Hemolytic anemia

1) Intravascular
2) Extravascular.

① Classification

1) Acquired (Extracorpuscular, Extrinsic):
   - ① Immune
     - a) Autoantibody
     - b) Alloantibody - (Transfusion, New Born).
   - ② Non-Immune
     - a) Mechanical → Microangiopathic (DIC, HUS, TTP)
       → March haemoglobinuria (vigour exercise)
     - b) Infection → Intracellular organism → Malaria
       Toxins → C-Perfringens
     - c) Chemical / Physical → Copper (Wilson disease)
       ↳ oxidative drugs, Burns, Drowning
     - d) Acquired abnormal membrane
       (Paroxysmal nocturnal Haemoglobinuria)

Autoimmune Hemolytic anemia

→ ↑ RBC destruction, due to red cell antibodies. which cause usually intravascular hemolysis, but if complement activation is low it might cause extravascular hemolysis

Classification:

i) Warm antibodies → 37°C, Most Common, IgG
ii) Cold antibodies → 4°C, Rare, IgM and complement

① Warm autoimmune hemolysis

Etiology → Unknown
→ Secondary to Autoimmune disease (SLE, RA), Drugs, Malignancy (leukemia, lymphoma) Injections, Cancers.

Pathology → IgG (Warm agglutins)
↓
Binds to Rh antigen
↓
Macrophage → Phagocytosis
Neutrophils → Granules
NK cells → CD8 positive cells.

② Cold autoimmune hemolysis

→ Mostly chronic Form:
IgM (Cold agglutin)
↓
Complement pathway
↓
Membrane attack complex (MAC).

→ In acute form may mimic like Raynauds Phenomena

Clinical Features

Intravascular Hemolysis (Mostly)

RBC destruction → ↑↑ LDH Enzyme

↓

Hemoglobin → Haptoglobin → Bile → Removed through feces.

Heme — Globin

↳ Unconjugated bilirubin.

↳ Jaundice, Gallstones.

In Kidney stored as Hemosiderin (Hemo is)

↓

Excreted as Hemoglobinuria and Hemosiderinuria → Renal Insufficiency ← Oliguria

Extravascular Hemolysis (↓ complement how)

→ In Spleen and etc. (Reticuloendothelial system).

→ Haptoglobin, LDH = Normal

→ No Hemoglobin or Hemosiderin in Urine.

Lab Investigation:

① Blood → ↑↑↑ Reticulocyte ↓ Haptoglobin, ↑↑ LDH

→ Normocytic Normochromic anemia

→ MCV, MCH, MCHC → Normal, RDW normal

② Urine → Urobilinogen, Stercobilinogen in stool, Hemoglobin etc.

③ Bone marrow → Proliferation.

④ Coomb's test

① Direct antiglobulin test (DAT) Coomb test.

Blood · RBC

→ RBC

→ RBC antigen + Antibody Bound to red cell antigen.

→ Coomb's reagent (Antibody against human globulin (antibody).

Y Y Y + ⊕

⇒ Agglutination occurs.

Used to detected

i) Autoimmune hemolytic anemia
ii) Hemolytic diseases of newborn
iii) Transfusion reactions

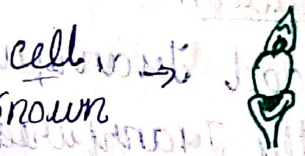
② Indirect antiglobulin test (IAT) Coomb's test

Patient + Plasma → Red cell with known antigen expression → Red cell with Ag-Ab complex

+ Coombs reagent

↓

RBCs Agglutinate.



Use for screening

1) Antibody screening before blood transfusion.
2) Screening in pregnancy for antibody that might cause hemolytic disease in newborn.

3) Alloimmune hemolytic anemia

Antibodies against non-self red cells.

i) Blood transfusions.

ii) Diseases of New Born.

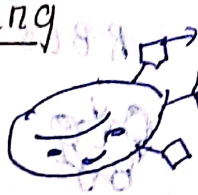
Introduction:

In Blood Transfusion elements of blood is usually Transfused (RBC, Platelet, WBC, etc)

① Homologous → From other person

② Autologous → planned before surgery.

Blood Typing



→ Only coprotein (A, B).

→ Rh Factor (D antigen) acts as antigen.

→ So If Type A person → Antibody against B,

B → Antibody to A

O → Antibody to Both

AB → No antibody

	Giving	Recieving
A^+	AB^+, B^+, AB^+, AB^-	A^+, A^-, O^+, O^-
B^+	B^+, AB^+	B^+, B^-, O^+, O^-
AB^+	AB^+.	Everyone.
O^+	Everyone	O^+, O^-

→ Rh positive will not have antibody against Rh, But negative will have antibody.

	Giving	Recieving
A^-	A^+, A^-, AB^+, AB^-	A^+, A^-, O^-
B^-	B^-, B^+, AB^+, AB^-	B^-, O^-
AB^-	AB^+, AB^-	A^-, B^-, AB^-, O^-
O^-	Everyone	O^-

Cross matching

Recipient Serum + Donor RBC → Agglutination occurs.
(If antibody present) (Then cannot give blood).

ABO incompatible red cell transfusion.

Wrong Blood Group (Antigen)
↓
Already present antibody (IgM usually).
↓
Binds to it and activates Complement System
↓
Anaphylotoxin, MAC complex, chemotaxins, opsonization
↓
Red cell lysis (Destruction)
↓
Systemic Immune response.

Rhesus D Blood Incompatability:
Usually negative in 15% Caucasians.

1st Pregnancy
Father RhD+ve
Mother RhD-ve
Fetus RhD+ve
→ Fetal-maternal Blood transfer labour
→ First newborn (RhD+ve) safe.
But mother (RhD-ve) is sensitized and produces RhD antibody (IgG)

Next Pregancy
Father RhD+ve
Mother RhD-ve
Fetus RhD+ve
→ Repeated encounter of fetal RhD antigen.
IgG from mother against RhD.
Crosses placenta
↓
Attacks to RBC of fetus and destructs.
← Fetal or Newborn hemolytic anemia.
Anemia, Jaundia, Kernicterus (CNS damage, death)

If Mother is sensitized to Rh D antigen prior itself then first fetal will be effected.

→ Mother Screened for Anti-red cell immuno globulin (IgG).

→ Anti-D immunoglobulin prophylaxis is given to pregnant women at 28-34 weeks which prevents antibody formation

5) Paroxysmal Nocturnal hemoglobin:

Irregular ↓ Night

→ Defect in glycosylphosphatidylinositol (GPI) an anchor protein.

↓

Increased sensitive to complement System ↓

Intravascular Hemolysis

↓

Haemoglobinuria in morning urine

→ Associated with thromborsis and aplastic anemia