HEMOLYTIC ANEMIAS

INCREASE RED CELL DESTRUCTION = REDUCED RED-CELL LIFE SPAN

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HEMOLYTIC ANEMIAS

- A red blood cell survives 90 to 120 days in the circulation; about 1% of human red blood cells break down each day.

- The spleen is the main organ which removes old and damaged RBCs from the circulation.
MECHANISMS OF HEMOLYSIS

- Extravascular
  - red cells destruction occurs in reticuloendothelial system

- Intravascular
  - red cells destruction occurs in vascular space
SIGNS OF HEMOLYTIC ANEMIAS

- Symptoms of anemia – pallor, fatigue, rapid pulse
- Jaundice
- Splenomegaly
DIAGNOSIS OF HEMOLYTIC ANEMIAS

- Anemia
- Reticulocytosis
- Indirect hyperbilirubinemia
  - Increased level of lactate dehydrogenase (LDH)
  - Absence or reduced of free serum haptoglobin
INTRAVASCULAR HEMOLYSIS

- laboratory signs of intravascular hemolysis:
  - tests for hemolysis
  and additionally:
  - hemoglobinemia
  - hemoglobinuria
  - hemosiderynuria
HEMOLYTIC ANEMIAS

Compensated hemolysis – increase erythropoiesis compensates increase destruction of erythrocytes

Decompensated hemolysis - erythropoiesis can not compensates increase destruction – patient needs therapy
COMPLICATIONS OF INCREASED, CHRONIC HEMOLYSIS

- Folinic acid deficiency
- Gallstones
- Thrombosis
- Hemolytic crisis
  - rapid destruction of large numbers of red blood cells
CLASSIFICATION OF HEMOLYTIC ANEMIAS

1. Hereditary
   a) Membrane defect (spherocytosis, elliptocytosis)
   b) Metabolic defect (Glucoze-6-Phosphate-Dehydrogenaze (G6PD) deficiency, Pyruvate kinase (PK) deficiency)
   c) Hemoglobinopathies (thalassemias, sickle cell anemia)

2. Acquired
   a) Immune hemolytic anemias
   b) Nonimmune hemolytic anemias
Hereditary membrane defects

I. Spherocytosis

- The most common defect of red cell membrane protein (1/2000 birth)
- Inheritance - autosomal dominant
- Deficient of membrane protein causes change of shape (round, no central pallor)
- Clinical features: jaundice, gallstones, splenomegaly, constitutional skeleton changes (ie tower cranium, gothic palate)
- Laboratory features: anemia, hiperbilirubinemia, retikulocytosis, ↑ LDH
  - blood smear - microspherocytes
  - abnormal osmotic fragility test
- Treatment - splenectomy
SPHEROCYTES
Hereditary membrane defects

2. Elliptocytosis
Hereditary metabolic defect

- Glucoze-6-Phosphate-Dehydrogenase (G6PD) deficiency
  - Hemolysis is induced by infections, drugs
  - Hemolysis is intravascular

- Pyruvate kinase (PK) deficiency
HEREDITARY HEMOGLOBINOPATHIES

- Thalassemias
  - Alfa thalassemia
  - Beta thalassemia: major, minor (trait), intermedia
  - Delta/Beta thalassemia
  - Hereditary persistence of fetal hemoglobin
- Sickle cell anemia
SICKLE CELL ANEMIA

**DEFINITION:** CHRONIC HEMOLYTIC ANEMIA CHARACTERIZED BY SICKLE-SHAPED RED CELLS CAUSED BY HOMOZYGOUS INHERITANCE OF HEMOGLOBIN S
SICKLE CELL ANEMIA - INCIDENCE

- Occurs mainly in people of African, Caribbean, Mediterranean descent
- Homozygous - about 0.3% of African Americans in the USA (have sickle cell anemia)
- Heterozygotes - 8-13% of African Americans (are not anemic, but the sickling trait = sicklemia can be demonstrated in vitro)
SICKLE CELL ANEMIA-PATHOGENESIS

- Hemolysis - because sickle RBCs are too fragile to withstand the mechanical trauma of circulation

- Occlusion in microvascular circulation caused by distorted, inflexible RBCs adhering to vascular endothelium
SICKLE CELL ANEMIA - CLINICAL FEATURES

IN HOMOZYGOTES

- Onset in the first or second year of life
- Period episodes of acute vascular occlusion (painful crisis)
- Consequences of vaso-occlusion of the microcirculations (tissue ischemia and infarction) - infarction of spleen, brain, marrow, kidney, lung, aseptic necrosis, central nervous system and ophtalmic vascular lesions
- Events which impair tissue oxygenation can precipitate crisis (f.e. pneumonia)
SICKLE CELL ANEMIA - THERAPY

Preventive measures:

prevention or remedy of: infections (penicillin prophylaxis and pneumococcal vaccination), fever, dehydration, acidosis, hypoxemia, cold exposure

Blood transfusions for very severe anemia

New approaches to therapy:

1. Activation of Hb F synthesis - 5-azacytidine
2. Antisickling agents acting on hemoglobin or membrane
3. Bone marrow transplantation
2. ACQUIRED

A. Immune hemolytic anemias
   1. **Autoimmune hemolytic anemia**
      - caused by warm-reactive antibodies
      - caused by cold-reactive antibodies
   2. Alloimmune hemolytic anemia (transfusion of incompatible blood)

B. Nonimmune hemolytic anemias
   1. Chemicals
   2. Bacterial infections, parasitic infections (malaria)
   3. Hemolysis due to physical trauma
      (e.g. microangiopathic hemolytic anemia)
   4. Hypersplenism
   5. Paroxysmal nocturnal hemoglobinuria (PNH)
AUTOIMMUNE HEMOLYTIC ANEMIA - AIHA

- caused by warm-reactive antibodies (70%)
  - infections, connective tissue disorders, drugs

- caused by cold-reactive antibodies (30%)
  - in temp. < 37 (4°)
  - infections, CLL, NHL

Laboratory findings: direct Coombs test (direct antiglobulin test)

Treatment: underlying disease, steroids, immunosuppressive
Avoid RBC transfusions
2. ACQUIRED

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   1. Chemicals
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ALLOIMMUNE HEMOLYTIC ANEMIA

- Transfusion of incompatible blood
- Serologic incompatibility
- After transplantation of bone marrow or organs
2. ACQUIRED

A. Immune hemolytic anemias

1. Autoimmune hemolytic anemia
   - caused by warm-reactive antibodies
   - caused by cold-reactive antibodies
2. Alloimmune hemolytic anemia

B. Nonimmune hemolytic anemias

1. Chemicals
2. Bacterial infections, parasitic infections (malaria)
3. Hemolysis due to physical trauma
   - microangiopathic hemolytic anemia
4. Hypersplenism
5. Paroxysmal nocturnal hemoglobinuria (PNH)
CLASSIFICATION OF MICROANGIOPATHIC HEMOLYTIC ANEMIA

- Thrombotic thrombocytopenic purpura (TTP)
- Hemolytic uremic syndrome (HUS)
MICROANGIOPATHIC HEMOLYTIC ANEMIA

- Intravascular hemolysis caused by fragmentation of normal red cells passing through abnormal arterioles
- Arterioles are changed by deposition of platelets and fibrin
- Microvascular lesion cause organ damage (kidney, CNS)
Normal red blood cell

Damaged red blood cell

Thrombotic Red Blood Cells
MICROANGIOPATHIC HEMOLYTIC ANAEMIA

Underlying disease

- Invasive carcinoma
- Complication of pregnancy
- Serious infection
- Drugs
MICROANGIOPATHIC HEMOLYTIC ANAEMIA

- Symptoms:
  - Related to the primary disease
  - Related to organs damage

- Laboratory findings

- Blood film: schistocytes
2. ACQUIRED

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   1. Autoimmune hemolytic anemia
      - caused by warm-reactive antibodies
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   2. Transfusion of incompatible blood

B. Nonimmune hemolytic anemias
   1. Chemicals
   2. Bacterial infections, parasitic infections (malaria)
   3. Hemolysis due to physical trauma
      - hemolytic - uremic syndrome (HUS)
      - thrombotic thrombocytopenic purpura (TTP)
      - prosthetic heart valves
   4. Hypersplenism
   5. Paroxysmal nocturnal hemoglobinuria (PNH)
HYPERSPLENISM

- State of hyperactivity of the spleen
- Causes of hypersplenism
  - Infection – bacterial, viruses, fungi
  - Inflammatory diseases -
  - Neoplasm
  - Storage disorders (Gaucher disease)
  - Other – amyloidosis, sarcoidosis
2. ACQUIRED

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Paroxysmal nocturnal hemoglobinuria (PNH)

PATHOGENESIS

- AN ACQUIRED CLONAL DISEASE, ARISING FROM A SOMATIC MUTATION IN A SINGLE ABNORMAL STEM CELL

- DEFICIENCY OF THE GPI (GLYCOSYL-PHOSPHATIDYL-INOSITOL) ANCHOR ON THE SURFACE OF HEMATOPOIETIC CELLS

- RED CELLS ARE MORE SENSITIVE TO THE LYTIC EFFECT OF COMPLEMENT

- INTRAVASCULAR HEMOLYSIS
PAROXYSMAL NOCTURNAL HEMOGLOBINURIA (PNH)

Symptoms

- Irregularly hemoglobinuria occurs with dark brown urine in the morning
- Hemolysis is released by infection, surgery or other events
- Increased risk of thrombosis
- Renal failure
- Neurologic manifestation - headaches
Paroxysmal nocturnal hemoglobinuria (PNH)

LABORATORY FEATURES
- HEMOGLOBINURIA
- HEMOSIDERINURIA
- PANCYTOPENIA
- CHRONIC URINARY IRON LOSS
- SERUM IRON CONCENTRATION DECREASED
- POSITIVE HAM’S TEST (ACID HEMOLYSIS TEST)
- SPECIFIC IMMUNOPHENOTYPE OF ERYTROCYTES (CD59, CD55)
Paroxysmal nocturnal hemoglobinuria (PNH)

TREATMENT

- WASHED RBC TRANSFUSION
- IRON THERAPY
- ALLOGENIC BONE MARROW TRANSPLANTATION

MONOCLONAL ANTIBODY ECULIZUMAB (TRADE NAME SOLIRIS)
WHAT DO YOU HAVE TO REMEMBER

Anemia +
1. Retikulocytosis
2. \( \uparrow \) bilirubin (unconjugated), \( \uparrow \) LDH
3. \( \downarrow \) haptoglobin
4. Haemoglobin and haemosiderin in urine