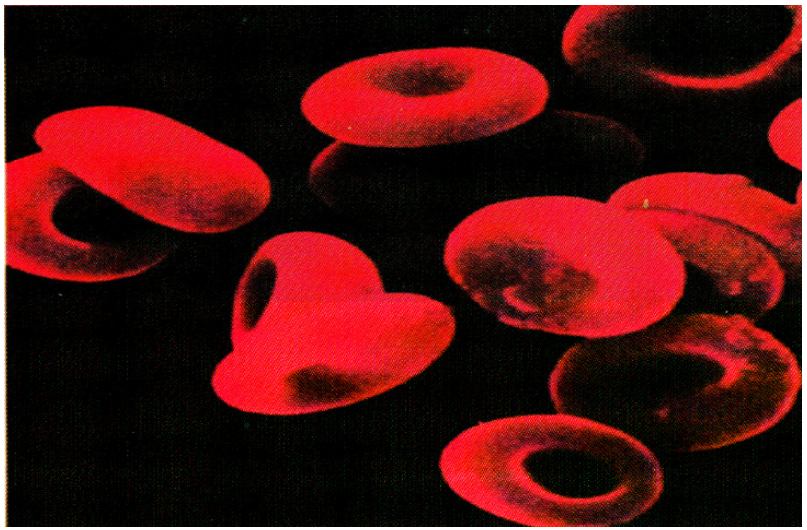
Red blood cell disorders



RBC disorders

- The Red Cell Disorders can be due to three major reasons:

1) Increased RBC Destruction (Hemolytic anemia).
2) Decreased RBC Production
3) Blood Loss .

Increased RBC Destruction

- **RBC disorders due to Increased RBC Destruction (Hemolytic anemia) include:**

1- Anemias secondary to **membrane disorders** (herditary spherocytosis, hereditary elliptocytosis)

2- **Enzyme deficiencies** (Glucose-6-phosphate dehydrogenase, pyruvate kinase).

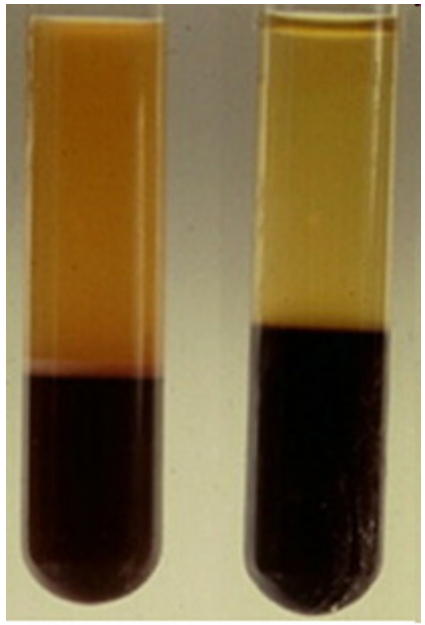
3- **Hemoglobin Abnormalities (hemoglobinopathies).**

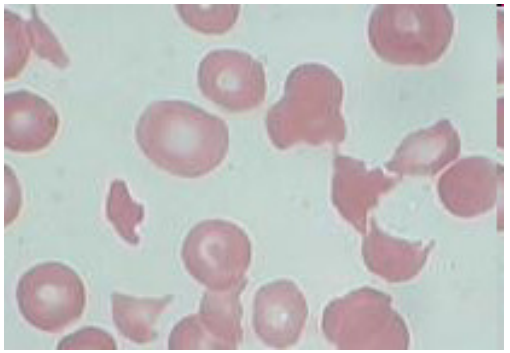
3- Antibody mediated destruction

4- Mechanical trauma.

Hemolytic anemia

- Increased destruction of red blood cells in the peripheral blood without evidence of ineffective erythropoiesis is known as hemolytic anemia.
- Normally when the RBCs become senescent (after 120 days) they are removed from the peripheral blood by macrophages in the spleen and liver.
- Hemolysis is the **premature destruction of RBCs** due to intrinsic inherited defects in the RBCs or because of acquired intravascular abnormalities.



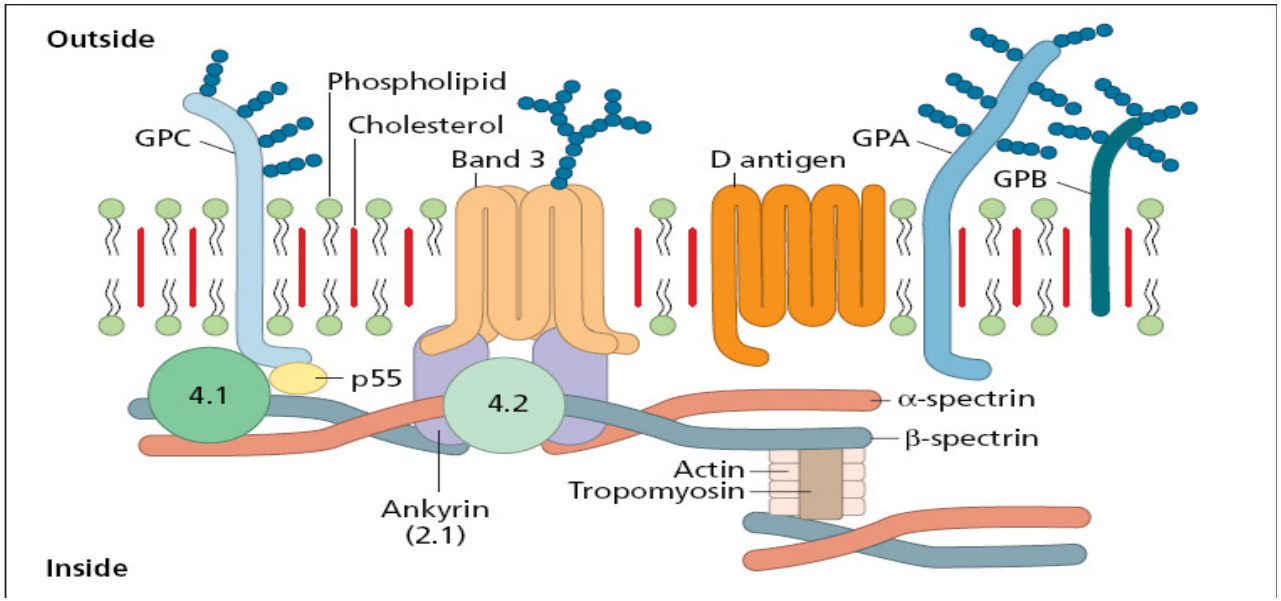


RBC morphology terms

- **Poikilocytosis** refer to an increase in abnormal red blood cells of any shape.

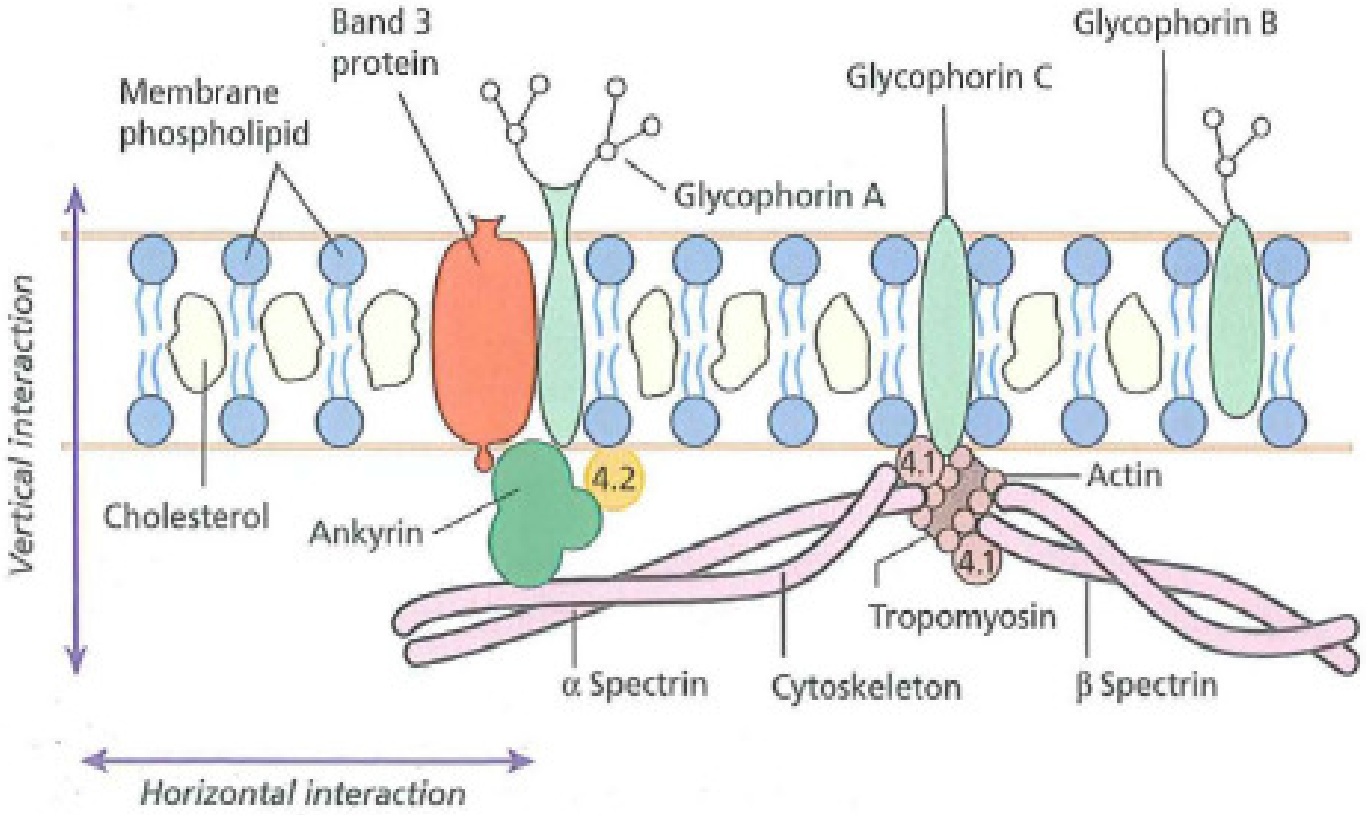
- **Anisocytosis** is a variation of the size of red blood cells.

Red cell membrane



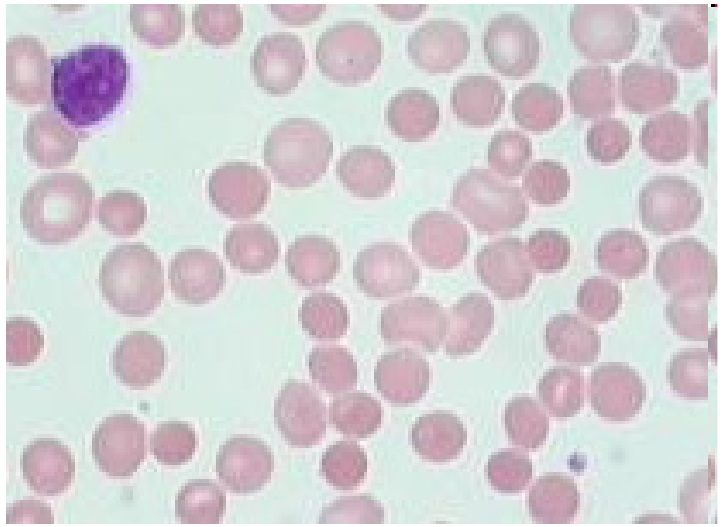
-The RBC membrane is a phospholipid bilayer with varying amounts of membrane cholesterol.
-A number of transmembrane (band 3 and several glycophorins) and membrane support [actin; ankryn (band2.1); band4.1; spectrin] proteins are present.
-The actin - spectrin - 4.1 complexes help maintain the structural strength and stability of the RBC membrane.
-The spectrin - ankryn - band 3 complexes stabilize the phospholipid bilayer.

Red cell membrane



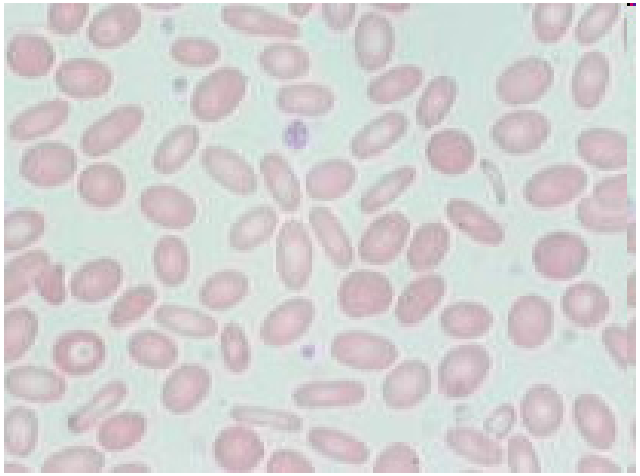
RBC Membrane Disorders

- Inherited red cell membrane defects include hereditary spherocytosis, hereditary elliptocytosis, hereditary stomatocytosis, and pyropoikilocytosis.
- Abnormalities of the red cell membrane result in hemolysis .
- **Hereditary spherocytosis** is characterized by numerous **spherocytes** on the PBS.
- It is caused by a molecular defect in one or more of the proteins of the red blood cell cytoskeleton, including, spectrin, ankyrin, Band 3, or Protein 4.2.
- Spherocytes have reduced surface membrane area relative to the RBC volume.
- Spherocytes are osmotically fragile compared to normal RBCs.

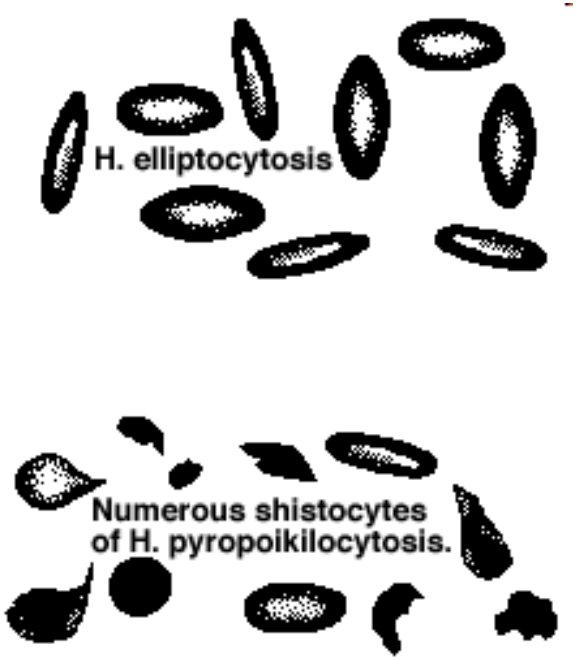


Hereditary spherocytosis

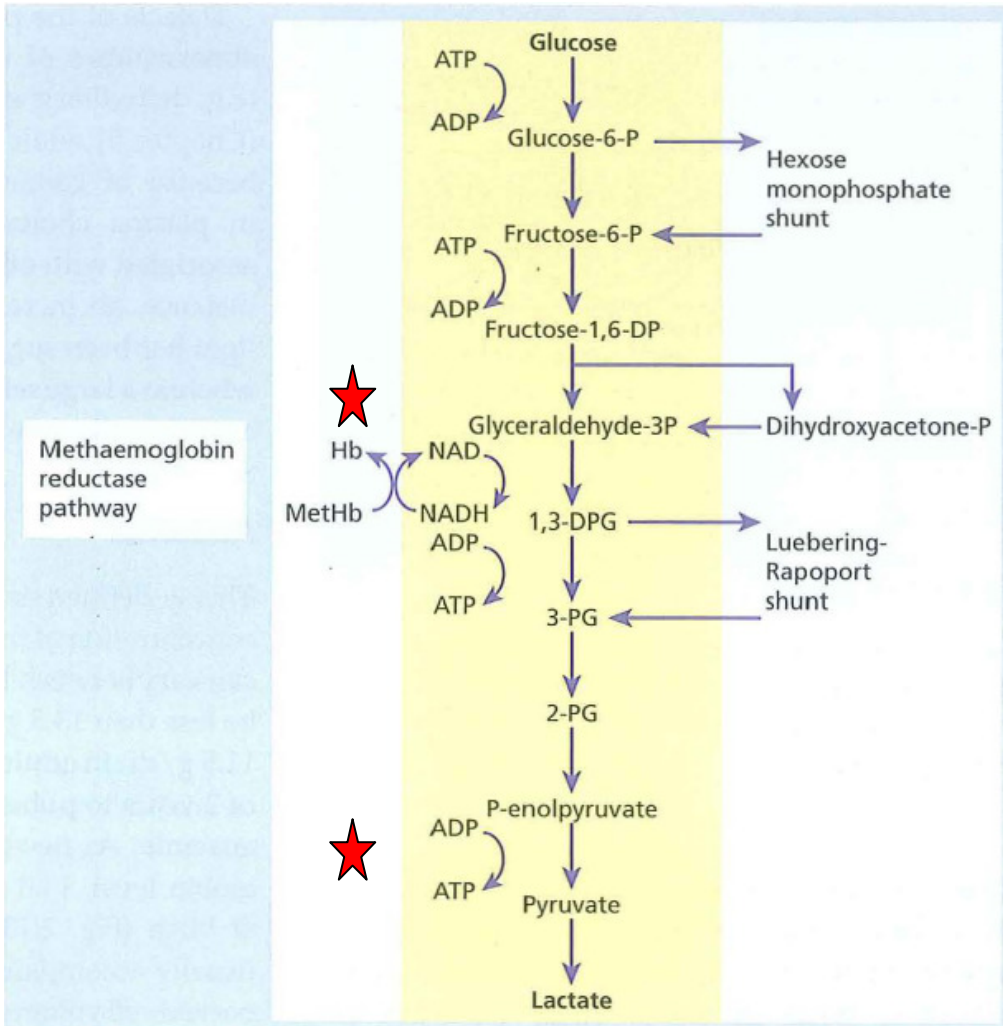
RBC Membrane Disorders



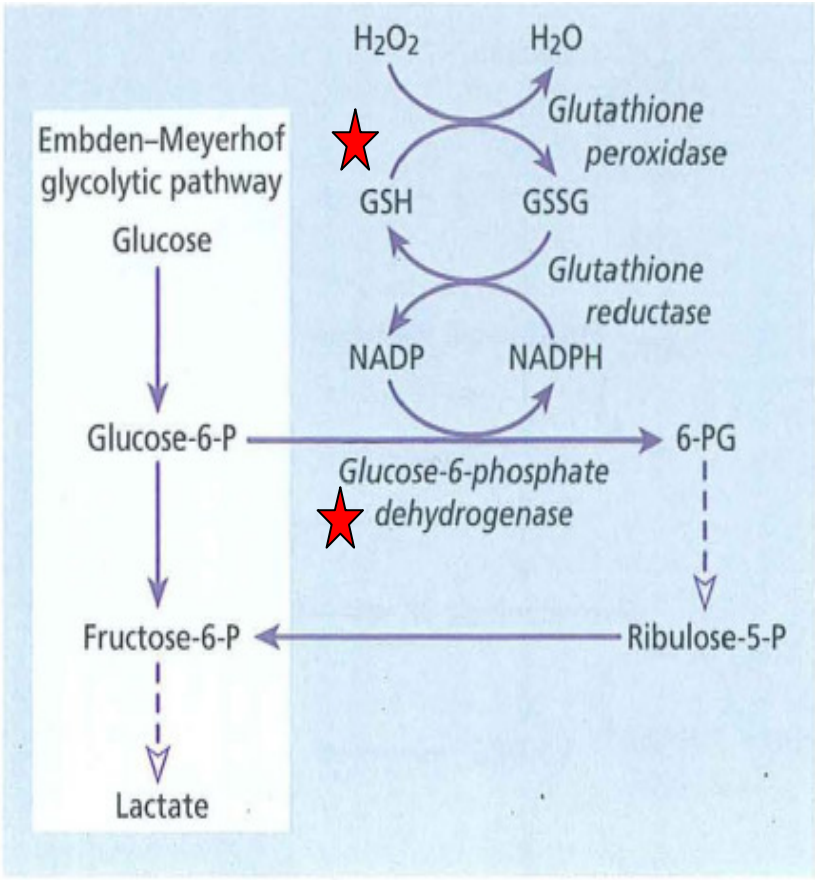
Hereditary elliptocytosis



Anemia related to RBC metabolism (enzymopathies)



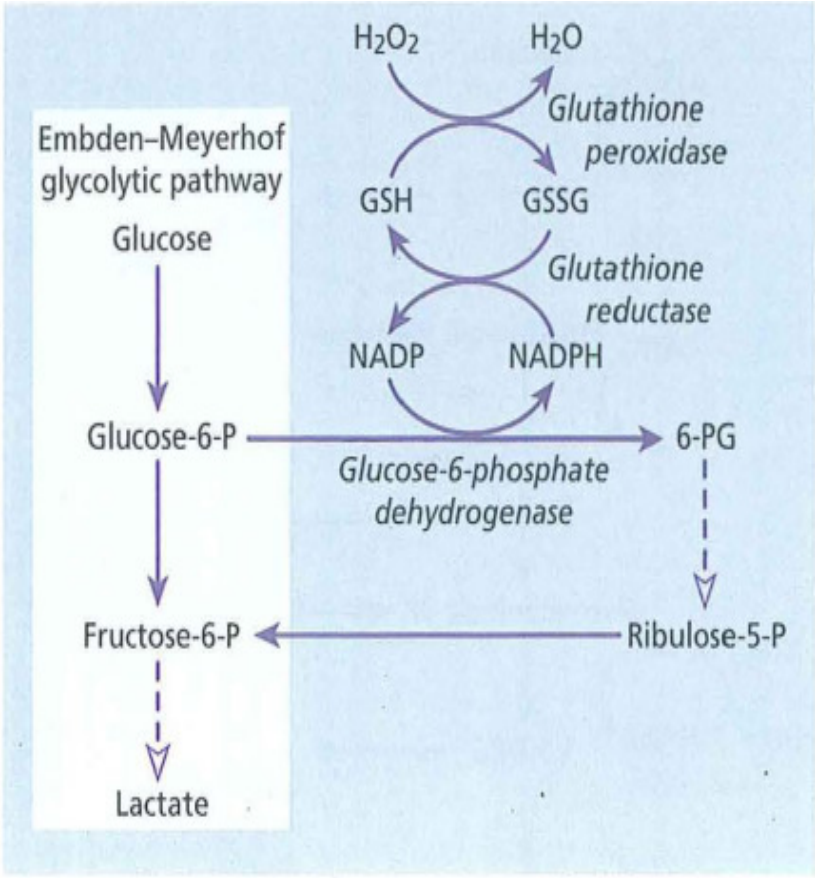
Embden-Meyerhof glycolytic pathway



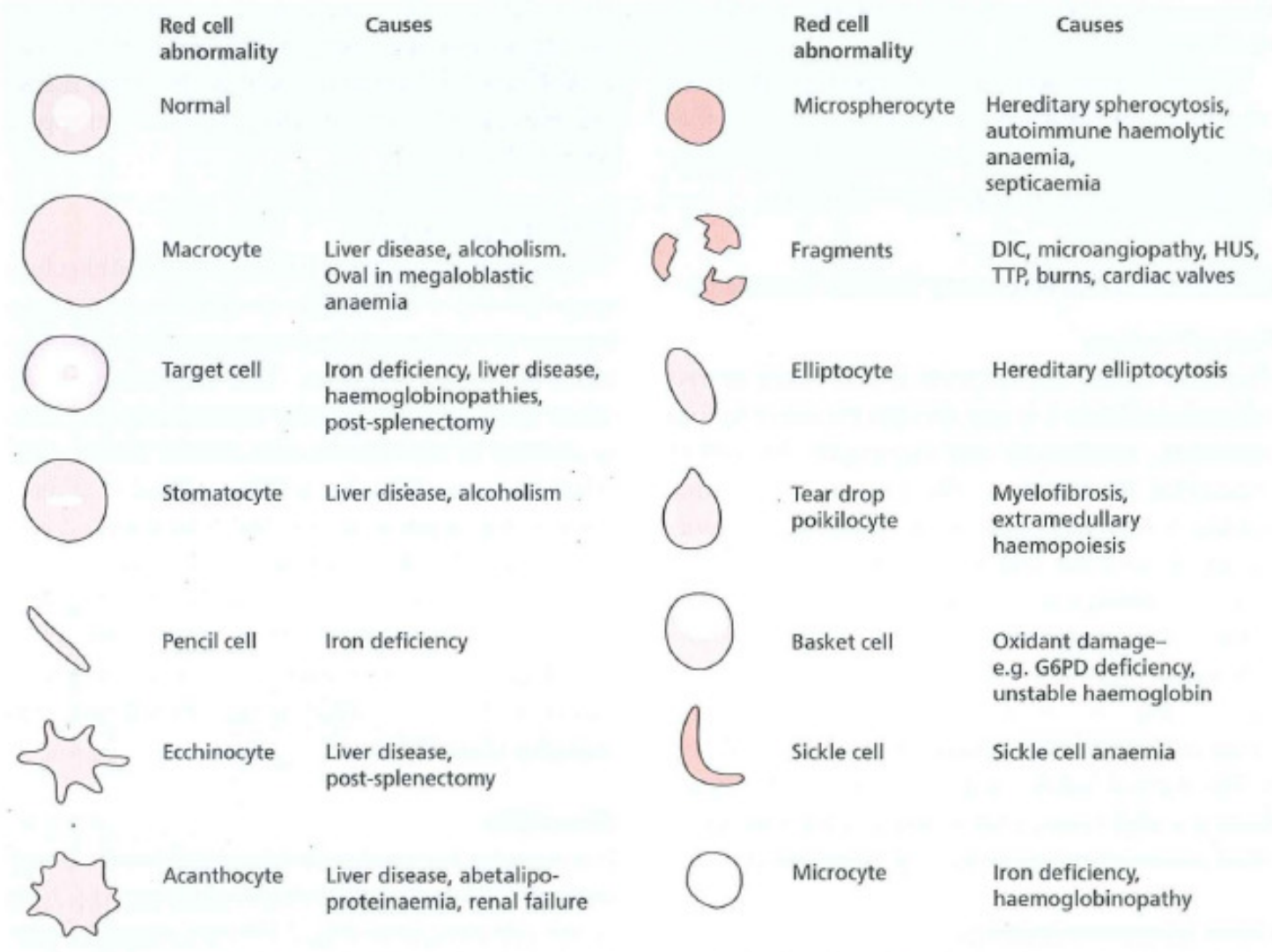
The hexose monophosphate shunt pathway

RBC Enzyme Deficiencies

- Glucose-6-phosphate dehydrogenase (**G-6-PD**) deficiency is the most common enzyme deficiency known to cause hemolysis.
- **G-6-PD** reduces NADP (nicotinamide-adenine-dinucleotide phosphate) to NADPH.
- NADPH reduces oxidized glutathione (GSSH) to its reduced form GSH.
- GSH prevents oxidation of RBC membranes and hemoglobin.



Some of the more frequent variations in size (anisocytosis) and shape (poikilocytosis) that may be found In different anaemias.

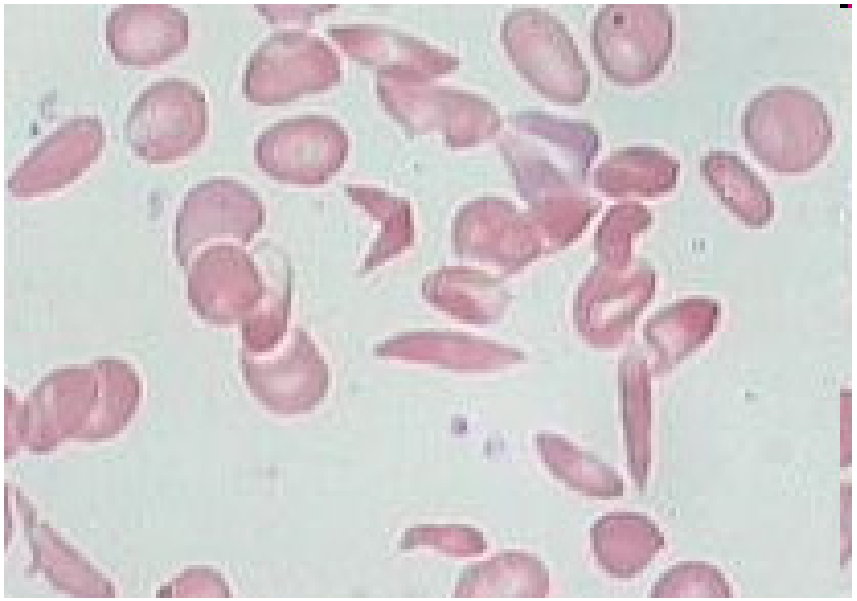


Red cell abnormality	Causes	Red cell abnormality	Causes
Normal		Microspherocyte	Hereditary spherocytosis, autoimmune haemolytic anaemia, septicaemia
Macrocyte	Liver disease, alcoholism. Oval in megaloblastic anaemia	Fragments	DIC, microangiopathy, HUS, TTP, burns, cardiac valves
Target cell	Iron deficiency, liver disease, haemoglobinopathies, post-splenectomy	Elliptocyte	Hereditary elliptocytosis
Stomatocyte	Liver disease, alcoholism	Tear drop poikilocyte	Myelofibrosis, extramedullary haemopoiesis
Pencil cell	Iron deficiency	Basket cell	Oxidant damage– e.g. G6PD deficiency, unstable haemoglobin
Ecchinocyte	Liver disease, post-splenectomy	Sickle cell	Sickle cell anaemia
Acanthocyte	Liver disease, abetalipo-proteinaemia, renal failure	Microcyte	Iron deficiency, haemoglobinopathy

Abnormalities of Hb synthesis

- Disorders of abnormal hemoglobin synthesis are called **hemoglobinopathies**.
- The hemoglobinopathies are inherited disorders.
- Hemoglobinopathies may result in hemolysis (25%) because of changes in hemoglobin solubility or because of instabilities in the hemoglobin molecule.
- Such changes are caused by either structural defects (eg, Sickle cell disease) or quantitative defects (beta-thalassemia; alpha-thalassemia).

Hemoglobinopathies



The most common example of the hemoglobinopathies is Hgb S or sickle cell anemia.

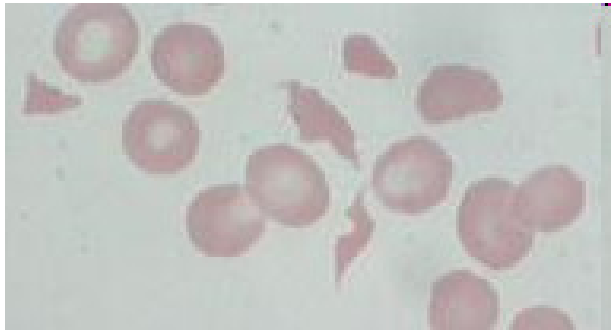
Antibody Mediated Hemolysis

- In autoimmune hemolytic anemia (AIHA) RBCs are destroyed by antibodies made by a person against their own RBCs.
- In AIHA the antibody coated RBC membrane is removed bit by bit, usually in the spleen.

DAT detects antibodies attached to the patient's RBCs

RBC destruction due to mechanical trauma.

- RBC fragmentation may be caused by RBCs striking against abnormal surfaces (aortic stenosis; atherosclerosis) or artificial surfaces (prosthetic heart valves; arterial grafts.(



Classification of haemolytic anaemias.

Hereditary	Acquired
Membrane Hereditary spherocytosis, hereditary elliptocytosis	**Immune** *Autoimmune* Warm antibody type (see Table 5.5) Cold antibody type
Metabolism G6PD deficiency, pyruvate kinase deficiency	*Alloimmune* Haemolytic transfusion reactions Haemolytic disease of the newborn Allografts, especially marrow transplantation
Haemoglobin Genetic abnormalities (Hb S, Hb C, unstable); see Chapter 6	*Drug associated* **Red cell fragmentation syndromes** See Table 5.6 **March haemoglobinuria** **Infections** Malaria, clostridia **Chemical and physical agents** Especially drugs, industrial/domestic substances, burns **Secondary** Liver and renal disease **Paroxysmal nocturnal haemoglobinuria**

G6PD, glucose-6-phosphate dehydrogenase; Hb, haemoglobin.

Decreased RBC Production

- **RBC disorders due to decreased RBC Production includes:**

1- Anemias secondary to decreased hemoglobin synthesis as in the microcytic anemias of **iron deficiency** and **thalessemia.**

2- The abnormalities of DNA synthesis as in the megaloblastic anemias (eg, lack of Vitamin B12).

3- Abnormalities of hematopoietic stem cell as in aplastic anemia.

4- Abnormalities of RBC precursors proliferation, and failure of differentiation as in anemia of chronic renal failure.

Decreased RBC Production

- **Decreased RBC production may result from a:**
- Defective stem cell (aplastic anemia).
- lack of a necessary structural component (eg, iron deficiency anemia).
- lack of an enzyme (Vitamin B12)
- unknown causes (anemia of chronic disease).

What is anemia ?

- Anemia is not a specific disease.

- Anemia can be defined as a reduction in the haemoglobin concentration of the blood.
- Symptoms of anemia include fatigue, weakness, Fainting , decreased appetite and occasionally chest pain, shock or congestive heart failure.
- Physical signs of anemia are manifest by pallor of the skin, nail beds, and mucous membranes (conjunctiva).
- It is critical to determine the cause of the anemia.
- The most useful parameters of the Complete Blood Count (CBC) to diagnose anemia are:

1-The Hematocrit (Hct)

2-Hemoglobin (Hgb)

3-Mean Corpuscular Volume (MCV).

Morphological Approach (big versus little)

First, measure the size of the RBCs:

- Use of volume-sensitive automated blood cell counters, such as the Coulter counter.
- The red cells pass through a small aperture and generate a signal directly proportional to their volume.
- Other automated counters measure red blood cell volume by means of techniques that measure refracted, diffracted, or scattered light
- By calculation from an independently-measured red blood cell count and hematocrit:

Red blood cell indices

- **Red blood cell indices** are blood tests that provide information about the Hb content and size of RBC.

RBC indices	Definition	Normal range	Formula
MCV	-Average size of a red blood cell. -calculated by dividing the hematocrit (Hct) by the red blood cell count.	80-95 fl	$MCV = \frac{Hct}{RBC}$
MCH	-Average amount of hemoglobin (Hb) per red blood. -calculated by dividing the hemoglobin by the red blood cell count	27-31 pg/cell	$MCH = \frac{Hb}{RBC}$
MCHC	- average concentration of hemoglobin per red blood. - calculated by dividing the hemoglobin by the hematocrit	32-36 g/dL	$MCHC = \frac{Hb}{Hct}$

Morphological classification of anemia

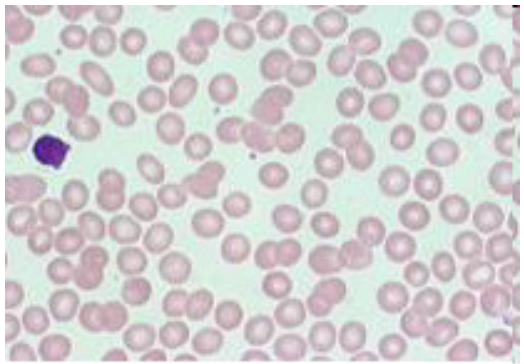
Table 2.4 Classification of anaemia.

Microcytic, hypochromic	Normocytic, normochromic	Macrocytic
MCV <80 fL	MCV 80–95 fL	MCV >95 fL
MCH <27 pg	MCH ≥27 pg	Megaloblastic: vitamin B_{12} or folate deficiency
Iron deficiency	Many haemolytic anaemias	Non-megaloblastic: alcohol, liver disease, myelodysplasia, aplastic anaemia, etc. (Table 4.11)
Thalassaemia	Anaemia of chronic disease (some cases)	
Anaemia of chronic disease (some cases)	After acute blood loss	
Lead poisoning	Renal disease	
Sideroblastic anaemia (some cases)	Mixed deficiencies	
	Bone marrow failure (e.g. post-chemotherapy, infiltration by carcinoma, etc.)	

MCH, mean corpuscular haemoglobin; MCV, mean corpuscular volume.

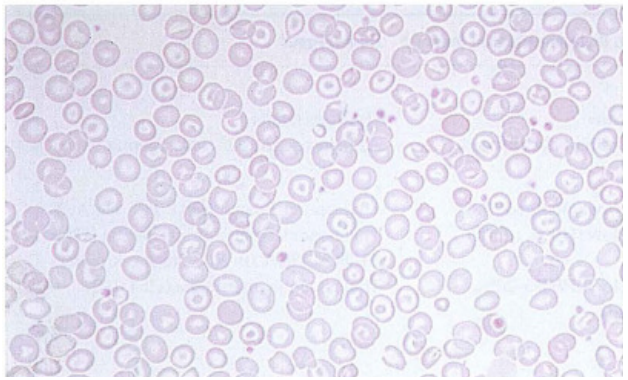
Morphological classification of anemia

Normocytic normochromic RBC

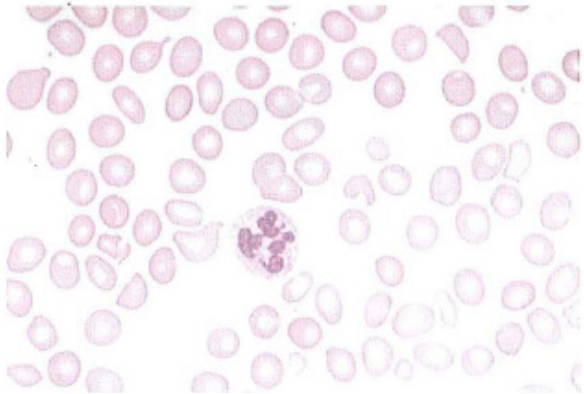


Normal PBS showing slight variation in the size and shape of the erythrocytes.

Microcytic hypochromic RBC



Macrocytic hypochromic RBC



Morphological classification of anemia

Table 2.4 Classification of anaemia.

Microcytic, hypochromic	Normocytic, normochromic	Macrocytic
MCV <80 fL	MCV 80–95 fL	MCV >95 fL
MCH <27 pg	MCH ≥27 pg	Megaloblastic: vitamin B_{12} or folate deficiency
Iron deficiency	Many haemolytic anaemias	Non-megaloblastic: alcohol, liver disease, myelodysplasia, aplastic anaemia, etc. (Table 4.11)
Thalassaemia	Anaemia of chronic disease (some cases)	
Anaemia of chronic disease (some cases)	After acute blood loss	
Lead poisoning	Renal disease	
Sideroblastic anaemia (some cases)	Mixed deficiencies	
	Bone marrow failure (e.g. post-chemotherapy, infiltration by carcinoma, etc.)	

MCH, mean corpuscular haemoglobin; MCV, mean corpuscular volume.