Hemolytic anemia

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Definition and Classification

- **destruction of RBCs**.
- It can be classified into two main categories:
  - **Congenital / Hereditary**:
    - hereditary spherocytosis,
    - G6PD deficiency, and
    - hemoglobinopathies.
  - **Acquired: Caused by external factors**
    - autoimmune reactions,
    - infections, and
    - mechanical trauma

Pathophysiology

- **Intracorpuscular defects**:
  - membrane abnormalities
  - enzyme deficiencies.
- **Extracorpuscular factors**: External factors that lead to RBC destruction,
  - autoimmune processes
  - infections

Immune-Mediated Hemolysis

- **Complement-Activated Autoantibodies**:
- antibodies bind to RBCs and activate the complement system, leading to the formation of the membrane attack complex, which causes lysis of RBCs either intravascularly or extravascularly, often in the spleen

- **Non-Complement-Activated Autoantibodies**:
- antibodies bind to RBCs without activating the complement system, leading to phagocytosis by macrophages

Types of Congenital Hemolytic Anemia

1. Hereditary Spherocytosis

- **Description:**
  - A condition where RBCs are spherical rather than the typical biconcave shape due to defects in membrane proteins (e.g., spectrin, ankyrin).
- **Symptoms**:
  - Chronic anemia, jaundice, splenomegaly, and increased risk of gallstones.
- **Genetics:**
  - Often inherited in an autosomal dominant pattern.

2. Hereditary Elliptocytosis

- **Description:**
  - Characterized by elliptical-shaped RBCs that are less stable and more prone to hemolysis.
- **Symptoms**:
  - Generally milder than HS but may include fatigue and jaundice.
- **Genetics:**
  - Typically inherited in an autosomal dominant manner

stomatocytosis

- Hereditary Stomatocytosis:
  - inherited as an autosomal dominant trait and can manifest as severe hemolytic anemia early in life.
  - It involves a defect in the red blood cell membrane that causes a leak of sodium and potassium ions.
  - Hereditary stomatocytosis includes xerocytosis (dehydrated hereditary stomatocytosis) and overhydrated hereditary stomatocytosis.
- Acquired Stomatocytosis:
  - This type can be associated with conditions like acute alcoholism, liver disease, Rh null phenotype, lead poisoning or certain medications

3. Glucose-6-Phosphate Dehydrogenase (G6PD) Deficiency

- **Description**:
  - An enzyme deficiency that leads to increased susceptibility of RBCs to oxidative stress.
- **Symptoms:**
  - Episodes of hemolytic anemia triggered by infections, certain medications, or foods (e.g., fava beans).
- **Genetics:**
  - X-linked recessive inheritance.

4. Pyruvate Kinase Deficiency

- **Description:**
  - A deficiency in the enzyme pyruvate kinase, crucial for glycolysis, leading to energy depletion in RBCs.
- **Symptoms:**
  - Chronic hemolytic anemia, jaundice, and splenomegaly.
- **Genetics:**
  - Autosomal recessive inheritance.

5. Congenital Dyserythropoietic Anemia

- **Description:**
  - ineffective erythropoiesis and morphological abnormalities in bone marrow erythroblasts.

- **Types:**
  - CDA Type I: Binucleated erythroblasts; caused by mutations in CDAN1 or c15orf41.
  - CDA Type II: multinucleated erythroblasts; caused by mutations in SEC23B.

6. Sickle Cell Disease

- **Description:**
  - mutation in the beta-globin gene leading to the production of abnormal hemoglobin (HbS), which distorts RBCs into a sickle shape under low oxygen conditions.
- **Symptoms:**
  - Severe pain episodes, anemia, increased risk of infections, and organ damage due to vaso-occlusive crises.

Acquired Hemolytic Anemia

Immune-mediated

- Autoimmune hemolytic anemia (AIHA)
  - Warm autoimmune hemolytic anemia (WAIHA)
  - Cold agglutinin disease
- Alloimmune hemolytic anemia (e.g., hemolytic disease of the newborn, transfusion reactions)
- Drug-induced hemolytic anemia (e.g., penicillin, methyldopa)

Non-immune-mediated

- Microangiopathic hemolytic anemia (MAHA) (e.g., thrombotic thrombocytopenic purpura, hemolytic uremic syndrome)
- Mechanical trauma (e.g., prosthetic heart valves)
- Infections (e.g., malaria)
- Toxins (e.g., snake venom)

Laboratory Evaluation

- Complete blood count (CBC):
  - To evaluate anemia severity.
- Reticulocyte count:
  - Indicates bone marrow response to anemia.
- Blood smear:
  - spherocytes, schistocytes, or bite cells depending on the type of hemolysis.
- Biochemical markers:
  - Elevated bilirubin, lactate dehydrogenase (LDH), and decreased haptoglobin levels are indicative of hemolysis.

Clinical Features

- Fatigue and weakness due to anemia.
- Jaundice from increased bilirubin levels.
- Dark urine due to hemoglobinuria in cases of intravascular hemolysis.
- Splenomegaly, particularly in hereditary forms.

Types of Immune-Mediated Hemolysis

1. Warm Autoimmune Hemolytic Anemia (WAIHA)

- **Mechanism:**
  - IgG antibodies bind to RBCs at body temperature (37°C).
  - This leads to extravascular hemolysis, primarily in the spleen and liver.
- Causes:
  - Often idiopathic
  - Lymphoproliferative disorders (e.g., lymphoma, leukemia)
  - Viral infections (e.g., HIV, hepatitis)
  - Autoimmune diseases (e.g., lupus)

2. Cold Agglutinin-Mediated Hemolytic Anemia (CAD)

- Mechanism:
  - In CAD, IgM antibodies bind to RBCs at lower temperatures (typically below 30°C).
  - This can lead to both intravascular and extravascular hemolysis.
- Causes:
  - Mycoplasma pneumoniae
  - Infectious mononucleosis (EBV)
  - Certain lymphoproliferative disorders

3. Paroxysmal Cold Hemoglobinuria (PCH)

- Mechanism:
  - PCH is characterized by the presence of Donath-Landsteiner antibodies that cause hemolysis when exposed to cold temperatures.
- Causes:
  - Often associated with viral infections, particularly in children, and can occur following exposure to cold environments.

Treatment Approaches

1. Supportive Care

- Blood Transfusions:
  - Used to increase red blood cell counts and alleviate symptoms of anemia, particularly in severe cases

- Iron Supplementation:
  - May be necessary if there is iron deficiency due to hemolysis or treatment

2. Pharmacological Treatments

- Corticosteroids:
  - Prednisone is commonly used to suppress the immune system in autoimmune hemolytic anemia (AIHA), limiting the destruction of red blood cells.
- Intravenous Immunoglobulin (IVIG):
  - This treatment can help decrease the destruction of red blood cells, especially in cases of AIHA.
- Immunosuppressive Therapy:
  - Medications like rituximab and cyclosporine are used for patients who do not respond to corticosteroids. Rituximab is particularly effective in steroid-refractory cases.
- Hydroxyurea:
  - Used in sickle cell anemia to increase fetal hemoglobin production and reduce sickling episodes

3. Surgical Interventions

- Splenectomy:
  - patients with hereditary spherocytosis or those with AIHA who do not respond to medical therapy.
  - This procedure can significantly reduce hemolysis since the spleen is a primary site for red blood cell destruction.
  - Contraindicated in Stomatocytes

4. Advanced Therapies

- **Plasmapheresis:**
  - removes antibodies from the bloodstream and can be beneficial in severe cases where other treatments have failed.
- **Stem Cell Transplantation:**
  - Considered in refractory cases, particularly for patients with severe autoimmune hemolytic anemia or those with underlying hematological disorders