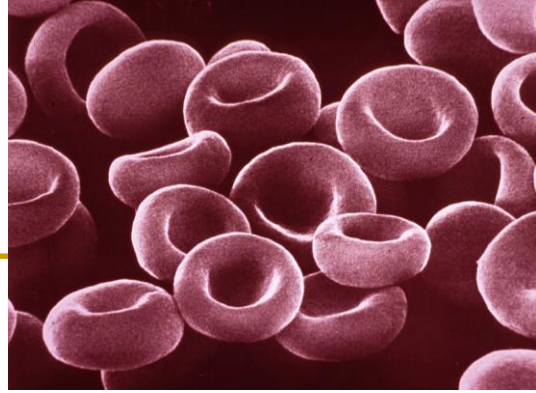


# Overview of Red Cell Haemolysis

MBCHB 3 Lecture series

Prof. J. N. Githang'a

# Lecture objective

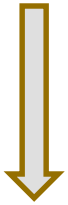
- *At the end of the lecture you should be able to:*
  - Define the terms: haemolysis, haemolytic disorder
  - Explain the pathophysiology of haemolysis
  - List the clinical features associated with haemolysis
  - Outline the investigation of a haemolytic condition

# Definitions

- **Haemolysis** is the destruction of erythrocytes with release of red cell contents
- **Haemolytic disorder:** There is premature destruction of the RBC with consequent shortening of the lifespan of the red cells
- Haemolysis leads to **hemolytic anemia** when bone marrow activity is unable to compensate for the red cell loss

# Consequences of haemolysis

- Increased catabolism of haemoglobin
- Compensatory bone marrow hyperplasia



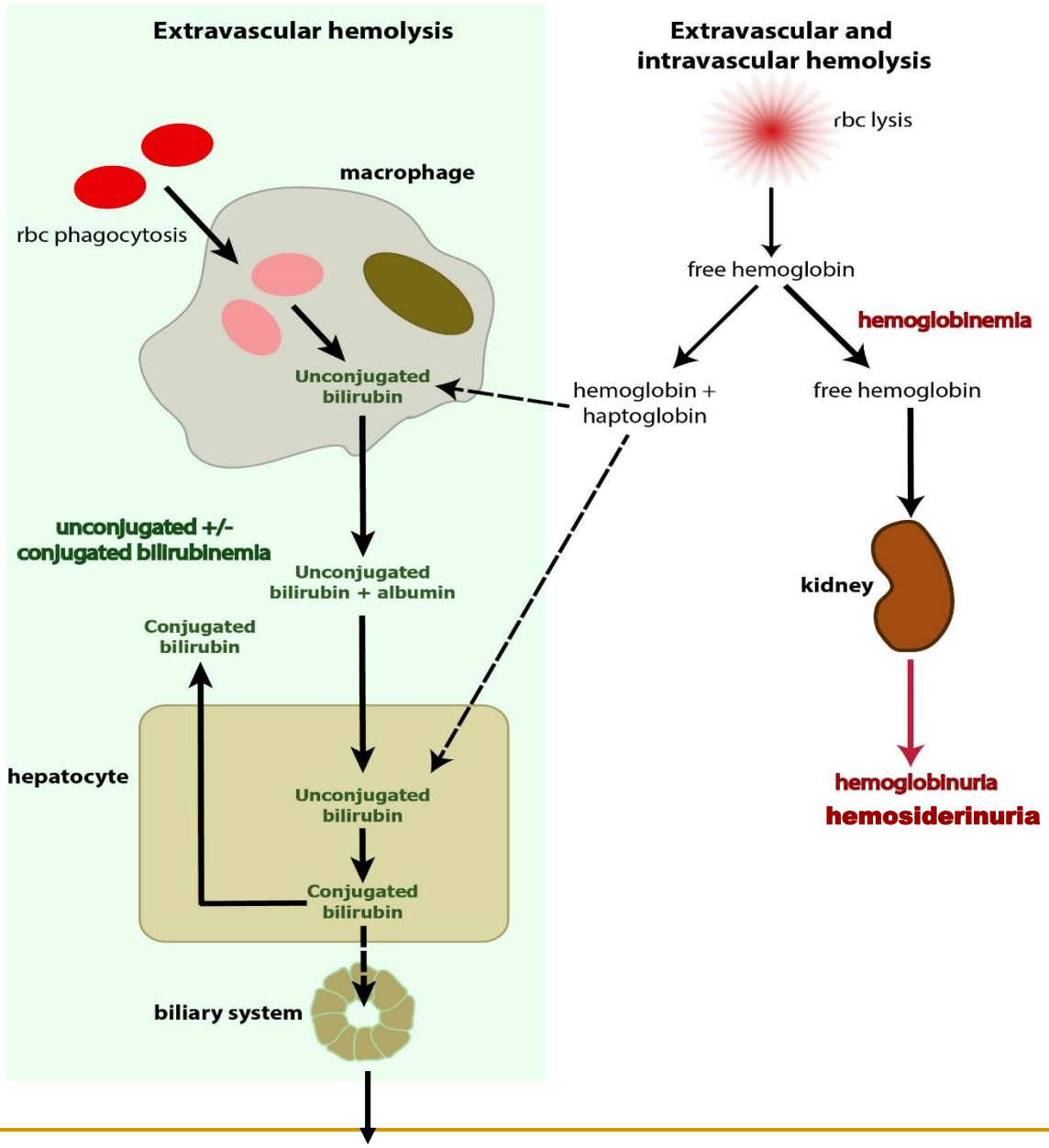
- These form basis for laboratory diagnostic tests for haemolysis

# Pathophysiology

- A large number of hereditary and acquired disorders cause haemolysis
  - Increased RBC destruction may be due to intrinsic RBC disorders - mostly hereditary;  or  extrinsic factors - mostly acquired

- Haemolysis may occur **extravascularly** or **intravascularly** or both

- Hemolysis may be acute, chronic, or episodic


Extravascular hemolysis
Extravascular and intravascular hemolysis
rbc lysis
macrophage
rbc phagocytosis
free hemoglobin
hemoglobinemia
Unconjugated bilirubin
hemoglobin + haptoglobin
free hemoglobin
unconjugated +/- conjugated bilirubinemia
Unconjugated bilirubin + albumin
kidney
Conjugated bilirubin
hepatocyte
Unconjugated bilirubin
hemoglobinuria
hemosiderinuria
Conjugated bilirubin
biliary system
Urobilinogen

## 1. Extravascular haemolysis (more common):

- Removal and destruction of damaged RBCs by the macrophages of the spleen and liver (may occur in BM)
- Damaged/abnormal RBCs are phagocytosed and destroyed by macrophages
- The iron released is recycled

## 2. Intravascular haemolysis

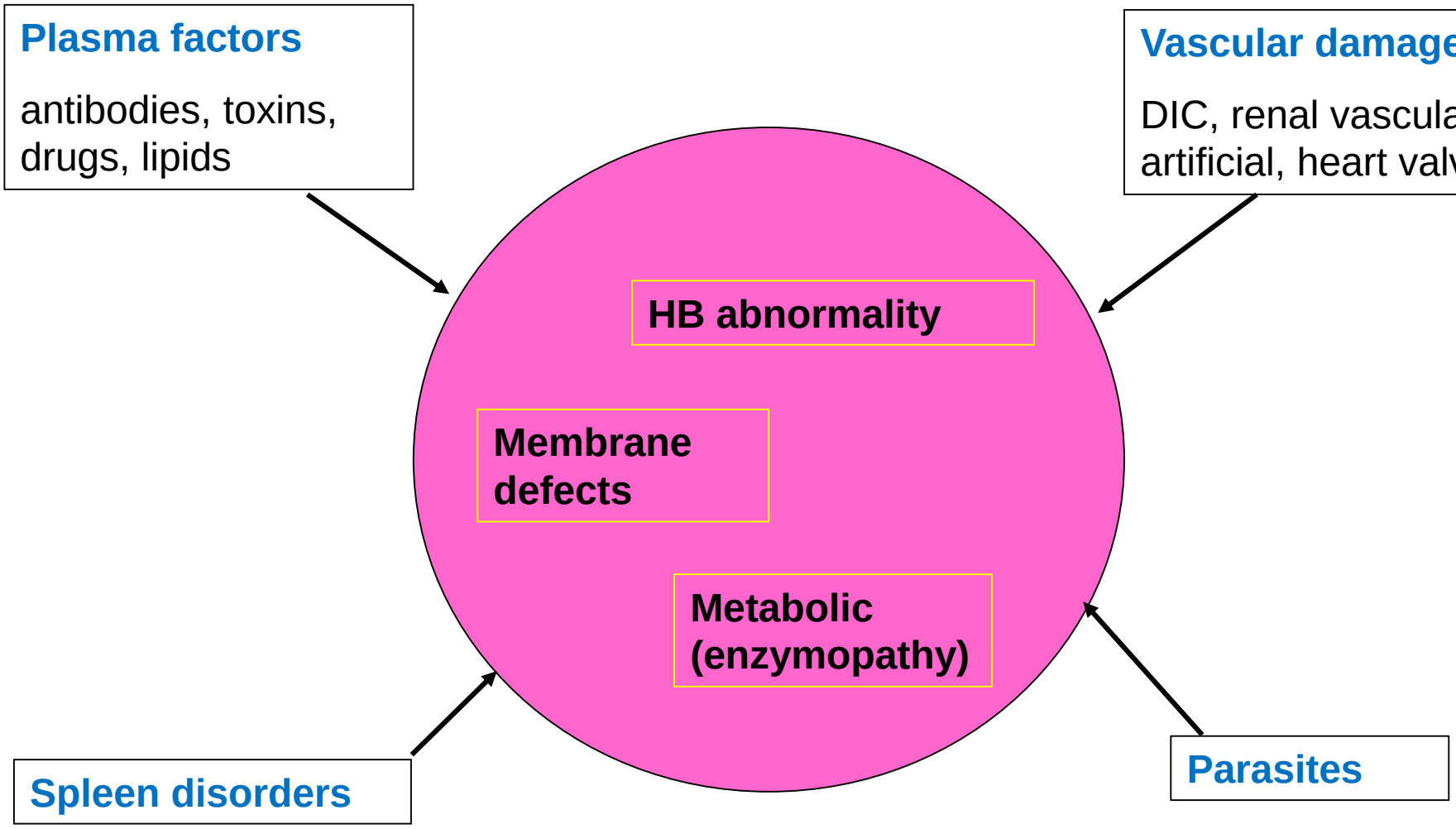
- The destruction of RBCs occurs in circulation with the release of cell contents into the plasma

- Mechanical trauma from a damaged endothelium, compliment fixation and activation on the cell surface, infectious agents may cause direct membrane degradation and cell destruction in circulation

- In intravascular haemolysis HB released is lost through kidneys resulting in **haemoglobinuria** and **haemosiderinuria**

- **Haemosiderin**
  - Excess HB released from RBCs in circulation is filtered by the kidney; in cells of the proximal tubule the iron removed and stored as haemosiderin
  - When the cells slough off they are excreted into the urine, producing a brownish/dirty colour due to the haemosiderin within

# *Factors causing red cell haemolysis*



# Classification

**Intracorpuscular* RBC Defects (Hereditary)**

- Membrane defects
- Haemoglobin defects
- Enzyme defects

**Extracorpuscular ** Defects (Acquired)**

- Immune causes
- Non-immune causes

*Intrinsic

** Extrinsic

## Intracorpuscular causes (mostly hereditary)

- Red cell membrane defects:
  - Hereditary sperocytosis,
  - Hereditary elliptocytosis and ovalocytosis
  - Hereditary stomatocytosis
  - Paroxysmal Nocturnal Haemoglobinuria* (acquired)

# Haemoglobin disorders:

- Structural variants:
  - HbS, Hb C, Hb E, Hb D etc
  - Unstable haemoglobins, and others
- Imbalance in globin chain synthesis
  - Thalassaemia syndromes ($\alpha$, $\beta$ thal)

- Red cell enzyme defects
  - G6PD deficiency
  - Pyruvate kinase deficiency
  - Others enzymes of pentose phosphate pathway

- Extracorpuscular causes (mostly acquired):

## 1. Non-immune causes:

- Infections (parasitic diseases - Malaria, bacterial sepsis - Clostridial infections)
- Toxins, chemicals, drugs
- Red cell fragmentation syndromes e.g. DIC, prosthetic cardiac valves, etc
- Hypersplenism

## 2. Immune mediated haemolysis:

- Autoimmune haemolytic anaemia (AIHA)
- Alloimmune HA
  - Haemolytic transfusion reaction
  - Haemolytic disease of the newborn
  - Allograft associated HA
- Drug induced immune haemolytic anaemia

# Clinical features

- History and physical examination can provide important clues
- Mild haemolysis may be asymptomatic
- Features of anaemia
  - Symptoms: Dyspnea, fatigue, weakness, oedema, angina and cardiopulmonary decompensation
  - Sign:  Pallor

## Clinical features cont…

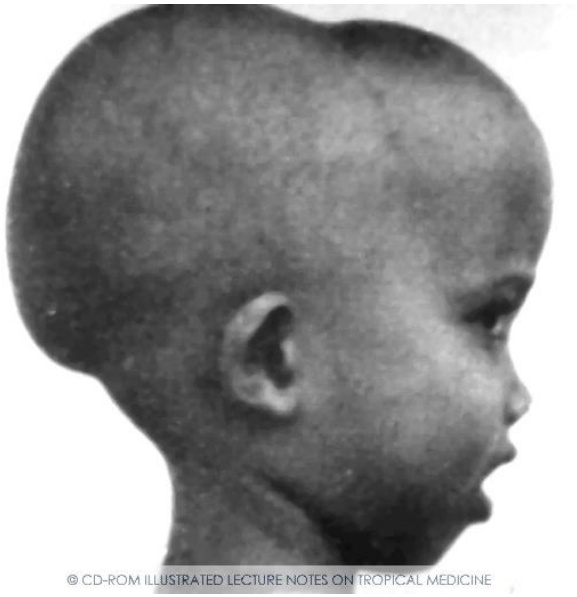
- Jaundice of skin & mucous membranes
- Enlarged spleen
- intravascular hemolysis - Dark urine, haemoglobinuria & haemosiderinuria

## Clinical features cont…

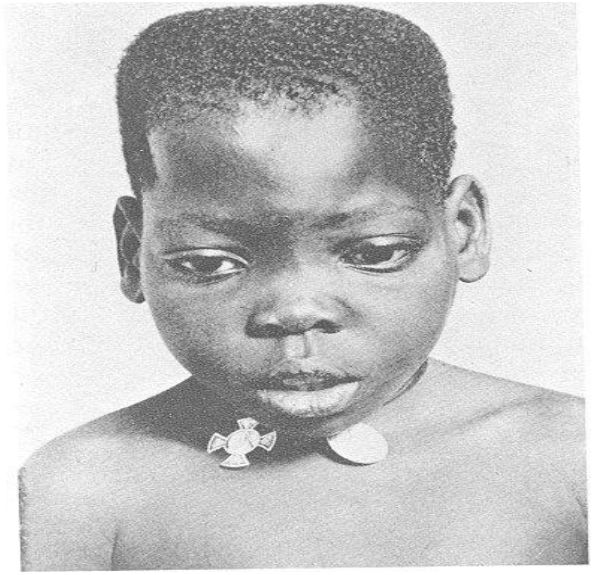
**Features reflecting the underlying cause for haemolysis e.g.**

- Painful occlusive crisis (SCD)
- Leg ulcers (eg SCD)
- Skull and skeletal deformities eg skull bossing (SCD, Thal, other chronic HA)
- Gallstones

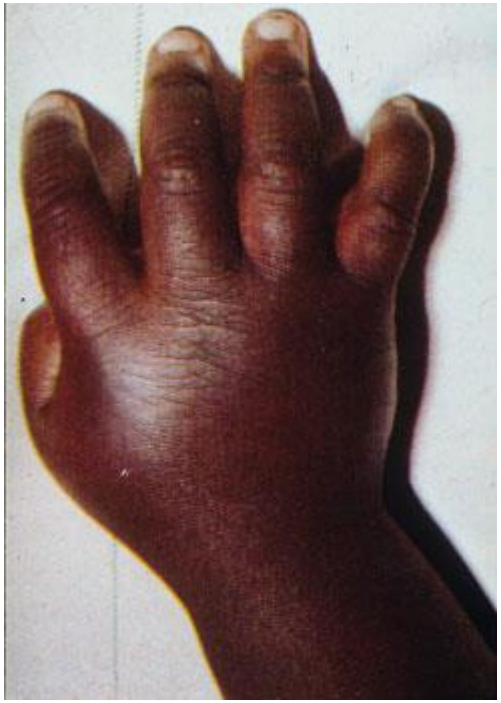
Jaundice of the sclera



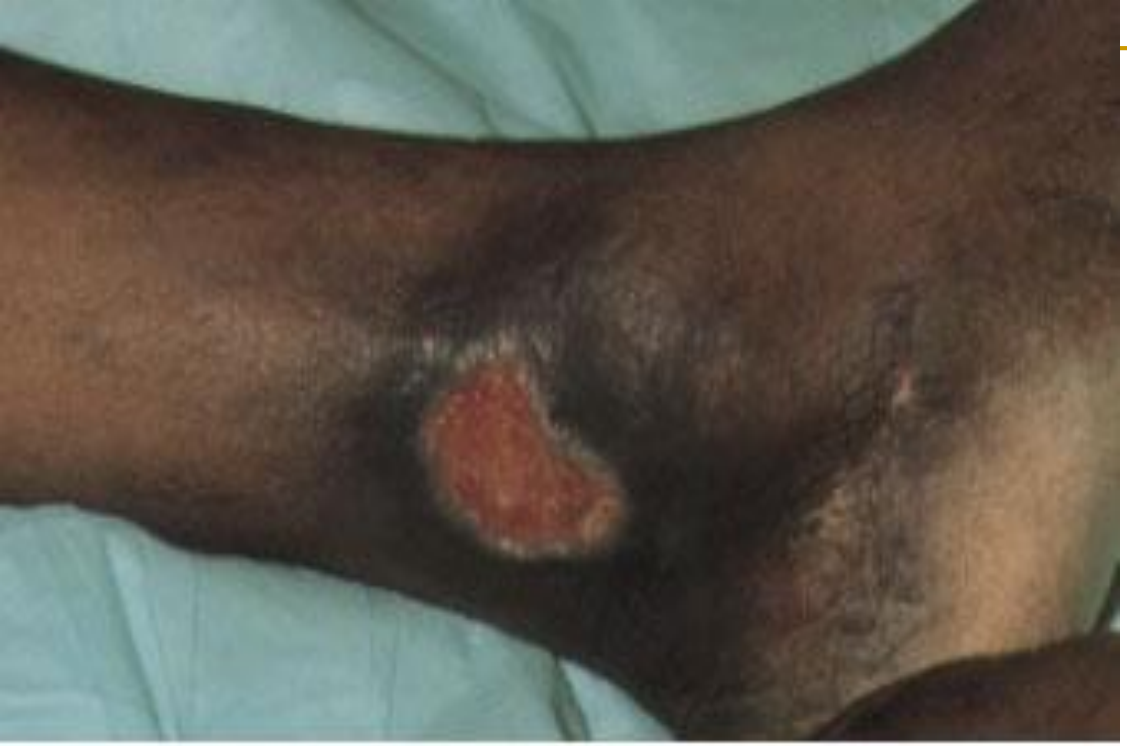

Skull bossing

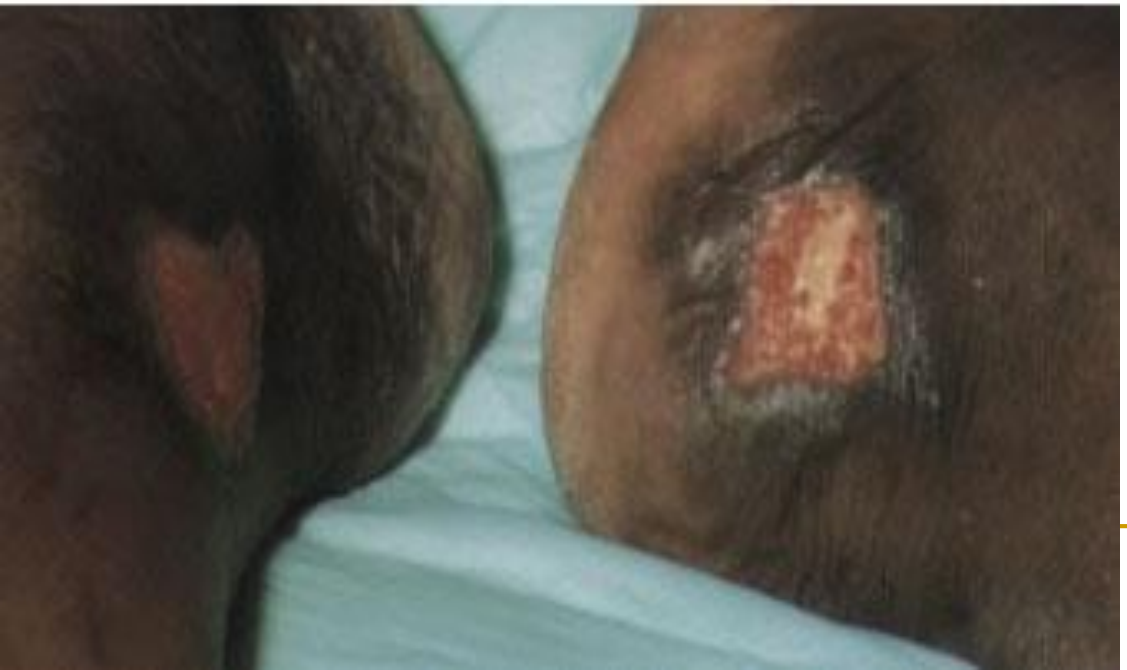


# Dactylitis (Hand-Foot syndrome)



Soft tissue swelling in hand in SCD



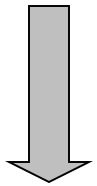


Pictographs showing chronic leg ulcers as seen in SCA.

# Laboratory evaluation

**AIM:**

- Test for haemolysis and anaemia
- Determine mechanism of haemolysis and the precise diagnosis



1. Initial tests: evidence of haemolysis, anaemia
2. Specific confirmatory tests
3. Additional studies

# Laboratory features: Initial tests

- CBC count
  - Low Hb, HCT/PCV, RBC  if anemia present
  - RBC indices (MCV, MCH, MCHC)
  - WBC counts and differential
  - Platelet count
- Reticulocyte count ↑

- Peripheral smear morphology:

  Can provide important clues as to cause of haemolysis

  - Demonstrates sickle cells, spherocytes, fragments target cells
  - Red cell inclusions
  - Polychromasia (reticulocytosis)
  - Nucleated red cells
  - Parasites

# Biochemical tests for haemolysis:

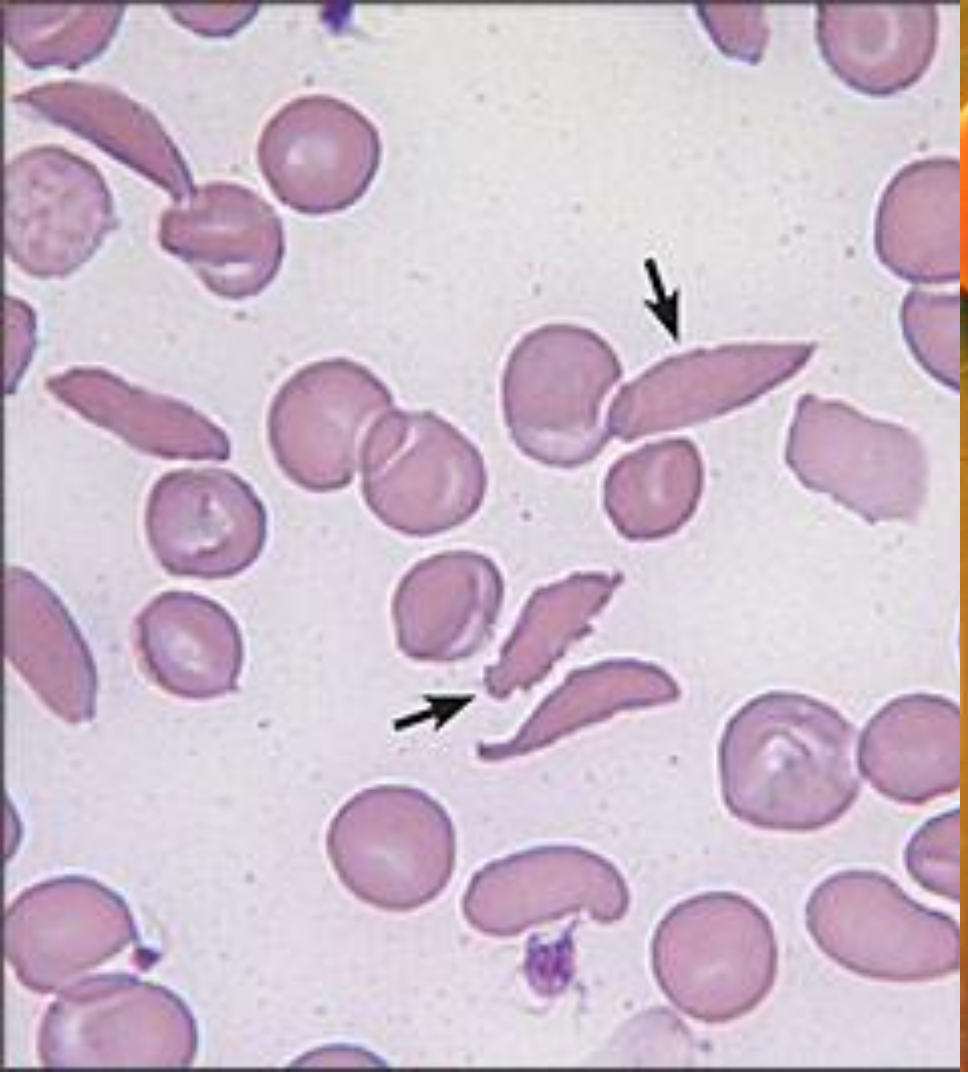
- Serum lactic acid dehydrogenase↑
- Serum haptoglobin ↓, serum hemopexin ↓
- Methaemalbumin (Intravascular haemolysis)
- Indirect bilirubin↑, urobilinogen in urine
- Urine hemoglobin present (hemoglobinuria)
- Urine haemosiderin

## Specific studies:

*Directed by clinical features, initial laboratory test findings:*

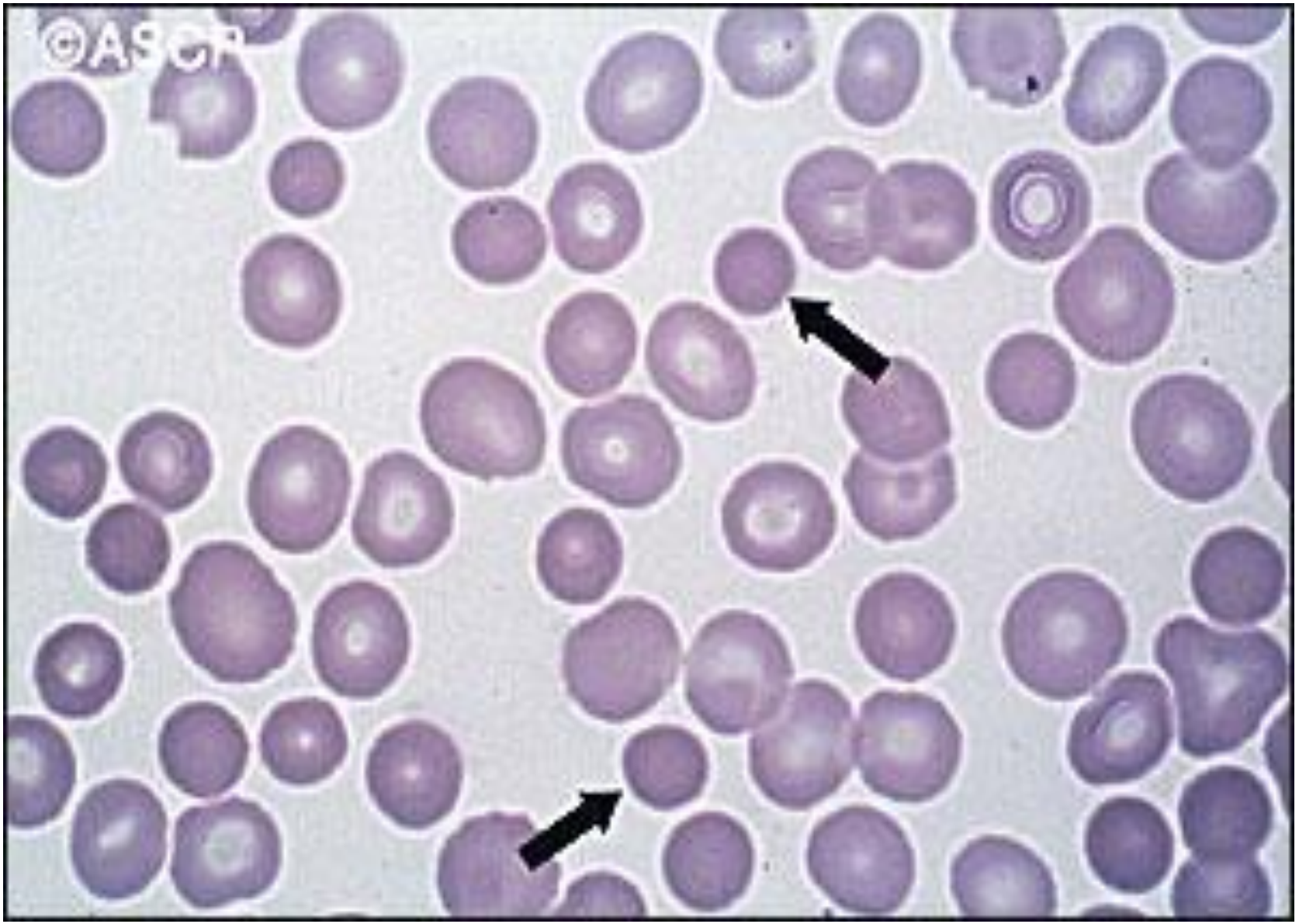
- Direct antiglobulin test (DAT)/Coombs test
- Sicklng test, HB electrophoresis, HB solubility,
- G-6-PD screening tests
- Enzyme assays
- Red cell membrane studies
- Osmotic fragility test
- Others

**Bone marrow examination is not necessary for diagnosis of straight forward haemolysis*

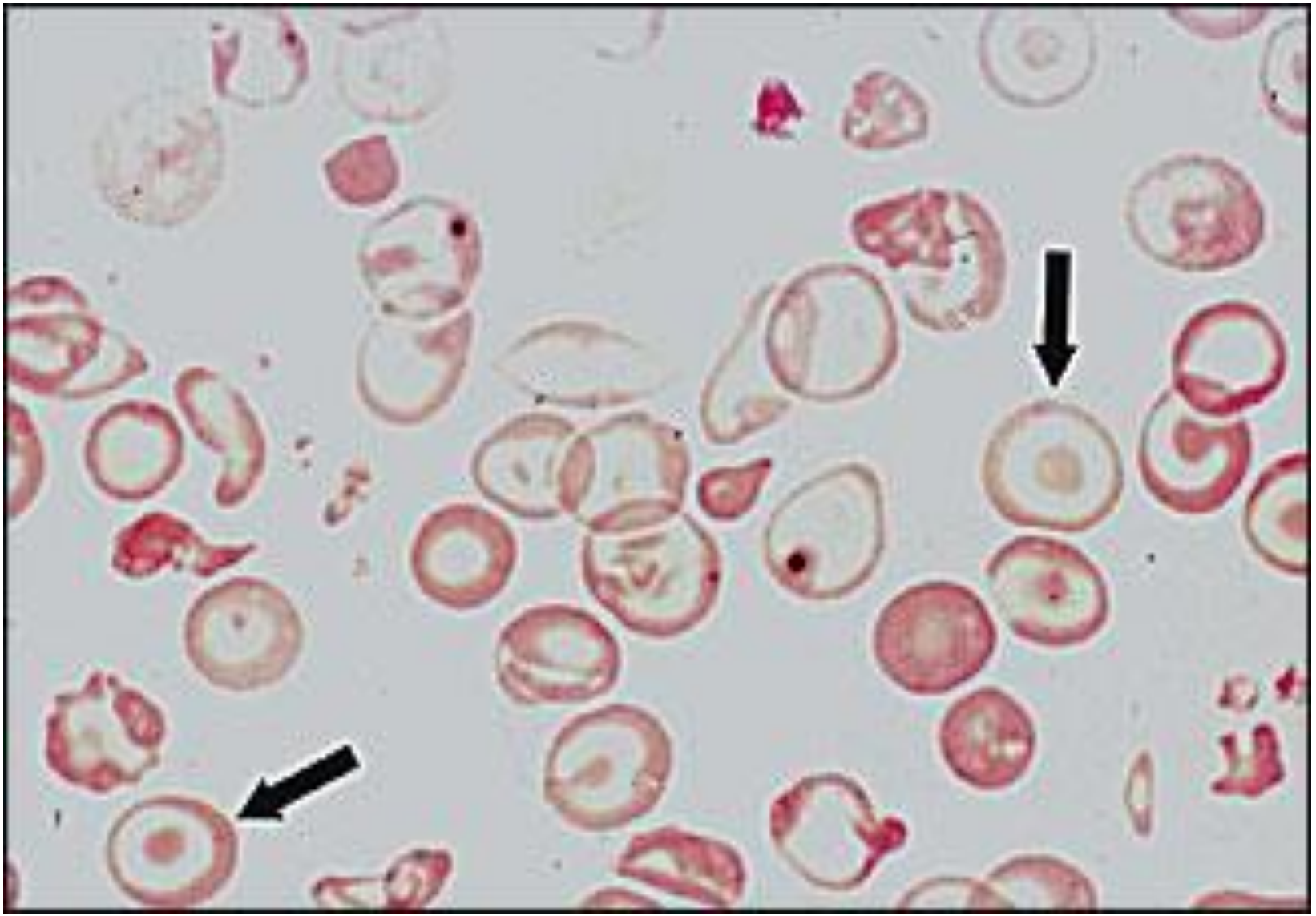


Appearance of sickle cells on a stained blood film.

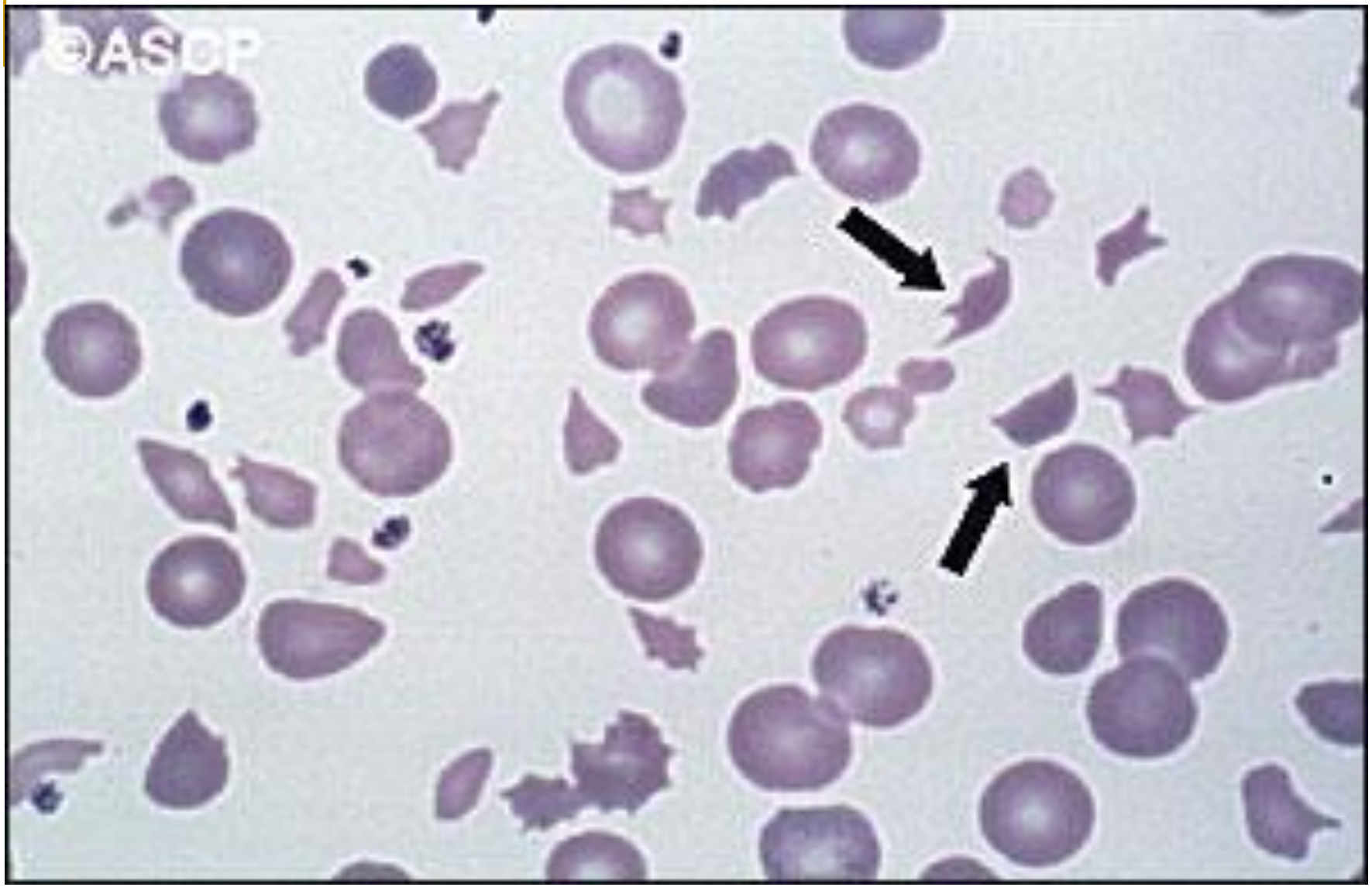
Appearance of a sickled cell in the blood



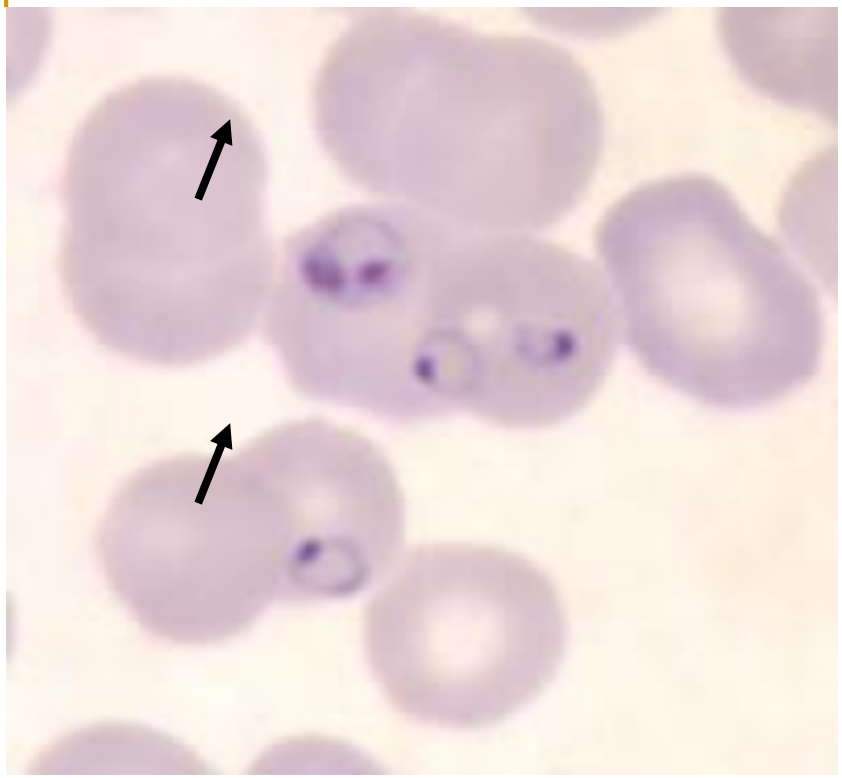
Spherocytes – HS, IHA etc

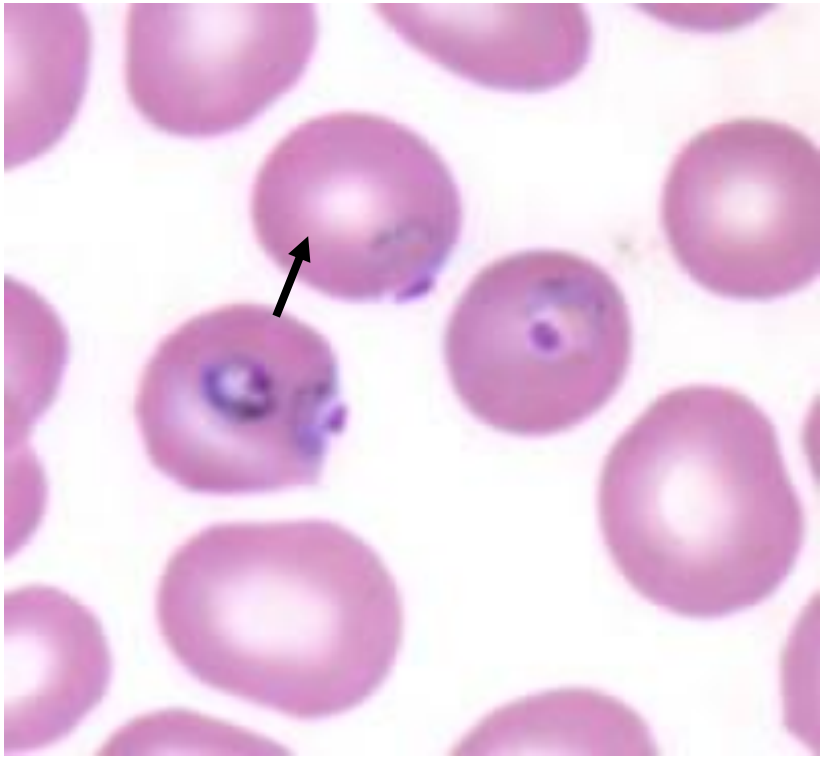


Target cells - Haemoglobinopathy



Fragments – Red cell fragmentation syndromes eg DIC etc





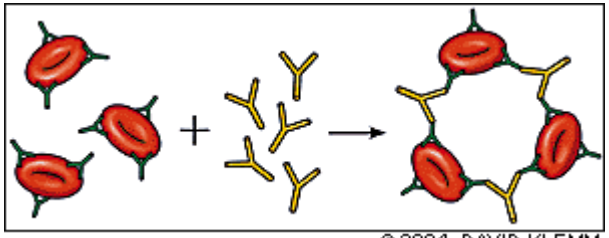
Malaria parasites in red blood cells

# Conclusion

- Haemolysis is the destruction of RBC
- Haemolytic disorders are caused by various hereditary or acquired conditions
- Clinical features include anaemia, jaundice, haemoglobinuria (intravascular haemolysis) and features attributable to particular disorder
- Diagnostic tests aim at
  - Detecting haemolysis and anaemia
  - Determining the mechanism of haemolysis and the precise diagnosis

# Thanks for listening!

# Questions??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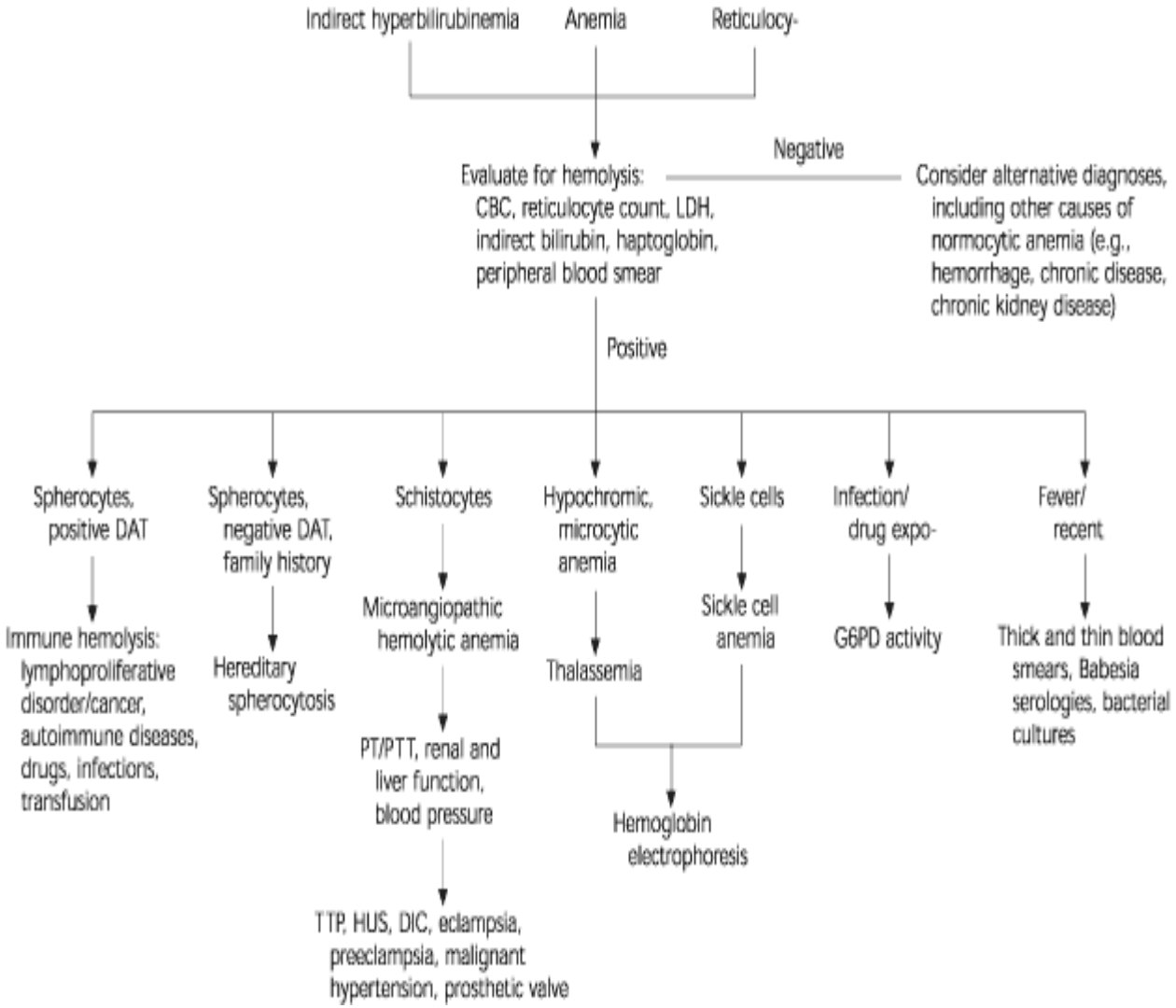
Indirect hyperbilirubinemia
Anemia
Reticulocy-
Evaluate for hemolysis:
CBC, reticulocyte count, LDH, indirect bilirubin, haptoglobin, peripheral blood smear
Negative
Consider alternative diagnoses, including other causes of normocytic anemia (e.g., hemorrhage, chronic disease, chronic kidney disease)
Positive
Spherocytes, positive DAT
Spherocytes, negative DAT, family history
Schistocytes
Hypochromic, microcytic anemia
Sickle cells
Infection/ drug expo-
Fever/ recent
Immune hemolysis: lymphoproliferative disorder/cancer, autoimmune diseases, drugs, infections, transfusion
Hereditary spherocytosis
Microangiopathic hemolytic anemia
Thalassemia
Sickle cell anemia
G6PD activity
Thick and thin blood smears, Babesia serologies, bacterial cultures
PT/PTT, renal and liver function, blood pressure
Hemoglobin electrophoresis
TTP, HUS, DIC, eclampsia, preeclampsia, malignant hypertension, prosthetic valve