

A 6-day-old girl has been in the hospital since birth due to persistent jaundice despite phototherapy. She was born at 39 weeks gestation to a primigravid 17-year-old woman. The mother had an unremarkable pregnancy, normal prenatal laboratory results, and O+ blood type. On the first day of life, the girl developed jaundice on the face that has now spread throughout her body. She has been breastfeeding well with good latch and making normal amounts of urine and "mustardy" stool. Family history is notable for anemia requiring blood transfusions in the father. The mother has no medical problems. The neonate's vital signs are normal. Examination shows scleral icterus and generalized jaundice. Splenomegaly is present. Laboratory results at 24 hours of life showed hemoglobin of 15.7 g/dL, total bilirubin of 10 mg/dL, and direct bilirubin of 0.4 mg/dL. Current laboratory results are as follows:

#### Complete blood count

Leukocytes	6000/ $\mu$ L
Hemoglobin	12.7 g/dL
Mean corpuscular volume	98 fL
Mean corpuscular hemoglobin concentration	42 g/dL
Platelets	230,000/ $\mu$ L
Reticulocytes	2.5%

#### Liver function studies

Albumin	4 g/dL
Total bilirubin	20 mg/dL
Direct bilirubin	0.4mg/dL
Aspartate aminotransferase (SGOT)	22 U/L
Alanine aminotransferase (SGPT)	24 U/L

#### Hematology

Blood type	A+
Serum lactate dehydrogenase	800 mg/dl



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#### Hematology

Blood type	A+
Serum lactate dehydrogenase	800 mg/dL
Coombs test	Negative

The neonate's peripheral smear shows spherocytes. Hemoglobin electrophoresis is normal. What is the most likely cause of this patient's anemia?

- ☐ A. ABO incompatibility
- ☐ B. Autoimmune hemolysis
- ☐ C. Defect of the alpha globin chain
- ☐ D. Defect of the beta globin chain
- ☐ E. Defect of the red blood cell membrane
- ☐ F. Erythrocyte glycolytic enzyme deficiency
- ☐ G. Folate deficiency

Submit



A 6-day-old girl has been in the hospital since birth due to persistent jaundice despite phototherapy. She was born at 39 weeks gestation to a primigravid 17-year-old woman. The mother had an unremarkable pregnancy, normal prenatal laboratory results, and O+ blood type. On the first day of life, the girl developed jaundice on the face that has now spread throughout her body. She has been breastfeeding well with good latch and making normal amounts of urine and "mustardy" stool. Family history is notable for anemia requiring blood transfusions in the father. The mother has no medical problems. The neonate's vital signs are normal. Examination shows scleral icterus and generalized jaundice. Splenomegaly is present. Laboratory results at 24 hours of life showed hemoglobin of 15.7 g/dL, total bilirubin of 10 mg/dL, and direct bilirubin of 0.4 mg/dL. Current laboratory results are as follows:

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Hematology

Blood type

A+

Serum lactate dehydrogenase

800 mg/dL

Coombs test

Negative

The neonate's peripheral smear shows spherocytes. Hemoglobin electrophoresis is normal. What is the most likely cause of this patient's anemia?

- ☐ A. ABO incompatibility [7%]
- ☐ B. Autoimmune hemolysis [4%]
- ☐ C. Defect of the alpha globin chain [1%]
- ☐ D. Defect of the beta globin chain [1%]
- ☒ E. Defect of the red blood cell membrane [84%]
- ☐ F. Erythrocyte glycolytic enzyme deficiency [3%]
- ☐ G. Folate deficiency [0%]

Proceed to Next Item

Explanation:

User Id:

Hereditary spherocytosis	
Epidemiology	<ul style="list-style-type: none"><li>Autosomal dominant inheritance (~75%)</li><li>Northern European descent</li></ul>
Clinical presentation	<ul style="list-style-type: none"><li>Hemolytic anemia</li><li>Jaundice</li><li>Splenomegaly</li></ul>
Laboratory findings	<ul style="list-style-type: none"><li>↑ Mean corpuscular hemoglobin concentration</li><li>Spherocytes on peripheral smear</li><li>Negative Coombs test</li><li>↑ Osmotic fragility on acidified glycerol lysis test</li><li>Abnormal eosin-5-maleimide binding test</li></ul>



Proceed to Next Item

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Treatment	<ul style="list-style-type: none"> <li>Folic acid supplementation</li> <li>Blood transfusions</li> <li>Splenectomy</li> </ul>
Complications	<ul style="list-style-type: none"> <li>Pigment gallstones</li> <li>Aplastic crises from parvovirus B19 infection</li> </ul>

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Hereditary spherocytosis is a common cause of hemolytic anemia in persons of Northern European descent. The classic triad of **hemolytic anemia**, **jaundice**, and **splenomegaly** can present at any time of life, including the newborn period. Most normal newborns develop some jaundice due to high fetal red blood cell turnover and physiologic immaturity of bilirubin clearance. However, jaundice on the first day of life and persistent, worsening jaundice are concerning for a pathologic process.

This infant's clinical presentation, family history, and laboratory findings of decreasing hemoglobin, elevated lactate dehydrogenase, **increased mean corpuscular hemoglobin concentration**, spherocytes on peripheral smear, and **negative Coombs test** are concerning for hereditary spherocytosis. Autosomal dominant mutation of the **ankyrin gene** causes decreased ankyrin in the red blood cell membrane, resulting in



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This infant's clinical presentation, family history, and laboratory findings of decreasing hemoglobin, elevated lactate dehydrogenase, **increased mean corpuscular hemoglobin concentration**, spherocytes on peripheral smear, and **negative Coombs test** are concerning for hereditary spherocytosis. Autosomal dominant mutation of the **ankyrin gene** causes decreased ankyrin in the red blood cell membrane, resulting in **spectrin deficiency**. The cell membrane becomes round (normal red blood cells are biconcave) and unstable. The **fragile** spherocytes are less able to traverse through tight spaces in the microcirculation such as the spleen, which results in hemolytic anemia and splenomegaly. The diagnosis is confirmed by the acidified glycerol lysis and eosin-5-maleimide binding tests.

Although the reticulocyte count is normally high in hemolytic anemia, neonates are unable to produce appropriate erythropoiesis in response to anemia, as seen in this patient. They are thus predisposed to severe anemia and often require transfusions.

**(Choices A and B)** Isoimmune hemolytic disease of the newborn (eg, ABO incompatibility) and autoimmune hemolytic anemia can cause decreased hemoglobin, increased lactate dehydrogenase, and hyperbilirubinemia. Antibody-mediated hemolysis would cause a positive Coombs test. This patient's negative Coombs test rules out an antibody-mediated process.

**(Choices C and D)** Hemoglobinopathies (eg, alpha and beta thalassemias, sickle cell anemia) are unlikely due to normal hemoglobin electrophoresis.

**(Choice F)** Pyruvate kinase deficiency and glucose-6-phosphate dehydrogenase deficiency can cause hemolytic anemia due to inherited defects of erythrocyte glycolytic enzymes. However, spherocytes would not be seen on peripheral blood smear.

**(Choice G)** Folate deficiency can cause macrocytosis. Patients with hemolytic anemia are at risk of becoming folate deficient due to high cell turnover. This is unlikely to occur in the immediate neonatal period and when laboratory results show normal mean corpuscular volume.

**Educational objective:**

Hereditary spherocytosis should be suspected in a patient with persistent jaundice,



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#### Educational objective:

Hereditary spherocytosis should be suspected in a patient with persistent jaundice, hemolytic anemia, splenomegaly, positive family history, and spherocytes on peripheral blood smear. Red blood cell fragility on acidified glycerol lysis and eosin-5-maleimide binding tests confirms the diagnosis.

#### References:

1. [Natural history of hereditary spherocytosis during the first year of life.](#)
2. [Guidelines for the diagnosis and management of hereditary spherocytosis-2011 update.](#)