🩸 IMMUNOHEMOLYTIC ANEMIA

Immunohemolytic anemia results from antibodies directed against antigens on red blood cell (RBC) membranes, leading to premature RBC destruction ⚠️

🧠 Basic Concept

- Antibodies bind to RBC surface antigens
- Antibodies may:
  - Arise spontaneously (autoimmune)
  - Be drug-induced 💊
- Condition is uncommon but clinically important

🧪 Basis of Classification

Immunohemolytic anemia is classified based on:

1️⃣ Type of antibody involved

2️⃣ Associated or predisposing conditions

📊 CLASSIFICATION OF IMMUNOHEMOLYTIC ANEMIAS

🔥 Warm Antibody Type

- Primary (Idiopathic)
- Secondary:
  - B-cell neoplasms (e.g., CLL)
  - Autoimmune disorders (e.g., SLE)
  - Drugs:
    - α-methyldopa
    - Penicillin
    - Quinidine

❄️ Cold Antibody Type

- Acute:
  - Mycoplasma pneumoniae infection

- Infectious mononucleosis

- Chronic:
  - Idiopathic
  - B-cell lymphoid neoplasms (e.g., lymphoplasmacytic lymphoma)

📌 *This table is very commonly tested in SAQs*

🧪 DIAGNOSIS — COOMBS TESTS 🔍

🔴 Direct Coombs Test (DAT)

Purpose: Detect antibodies and/or complement already bound to patient's RBCs

Procedure Flowchart:

Patient's RBCs → Incubated with anti-human Ig or anti-complement antibodies → Agglutination occurs → Positive test = RBCs coated with Ig and/or complement

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🔵 Indirect Coombs Test

Purpose: Detect antibodies in patient's serum

Flowchart:

Patient's serum → Mixed with test RBCs (known antigens) → Agglutination → Identifies specific antibody target

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🔥 WARM ANTIBODY IMMUNOHEMOLYTIC ANEMIA

🧬 Antibody Characteristics

- Mainly IgG
- Rarely IgA
- React optimally at 37°C 🌡️

⚙️ PATHOGENESIS — STEPWISE FLOWCHART

IgG binds RBC membrane antigens → RBCs opsonized with IgG → Splenic macrophages recognize Fc receptors

→ Partial phagocytosis ("nibbling") 🦷 → Loss of RBC membrane → Formation of spherocytes 🔴 → Sequestration & destruction in spleen → Extravascular hemolysis

📌 Mechanism resembles hereditary spherocytosis

🧪 Morphologic Feature

- Presence of spherocytes in peripheral smear
- Due to membrane loss, not cytoskeletal defect

🧠 Etiology

- >60% idiopathic (primary)
- ~25% secondary to:
  - Autoimmune diseases (e.g., SLE)
  - B-cell malignancies
  - Drugs 💊

💊 Drug-Induced Mechanisms

1️⃣ Autoantibody Induction (α-methyldopa)

Drug alters RBC antigenicity
→ Loss of self-tolerance
→ Autoantibodies against intrinsic RBC antigens
→ IgG-mediated hemolysis

2️⃣ Hapten Mechanism (Penicillin)

Drug binds RBC membrane proteins
→ Formation of neoantigen
→ Antibody binds drug-RBC complex
→ RBC destruction

3️⃣ Immune Complex Mechanism

Drug + antibody in plasma

→ Immune complex deposits on RBC

→ Complement activation

→ Hemolysis

🩺 Clinical Features

- Chronic, mild to moderate anemia
- Moderate splenomegaly
- Many patients require no treatment 😊

❄️ COLD ANTIBODY IMMUNOHEMOLYTIC ANEMIA

🧬 Antibody Characteristics

- Usually IgM
- Low-affinity antibodies
- Bind RBCs at <30°C 🧊
- Act in:
    - Fingers

- Toes
- Ears

⚙️ Pathogenesis — Clean Flowchart

Cold exposure → IgM binds RBC surface → Complement activation begins → C3b & C3d deposited on RBC → RBC travels to warmer areas → IgM dissociates → Complement remains bound → Macrophage recognition (spleen & liver) → Extravascular hemolysis

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🩸 Key Mechanistic Points

- Complement cascade does NOT complete
- No MAC formation
- Hence:
  - ❌ Minimal intravascular hemolysis
  - ✅ Predominantly extravascular hemolysis

❄️ Agglutination & Raynaud Phenomenon

- IgM is pentameric
- One IgM binds multiple RBCs → RBC cross-linking → Agglutination (clumping) 🧱 → Sludging in capillaries → Raynaud phenomenon (color changes, pain) ❄️🖐️

🦠 Associated Conditions

Acute (Transient)

- Mycoplasma pneumoniae
- Infectious mononucleosis
  ➡ Mild, self-limited anemia

Chronic

- B-cell neoplasms
- Idiopathic cold agglutinin disease

📌 One-Look Exam Comparison

Feature	Warm Antibody	Cold Antibody
Antibody	IgG (± IgA)	IgM
Temp	37°C	<30°C
Hemolysis	Extravascular (spleen)	Extravascular (liver/spleen)
Smear	Spherocytes	RBC agglutination
Special feature	Splenomegaly	Raynaud phenomenon

-> The End <-