBC	2-6 °C	42d max	4hrs	1g/dl 3% Hct
Platelet: Pooled SDAP	24-28°C ↑ bact contamⁿ	5d	30min	↑5-10k
FFP Cryoppt	-18 °C -30°C	1yr	30 min	cryoppt: Fibrinogen vWF - f8 f13

Complication	Signs/Symptoms	Treatment
Febrile NHTR (MC)	Fever, Chills, Malaise WBCs	Supportive- acetaminophen
Hemolytic transfusion rxn	Fever, chills, pain at the site of reaction, nausea/vomiting, shock, dark urine	STOP the transfusion IV fluids +/- diuretics MCC: ABO incompat
Allergic	Urticaria, pruritis, hives ↑ IgA deficiency	Symptomatic- antihistamines.
TRALI (≤in 6hrs) anti-HLA donor	Dyspnea, hypoxemia, bilateral chest infiltrates crepts	STOP the transfusion airway control, supportive care
TACO	Dyspnea, edema, JVP Raised	Slow infusion + Diuretics

Leukoreduction filter
↓ WBC
↓ febrile
↓ CMV
↓
mc blood transfusions



PH agitator

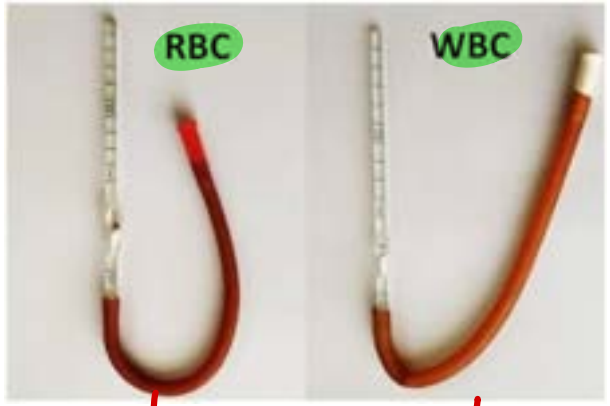
1° prevention
Prospective screening
x dengue

Screen for: HIV/ HBV/ HCV/ SYPHILIS /MALARIA

- Massive transfusions
- Drowning
- Tumor lysis Sx
- Refeeding Sx

MISCELLANEOUS

ESR

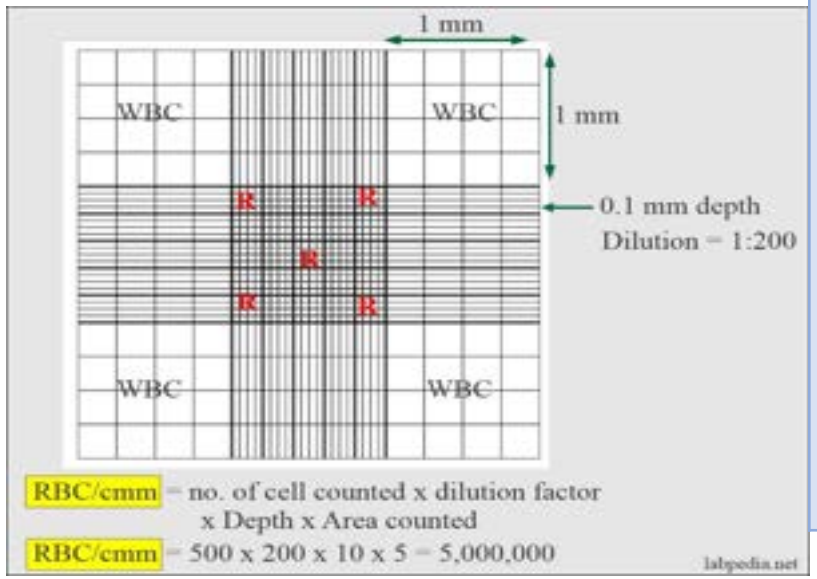


200x dilution

20x dilution

Plt

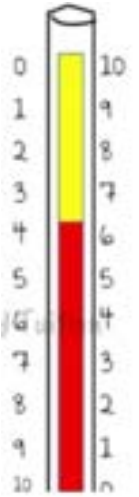
Neubauer chamber

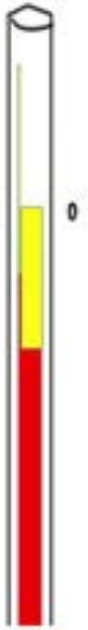


Plt : RBC chamber

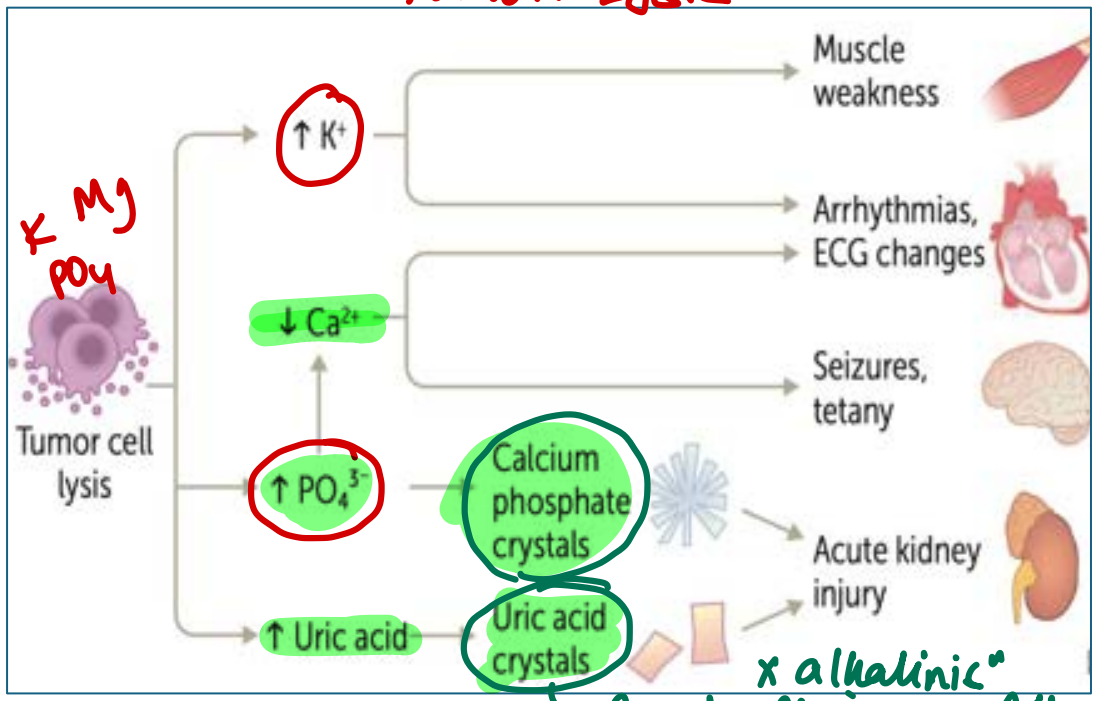
Rees Ecker fluid

Wintrobe	Westergren
• Tube is closed at lower end & open at upper end	• The tube is opened at both ends
• It contains less vol. blood sample	• It contains large vol. of blood sample
• EDTA as anticoagulant	• Sodium citrate as anticoagulant
• Values are less sensitive	• Values are more sensitive
• Tube is 11 cm.	• Tube is 30 cm long
• Dia-2.5mm	• Diameter internal-2.5mm





TUMOR LYSIS



K MJ PO4

x alkalinic"

Rx: iv fluids + Allopurinol/ Rasburicase

Svc syndrome: SVC stent

Acute back pain due to bone mets: aa Dexamethasone

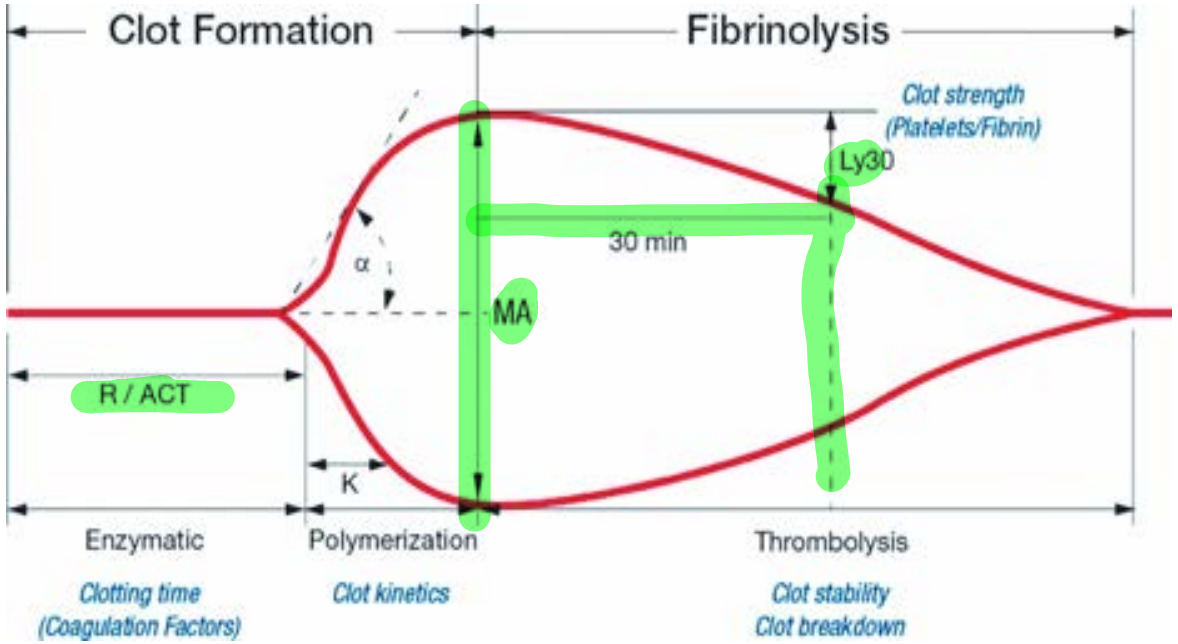
palliative: RT ← MRI

TEG: Thrombo elastography

↓

all steps of coagn pathway

ROTEM



TEG	ROTEM	Description	Normal	Abnormality: Cause	Treatment
Reaction Time (R value)	Clotting Time (CT)	Time till initiation of fibrin clot formation	5 - 10 min	↑ R value: ↓ factors	FFP protamine
K value	Clot Formation Time (CFT)	Time to achieve 20 mm clot on assay representing thrombin-platelet interaction	1 - 5 min	↑ K/CFT value: ↓ fibrinogen	Cryoprecipitate Fibrinogen
α-angle	α-angle	Rate at which fibrin cross-linking occurs	45 - 75°	↓ α angle: ↓ fibrinogen	Cryoprecipitate Fibrinogen
Maximum Amplitude (MA)	Maximum Clot Firmness (MCF)	Maximum strength of clot	50 - 75 mm	↓ MA/MCF: ↓ platelet count and/or function	Platelets DDAVP
LY-30	Clot Lysis (CL)	Degradation of clot 30 minutes after MA/MCF	0 - 10%	↑ LY-30/CL: ↑ clot breakdown	TXA Amicar

R, K → Coagn factors

α → ⊕ fibrinogen

Ma → Plt ↓↓

Ly 30 → fibrinolysis

MAP