عنوان المحاضرة:
Hemolytic anemia

SAWA UNIVERSITY

جامعة ساوة

كلية التقنيات الصحية والطبية

قسم تقنيات المختبرات الطبية

المرحلة الثالثة

رقم المحاضرة **التاسعة**

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- Classification
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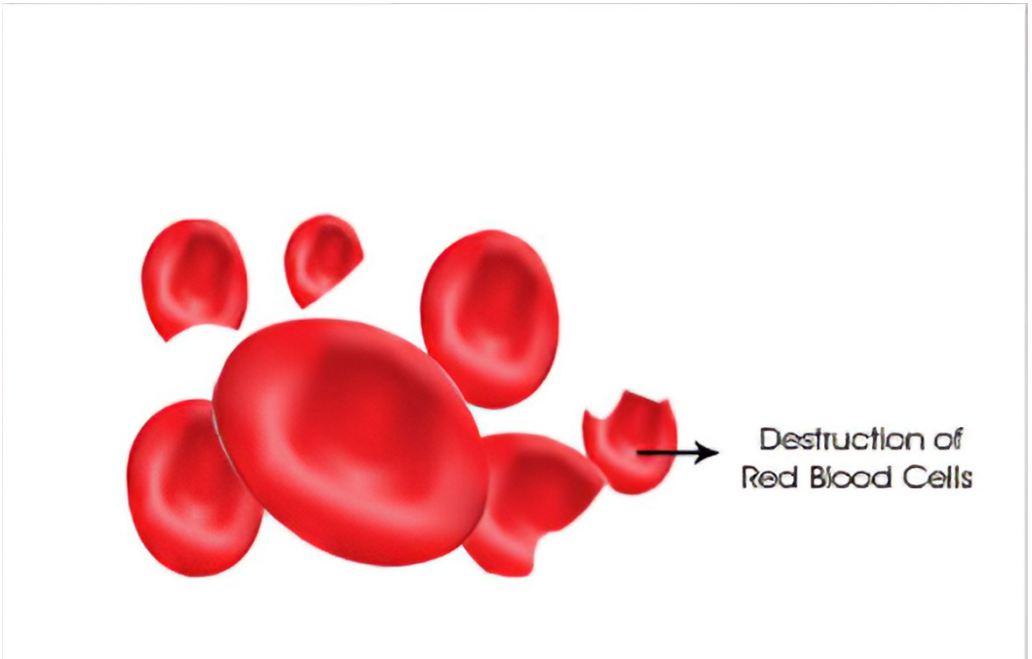
Hemolytic anemia



Normal red cell destruction

- Red blood cell destruction usually occurs after a mean lifespan of 120 days, as the cells have no nucleus, red cell metabolism gradually deteriorates as enzymes are degraded and the cells become non-viable.
- The aged red cells are removed by the macrophages of the reticuloendothelial (RE) system in the bone marrow and liver and spleen.
- Intravascular hemolysis plays little or no part in normal red cell destruction

Hemolytic anemia

- Anemia that result from an increased rate of red cell destruction (premature destruction of RBC).

- The normal bone marrow, is able to produce red cells at about 7 times the normal rate.

- Anemia due to hemolysis may not be seen until the red cell lifespan is less than 30 days

Clinical features of hemolytic anemia

- Pallor.
- Jaundice.
- Splenomegaly.
- Dark urine.
- Pigment gallstones

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- The laboratory findings :

1- Features of increased red cell breakdown:

- serum indirect bilirubin raised.
- urine urinobilinogen increased.
- serum haptoglobins absent because the haptoglobins become saturated with hemoglobin.

2- Features of increased red cell production:

- Increased retic count (reticulocytosis)
- bone marrow erythroid hyperplasia.

3- Damaged red cells:

- morphology (e.g. microspherocytes, fragments).
- osmotic fragility.

Bite RBC

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Classification

Classifications according to the 1. site of destruction of the red cells:

Extravascular hemolysis

(removal of red cells by cells of the RE system).

Intravascular hemolysis

(destruction directly in the circulation).

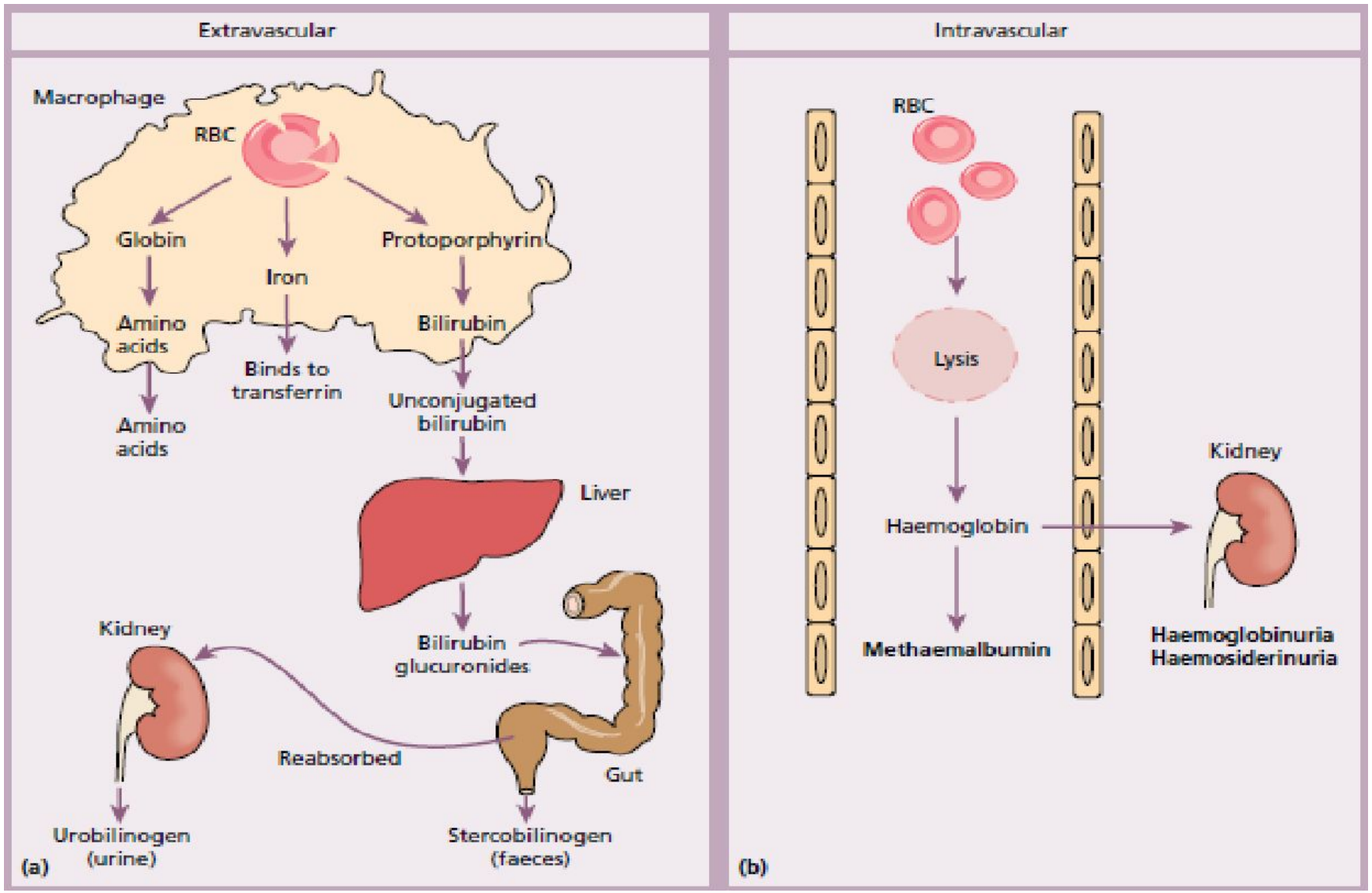
Classifications according to 2. underlying pathology:

Hereditary hemolytic anemia are the result of

'intrinsic' red cell defects.

Acquired hemolytic anemia .

According to the site of RBC breakdown (Mechanism of haemolysis)



Classification of haemolytic anemia :

Hereditary	Acquired
Membrane Hereditary spherocytosis, hereditary elliptocytosis	**Immune** *Autoimmune* Warm antibody type Cold antibody type
Metabolism G6PD deficiency, pyruvate kinase deficiency	*Alloimmune* Haemolytic transfusion reactions Haemolytic disease of the newborn Allografts, especially stem cell transplantation
Haemoglobin Genetic abnormalities (Hb S, Hb C, unstable); see Chapter 7	*Drug associated*
	Red cell fragmentation syndromes See Table 6.6
	March haemoglobinuria
	Infections Malaria, clostridia
	Chemical and physical agents Especially drugs, industrial/domestic substances, burns
	Secondary Liver and renal disease
	Paroxysmal nocturnal haemoglobinuria

Hereditary hemolytic anemia

- Red cell Membrane defects

  Hereditary Spherocytosis (HS)

- HS is usually caused by defects in the proteins:

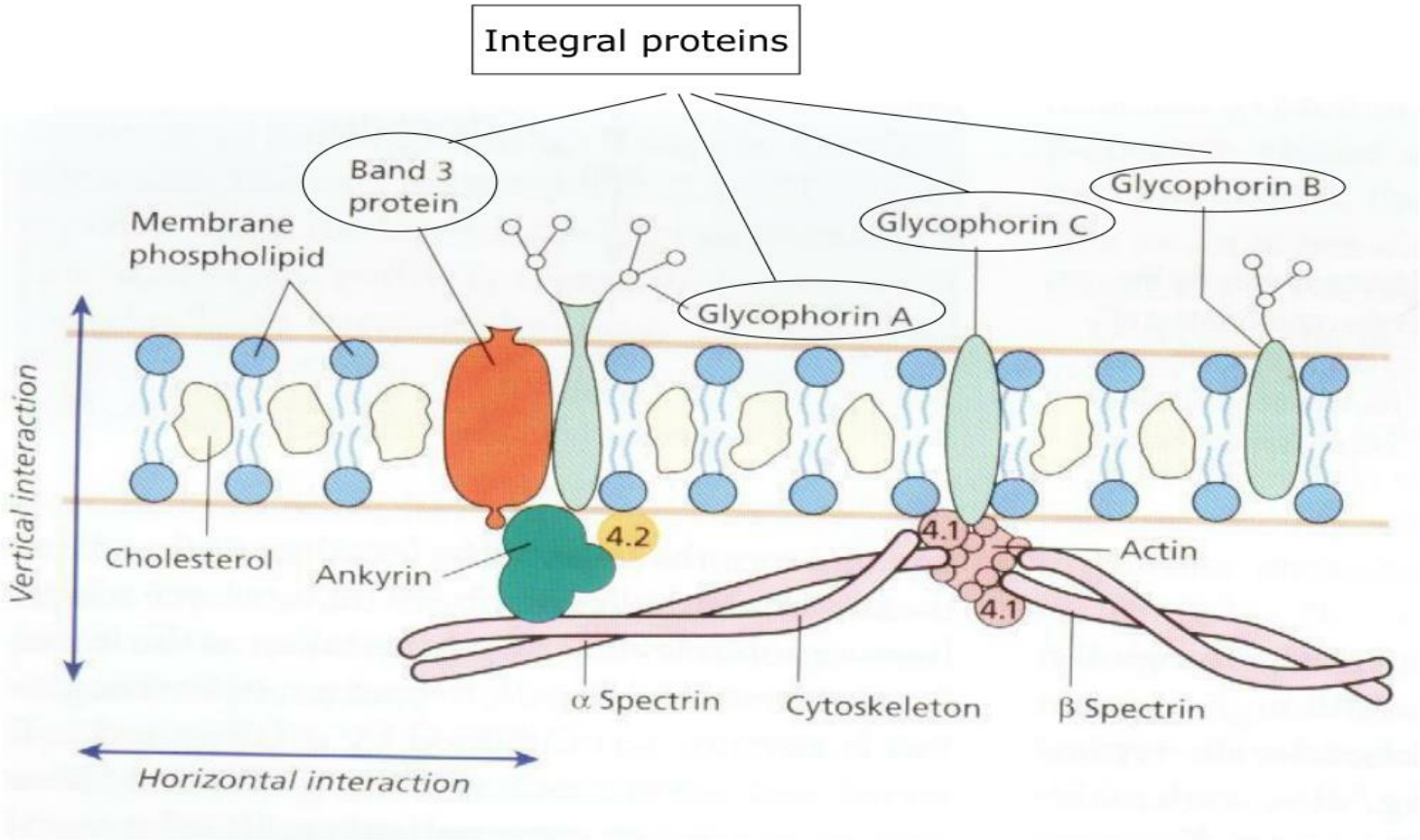
o Ankyrin

o α- or β-spectrin

o Band 3

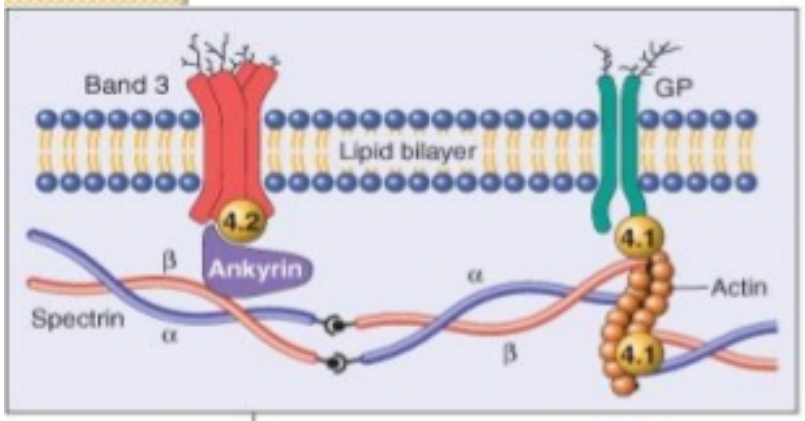
o protein 4.2

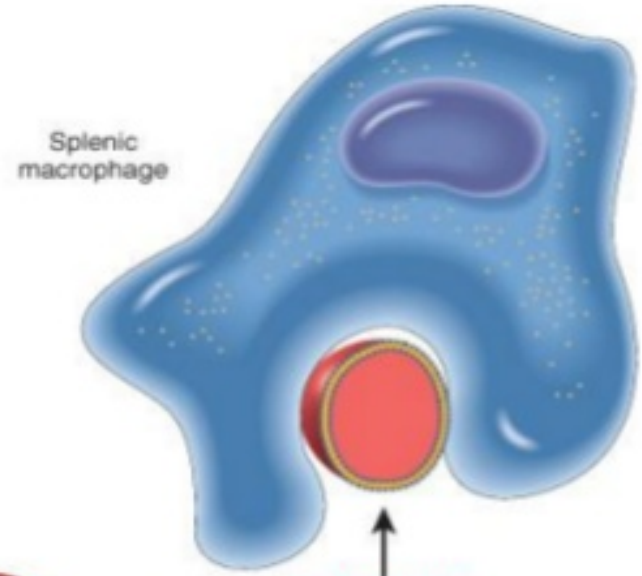
involved in the vertical interactions between cell membrane skeleton and lipid bilayer of the red cell.

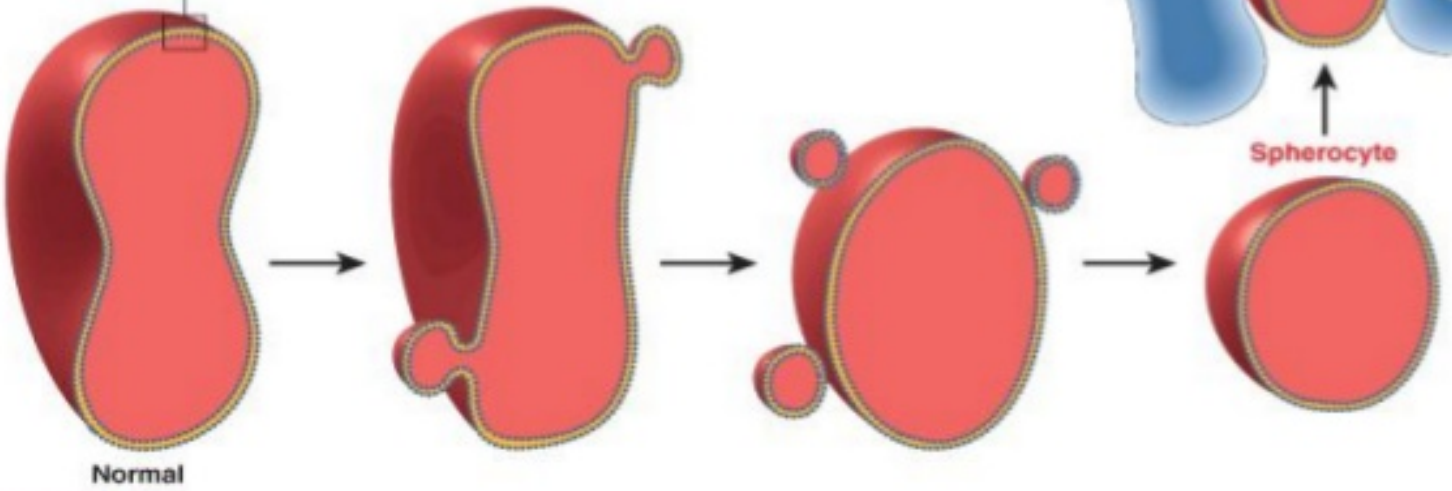

Integral proteins
Band 3 protein
Membrane phospholipid
Glycophorin A
Glycophorin C
Glycophorin B
Vertical interaction
Cholesterol
Ankyrin
4.2
4.1
Actin
4.1
α Spectrin
Cytoskeleton
β Spectrin
Horizontal interaction

- The bone marrow produces red cells of normal biconcave shape but these lose membrane and become spherical (loss of surface area relative to volume).
- • The loss of membrane caused by the release of parts of the lipid bilayer that are not supported by the skeleton.
- • the spherocytes are unable to pass through the microcirculation, especially in the spleen, and die prematurely

spherocytosis







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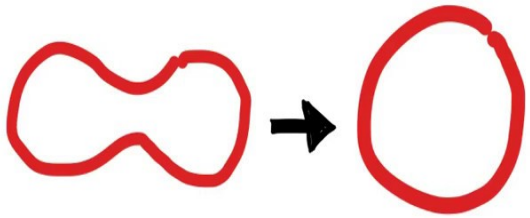
- HS autosomal dominant; rarely autosomal recessive.

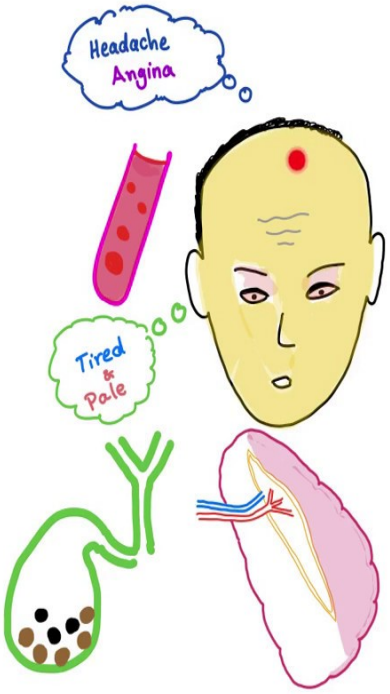
Investigation

- Anemia.
  Jaundice
- Reticulocytosis.
- The blood film shows microspherocytes, which are densely staining with smaller diameters than normal red cells.

- Osmotic fragility test.

Hereditary Spherocytosis





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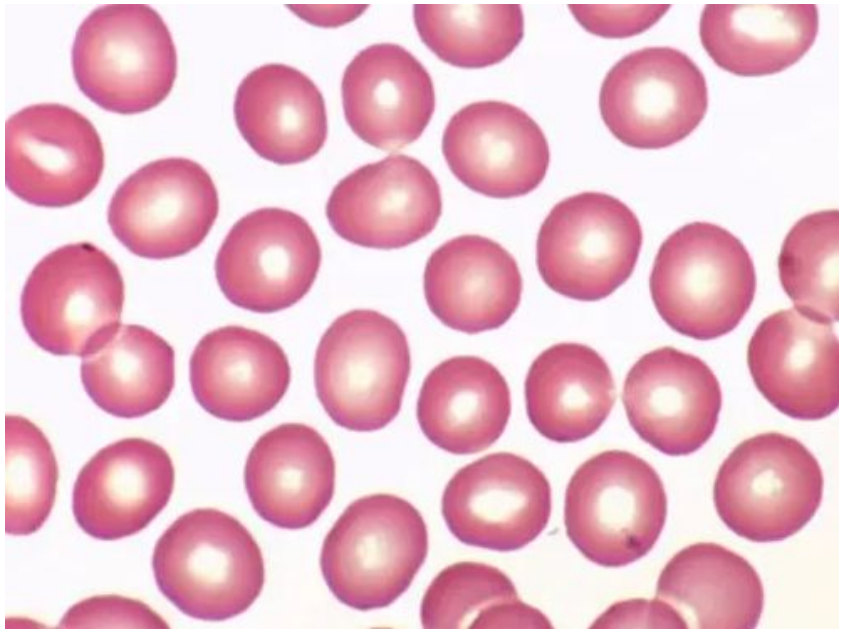
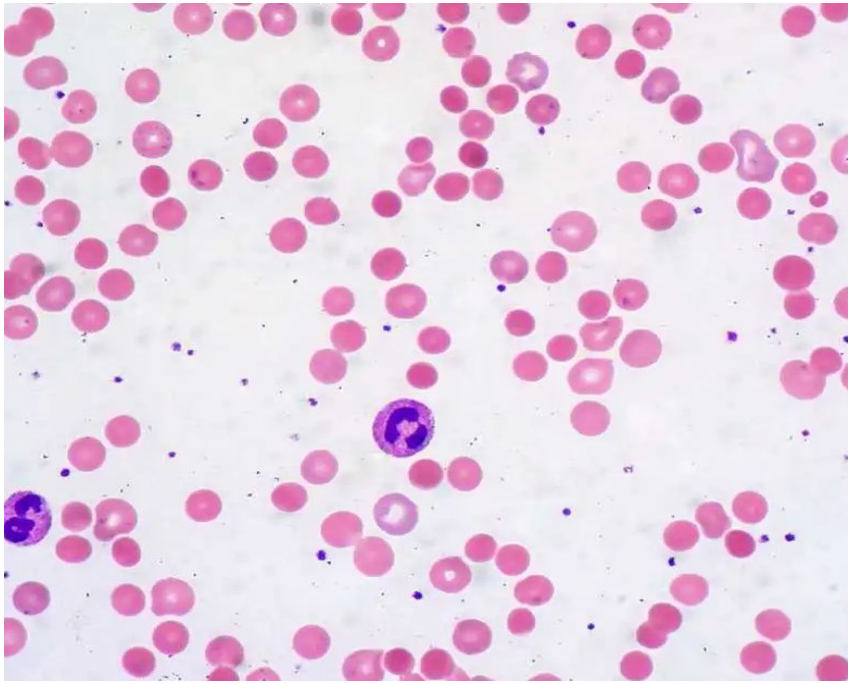
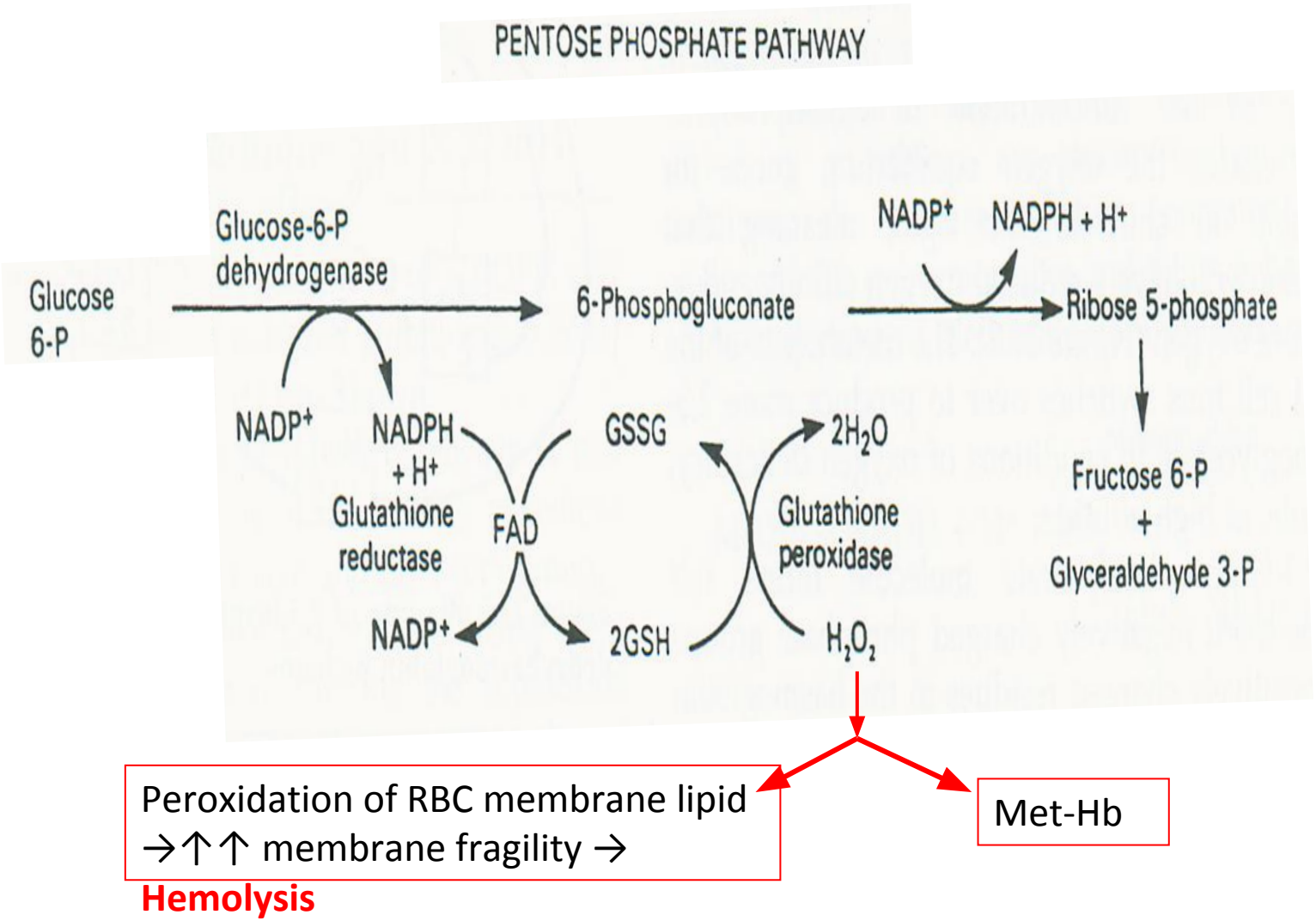




Metabolism defects G6PD deficiency

- Glucose-6-phosphate dehydrogenase (G6PD) is reducing agent, which is needed for the production of reduced glutathione; a deficiency renders the red cell susceptible to oxidant stress.
- There is a wide variety of normal genetic variants of the enzyme G6PD, the most common being type B in Western and type A in Africans.
- In addition, more than 400 variants caused by point mutations or deletions, producing G6PD enzyme with less activity than normal result in G6PD deficiency



damage by H_2O_2The function G6PD in the red cell is to generate NADPH → reduced glutathione → protect the RBCs from the oxidative

Inheritance:

- X -linked, affecting males, and carried by females who show approximately half the normal red cell G6PD values. The female heterozygotes

Clinical features:

G6PD deficiency does not cause any symptoms unless the patient takes fava beans or drugs, such as the anti-malarial primaquine.

The administration of these drugs causes rapid and often severe hemolysis and jaundice (intravascular) in response to oxidant stress

Normal blood count between attacks of hemolysis.

1- Acute haemolytic anaemia in response to oxidant stress

Infections and other acute illnesses (e.g. diabetic ketoacidosis)
Drugs
Antimalarials (e.g. primaquine, pamaquine, chloroquine, Fansidar®, Maloprim®)
Sulphonamides and sulphones (e.g. co-trimoxazole, sulfanilamide, dapsone, Salazopyrin®)
Other antibacterial agents (e.g. nitrofurans, chloramphenicol)
Analgesics (e.g. aspirin), moderate doses are safe
Antihelminths (e.g. β-naphthol, stibophen)
Miscellaneous (e.g. vitamin K analogues, naphthalene (mothballs), probenecid)
Fava beans (possibly other vegetables)

Diagnosis

Between hemolysis :

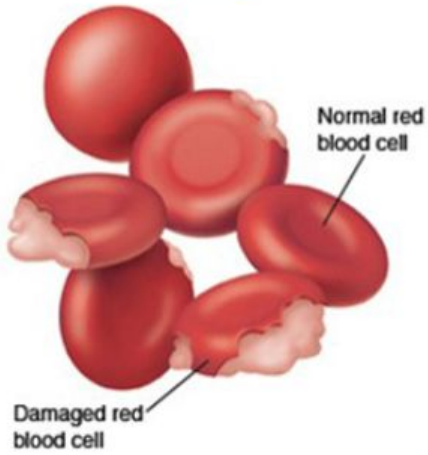
the blood count is normal.

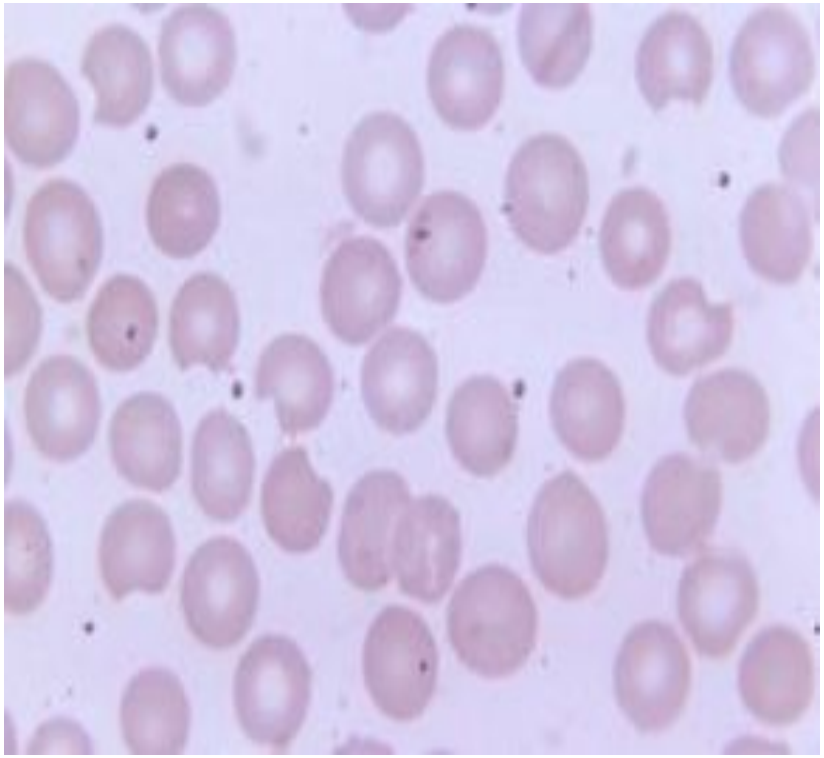
The enzyme deficiency is detected by G6PD enzyme assay.

During hemolysis :

- The blood film may show contracted and fragmented cells, bite cells and blister cells with reticulocytosis
- Because of the higher enzyme level in young red cells (reticulocyte), enzyme assay may give a ‘false’ normal level in the phase of acute hemolysis.

SYMPTOMS OF G6PD DEFICIENCY





Acquired hemolytic anemia

- Immune hemolytic anemia

Autoimmune hemolytic anemia

- (AIHA) are caused by autoantibody produced by the body against its own red cells.

They are characterized by a positive direct antiglobulin test (DAT), also known as the Coombs' test, and divided into 'warm' and 'cold' types according to whether the antibody reacts more strongly with red cells at 37°C or 4°C

Alloimmune hemolytic anemia

- In these anemia, antibody produced by one individual reacts with red cells of another.

Example:

o Transfusion of ABO-incompatible blood (hemolytic transfusion reaction).

o Rh hemolytic disease of the newborn.

o Allogeneic transplantation for renal, hepatic, cardiac or bone marrow grafts.

Drug-induced immune hemolytic anemia

- Drugs may cause immune hemolytic anemia via three mechanisms:

1. Antibody directed against a drug–red cell membrane complex (e.g. penicillin, ampicillin); this only occurs with massive doses of the antibiotic.

2. Deposition of complement via a drug–protein (antigen) – antibody complex onto the red cell surface (e.g. quinidine, rifampicin).

3. A true autoimmune hemolytic anemia in which the role of the drug is unclear (e.g. methyldopa). In each case, the hemolytic anemia gradually disappears when the drug is discontinued.

Red cell fragmentation syndromes MAHA

- These arise through physical damage to red cells either on abnormal surfaces (e.g. artificial heart valves or arterial grafts), arteriovenous malformations or as red cells passing through abnormal small vessels (microangiopathic hemolytic anemia), such as in DIC, TTP or vasculitis.
- The blood film contains many deeply staining red cell fragments.

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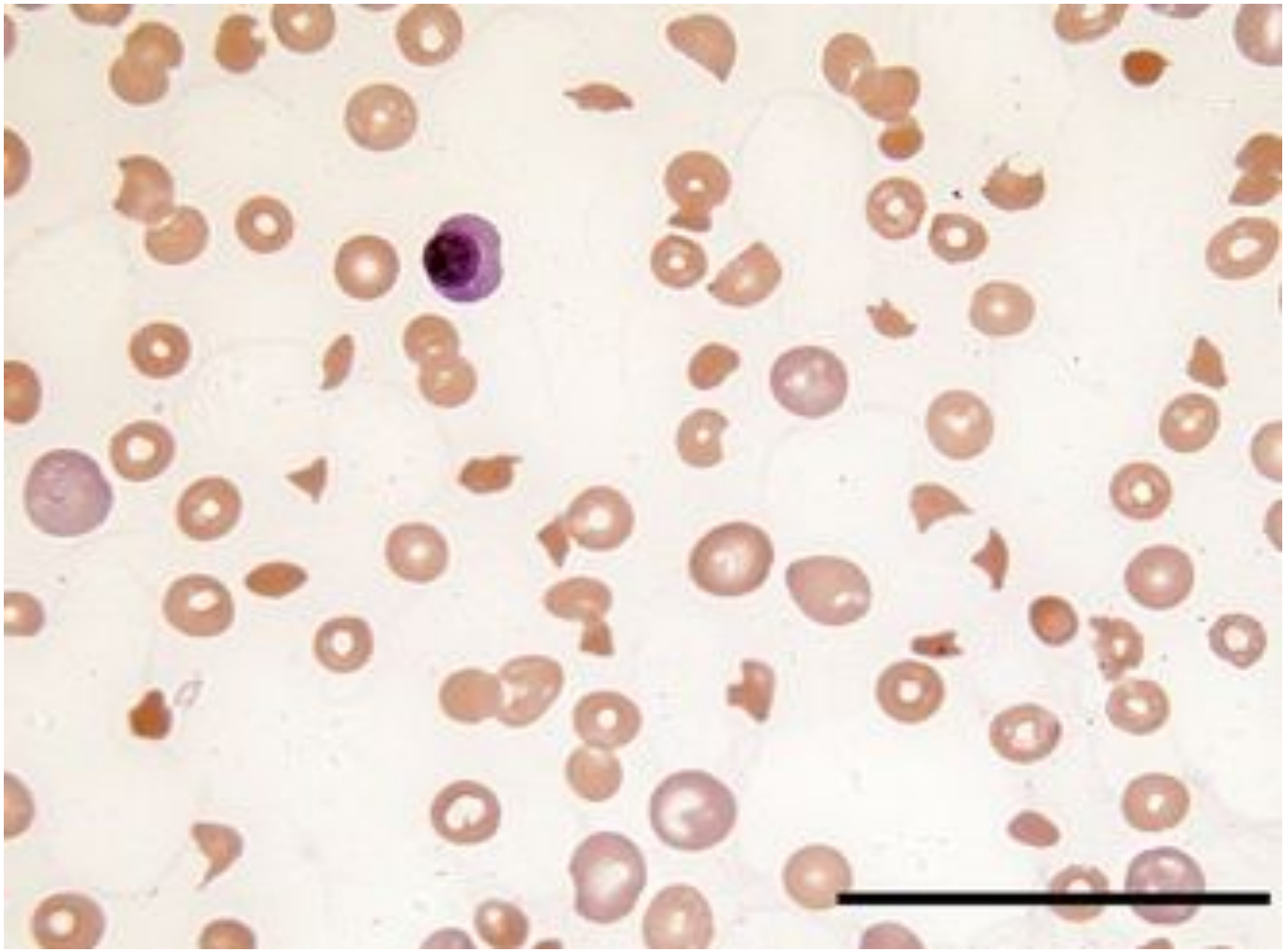


- March hemoglobinuria
- • This is caused by damage to red cells between the small bones of the feet, usually during prolonged marching or running.
- • The blood film does not show fragments.

- • Infections can cause hemolysis in a variety of ways:
- 1. Precipitate an acute hemolytic crisis in G6PD deficiency.
- 2. Microangiopathic hemolytic anemia (e.g. meningococcal or pneumococcal septicemia).
- 3. Malaria causes hemolysis by extravascular destruction of parasitized red cells as well as by direct intravascular lysis.
- 4. Clostridium perfringens septicemia can cause intravascular hemolysis with marked microspherocytosis

* T or F

Q1 Clinical features of hemolytic anemia

A. Pallor. B. Jaundice. C. Splenomegaly. D. Dark urine. E. Pigment gallstones

Q2 The laboratory findings OF hemolytic anemia :

A. serum indirect bilirubin raised .B. urine urinobilinogen increased. C. serum haptoglobins absent.

D. Increased retic count (reticulocytosis)

. Q3 In Hereditary hemolytic anemia

A. Anemia and Jaundice are presenting features B. Reticulocytosis.

C. The blood film shows microspherocytes, D. Osmotic fragility test. Positive

D. autosomal dominant; rarely autosomal recessive.

Q4 Hereditary spherocytosis hemolytic anemia

A. its Red cell Membrane defects

B. usually caused by defects in the proteins: Ankyrin , α- or β-spectrin

C. Its red cell enzyme defect D. globin chain synthesis defect E. autoantibodies against RBC

Q5 Autoimmune hemolytic anemia

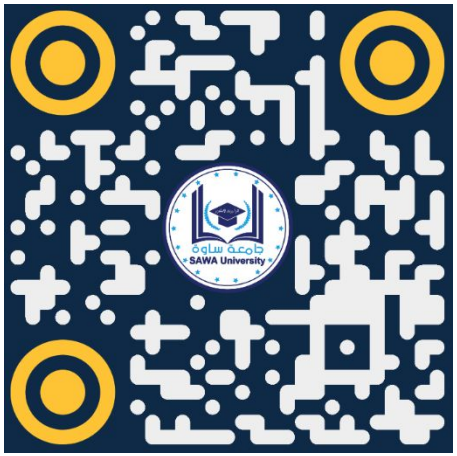
A. caused by autoantibody against own red cells.

B. diagnosed by a positive direct antiglobulin test (DAT)(Coombs' test)

C. divided into 'warm' and 'cold' antibodies

D. warm antibody reacts more strongly with red cells at 37°C

E . Cold antibody reacts more strongly with red cells at 4°C



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