1 Iron Deficiency Anemia

* Causes :-
1- lack of iron in diet
2- Blood loss
3- malabsorption
4- Increase needs
5- Inflammation

* ↓ Ferritin , ↑ TIBC , ↑ RDW
↓ Transferrin saturation , ↑ Transferrin
↓ hepcidin

2 Anemia of chronic disease

* ↑ Ferritin , ↓ TIBC
↑ erythrocyte , ↓ Transferrin
Free Protoporphyrin , ↓ Iron absorption
↑ hepcidin

1 + 2 ⇒ microcytic anemia

3 Macrocytic Anemia (B12. Folate deficiency)

- Reticulocyte count low
- Hypersegmented neutrophil
- Neurological symptoms (Numbness, Unsteady gate, loss position sense) with ↓ B12
- No neurological symptoms with ↓ Folate

* Pernicious anemia
- autoimmune attack on gastric mucosa
3 type of Abs :-
1- Parietal canalicular Ab
2- blocking Ab
3- Intrinsic factor-B 12 complex Ab

* ↑ risk of malignancy in = Patient with pernicious anemia

4 Normocytic anemia

- anemia of chronic disease :
- under production

Aplastic anemia
↳ Pancytopenia
- No ↑ reticulocyte count
- No splenomegaly
- BM exam must For diagnosis
- BM transplantation is the treatment of choic
- well response to immunosuppressive therapy
- Any age , Any gender

Myelophthisic
↳ TB , Osteosclerosis , lipid storage disorders , Metastatic cancer

5 Anemia in liver disease

Causes :- 1- Iron deficiency (most common)
2- Hypersplenism
3- Alcoholic cirrhosis
4- Therapy related hemolytic anemia and ↓ EPO receptor

6 Anemia of renal disease

- ↓ EPO production by damage Kidney
- ↑ inflammatory cytokines
- Hemolysis
- Chronic bleeding
- Folate deficiency

Hemolytic anemia (accelerated RBC destruction) – Hemolysis –

↳ Due to: - Infection
- Plasma Factor
- Mechanical
- Intrinsic

– Intravascular Hemolysis

① Activation of complement on RBC
- Paroxysmal nocturnal hemoglobinuria (PNH)
- " Cold "
- transfusion reaction
- autoimmune hemolytic anemia

② Physical or mechanical trauma

③ Toxic Microenvironment of RBC

– Intra corpuscular :-

Hereditary defect
- enzyme defect
- Hemoglobinopathies
- Thalassemia syndrom
- defect RBC membrane

Aquired defect
- PNH

– Extracorpuscular :- – Infection

- Drug
- Toxic
- microangiopathic
- Immunhemolytic anemia

* Features of Hemolytic anemia :

- ↓ RBC survival
- reticylostosis
- ↑ erythropoietin
- ↑ Product of Hb catabolism
- ↑ LDH, Bilirubin
- * ↓ haptoglobin *

in intravascular Hemolysis there is *Hburia, Hbemia and Hemosiderinuria but No in extravascular.

extra vascular → splenomegaly

Sickle cell disease (SCD)

(valine → glutamic acid , 6th Position , β chain)

- Ca^{+2} influx , K and H_2O efflux
- ↑ MCHC
- ↑ Hb
- ↓ No → narrow vessel
- Vaso - occlusive phenomena

- life span of RBC 10 - 12 day (RBC destraction)

* Consequences of

1. chronic hemolysis
2. Ischemic manifestation
3. ↑ risk of infection
4. crises (painful, Hemolytic, aplastic crises)

* autosplenectomy

* factor affect The degree of SCD?

1. Type Hb
   - Heterozygous: 50 : 50, HbA : Hbs
   - Homozygous: Hbs 100%
   - HbF → protect
2. Hb conc.
   - α-thalassemia
   - ↓ MCHC, ↓ sickling
3. blood circulation
   - spleen
   - BM
   - inflammation
   - ↓ blood flow
   - more sickling

* Diagnosis :-

- History , - CBC , smear
- Hb electrophoresis

* Rx (treatment) :-

- pain relief
- hydration
- antibiotic therap
- exchange transfusion to ↓ Hbs

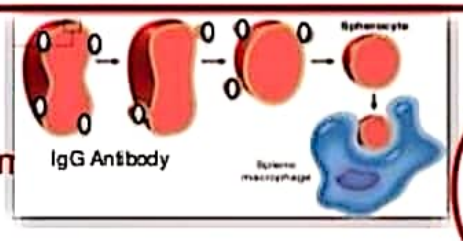
Hemolytic Anemia due to Autoantibodies

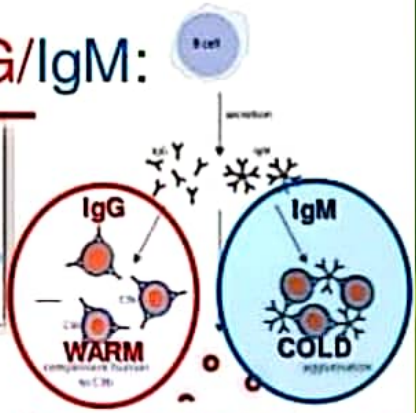
Warm Antibody: IgG/IgA type

- Activated at body temp. (37 c)
- Opsonization, phagocytosis and spherocytosis
- 80% of immune hemolytic anemias
  - Primary (50-70%)
  - Secondary:
    - lymphomas &leukemias
    - Hepatitis B and A
    - SLE
    - Drugs

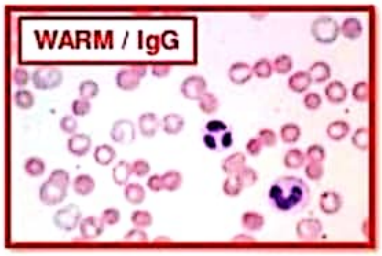
- **Cold Antibody:** IgM type active at 0-4°C
- (seasonal) or at periphery (fingers, toes)
- IgM/C3b: late complement fixation does not occur, blood moves to warm are (spleen)
- Dissociation of IgM and Opsonization through C3b in spleen (extravascular hemolysis)
- IgM agglutination (Raynaud phenomena)
  - Acute
    - Infectious mono
    - Mycoplasma
  - Chronic:
    - idiopathic
    - Lymphomas
- Cold hemolysin (paroxysmal cold hemoglobinuria 1-7%)
  - IgG type
  - Post infections: measles, mumps, mycoplasma, others

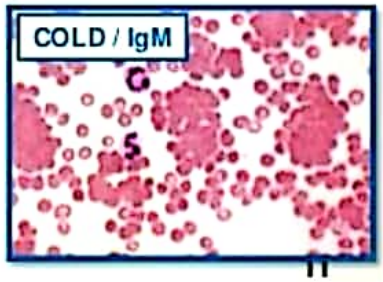
Immune Hemolytic anemia IgG/IgM:





- Causes:
  - RBC Antibody (Comm
- Pathogenesis:
  - Warm / IgG coated RBC lysis in spleen. Drugs, Idiopathic. (predominantly extravascular)
  - Cold / IgM - (Infections, Lymphoma) RBC Clumping & complement fixation lysis in BV & Liver. (predominantly intravascular)
- Morphology:
  - Spherocytes (warm) / RBC clumps (cold).
- Clinical Features:
  - Anemia, Jaundice. Splenomegaly in chronic.
  - Diagnosis: Comb's test *.





Thalassemia (mutation in globin gene) (in malaria endemic)

- microcytic hypochromic anemia
- ↑ Hgb A2 . Hgb F

* β-Thalassemia (11 mutations)

- common mutation @
① Promoter region (β^+)
② in exons (β^0)
③ with MRNA (b^+ or b^0)

* α- Thalassemia (16 deletion)

- Hydrops Fetalis → incompatibe with life

* Classification of β thalassemia

major
- β^0/β^0 , β^+/β^+ , β^0/β^+
- Transfusion dependent
- ↑ Hbf , ↓↓ HbA
- expansion bone marrow (skull . Facial)
- stunted growth
- hepatosplemamegaly

minor
- Heterozygous β^0 or β^+
- D.D → iron deficiency anemia

* ① Inclusion body
- excessive β-chain or α-chain
- Precipitate as Hb H (β4)

② Heinz body
- ass. with G6PD deficiency (bite cell)

③ Howell- Jolly body .
- Type of inclusion body with DNA

Hgb "H" disease @-

↳ 3 gene deletion
= Tetramer of 4β chains)
↑ affinity to O2
short RBC life span

G6PD

* X-linked , ↑ in males , Heinz body , ↓ GSH production
* asymptomatic unless exposed to oxidizing agent .

Hereditary spherocytosis (HS) → Non immune , weak interaction btw skeleton and intrinsic Factor

(Spectrin deficiency)

- mutation in (spectrin, ankyrin, band 3)
- AD , ↑ reticulocyte count)
- Splenomegaly (500 - 1600)
- Splenectomy help

Complication of-
- Gallbladder stones
- Foot ulcer
- Aplastic crisis
- Skeletal abnormalities

Immune Hemolytic anemia

due to Abs

Warm
- IgG
- spherocyte
- extravascular

Cold
- IgM
- RBC clump
- intravascular

* [illegible]
* [illegible]

Lec 11 : Coagulation and DIC

* Test for Coagulation :-

1. PT : extrinsic (VII, X, V, II, fibronogen) → add thromboplastin and Ca^{+2}
2. PTT : intrinsic (VIII, X, V, II, fibronogen + XII, XI, IX) → add Kaolin, cephalin, Ca^{+2}
3. Platelet count : (150000 - 450000)
4. Tests of Platelet Function

* aquired difficency in clot Factor is most common.

* Hemophilia "A"

- deficiency of factor VIII
- X - linked
- Affect male
- heterozygous female (inactiv X chr.) ⇒ unfavorable lyonization
- C/P → bruising, massive hemorrhage after trauma, *Petechia is absent
- site of bleeding → large joint, soft tissue, Nose, Brain, GI tract, Urinary tract (deep hemorrhage)
- PTT prolong, replacement therapy

Hemophilia "B"

- X - linked
- deficiency in Factor IX
- Prolong PTT

VWf

* most common hereditary bleeding disorder
* AD → Prolong BT and PTT → Mucocutaneous bleeding
* 3 main Type, Type 2 subdivided into 4 subtye, normal Platelet count, PT

DIC

disseminated intravascular coagulation (Consumptive Coagulopathy)

* Caused by systemic activation of Coagulation
* thrombi throughout microcirculation
* Consequence → Fibrinolysis is activated
* tissue hypoxia, or bleeding due to fibrinolysis
- acceterated platelet destruction in combination with coagulation Factor consumption

* Acute Presentation → (bleeding) Anemia, Thrombocytopenia
* chronic → Thrombosis

Triad of DIC ⟹ (Thrombosis , fibrinolysis , bleeding)

obstetric complication , infection , cancer , injury

lab ⟶ ↓ Platelet , ↑ fibrinogen . PT . PTT , FDP

Platelet disorders

Classification :-

1. Failure of production
2. Abnormal distribution
3. ↑ Platelet destruction
   - ↳ Immuno Thrombocytopenic Purpura (ITP)

* Causes :-

1. SLE
2. drug (heparin , quinidine)
3. Post transfusion
4. Neonatal due to autoantibody
5. DIC , microangiopathic hemolytic

Classification of ITP :-

1- Acute ITP (Idiopathic)

- children
- Petechia , bruising
- Preceded by vaccin . infection
- Plt. count < 20.000
- self limit
- sever case ⟶ steroid , IV immunoglobulins

2- chronic ITP

- women (20 - 50)
- life span Plt. (hours)
- ↑ megakaryocytes
- Petechial , menorrhagia

Treatment of ITP :-

1- steroid
2- IV immunoglobulins
3- spleenectomy
4- Immunosuppressive therapy

Microangiopathic Thrombocytopenia

Thrombotic Thrombocytopenic Purpura (TTP)

- adult → female > male , 3th - 4th decade
- inherited and sporadic
  - ↓ ADAMTS 13 &
    - (*) Ab against ADAMTS 13
    - signs and symptoms:
      - (1) Hyaline microthrombi of skin, gingiva
      - (3) fever, neurologic abnormalities
      - (9) acute Thrombocytopenia, renal dysfunction
- ↑ LDH . ↑ bilirubin . ↓ haptoglobin
- ↑ BT
- Plasma exchange

Hemolytic uremic syndrom (HUS)

- Pediatric
- E. coli
- blood diarrhea
- hyaline microthrombi
- ↑ BT
- dialysis . antihypertensin
- thrombi limit to glomerular capillary