

A 2-day-old Asian girl in the newborn nursery has jaundice. She was born at 40 weeks gestation to a 30-year-old woman by uncomplicated vaginal delivery. Membranes ruptured spontaneously 1 hour prior to delivery. Prenatal laboratory testing was normal. Group B streptococcus screen was negative. Maternal blood type is A-positive. The neonate has been exclusively breastfeeding with good latch, voiding appropriately, and passing meconium. Weight and length are at the 50th percentile. Vital signs are normal. On examination, **jaundice of the face and neck** is present. The remainder of the examination is unremarkable.

Laboratory results at 24 hours of life are as follows:

Total bilirubin 7 mg/dL

Conjugated bilirubin 0.4 mg/dL

Which of the following is the most likely cause of this newborn's condition?

- ☐ A. Congenital obliteration of the extrahepatic biliary tree
- ☐ B. Decreased hepatic uridine diphosphogluconurate glucuronosyltransferase activity
- ☐ C. Decreased production of beta globin chains
- ☐ D. Deficiency of galactose-1-uridyl transferase
- ☐ E. Isoimmune-mediated hemolysis
- ☐ F. Sepsis-mediated hemolysis

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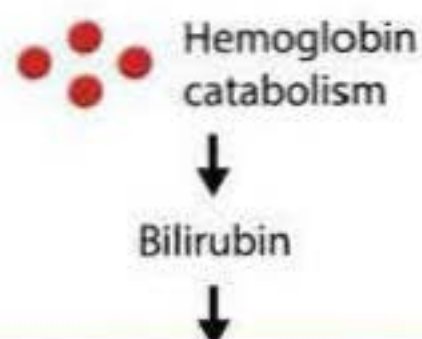
- ☐ A. Congenital obliteration of the extrahepatic biliary tree [2%]
- ☒ B. **Decreased hepatic uridine diphosphoglucuronate glucuronosyltransferase activity** [82%]
- ☐ C. Decreased production of beta globin chains [2%]
- ☐ D. Deficiency of galactose-1-uridyl transferase [5%]
- ☐ E. Isoimmune-mediated hemolysis [9%]
- ☐ F. Sepsis-mediated hemolysis [0%]

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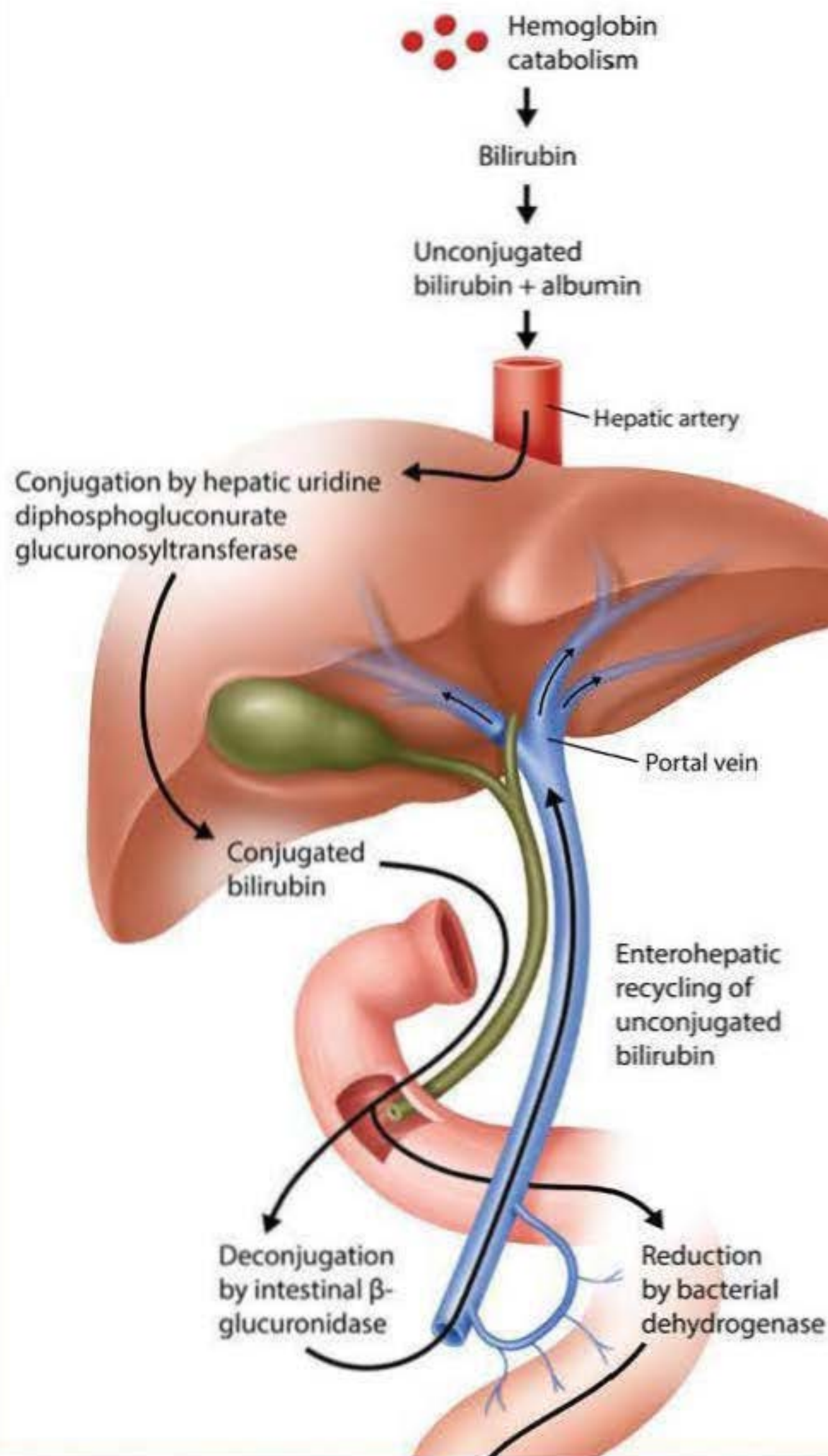
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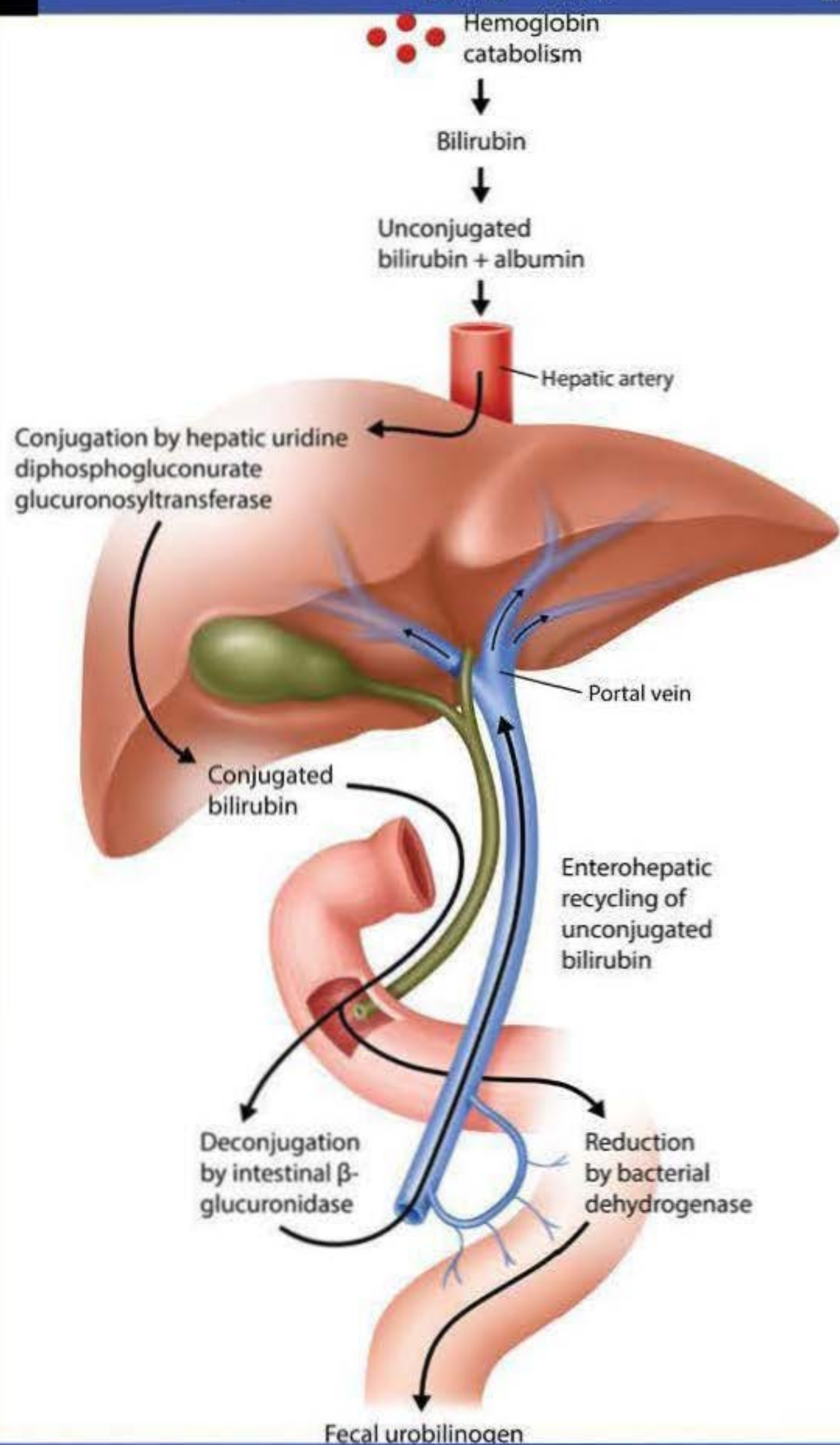
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Bilirubin metabolism



Bilirubin metabolism





Fecal urobilinogen

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Almost all newborns have jaundice that appears on **days 2-4 of life**. Although total bilirubin is normally <1 mg/dL in adults, newborns have **unconjugated hyperbilirubinemia** due to several physiologic differences in bilirubin metabolism.

1. At birth, red blood cell concentration is elevated (**hematocrit 50%-60%**) with shorter life span (~90 days), resulting in **high hemoglobin turnover** and bilirubin production.
2. Bilirubin clearance is initially slow because hepatic uridine diphosphoglucuronate glucuronosyltransferase (UGT) does not reach adult levels until age 2 weeks. **Asian newborns have decreased UGT activity** compared to other ethnicities.
3. Enterohepatic recycling is increased as the **sterile newborn gut** cannot break down bilirubin to urobilinogen for fecal excretion. More bilirubin is resorbed in the gut and recycled in the enterohepatic circulation until the gut is colonized and produces bacterial enzymes for reduction to urobilinogen.

Physiologic jaundice of the newborn is usually benign and resolves on its own by age 1-2 weeks. Newborns should be monitored for persistent or worsening jaundice as high levels can cause brain damage. Frequent feeding should be encouraged to promote gut colonization and fecal excretion. Natural sunlight can help decrease bilirubin but is not recommended due to risk of sunburn. Sometimes rapidly rising hyperbilirubinemia requires **phototherapy** for **kernicterus** prevention. **Exchange transfusion** is indicated for total bilirubin levels >20 - 25 mg/dL.

(Choice A) Jaundice is usually the first sign of biliary atresia. The neonatal liver can conjugate bilirubin, but the obstructed biliary tract cannot transport bile to the intestine, resulting in hepatic bile retention (cholestasis), direct hyperbilirubinemia, and jaundice. Direct hyperbilirubinemia is defined as conjugated bilirubin >2 mg/dL (34.2 mmol/L) or $>20\%$ of total bilirubin, which is not seen in this patient.

(Choice C) Although beta thalassemia can cause hemolysis and unconjugated hyperbilirubinemia, newborns are asymptomatic as they have mostly fetal hemoglobin, which is comprised of alpha and gamma globin chains. After age 6 months, symptoms of hemolytic anemia emerge as gamma globin chains are replaced with beta for the production of adult hemoglobin.

(Choice D) Galactosemia can cause hyperbilirubinemia but also feeding intolerance (eg, vomiting, diarrhea), which is not seen in this patient. It is also uncommon in contrast to physiologic jaundice of the newborn.

(Choice E) Newborns of mothers with blood group O- or Rh-negative are at risk for hemolytic anemia and severe hyperbilirubinemia. ABO and Rh incompatibility is unlikely

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(Choice E) Newborns of mothers with blood group O- or Rh-negative are at risk for hemolytic anemia and severe hyperbilirubinemia. ABO and Rh incompatibility is unlikely in this case with maternal blood type A-positive.

(Choice F) Sepsis can cause hemolysis and exacerbate hyperbilirubinemia. This patient does not have fever or risk factors for neonatal sepsis (eg, prolonged rupture of membranes, positive group B streptococcal screen, fever), making this etiology unlikely.

Educational objective:

Physiologic jaundice of the newborn is common and usually benign. The indirect hyperbilirubinemia is due to increased bilirubin production, decreased bilirubin clearance, and increased enterohepatic recycling. Phototherapy is the gold standard treatment for rapidly rising hyperbilirubinemia to prevent kernicterus.

References:

1. Neonatal hyperbilirubinemia in the low-intermediate-risk category on the bilirubin nomogram.
2. Management of hyperbilirubinemia in the newborn infant 35 or more weeks of gestation.
3. Assessing jaundice in infants of 35-week gestation and greater.
4. A practical approach to neonatal jaundice.