By Hanadi MJ

* Anemia *

① Microcytic MCV (<80 fL/cell) :-

A) Iron deficiency   B) Anemia of Chronic disease   C) Thalassemia

(A & B) → problem in heme (iron)   (C) → problem in globin

A) **Cause:** malabsorption as in celiac disease (damaged villi of duodenum) or gastrectomy (we need acid to absorp Fe) or in chronic blood loss (GIT, menstrup.)

lab msrmnt: Serum Fe ↓, TIBC ↑, % Saturation ↓, Serum ferritin ↓, RDW

ferritin ↓, TIBC ↑ & vise versa

clinical: koilonychia, glossitis, Angular stomatitis

B) **Cause:** inflammation or chronic disease which leads to reducing serum Fe so that body can protect itself & not allow bacteria to feed on Fe.

lab msrmnt: ↑ ferritin, TIBC ↓, ↓ Serum Fe, % Saturation ↓.

↳ ferritin increased ↑ bcz hepcidin didn't allow macrophages to release it

C) we have α-Thal. & β-Thal. To start with α-Thal → Chromosome 16:- gene deletion of alpha chain of hemoglobin, inherited autosomal recessive.

↓ HB, ↓ MCV, ↓ MCH & it's of 4 types ↓

severe 1) Barts Syndrome (hydrops fetalis) absence of all α chains → No HbA. (γ4)

decreased 2) HB H disease absence of 3 α chains. (β4) transfusion rare need

mild 3) α-thal. trait absence of 2 " (cis / trans) → no treatment

Normal 4) " Silent carrier " " 1 " → no abnormalities

(Note: RDW Changes < shape → poikylocytosis ; size → anisocytosis

10) Now for B-thalasemia → mutation of their genes on Chromo. 11

* Note: عنا كل كروموسوم فيه جين واحد من بيتا، لكن ألفا كان جينين ع كل كروموسوم.

* Mutations : 1) absent (B0) 2) diminshed (B+) → 3 types :

1) Minor (heterozygos) only 1 has mutation B/B+ or B/B° (normal)

2) Intermedia (homozygous) B+/B+ or B+/Bo (normal-mild)

3) Major (homozygous) B°/B° → no Beta Production (severe)

(bone marrow) Intramedullary → Apoptosis of RBC Extramedullary → RBC hemolysis (liver and spleen)

bcz 2 appear
* Major → target cells & bone marrow → erythroid hyperplasia & splenomegly

ineffective erythropoisis → ↑ erythropoitin → erythroid hyperplasia + deformities

→ "hair on end" on skull + "chipmunk" appearnce of face + 2ndry hemochromtosis

lab msrmnt → ↓ HBA , ↑ HBA2 treat → iron chelate + splenoctomy

Note:- B12 vit is close RBC production , thalsmia protect from malaria

* Iron Fe absorbed in "duedenum"

* B12 absorbed in "ileum"

* Folic Acid absorbed in "jejunum"

Notes

• Cobalamin → B12 , • pyridoxine → B6

for DNA synthesis ; for iron formation

* Megaloblasts: enlargment of erythrocyte precursors

* Giant Metamyelocytes: enlargment of granulocytes precursor

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* Anemia *

② Macrocytic (MCV > 100 FL/cell)

A) Megaloblastic cause B) Non-Megaloblastic

A) Cause ↓ deficency in B12 or in folate → both imp for DNA & protein we will have * megaloblasts (large abnormal erythroid precursor) ° showing "Nuclear-cytoplasmic dyssynchrony" & will have macrocytes (mature RBC with ↑MCV) impaired DNA synthesis → ineffective erythropoesis → macrocytes in peripheal blood & hypersegmented neutrophils & nucleated RBC (immature nucleus) & Pancytopenia (↓WBC ↓RBC ↓Platelet) & ↓retic count & giant metamyelocytes

Cobalamin (B12) dificiency leads → Neurological disorders !

*B12 defncy → ① intake ② disorder ③ absorption.

2 → Autoimmune antibodies against IF (intrinsic factor) or against Parietal cells as in (Pernicious Anemia)* so no absorption of B12 (becz. disease)

3 → damage to ileum as in Crohn's disease.

*Note → ② ↑ homocystein → ↑ thrombosis

↑

① ↓ B12 / ↓ folate why ?

متن مهم كثير لل pathw

ركن مهم لغير مواد

③ becz. activated tetrahydrofolate THF will give methy → B12 → methylated → give methy to homocysteine → methione.

* Anemia *

③ Normocytic. (80-100 fL/cell) → RT count ↗ low / ↘ high

if RT is low → "Aplastic Anemia", but first remember ↓

* corrected reticulocyte count = RT % × $\frac{\text{Actual HCT} \to ?}{\text{Normal HCT} \to 45}$ — >2% high, <2% low

Ⓐ "Aplastic Anemia": bone marrow disorder → Pancytopenia

normochromic normocytic Anemia with low reticulocyte count (<3%)

(it's Aplastic anemia in case of NO neoplasia or fibrosis) but may be becz of drugs, disease (SLE → autoimmune), Infections (B19, EBV)

you should give immunosupression for T-cell activation

Ⓑ "Hemolytic Anemia" → Sickle, G6PD, heriditary sphero, Autoimmun...

↳ ↓RBC survival, ↑RT, ↑indirect Bilirubin, ↑LDH

① Intravascular	② Extravascular
No break of Hb & ↓↓ in haptoglobin that captures it hemoglobinemia, "urea, hemosidremia after days, ↑LDH	break down of Hb so ↑↑ in unconjugated bilirubin but no Hb in urine or blood, ↑LDH

① hemoglobin-opathies: Sickle — ② membrane defects: Spherocytosis — ③ Enzyme defiency: G6PD

We will start with sickle on next page →

* Anemia *

* **Sickle Cell Anemia** (Normocytic) → autosomal recessive

1) more common than B-thalsmia 2) Point mutation on chrom. 11 it's reversibly sickling due to hypoxia, dehydration, acidosis but may later be irreversible & damage its membrane & closes narrow vessels "vasoocclussion" → infarction (kidney, liver, splen, BM)

Hb S (Glu → val) Hb C (Glu → lys) • We will have ↓

(1 Chronic hemolysis gall stones ↑, erythropoesis ↑, "hair on end skull", ...

(2 Ischemic Manfistation obstructions, "Dactylitis" → infarcts in bones ✍ swelling also autosplenoctomy → ↑encapsulated infections & will show Howel-Jolly bodies

* G6PD deficiency aka "favasism" → **↓G6PD Anemia** (✓)

X linked recessive disorder, ↓G6PD → ↑ ROS (oxidative stress ↑) → ↑ hemolytic Anemia

Why G6PD? "PPP" pentose phosphate pathway → ↑NADPH → ↑ reduced glutathione

Oxidant Stress? Drugs (sulfonamides, Furantoins, antimalarial, ...) + favism + ROS leads to Heinz bodies & bite cells (by denaturation of globin chains)

* **Hereditary Spherocytosis** → congenital hemolytic Anemia

abnormal spectin and Ankyrin tathering proteins → RBC membrane blebs → Spherical RBC → killed at spleen befor 120 days → Splenomegaly + Jaundice + Anemia + ↑RT • loss of central Pallor + high MCHC ↑ + howel-Jelly bodies (anuclear DNA reminant) to treat → splenectomy (to reduce hemolysis)

↑ Osmotic fragility (when kept in hypotonic saline solution)

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* Anemia *

* **Immune Hemolytic Anemia (AIHA)** → 3 categories: allo, auto, drug-induced

Complement cascade → Classical (extravascular) + Alternative (Intravascular)

Classical → C1 complex (Antigen + IgG) Alternative → C3 → MAC

① Warm antibody (IgG / IgA) → extravas, spherocytes, Primary & 2ndry reasons

2ndry :- lymphoproliferative disorders, Autoimmune disease (SLE), Drugs (cephalosporins & Penicillin)

② Cold Antibody (IgM) → clumping & complement fixation → IgM agglutinate

(intra & extra vascular) → hemolysis in hand/feet in cold weather.

reasons :- Infectious Mononucleosis (EBV), mycoplasma infection, lymphoproliferative disorders

* **Paroxysmal nocturnal hemoglobinuria (PNH)**

Caused by acquired somatic mutation in X-linked PIGA gene.

↑CO_2 → ↑acidosis (PH↓) → fixation of complement system → bcz of mutated PIGA gene there's no GPI anchor protein to hold CD55 & CD59 then → activation of complements → MAC complex → hemolyse RBC

* **Anemias due to mechanical trauma to RBC's**

Cells disrupted by physical trauma due to :- cardiac valve prosthesis, Microangiopathic hemolytic Anemia, HUS, TTP so RBC appear as :- schistocytes, burr cells, helmet cells

خلص كذا عن أنواع الأنيميا ، آخر ملف عن coagulation disorders وهو الأخير

* Coagulation Disorders *

1) Primary Hemostasis → vessel / Platelet / VWF

2) Secondary " → Coagulation & Anticoagulant factors

3) Plasmin Activation & fibrin dissolution

	extrinsic	common	intrinsic
1 → prothrombin	7	1, 2, 5, 10	9, 11, 12, 8
2 → fibrinogen			

9 → vitamin K dependent / 8 → bound to VWF

Anticoagulants → Protein S, protein C

BT (bleeding time), PTT (Partial thromboplastin time : intrinsic), PT (prothrombin : extrinsic)

FT (Thrombin time : final step of converting to → fibrin)

Primary Clinical Presentation → mucosal / skin bleeding, 2nd → deep bleeding

* Hemostasis disease *

① Hypocoagulability	② Hypercoagulability	③ Platelet disease
A) hemophilia A (factor 8↓)	A) factor 5 leiden disease	
B) " B (" 9) chismas	(most common) → makes it	
C) VWD (most common)	resistant to Protein C	type → ① thrombocytopenia
A → X-linked recessive, 2nd hemo		type → ② Qualitative
B → " "		
C → binds to GP1b & we use		
Ristocetin test		
C → Autosomal dominant disorder		
to treat we use desmopressin		
"DDAVP"		

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continue

autosomal R 1805

② A: Bernard Soulier ... B: Glanzman thrombasth.

↓GP1b, enlarged platelet, ↑BT — ↓G2b, ↓G3A, ↑BT

response to ADP ✓ — normal morphology, agg. to

" to vWf & ristocetin ✗ — ADP ✗, to vWf ✓

A:

① Idiopathic (most common) < acute / chronic ↑BT

child: acute → infection / vaccine, bruising & petechia, IgG against GP2B & 3A

adult: chronic → same but no infection. 2nd: SLE, HIV, drugs, ...

treat → IV immunoglobins + steroids & immunosupression + splenectomy (severe)

B:

① Microangiopathic thrombocytopenia / hemolytic Anemia (MAHA)

نفس الأعراض — intravascular hemolysis

1) TTP → inherited / sporadic → antibodies to ADAMTS(13) (cleaves vWf)

2) HUS → E-coli → bloody diarrhea, ... → more in children

3) DIC → Consumptive coagulopathy → thrombo hemorrhagic disorder

إضافة ↓

DIC: dissemenated intravascular coagulation → D↑ dimers, widespread

HUS: hemolytic uremic syndrome → non immune → kidney

TTP: thrombotic thrombocytopenic purpura → Neurologic & fever