HEREDITARY SPHEROCYTOSIS (HS) 🩸

Definition

Hereditary spherocytosis is an inherited hemolytic anemia caused by intrinsic defects of the red cell membrane, leading to:

- Formation of spherocytes
- Reduced deformability
- Premature destruction in the spleen (extravascular hemolysis)

📌 One-liner for exams:

HS is an autosomal inherited disorder of RBC membrane skeleton proteins causing spherocytes and splenic hemolysis.

Mode of Inheritance 🧬

- Autosomal dominant → *most common*
- Autosomal recessive → *rare, more severe form*

PATHOGENESIS ⚙️

Normal RBC Membrane Skeleton (Concept)

The RBC membrane is stabilized by a protein meshwork called the membrane skeleton, which maintains:

- Biconcave shape
- Flexibility
- Surface area-to-volume ratio

Key Proteins Involved 🧩

Protein	Function

Spectrin	Main structural protein; forms flexible mesh
Actin	Short filaments anchoring spectrin
Ankyrin	Links spectrin to band 3
Band 3	Intrinsic membrane protein
Glycophorin	Intrinsic membrane protein
Band 4.1	Stabilizes spectrin–actin junction

📌 Most common defect: Spectrin

Step-by-Step Pathogenesis Flowchart 🔄

- Inherited mutation in membrane skeleton proteins → Weak interaction between skeleton & membrane proteins → Membrane instability → Progressive loss of membrane vesicles with aging → Cytoplasm

relatively preserved → ↓ Surface area : volume ratio → RBC becomes spherical (spherocyte)

Why Spherocytes Are Destroyed 🧠

- Normal RBCs: flexible, biconcave
- Spherocytes: rigid, non-deformable

Splenic mechanism:

- Spherocytes enter splenic cords → Fail to pass through narrow sinusoids → Sequestration → Phagocytosis by splenic macrophages

📌 Site of hemolysis: Spleen (extravascular)

Role of Spleen (Clinical Correlation) ⭐

- Splenectomy → Removes major site of RBC destruction → Corrects anemia → BUT RBC defect & spherocytes persist

MORPHOLOGY 🔬

Peripheral Blood Smear

- Spherocytes:
  - Dark red
  - No central pallor
  - Smaller, dense cells

Bone Marrow

- Erythroid hyperplasia
- Compensatory ↑ RBC production
- Reticulocytosis present

Spleen

- Marked splenomegaly

- Weight: 500–1000 g
  (Normal: 150–200 g)

Histological features:

- Congested splenic cords
- ↑ Macrophages
- Phagocytosed RBCs within:
  - Sinusoids
  - Splenic cords

Other Morphologic Features

- Cholelithiasis (bilirubin pigment stones)
  - Seen in 40–50% of patients
  - Due to chronic hemolysis

CLINICAL FEATURES 🩺

Classical Triad ⭐

- Anemia
- Splenomegaly
- Jaundice

Severity of Anemia

- Variable:
  - Subclinical
  - Mild
  - Moderate (most common)
  - Severe (rare)

Laboratory Hallmark

Increased osmotic fragility 🧪

📌 Explanation:

- Spherocytes cannot tolerate hypotonic solutions
- They lyse earlier than normal RBCs

APLASTIC CRISIS ⚠️

Trigger

- Parvovirus B19 infection

Mechanism Flowchart 🔄

- Parvovirus B19 infection → Virus infects erythroblasts → Apoptosis of erythroid precursors → Temporary cessation of erythropoiesis → Rapid fall in Hb (short RBC lifespan) → Severe anemia (aplastic crisis)

📌 Bone marrow may become virtually devoid of RBC precursors

Clinical Course

- Lasts 10–14 days
- May require:

    - Blood transfusions
- Recovery occurs after immune control of infection

TREATMENT 💊

No Definitive Cure

- Defect is genetic
- Treatment is supportive and surgical

Splenectomy 🩸

- Improves anemia
- Reduces hemolysis
- Corrects Hb levels

📌 Indication: Moderate to severe disease

Risks of Splenectomy ⚠️

- ↑ Risk of infections by encapsulated bacteria:
  - *Streptococcus pneumoniae*
  - *Haemophilus influenzae*
  - *Neisseria meningitidis*

📌 Risk is highest in children

Partial Splenectomy (Modern Approach) ⭐

- Preferred in young children
- Benefits:
  - Improves anemia
  - Preserves some immune function

❌ Limitation:

- Residual spleen may regrow
- Some patients require repeat surgery later

High-Yield Summary Table 📊

Feature	Hereditary Spherocytosis
Defect	RBC membrane skeleton
Shape	Spherocytes
Hemolysis type	Extravascular
Site	Spleen
Osmotic fragility	Increased
Reticulocytes	Increased
Splenectomy	Corrects anemia
Gallstones	Common

-> The End <-