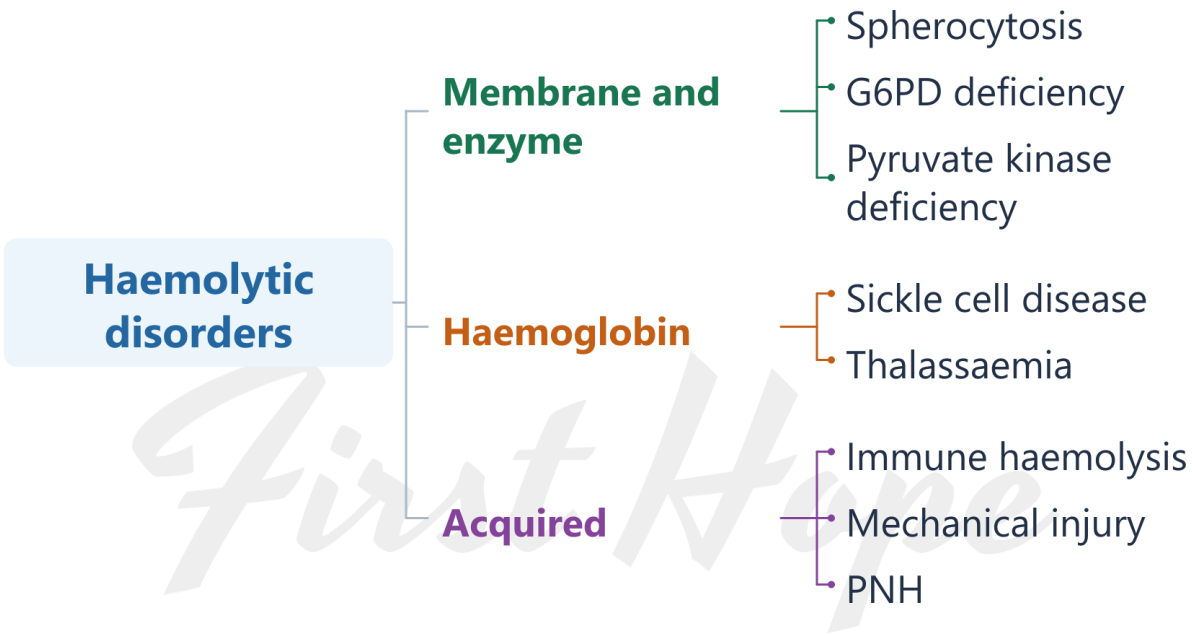
Pathology - Topic 16 - Hemolytic anemia

Haemolysis and Its Recognition

- **Haemolysis** is premature destruction of red cells, which normally circulate for about 120 days.

Marrow Compensation and Haemolysis Patterns

- Haemolytic anaemia develops when marrow compensation cannot fully replace the destroyed cells.
    - A compensated haemolytic disorder can have increased red-cell turnover without a low haemoglobin concentration.



1. Intrinsic Red-Cell Defects

- Inherited defects of the membrane, enzymes or haemoglobin make red cells vulnerable to destruction.
    - Hereditary spherocytosis, G6PD deficiency, sickle cell disease and thalassaemia are important examples.
- Most intrinsic defects are inherited, but paroxysmal nocturnal haemoglobinuria is an acquired intrinsic defect of a blood-cell clone.

2. Extrinsic Causes

- Antibodies, mechanical damage, infection, toxins and abnormal vascular conditions can destroy otherwise normal cells.
    - Most extrinsic causes are acquired, but the intrinsic–extrinsic and inherited–acquired classifications are not identical.

Sites of Red-Cell Destruction

1. Extravascular Haemolysis

- Splenic and hepatic macrophages remove damaged or antibody-coated red cells.

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

- Poorly deformable cells are trapped in the spleen and lose membrane or are completely phagocytosed.

➢ Typical consequences include anaemia, unconjugated hyperbilirubinaemia and splenomegaly.

- Longstanding increased bilirubin production can lead to pigment gallstones.

2. Intravascular Haemolysis

➢ Red cells rupture inside the circulation and release free haemoglobin into plasma.

- Haptoglobin binds free haemoglobin and is consumed, so its concentration often falls.

➢ Severe haemolysis can produce haemoglobinaemia and haemoglobinuria.

- Tubular uptake of filtered haemoglobin can later produce urinary haemosiderin, and acute kidney injury may develop.

➢ Several disorders have both intravascular and extravascular components rather than fitting a pure category.

Symptoms and Evidence of Red-Cell Destruction

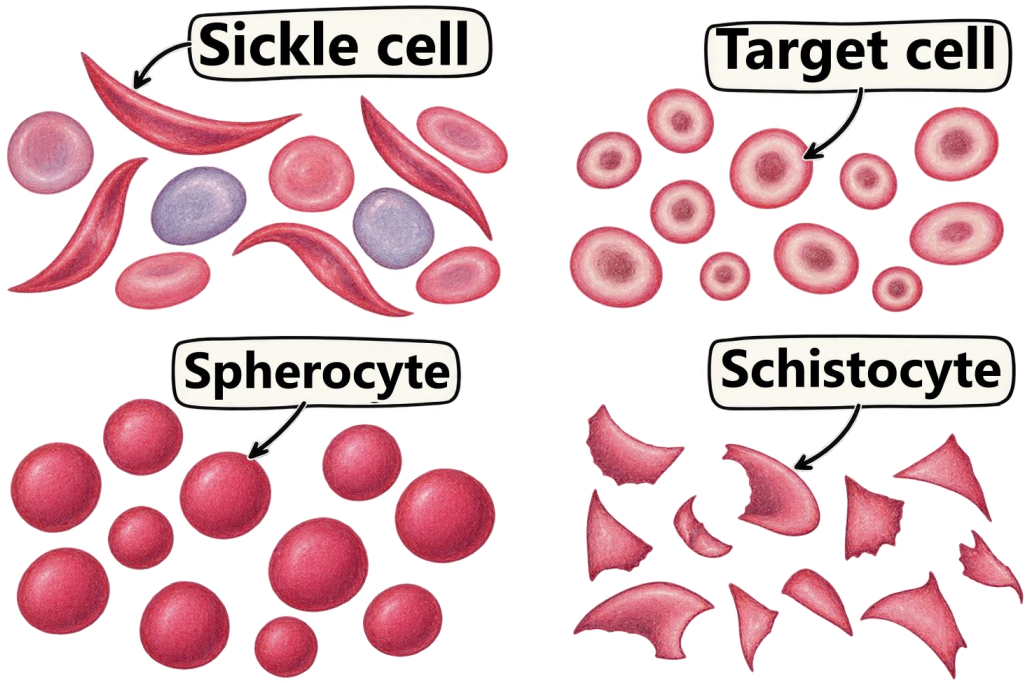
- Symptoms of anaemia may accompany jaundice, dark urine, splenic enlargement or a history of intermittent episodes.
- The usual laboratory pattern includes increased reticulocytes, LDH and unconjugated bilirubin with reduced haptoglobin.
  - Reticulocytes may be low if the marrow is suppressed, a nutrient is deficient or an aplastic crisis has occurred.
- Haptoglobin may also be low in severe liver disease and can rise during inflammation.
  - Interpret the full pattern rather than diagnosing haemolysis from one marker.
- The MCV is often normal or slightly increased because reticulocytes are large, but thalassaemia is characteristically microcytic.

Distinguishing Haemolysis from a Haemolysed Sample

- In-vitro red-cell rupture during collection or transport can raise measured potassium, LDH and plasma haemoglobin without true haemolytic disease in the patient.
- The laboratory haemolysis index, repeat collection and the wider clinical pattern help identify this preanalytical problem.
- Reticulocytosis and unconjugated hyperbilirubinaemia support an in-vivo process when the marrow can respond.
- An isolated high LDH may arise from many tissue injuries and is not specific for red-cell destruction.

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

Morphological Clues



Red cell shapes that guide the investigation of haemolysis

- **Spherocytes** suggest membrane loss and occur in hereditary spherocytosis and immune haemolysis.
- **Schistocytes** are fragments that suggest mechanical or microangiopathic red-cell injury.
- Sickle cells, target cells, bite cells and polychromasia direct further testing but require clinical correlation.
    - An apparent red-cell agglutination can distort automated indices and should prompt laboratory assessment for a cold-reactive antibody or other cause.

Hereditary Spherocytosis

- Hereditary spherocytosis is an inherited red-cell membrane disorder that produces spherical cells prone to splenic destruction.

Mechanism and Features

- Defects in membrane-skeleton proteins, such as spectrin, ankyrin or band 3, lead to progressive loss of membrane.
    - The cell becomes more spherical and less deformable, so the spleen removes it prematurely.
- Many cases are autosomal dominant, although other inheritance patterns and new mutations occur.
- Anaemia, jaundice, splenomegaly and pigment stones vary in severity.
    - Parvovirus B19 can temporarily suppress erythropoiesis and precipitate a severe aplastic crisis.

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

Laboratory Findings

Blood-Film and Immune-Test Findings

- The smear shows small dense cells without central pallor, with reticulocytosis when compensation is intact.
- MCHC is often increased, and the direct antiglobulin test is usually negative.
- A positive immune test instead raises the possibility of immune spherocytosis.

Membrane Screening Tests

- Reduced eosin-5-maleimide binding on flow cytometry supports the diagnosis in the appropriate setting.
- Osmotic fragility testing is a classical method but has limitations and is not a universal first choice.

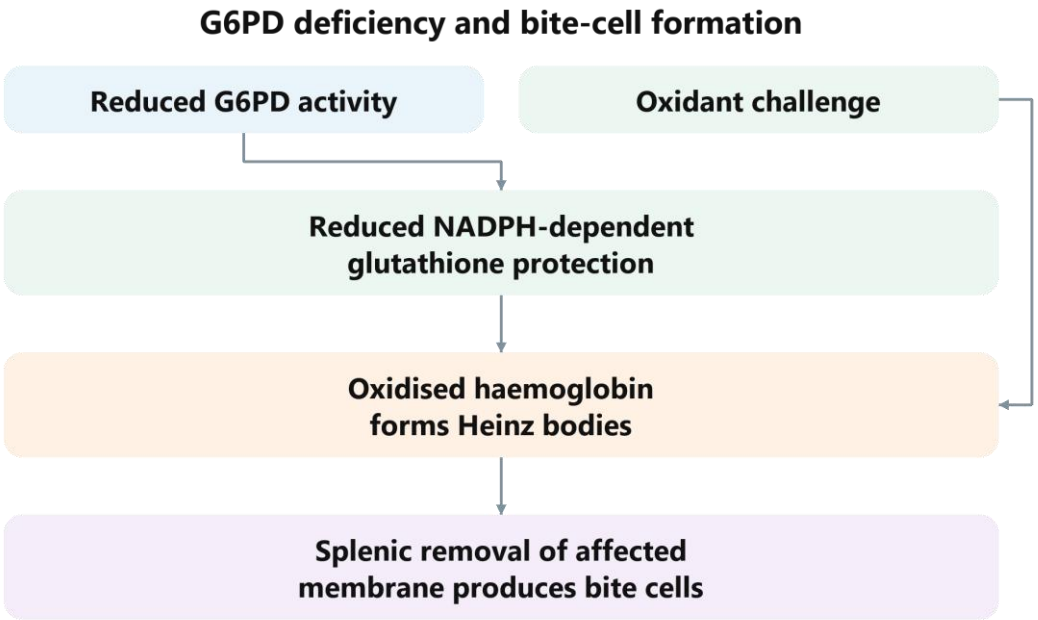
Basis and Limits of Membrane Tests

- Spherocytes have a reduced surface-area-to-volume ratio and may lyse at a higher saline concentration than normal disc-shaped cells in an osmotic fragility test.
- Eosin-5-maleimide binding assesses selected membrane-associated proteins, but the result must be interpreted with morphology and the family or clinical history.
- Splenic removal of abnormal cells is central to the disease; the intrinsic membrane defect remains even if splenic destruction is reduced.

G6PD Deficiency

- G6PD deficiency is an inherited enzyme defect that reduces red-cell protection against oxidative injury.

Mechanism and Triggers



Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

- Glucose-6-phosphate dehydrogenase helps generate NADPH, which keeps glutathione available to protect red cells from oxidation.
    - The defect is X-linked, and older red cells are especially vulnerable because their enzyme activity is lower.
- Infection, fava beans and certain oxidant medicines can precipitate haemolysis.
    - The specific medicine and exposure must be checked because risk differs between agents and variants.

Smear and Testing

Oxidative Blood-Film Changes

- Oxidised haemoglobin forms **Heinz bodies**, which are demonstrated by a supravital stain.
- Splenic removal of Heinz-body-containing membrane produces bite cells, and blister cells may also be seen.

Enzyme Testing and Interpretation

- An enzyme assay confirms reduced G6PD activity, but testing during an acute episode may be falsely reassuring.
- Older deficient cells may already have been destroyed, leaving reticulocytes with higher activity; repeat testing after recovery may be needed.
- Oxidative episodes are often self-limiting as the most enzyme-deficient older cells are removed and a younger population remains.
- Heterozygous females may have clinically significant disease because X-chromosome inactivation creates variable proportions of deficient erythrocytes.
- Recent transfusion can introduce normal donor cells and mask the enzyme-deficient population during testing.

Pyruvate Kinase Deficiency

- Pyruvate kinase deficiency reduces red-cell ATP production and can cause chronic non-immune haemolysis.

Mechanism and Diagnosis

- Membrane maintenance becomes inefficient when the cell's energy supply is inadequate.
- The diagnosis depends on enzyme or molecular testing after other causes have been considered.

Sickle Cell Disease

- Sickle cell disease is an inherited haemoglobin disorder in which haemoglobin S can polymerise and distort red cells.

Copyright by Engacy Learning Private Limited. All rights reserved. Reproduction or distribution without written consent is strictly prohibited.

FREE PREVIEW

Click here to visit our website

MBBS PREMIUM NOTES

Complete MBBS notes for every subject and year are available only in the FirstHope app.

Scan or click here

Click here to get the app >

Available on Google Play

Browse MBBS notes by year

firsthope.co.in/mbbs

Click here to explore MBBS >

Scan or click here

FirstHope Medical on Instagram

@firsthope.medical

Click here to follow

App and notes help

Find answers about access and downloads

Click here for help

YEAR 1 / YEAR 2 / YEAR 3 / YEAR 4