

A 7-year-old boy is brought to the physician for "yellow eyes." He has been tired and does not feel like playing. The boy has a history of periodic pallor, and his father has had similar symptoms throughout his life. His family recently emigrated from England and his parents are nonconsanguineous. Examination shows a tired-appearing boy with pale conjunctivae, scleral icterus and generalized jaundice. The tip of the spleen is palpable. Laboratory results are as follows:

Complete blood count

Hemoglobin	10 g/dL
Reticulocytes	10%
Platelets	240,000/ μ L
Leukocytes	8,000/ μ L
Mean corpuscular volume	96 fL
Mean corpuscular hemoglobin concentration	38% Hb/cell

Liver function studies

Total bilirubin	3 mg/dL
Direct bilirubin	0.2 mg/dL
Aspartate aminotransferase (SGOT)	27 U/L
Alanine aminotransferase (SGPT)	32 U/L

Peripheral smear shows anisocytosis, spherocytes, and polychromatophilia. Direct and indirect antiglobulin (Coombs) tests are negative. Which of the following is the most appropriate next step in management of this patient?

- ☐ A. Acidified glycerol lysis test
- ☐ B. Bone marrow biopsy
- ☐ C. Erythrocyte CD55 and CD59 protein testing
- ☐ D. Glucocorticoid therapy

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- ☐ E. Hemoglobin electrophoresis
- ☐ F. Serum B12 level
- ☐ G. Serum iron level

Submit

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- ☒ A. Acidified glycerol lysis test [68%]
- ☐ B. Bone marrow biopsy [2%]
- ☐ C. Erythrocyte CD55 and CD59 protein testing [14%]
- ☐ D. Glucocorticoid therapy [3%]

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- ☐ E. Hemoglobin electrophoresis [12%]
- ☐ F. Serum B12 level [1%]
- ☐ G. Serum iron level [1%]

Proceed to Next Item

Explanation:

User Id: [REDACTED]

Hereditary spherocytosis	
Epidemiology	<ul style="list-style-type: none">• Autosomal dominant inheritance (~75%)• Northern European descent
Clinical presentation	<ul style="list-style-type: none">• Hemolytic anemia• Jaundice• Splenomegaly
Laboratory findings	<ul style="list-style-type: none">• ↑ Mean corpuscular hemoglobin concentration• Spherocytes on peripheral smear• Negative Coombs test• ↑ Osmotic fragility on acidified glycerol lysis test• Abnormal eosin-5-maleimide binding test
Treatment	<ul style="list-style-type: none">• Folic acid supplementation• Blood transfusions• Splenectomy
Complications	<ul style="list-style-type: none">• Pigment gallstones• Aplastic crises from parvovirus B19 infection

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This patient's **Coombs-negative hemolytic anemia** (low hemoglobin, reticulocytosis, **jaundice**/hyperbilirubinemia), **splenomegaly**, family history, and **spherocytes** on peripheral smear are concerning for hereditary spherocytosis (HS). HS is the most common hereditary hemolytic anemia in the northern European population and is usually inherited in an **autosomal-dominant** pattern. HS is due to a red blood cell membrane defect that results in extravascular hemolysis as red blood cells pass through the splenic circulation system.

Symptoms vary from asymptomatic to severe disease and can manifest any time between infancy and early adulthood. A key laboratory finding is elevation of the **mean corpuscular hemoglobin concentration** (>36% Hb/cell) due to cellular dehydration

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Symptoms vary from asymptomatic to severe disease and can manifest any time between infancy and early adulthood. A key laboratory finding is elevation of the **mean corpuscular hemoglobin concentration** ($>36\%$ Hb/cell) due to cellular dehydration and membrane loss. In addition, spherocytes burst more easily due to their decreased surface area to volume ratio, and the diagnosis can be confirmed by assessing red blood cell fragility. The traditional sodium-chloride osmotic fragility test has poor sensitivity. The current gold standard for diagnosis is a combination of the **eosin-5-maleimide binding test** (flow cytometry) with the **acidified glycerol lysis test**.

(Choice B) Bone marrow biopsy is not required. The disease can be diagnosed by clinical presentation, hematologic parameters, and noninvasive eosin-5-maleimide binding and acidified glycerol lysis tests.

(Choice C) Paroxysmal nocturnal hemoglobinuria (PNH) is diagnosed by erythrocyte CD55 and CD59 protein testing. Clinical manifestations of PNH include hemolytic anemia, cytopenias, and hypercoagulability. However, spherocytes are not seen in PNH, making testing for this condition unnecessary in this patient.

(Choice D) Glucocorticoid therapy can be helpful for warm-agglutinin autoimmune hemolytic anemia, which manifests as low hemoglobin, reticulocytosis, and positive Coombs testing. This patient is Coombs negative; steroids are not indicated in non-autoimmune hemolytic anemias such as HS.

(Choice E) Hemoglobin electrophoresis is used to diagnose hemoglobinopathies such as sickle cell disease or thalassemia. The hemoglobin itself is normal in HS.

(Choice F) Macrocytic anemia (mean corpuscular volume >100 fL) can be caused by vitamin B12 or folate deficiency. High red blood cell turnover from hemolysis can deplete folate, but B12 levels should not be affected.

(Choice G) Iron deficiency can cause a hypochromic, microcytic anemia. Mean corpuscular hemoglobin concentration should be normal and spherocytes would not be seen. Measuring iron level would be low yield in this case.

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Educational objective:

Hereditary spherocytosis has varying degrees of severity but typically manifests as the triad of Coombs-negative hemolytic anemia, jaundice, and splenomegaly. It should be suspected in patients with reticulocytosis, hyperbilirubinemia, spherocytosis, and family history of anemia. The diagnosis should be confirmed with eosin-5-maleimide binding and acidified glycerol lysis tests.

References:

1. [Hereditary spherocytosis, elliptocytosis, and other red cell membrane disorders.](#)
2. [Diagnostic power of laboratory tests for hereditary spherocytosis: a comparison study in 150 patients grouped according to molecular and clinical characteristics.](#)
3. [Guidelines for the diagnosis and management of hereditary spherocytosis--2011 update.](#)

Media Exhibit

ary spherocytosis

