CP Presentation

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HPI

- 20-year-old white college student, diagnosed with infectious mononucleosis 6 months ago
- He recovered, but a follow-up CBC revealed a hemoglobin of 9.3 gm/dl and a reticulocytosis of 7.4%
- A direct Coombs test (direct anti-globulin test) was negative, and liver function tests normal except for an indirect bilirubin at 2.5 mg/dl

Physical Exam

- He is a healthy young man who has minimal scleral icterus
- Non-tender liver with a vertical span of 10 cm, and a soft spleen tip which descended 4 cm below the LCM with deep inspiration

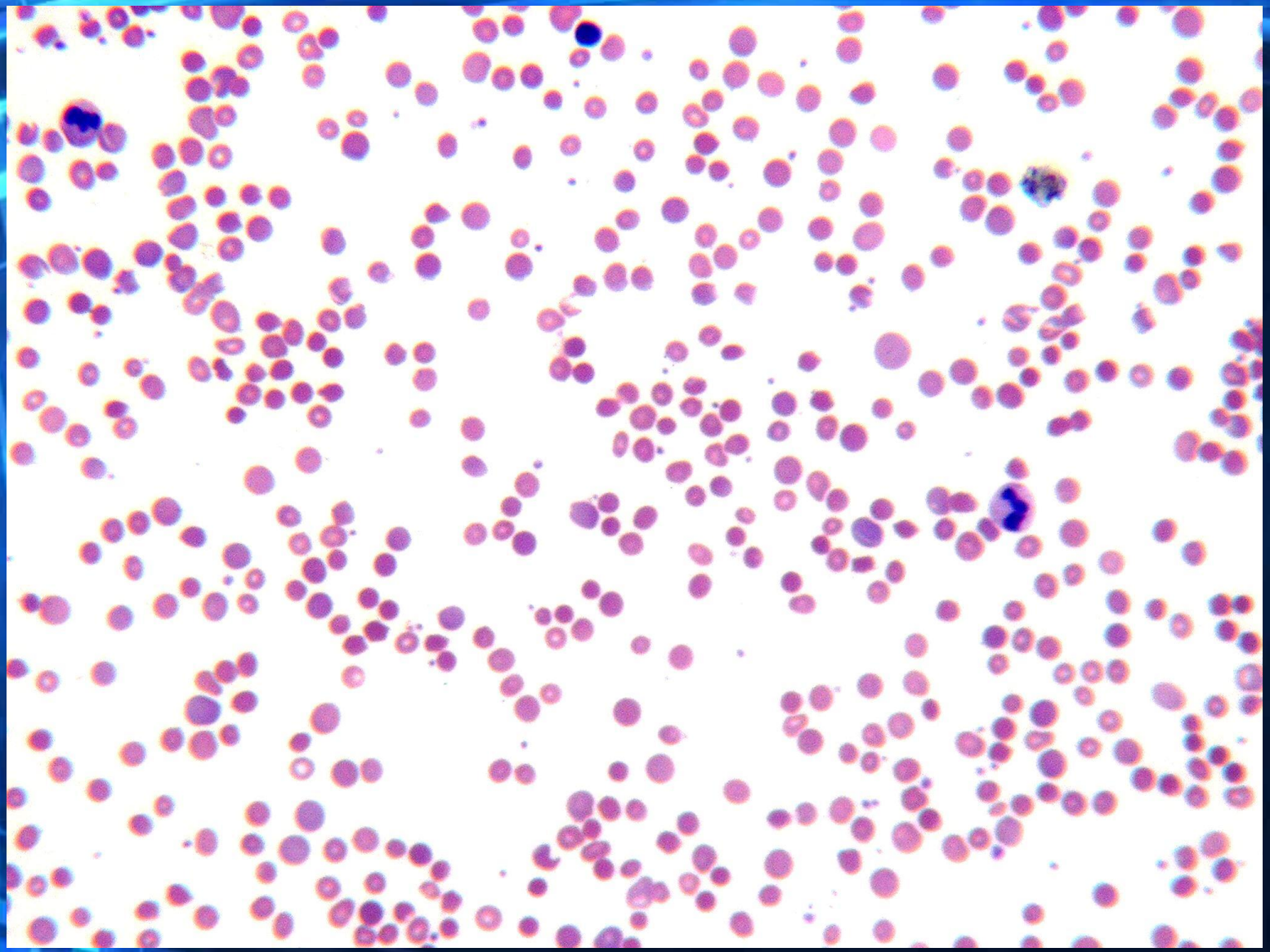
Labs

- WBC 6400
- Platelets 195,000
- Red blood cell indicies
  - Hgb 10.8
  - Hct 30
  - RBC 3.2
  - MCV 94
  - MCH 34
  - MCHC 36
  - Retics 6.8%

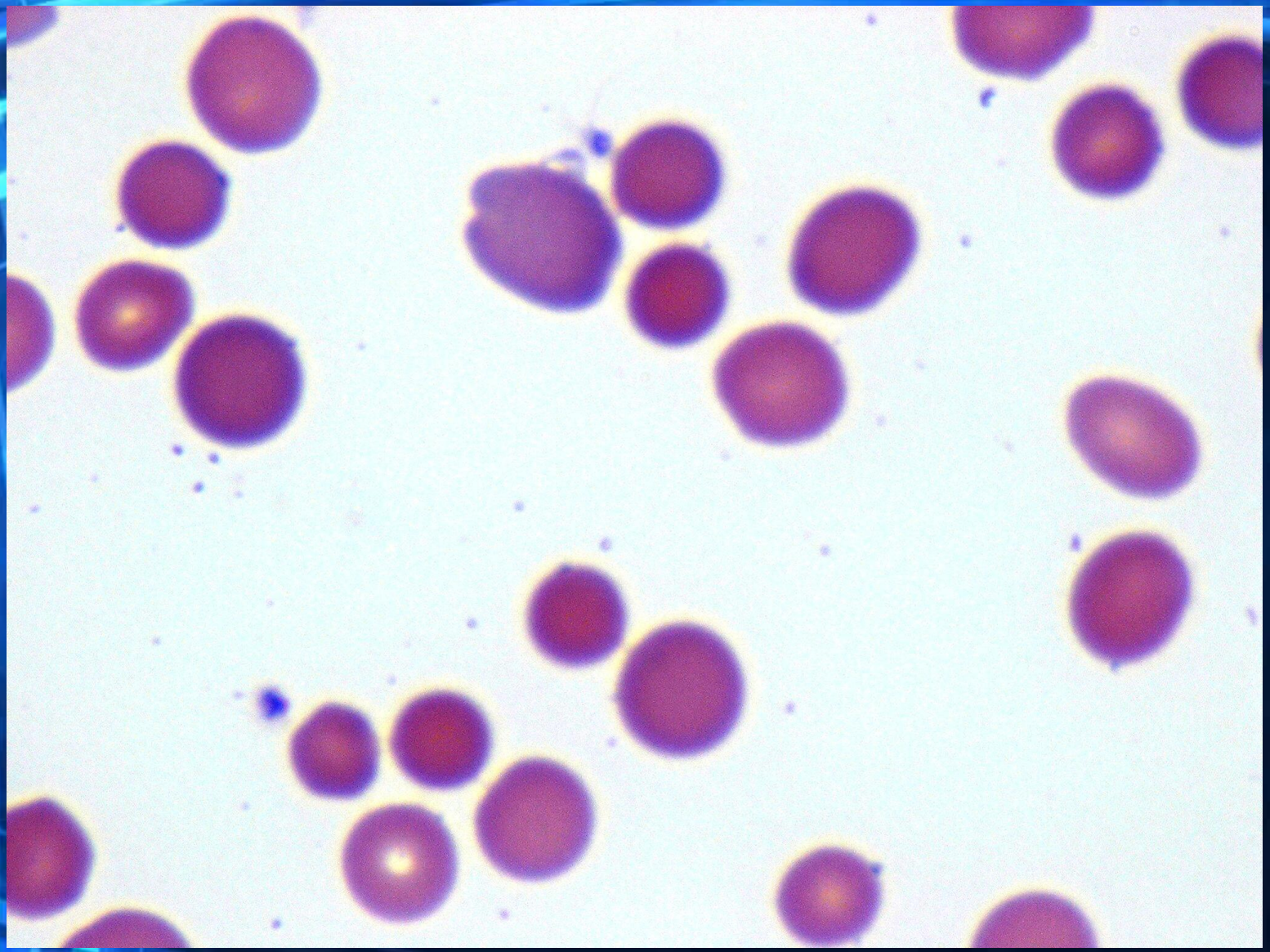
Labs- cont.

- LFTs normal except for indirect bilirubin of 2.2mg/dl
- LDH elevated to 290
- Direct anti-globulin (DAT) test is negative

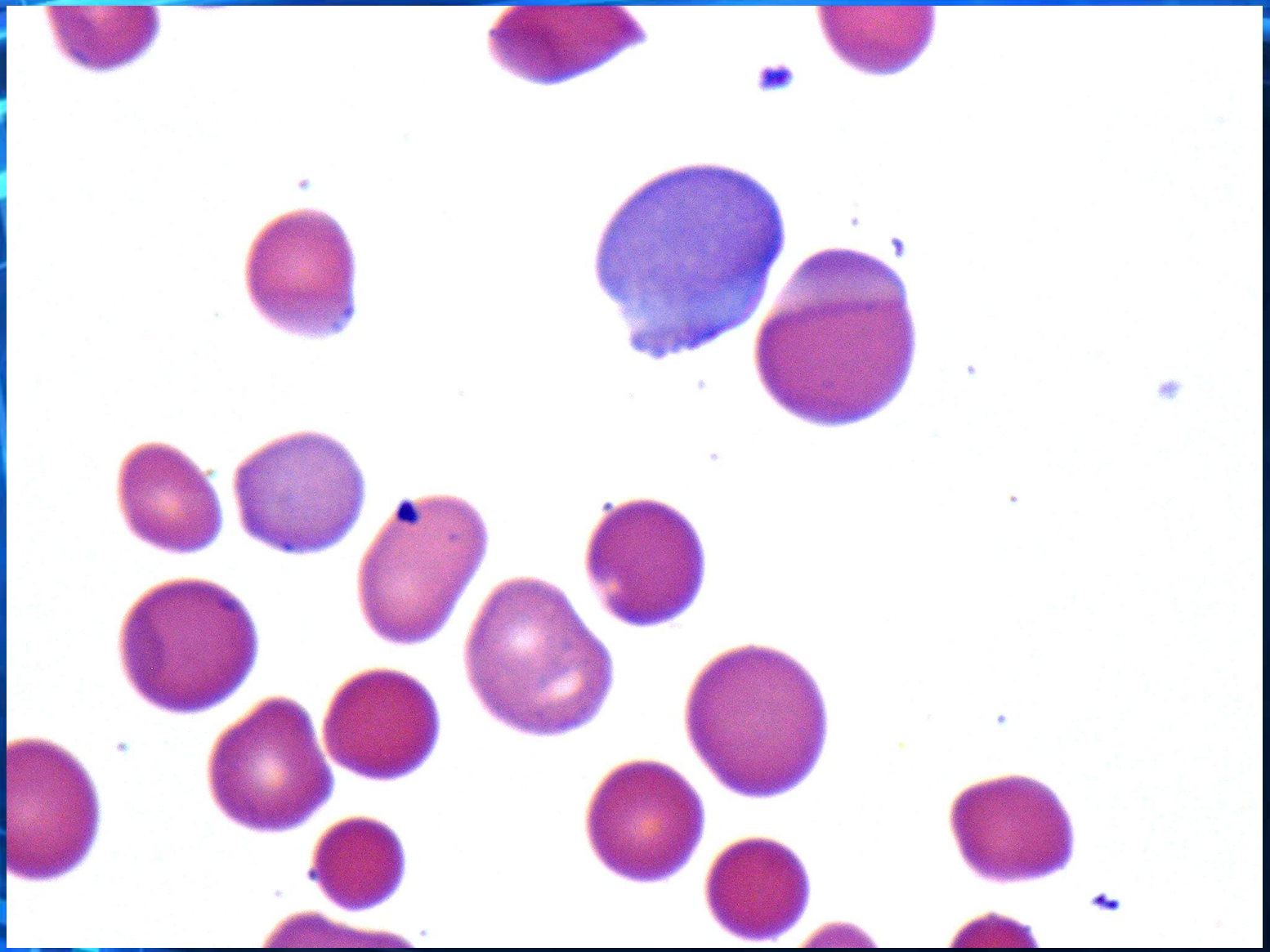
Peripheral Blood Smear



Peripheral Blood Smear (cont'd)



Peripheral Blood Smear (cont'd)



Hereditary spherocytosis (HS)

- Initially described in 1871
- Increased in persons of northern European descent
- In the US: 1 in 5000
- Most cases inherited in an autosomal dominant fashion

Structure

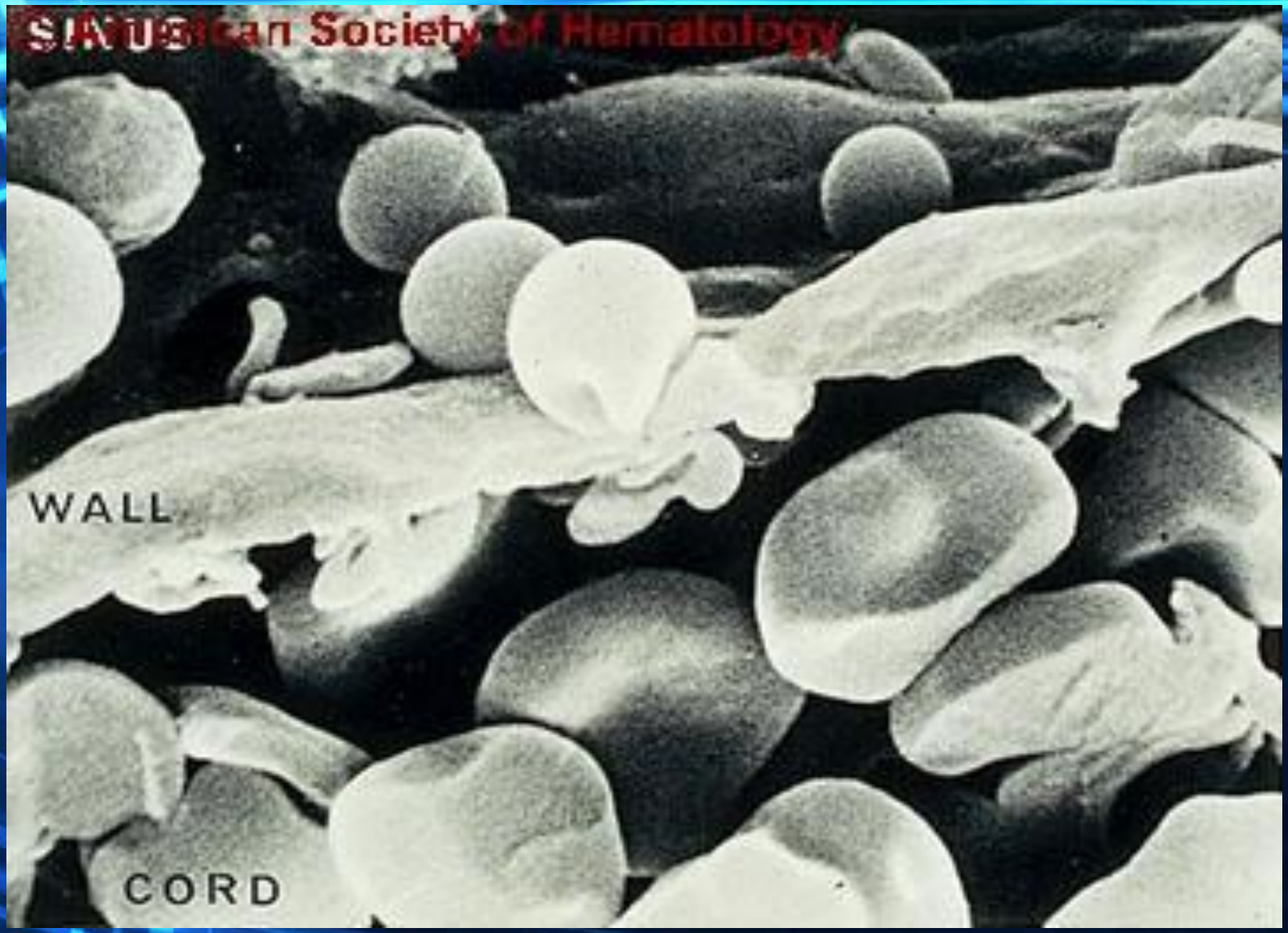
- The RBC membrane is composed of a lipid bilayer with associated proteins
- This is linked to a protein network “membrane cytoskeleton”
- This specific structural configuration gives the red blood cell flexibility (to squeeze through capillaries)

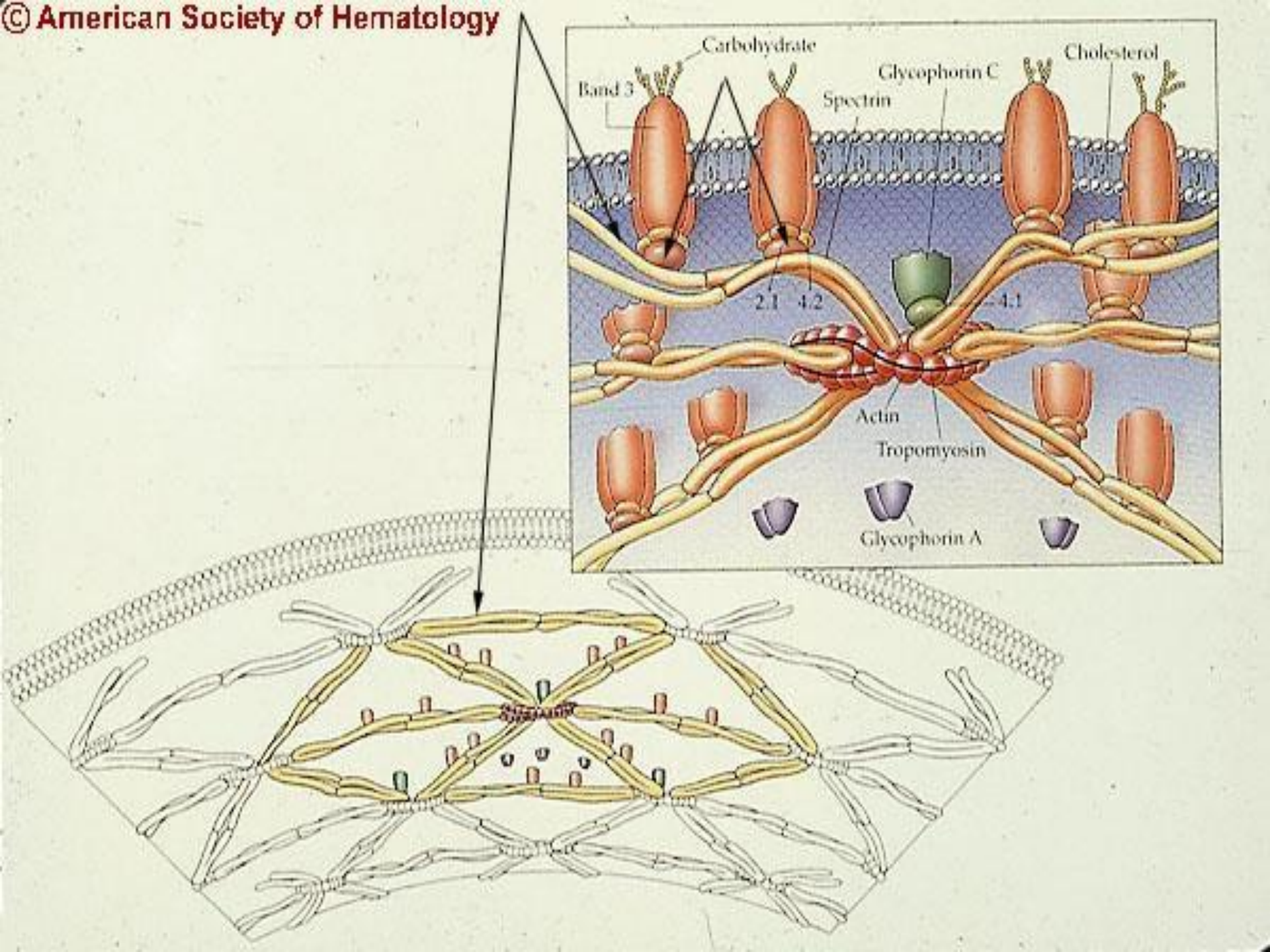
Membrane Protein Defects- resulting in spherocytes

- Spectrin deficiency alone
- Spectrin and ankyrin deficiency
- Band 3 deficiency
- Protein 4.2 defects

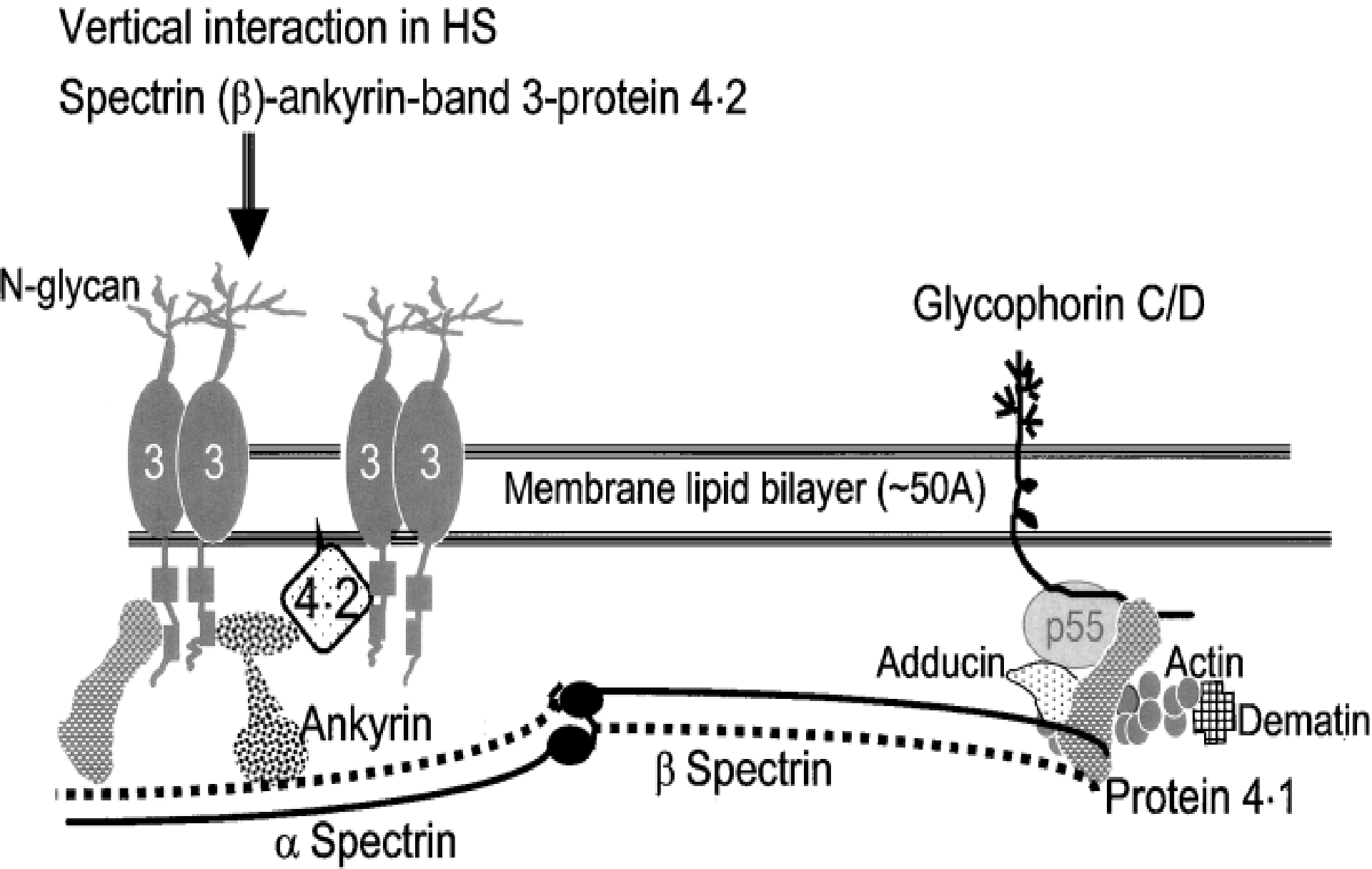
Pathophysiology

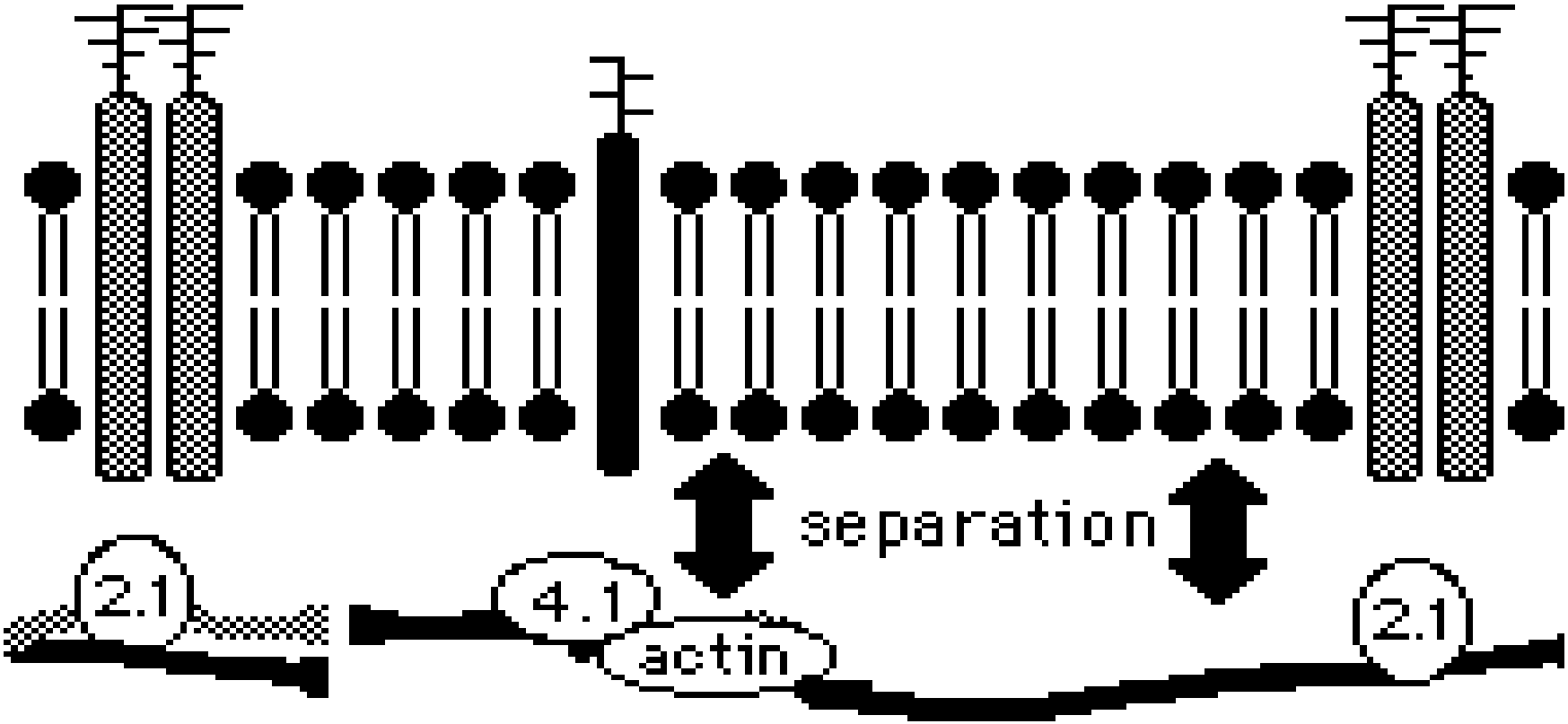
- Spherocytes are rounded red cells
  - Reduced surface membrane area
  - Losing their ability to change shape
  - Osmotically fragile compared to normal RBCs
- Spherocytes, being less flexible than normal RBCs, are destroyed in the spleen, causing splenomegaly

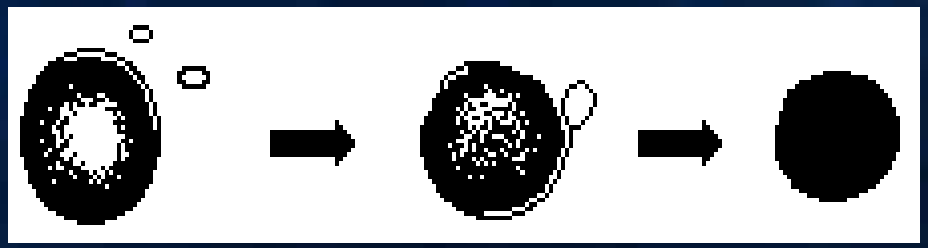

American Society of Hematology
WALL
CORD



Red Cell Cytoskeleton




separation
2.1
4.1
actin
2.1

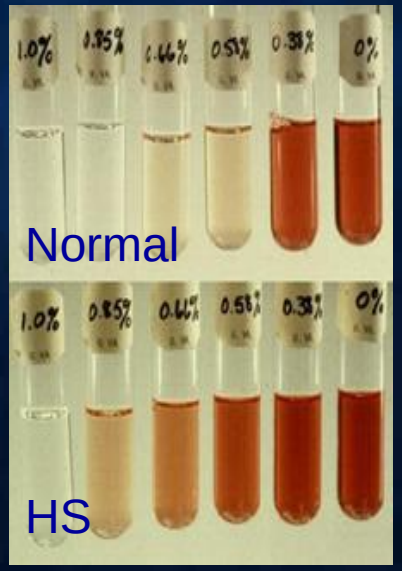


Diagnosis

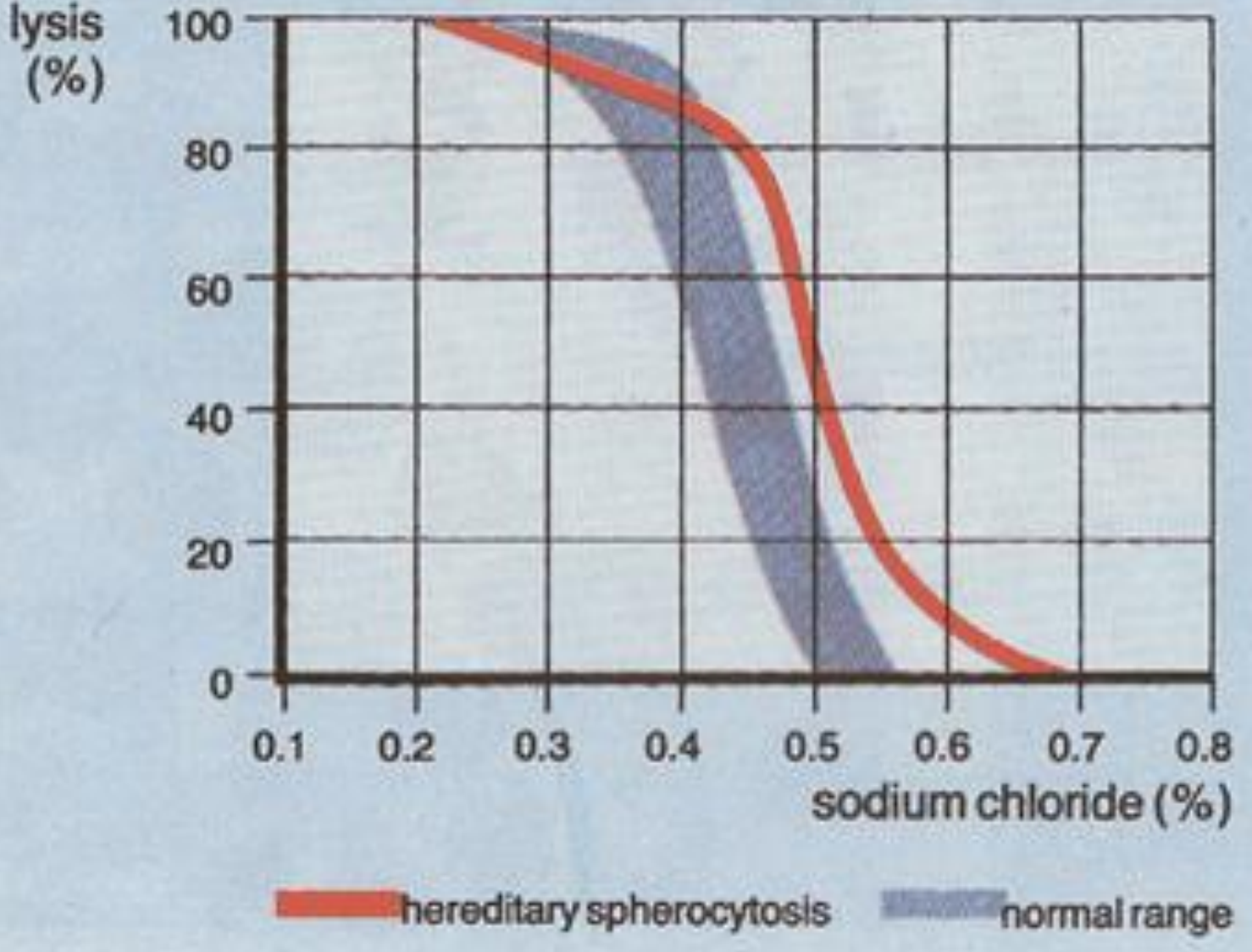
- Clinical picture
- Low hemoglobin, high MCHC, and high retics
- Increased indirect bilirubin, LDH, low haptoglobin
- PBS with spherocytes
- Negative DAT
- Positive osmotic fragility test

Osmotic Fragility Test

- Equal volumes of blood are placed in a series of hypotonic solutions
- Allowed to reach equilibrium (24 hr, 37 C); centrifuged and the optical density determined
- The RBC swells at 1.8x size
- Lysis occurs
- As the % saline decreases further, the amount of lysis increases

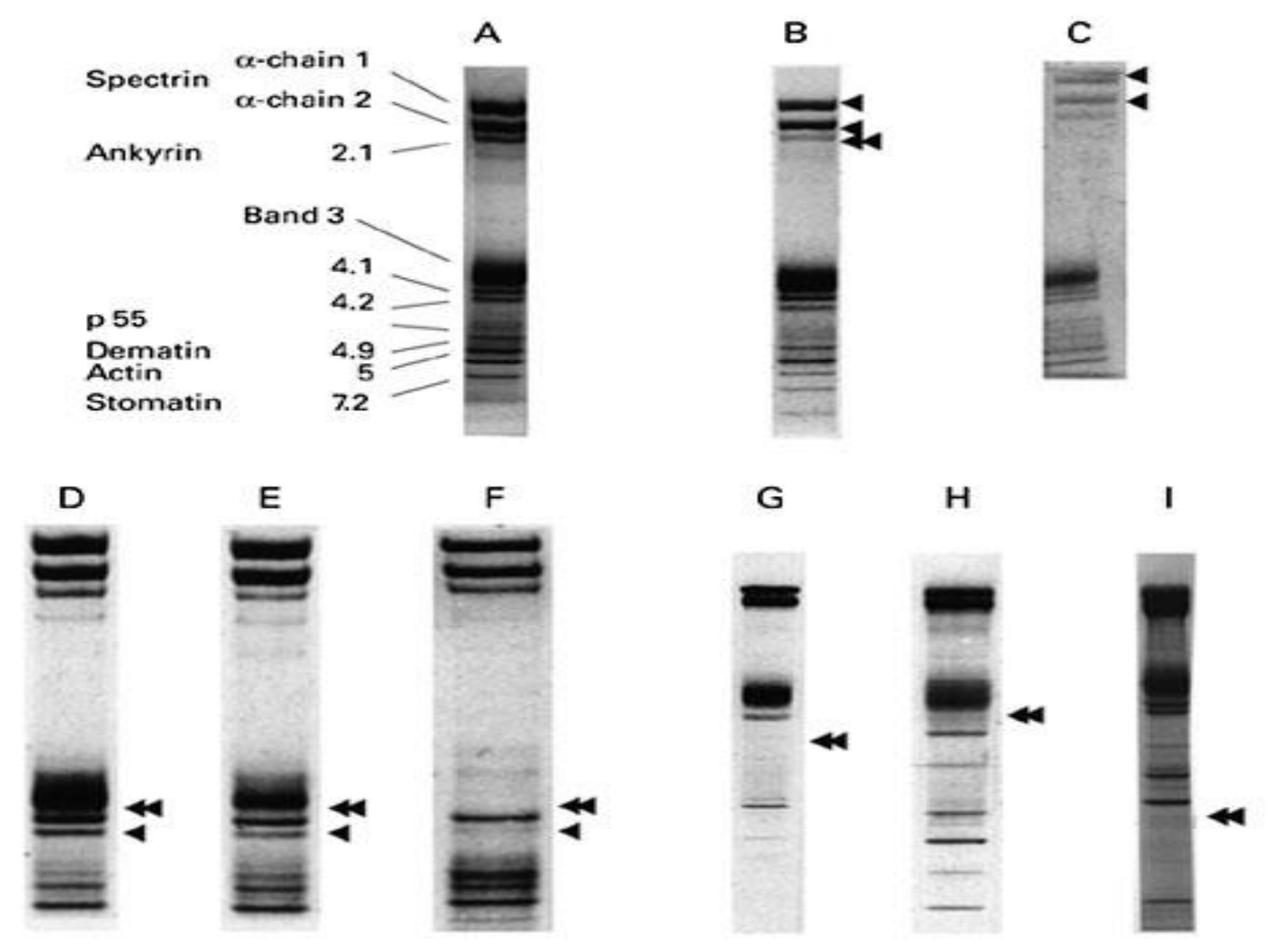


Osmotic Fragility



Alternative Tests

- Autohemolysis test
- Acidified glycerol test
- Pink test
- To specifically diagnose the protein abnormalities of hereditary spherocytosis, one must analyze red cell membrane proteins in gels, which separate proteins based on size and change


A
B
C
Spectrin
α-chain 1
α-chain 2
Ankyrin
2.1
Band 3
4.1
4.2
p 55
Dematin
4.9
Actin
5
Stomatin
7.2
D
E
F
G
H
I

Spectrin Deficiency

- Alpha spectrin mutations are associated with recessive forms of HS
- Beta spectrin mutations are associated with autosomal dominant forms

Ankyrin Defects

- Ankyrin is the binding site for spectrin
- Translocation of chromosome 8
- Deletion of short arm of chromosome 8
- In HS caused by ankyrin deficiency, decrease in spectrin occurs (equally diminished in 70% of cases)

Band 3 Deficiency

- 10-20% of patients with mild HS
- Autosomal dominant
- Proportionate decrease in 4.2 content

Protein 4.2 Deficiency

- Relatively common in Japanese

Management

- Depends on clinical picture
  - Splenectomy
  - Cholecystectomy (bilirubin stones)
  - Folic acid

References

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