Board Review in Neonatology 2020

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Q1

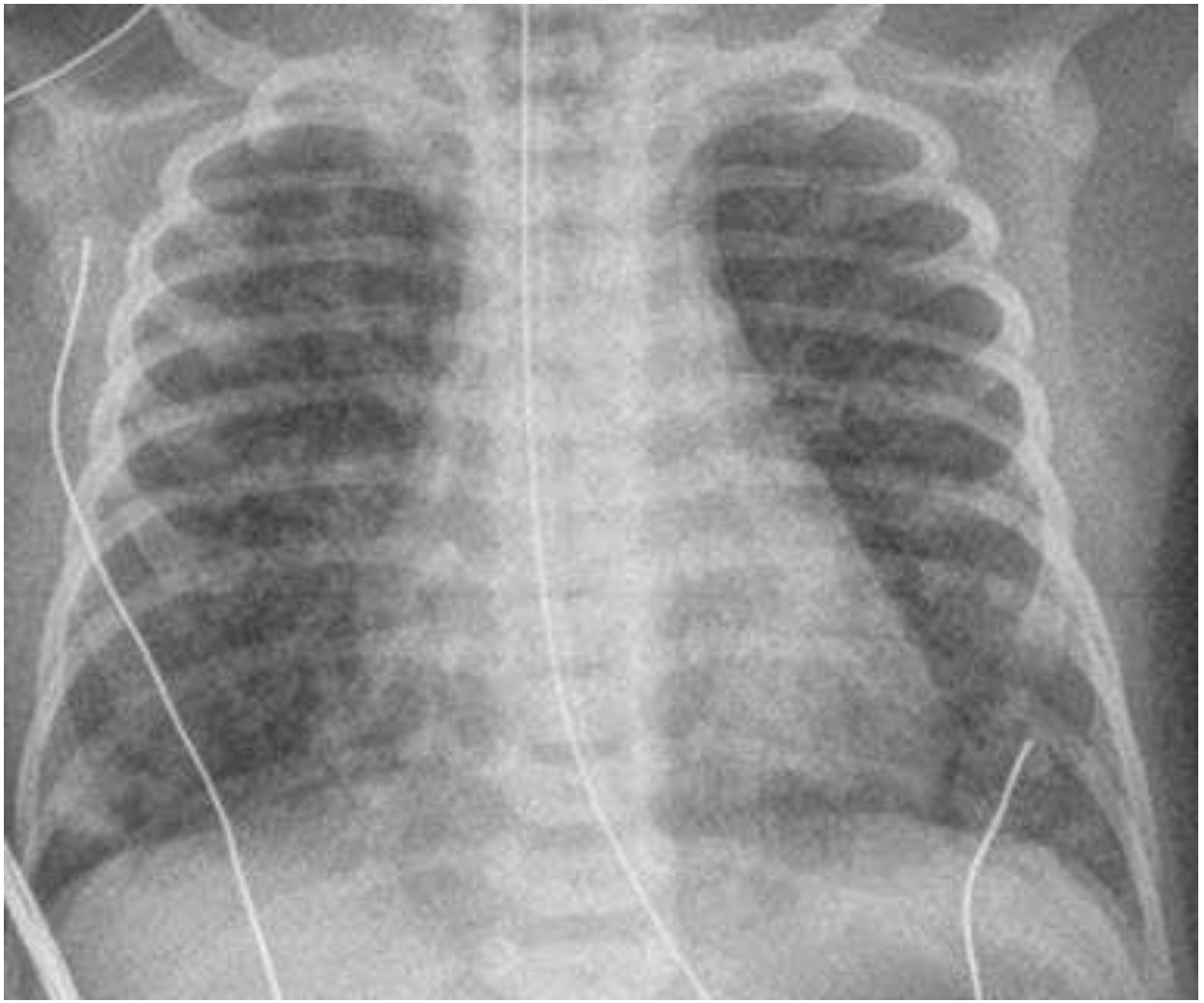
Q1

- A 40-week-gestation neonate with tachypnea is being evaluated 2 hours after birth. Maternal prenatal serologic test results were negative. Group B *Streptococcus* status is unknown. The neonate was born via cesarean section with meconium stained amniotic fluid noted at delivery. She cried immediately and received routine initial steps of care.

Q1

- Apgar scores were 6 and 8 at 1 and 5 minutes, respectively. Vital signs include a heart rate of 186 beats/min, respiratory rate of 67 breaths/min, blood pressure of 76/45 mm Hg,temperature of 37.6°C, and room air oxygen saturation of 87% on the left foot.
- Physical examination reveals nasal flaring with intermittent grunting, no cardiac murmur, peripheral pulses was felt, and no hepatosplenomegaly.

- **Her chest radiograph is shown**



Q1

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  A. Meconium aspiration syndrome
  B. Pneumonia
  C. Pneumothorax
  D. Respiratory distress syndrome

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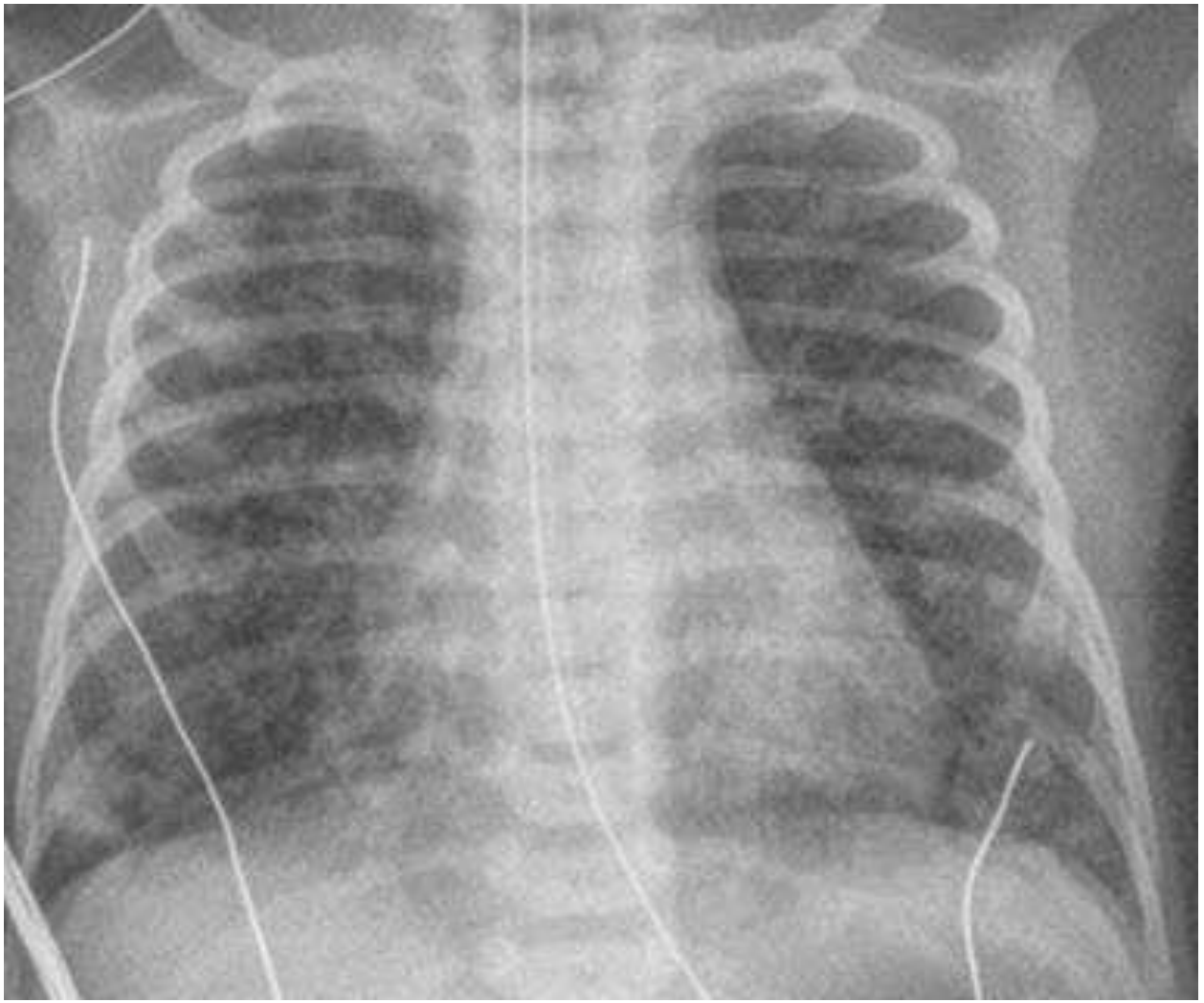

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Correct Answer: A

Meconium aspiration syndrome

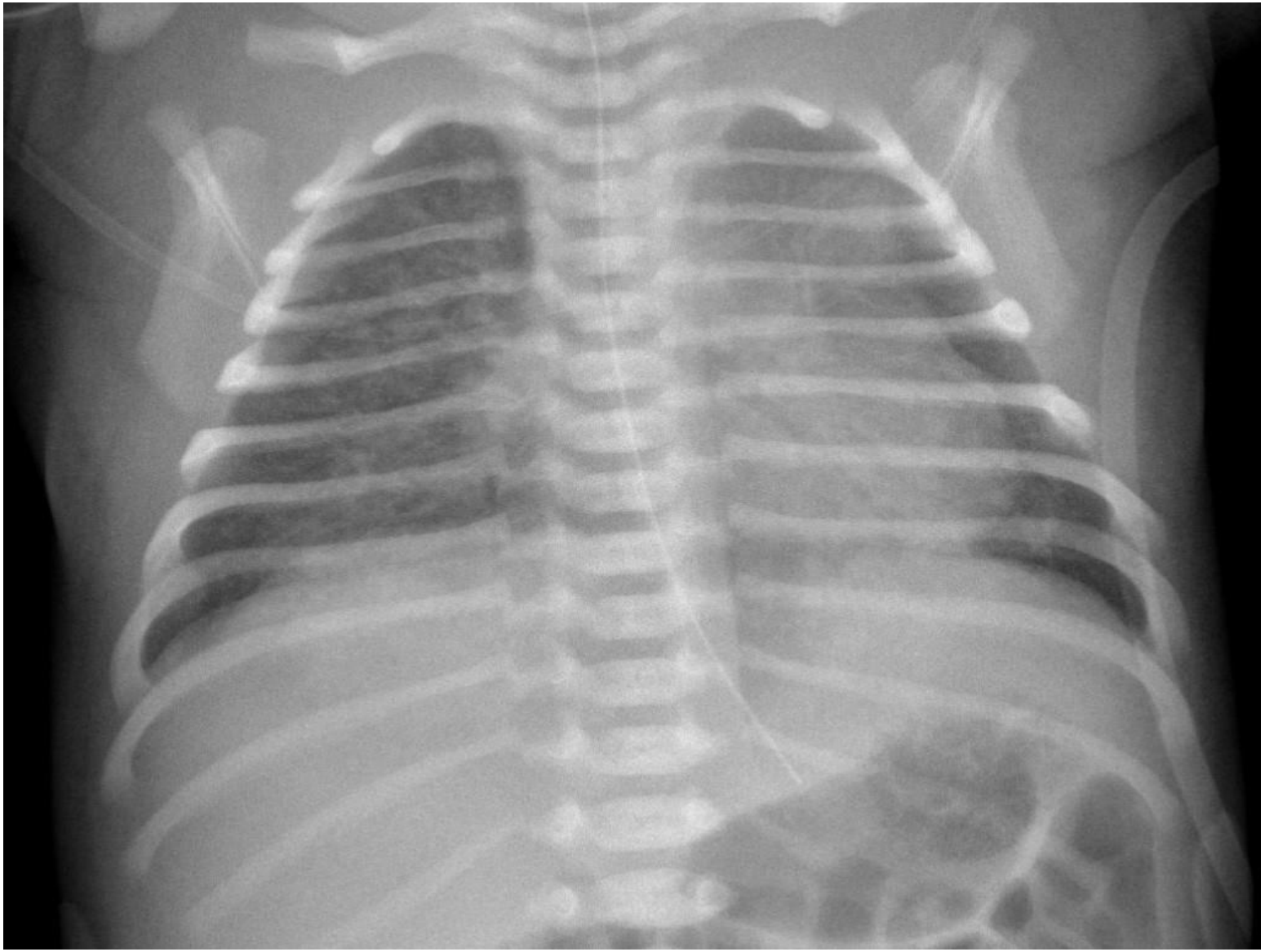
- The chest radiograph of the neonate in the vignette, in combination **with meconium-stained amniotic fluid and respiratory distress, is most consistent with a diagnosis of Meconium aspiration syndrome (MAS).**

- **Meconium aspiration syndrome** affects 0.4 to 1.6 neonates per 1,000 live births, with higher rates noted among late term (41 to 41 6/7 weeks') and post-term (42 to 42 6/7 weeks') gestation neonates.
- Risk factors for MAS include Cesarean delivery and fetal compromise. It may be associated with neonatal respiratory failure and pulmonary hypertension.

- After delivery, meconium acts via a ball valve mechanism, obstructing air flow and causing patchy areas of atelectasis and over distention which can be seen on chest radiography.
- Because of changes in the neonatal resuscitation program in 2015, vigorous neonates born through meconium-stained amniotic fluid no longer undergo elective intubation.
- This change in practice may be associated with an increase in admissions to the neonatal intensive care unit.

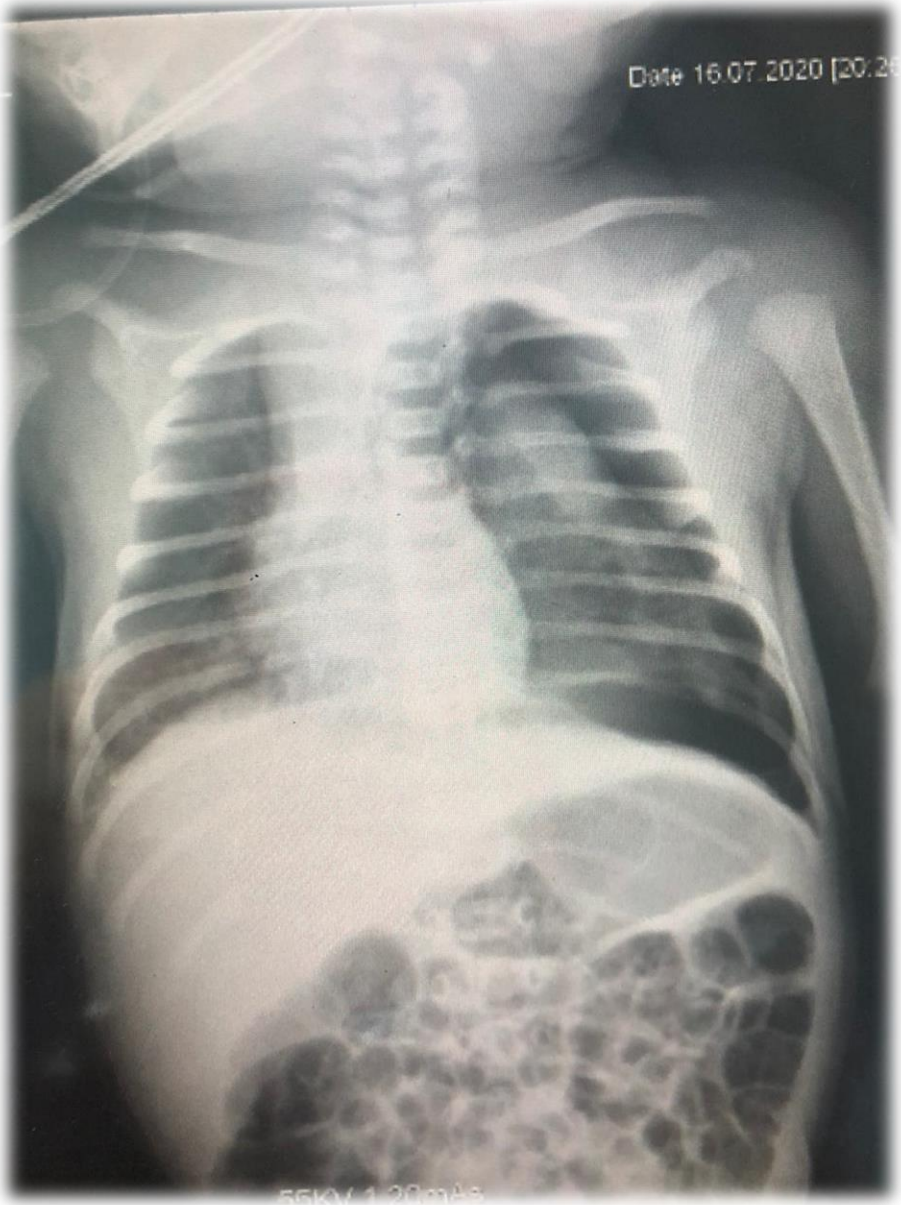
Pneumonia

- Group B streptococcal (GBS) pneumonia typically has a similar clinical presentation to respiratory distress syndrome (RDS) and MAS. Neonates exhibit tachypnea, grunting, flaring, and poor lung expansion.
- Maternal status may be GBS negative or positive with inadequate prophylaxis before delivery.
- Chest radiograph has a diffuse **reticulogranular appearance**.



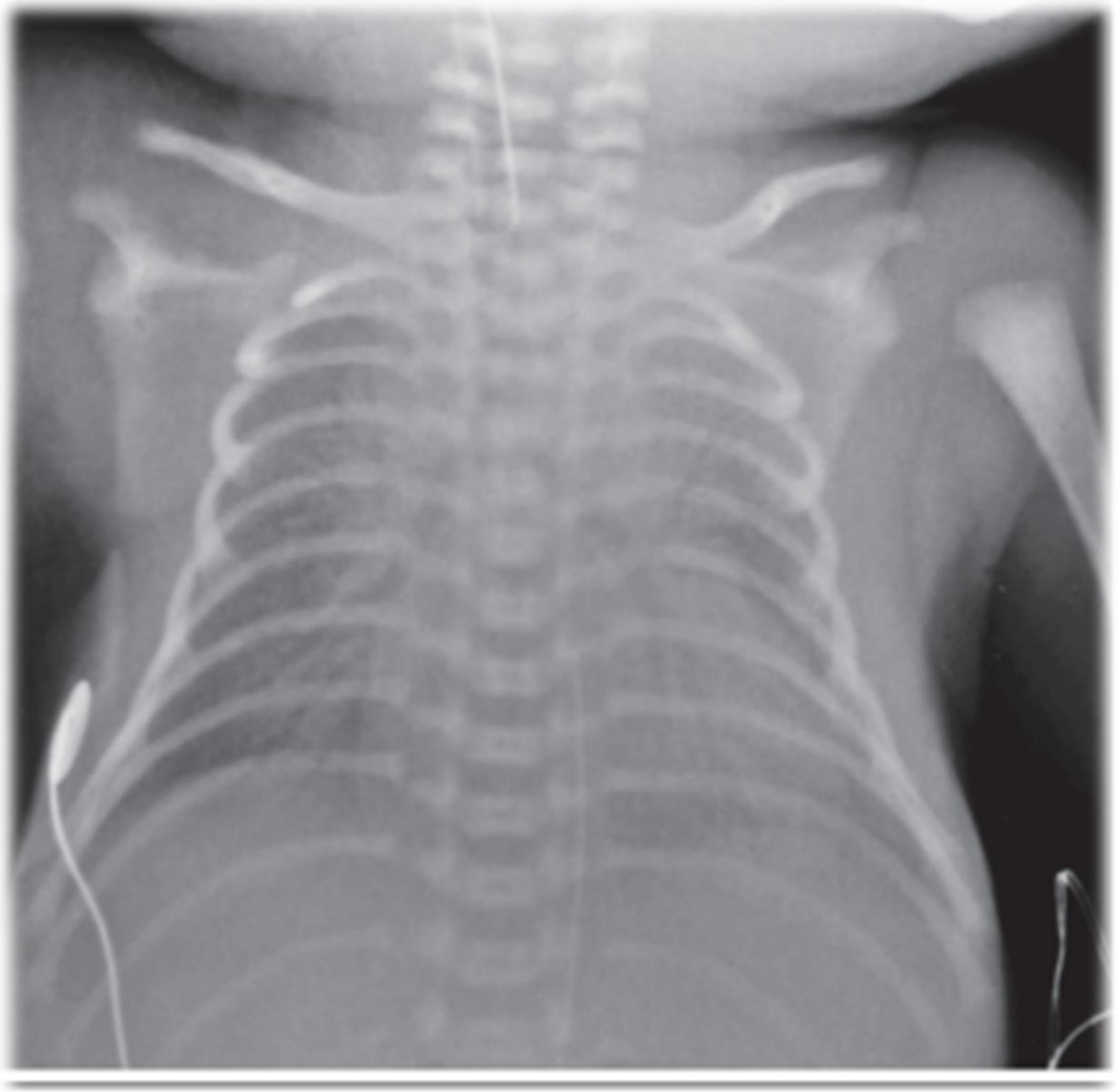
Pneumothorax

- A pneumothorax may occur as part of an air leak syndrome. Neonates requiring positive pressure ventilation after delivery have an increased risk of pneumothorax. In addition, both RDS and MAS are associated with an increased risk of pneumothorax.
- A large pneumothorax may compress the heart, requiring evacuation with a needle thoracostomy. Less often, a thoracotomy may be required.


Date 16.07.2020

Respiratory distress syndrome

- **Respiratory distress syndrome** is a disease of premature neonates caused by inadequate surfactant production.
- The severity of RDS is proportional to the degree of prematurity. Affected neonates present with tachypnea, grunting, flaring, and poor lung expansion.
- Chest radiography shows decreased lung volumes and a **homogenous ground glass appearance**, identical to that seen in GBS.



Q2

Q2

- A 6-day-old female neonate is brought to the emergency department for evaluation of abnormal movements. She was born at 39 weeks' gestation to a gravida 2 para 2 mother with an uncomplicated pregnancy via normal spontaneous vaginal delivery. Apgar scores were 9 and 9 at 1 and 5 minutes, respectively.
- Her neonatal course was unremarkable, and she was discharged home on the second day after birth.

Q2

- On the day of presentation, her parents noted abnormal movements that were described as asymmetric twitching of her legs with accompanying lip smacking and perioral cyanosis with periods where she appeared to hold her breath.
- These periods would last up to 2 minutes before self-resolving with return to her typical feeding and activity. Family history is significant for her mother and a maternal uncle with seizures around the time they were born, which subsequently resolved.

- The neonate's vital signs are within normal limits. She appears alert and has normal neurological examination findings.

- During examination, she has a typical event where her eyes open and she stares straight ahead with clonic movements of her legs and lip smacking with apnea. Intravenous phenobarbital (20 mg/kg) is administered, and the movements stop.

- Results of noncontrast computed tomography of the head are normal.
- Results of a complete blood cell count, comprehensive metabolic panel, urinalysis, ammonia level, C-reactive protein, lactate, serum and urine toxicology screen, and capillary blood glucose are within normal limits. Lumbar puncture yields clear cerebrospinal fluid.

- Laboratory data from cerebrospinal fluid analysis are shown:
- Cultures are pending.

Laboratory test	Result
White blood cell count	4/μL
Lymphocytes	75%
Red blood cell count	0/μL
Protein	120 mg/dL
Glucose	100 mg/dL (5.6 mmol/L)

Cultures are pending.

- Of the following, the MOST likely diagnosis is
  A. bacterial meningitis
  B. benign familial neonatal convulsions
  C. hypoxic-ischemic encephalopathy
  D. pyridoxine-dependent epilepsy

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Correct Answer: B

Benign familial neonatal convulsions

- The clinical presentation of the neonate in this vignette is consistent with benign familial neonatal convulsions, 1 of 2 recognized benign neonatal seizure syndromes.
- An affected neonate will present with focal clonic seizures responsive to antiepileptic medication
- The seizures typically resolve spontaneously in the first few days to week after birth. A positive family history of neonatal seizures distinguishes benign familial neonatal convulsions from benign neonatal seizures, or "fifth-day fits.“
-

Benign familial neonatal convulsions

- Key features supportive of the diagnosis of benign familial neonatal convulsions include a positive family history and lack of clinical, radiologic, or laboratory risk factors for seizure in a neonate with normal neurological examination findings and normal interictal electroencephalography (EEG) background.

- In both syndromes, prognosis is excellent with a benign clinical course. Antiepileptic medication can be withdrawn after a few weeks to months of therapy.

Neonatal seizures

- Neonatal seizures are a relatively common condition, typically occurring secondary to a variety of etiologies in the first week after birth.
- Causes include symptomatic seizures in the setting of hypoxic-ischemic encephalopathy, infection, a vascular event, congenital malformations, or an underlying genetic or metabolic disorder.
- The neonatal brain is immature with incomplete myelination and reduced capacity for sufficient inhibition of the hypersynchronous excitatory neuronal firing that causes seizures
-

Neonatal seizures

- As a result, neonatal seizures clinically can be subtle, arising from either a single focus or multiple foci that may not generalize. Neonatal seizures are classified as focal/multifocal clonic , focal tonic, generalized tonic, myoclonic and subtle.

- Close clinical observation and a high suspicion for seizure is crucial for prompt diagnosis and treatment.

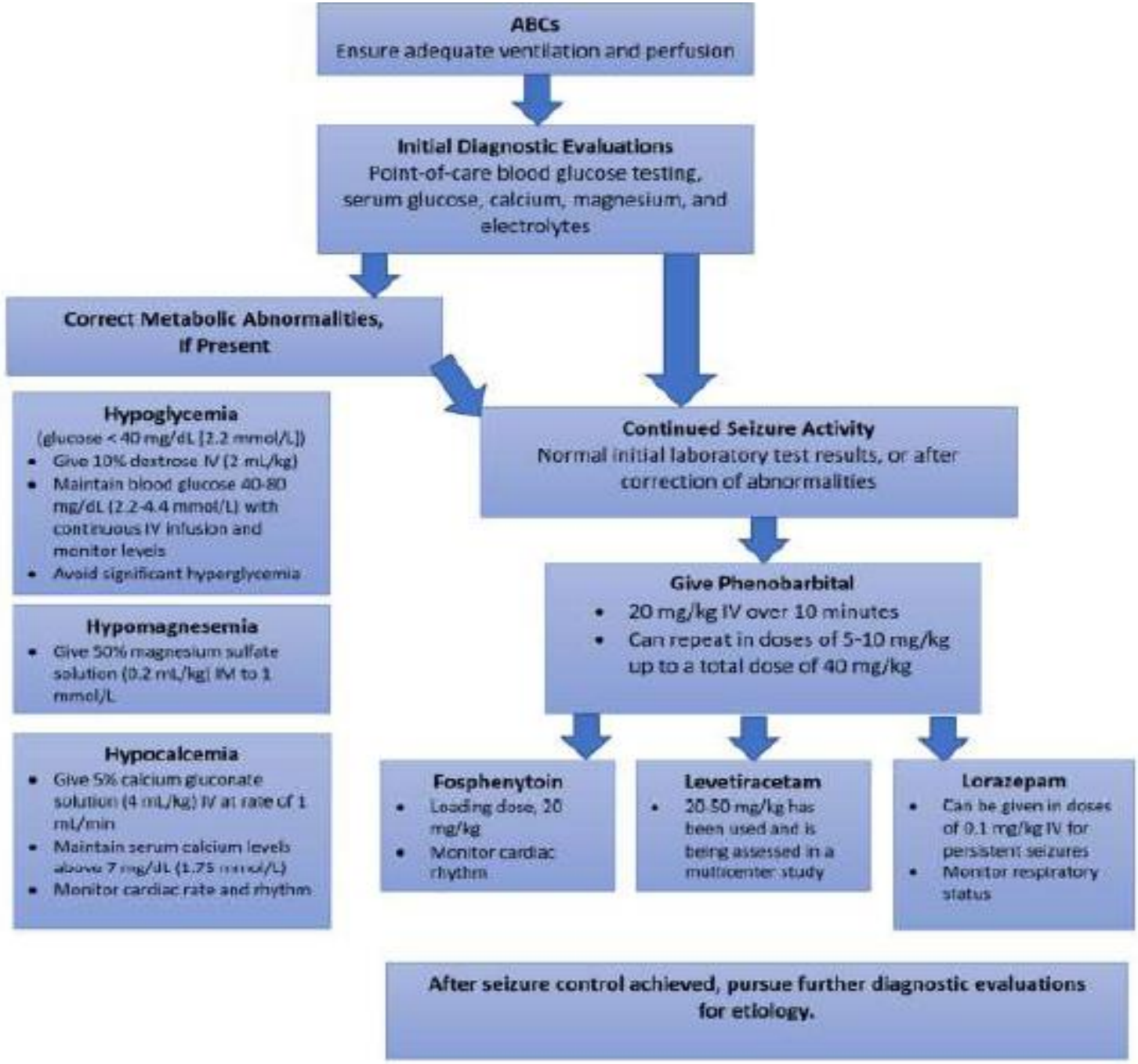
Neonatal seizures

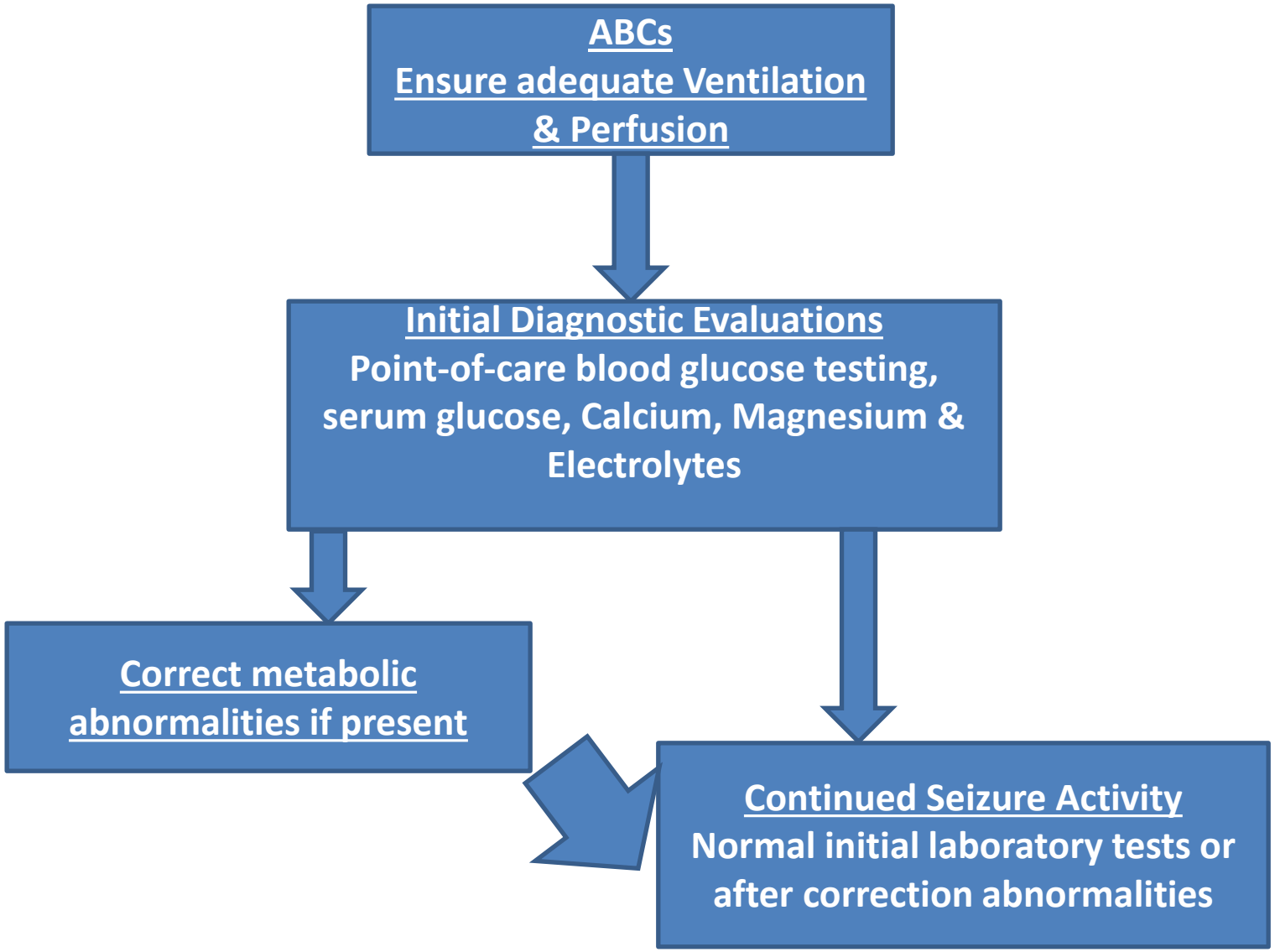
- Once the neonate is stabilized, a diagnostic evaluation to identify an etiology initial testing is aimed at treatable conditions such as correctable metabolic derangements (ie, hypoglycemia, hyponatremia). Hypoxic-ischemic encephalopathy is the most common cause of neonatal seizures.
- Affected neonates typically show some degree of clinical encephalopathy with abnormalities noted on interictal EEG and magnetic resonance imaging demonstrating brain injury.
- Central nervous system infections, such as meningitis and encephalitis, can cause seizures and are evaluated by cerebrospinal fluid analysis.

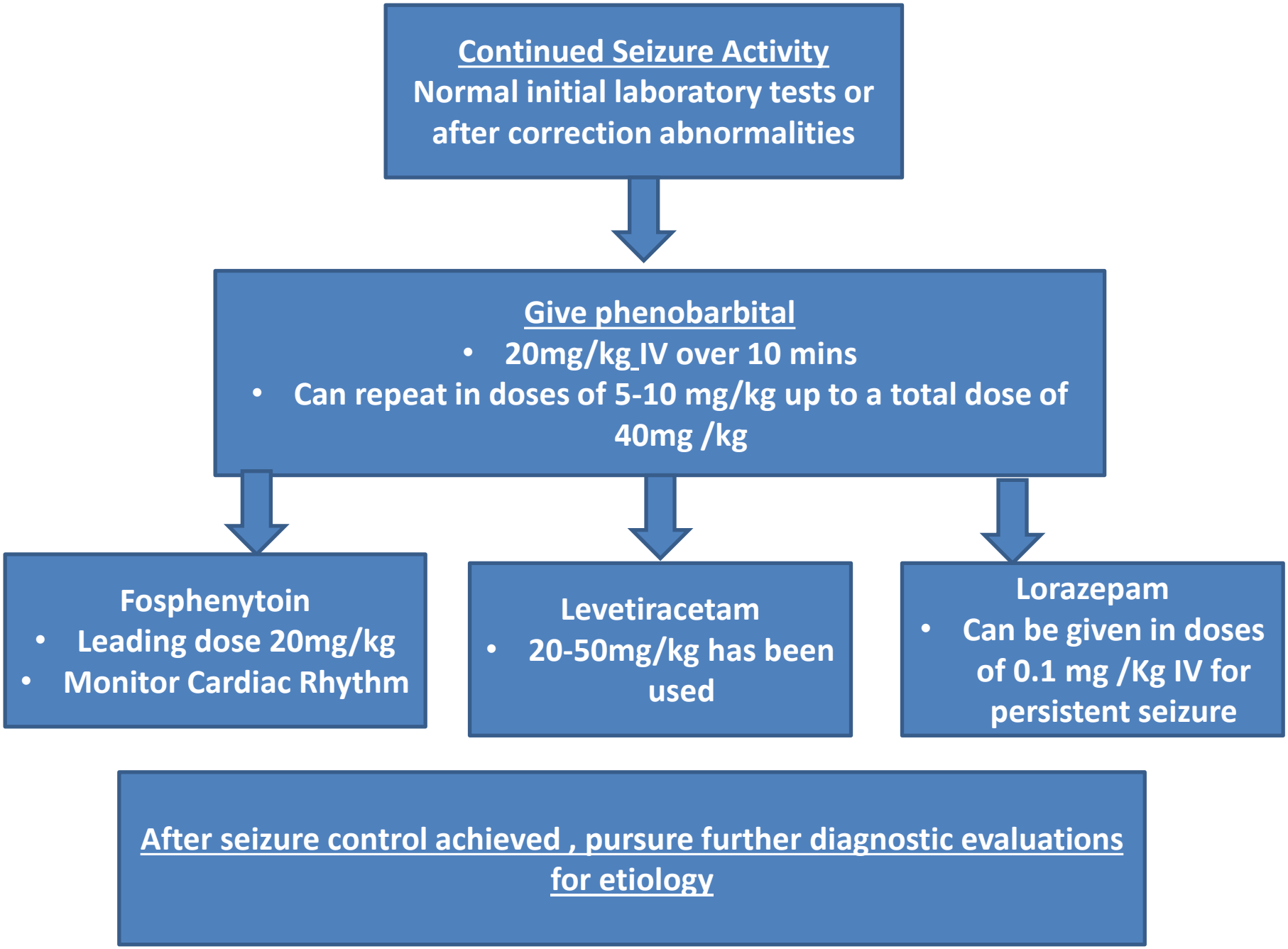
Neonatal seizures

- Congenital brain malformations and genetic/metabolic disorders can present with seizures at any age including the neonatal period.

- Pyridoxine-dependent epilepsy is a rare treatable cause of neonatal seizures that are refractory to typical antiepileptic medications but responsive to pyridoxine and/or folinic acid, administration of which can be both diagnostic and therapeutic.


ABCs
Ensure adequate ventilation and perfusion
Initial Diagnostic Evaluations
Point-of-care blood glucose testing, serum glucose, calcium, magnesium, and electrolytes
Correct Metabolic Abnormalities, If Present
Hypoglycemia
(glucose < 40 mg/dL [2.2 mmol/L])
Give 10% dextrose IV (2 mL/kg)
Maintain blood glucose 40-80 mg/dL (2.2-4.4 mmol/L) with continuous IV infusion and monitor levels
Avoid significant hyperglycemia
Hypomagnesemia
Give 50% magnesium sulfate solution (0.2 mL/kg) IV to 1 mmol/L
Hypocalcemia
Give 5% calcium gluconate solution (4 mL/kg) IV at rate of 1 mL/min
Maintain serum calcium levels above 7 mg/dL (1.75 mmol/L)
Monitor cardiac rate and rhythm
Continued Seizure Activity
Normal initial laboratory test results, or after correction of abnormalities
Give Phenobarbital
20 mg/kg IV over 10 minutes
Can repeat in doses of 5-10 mg/kg up to a total dose of 40 mg/kg
Fosphenytoin
Loading dose, 20 mg/kg
Monitor cardiac rhythm
Levetiracetam
20-50 mg/kg has been used and is being assessed in a multicenter study
Lorazepam
Can be given in doses of 0.1 mg/kg IV for persistent seizures
Monitor respiratory status
After seizure control achieved, pursue further diagnostic evaluations for etiology.


ABCs
Ensure adequate Ventilation & Perfusion
Initial Diagnostic Evaluations
Point-of-care blood glucose testing, serum glucose, Calcium, Magnesium & Electrolytes
Correct metabolic abnormalities if present
Continued Seizure Activity
Normal initial laboratory tests or after correction abnormalities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Correct metabolic abnormalities if present

- **Hypoglycemia**
- **Hypomagneimia**
- **Hypocalcemia**

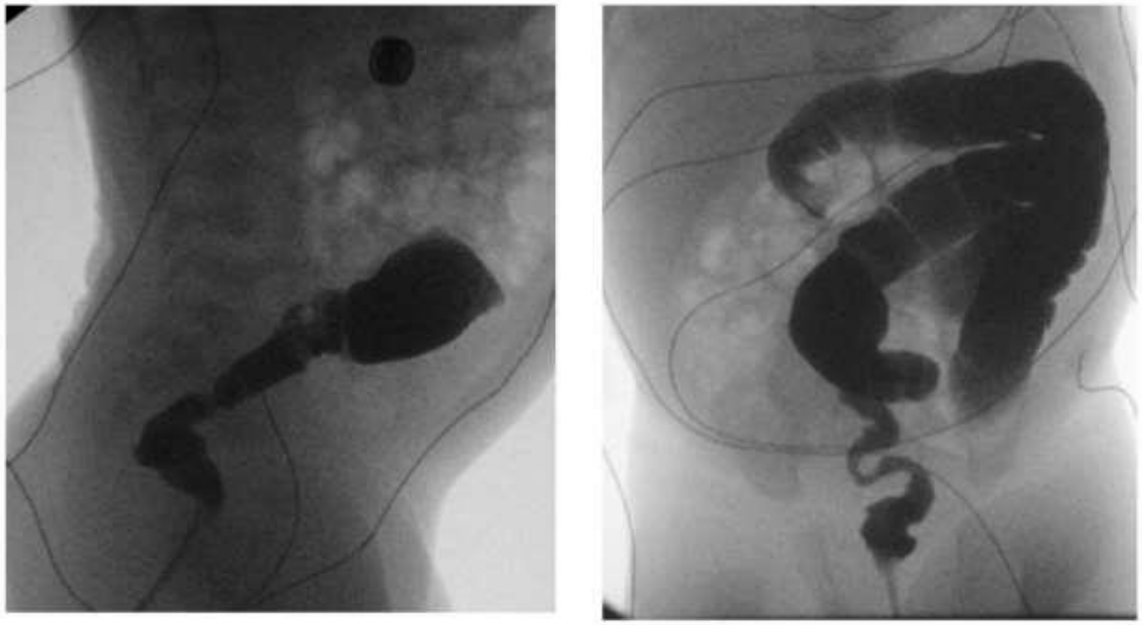
Q3

Q3

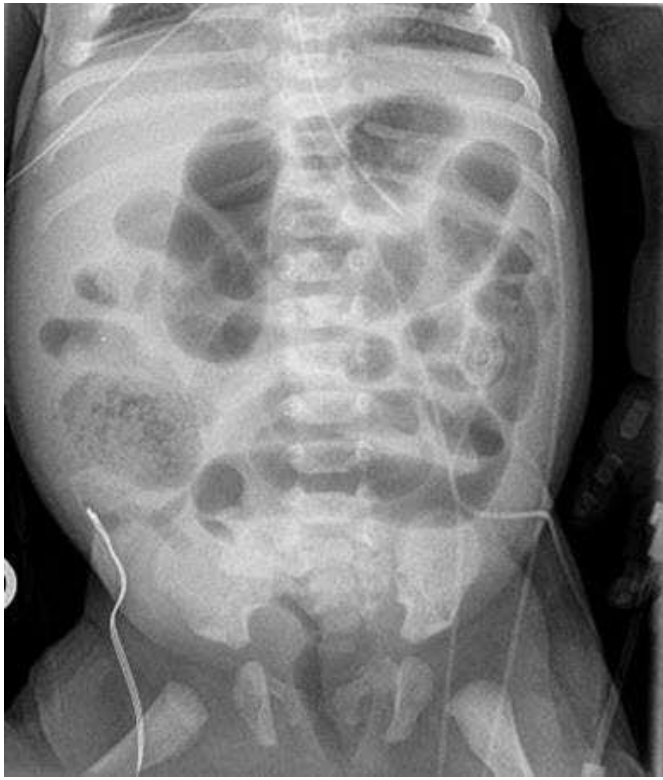
- A 26-hour-old male neonate, born at 36 weeks of gestation to a 24-year-old gravida 1, para 0 woman, is being evaluated.
- He was delivered via cesarean section because of breech presentation and had a birthweight of 2.9 kg. He has been both breast and bottle feeding.
- He has had 3 wet diapers since birth, but has not passed stool. His weight today is 2.8 kg.
- Physical examination reveals a comfortable neonate with no dysmorphic features, no murmur, and a soft abdomen with mild distention. An abdominal radiograph and a barium enema test are performed

Q3

Item Q192B



Barium enema findings for the neonate described in the vignette. Courtesy of M. Liszewski.



Item C192A

- Of the following, the neonate's MOST likely diagnosis is
  A. anal stenosis
  B. Hirschsprung disease
  C. inadequate oral intake
  D. small left colon syndrome

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  A. anal stenosis
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  C. inadequate oral intake
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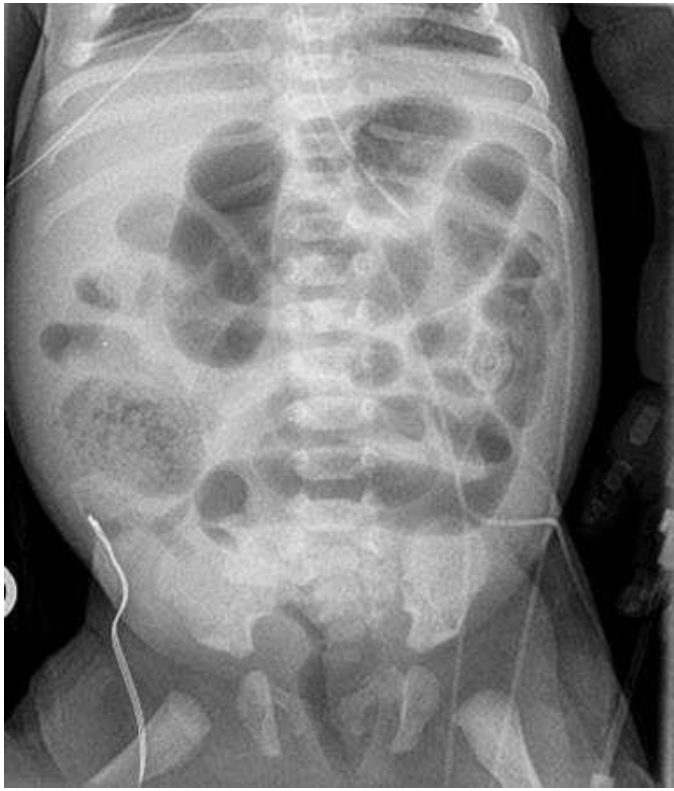
Correct Answer: B

Hirschsprung disease

- The neonate in the vignette failed to pass meconium in the first 24 hours after birth. No abdominal distention is noted. Abdominal radiograph reveals mild intestinal dilation.
- Barium enema shows a segment of narrowed bowel consistent with Hirschsprung disease.



- **Hirschsprung disease** affects approximately 1 in 5,000 live births and is more common among boys. Hirschsprung disease may occur in isolation but may also be associated with syndromes such as trisomy 21.

- It occurs because of an arrest in migration of ganglionic cells to the rectosigmoid region. Without adequate innervation, the colonic muscles do not relax properly.

- Affected neonates typically exhibit failure to pass meconium with or without abdominal distention. Abdominal radiography may show mild bowel dilation. Typically, digital rectal examination will result in a large foul-smelling bowel movement.

- Toxic mega-colon, a rare complication of Hirschsprung disease, is caused by increased luminal pressure, which compromises perfusion of the bowel wall causing bacterial translocation. On physical examination, affected neonates have abdominal tenderness, distention, and erythema.

Hirschsprung disease

- Barium enema is not diagnostic for Hirschsprung disease, but will show evidence of a transition zone of aganglionic cells in the sigmoid rectum. The diagnosis must be confirmed with suction rectal biopsy.
- Surgical repair is typically performed within the first week after birth and generally results in fecal continence. Children with surgically repaired Hirschsprung disease may develop constipation, fecal soiling, prolapse, and stricture.

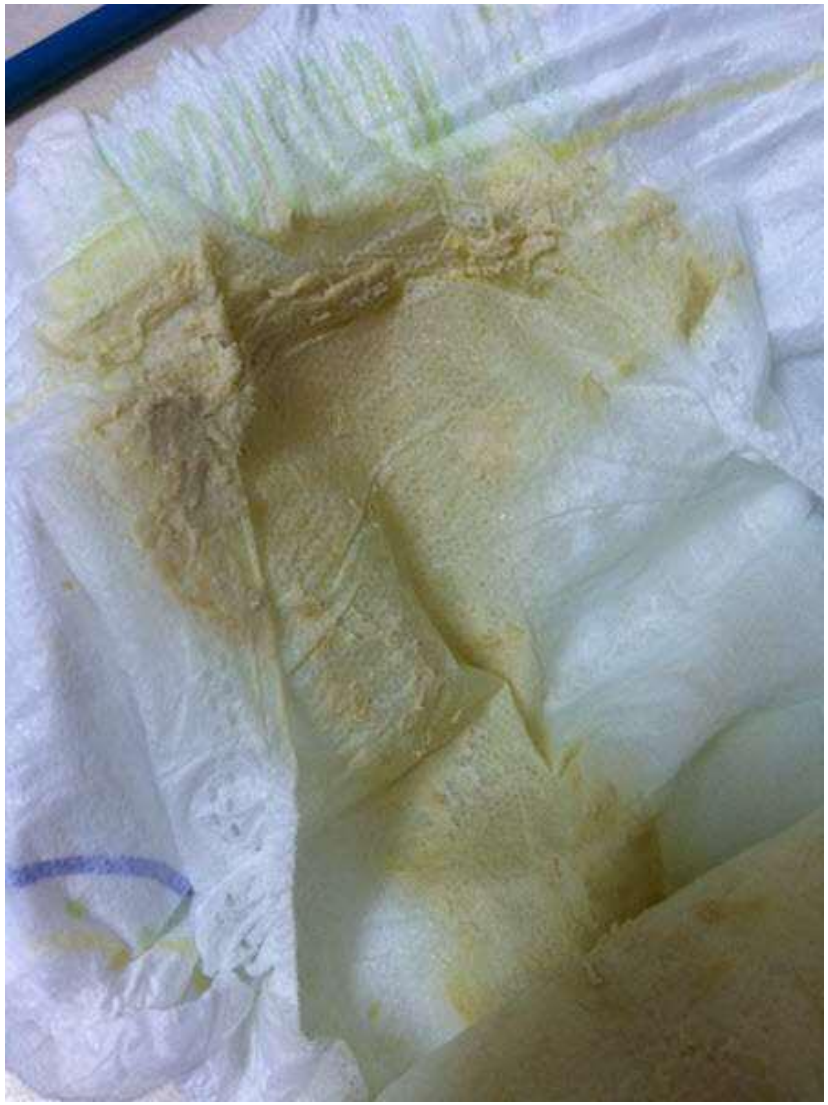
- Neonates with **anal stenosis** will have severe abdominal distention and require emergent surgical treatment. **Small left colon syndrome** has been associated with maternal diabetes; affected neonates have feeding intolerance and may have bilious emesis.
- A barium enema will reveal a left colon of reduced caliber. Because this neonate had 3 wet diapers in the first 24 hours, inadequate oral intake is not the correct response.

Q4

Q4

- A 20-day-old infant is seen for a routine health supervision visit. He was born at 38 weeks' gestation.
- He was noted to be mildly jaundiced.
- He has been breastfed exclusively and has been growing normally. He has no other significant medical history. He takes vitamin D daily.

- He appears well and in no distress. weight for length at the 60th percentile for age. His sclera are icteric. Cardiac and pulmonary examination findings are normal. His abdomen is mildly distended with a firm liver edge palpable 2 cm below the right sternal costal margin. There is no splenomegaly. Rectal examination findings are normal, and there is stool in his diaper



Laboratory data are shown:

Laboratory Test	Result
Conjugated bilirubin	3.7 mg/dL (63.3 µmol/L)
Unconjugated bilirubin	1.8 mg/dL (30.8 µmol/L)
Alanine aminotransferase	89 U/L
Aspartate aminotransferase	142 U/L
Alkaline phosphatase	1,314 U/L
γ-Glutamyl transferase	1,148 U/L

- **Of the following, the MOST likely diagnosis is**

  A. acute hepatitis C

  B. Crigler-Najjar syndrome type 1

  C. biliary atresia

  D. Gilbert syndrome

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Correct Answer: C

Neonatal Jaundice

- The infant in this vignette has biliary atresia, the most common cause of neonatal cholestasis. While cholestasis is defined as a conjugated bilirubin level of at least 2.0 mg/dL (34.2 µmol/L) and greater than 20% of total bilirubin, the most recent cholestasis management guidelines from the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition recommend consideration of cholestatic diseases in infants with a conjugated bilirubin level of greater than 1.0 mg/dL (17.1 µmol/L). Biliary atresia, a progressive fibro-obliterative disease of intrahepatic and extrahepatic bile ducts, presents in infants with jaundice after the first few weeks of age.

- As the disease progresses, acholic stools, poor feeding, and poor growth occur. Left untreated, cirrhosis and portal hypertension develop. Treatment of biliary atresia includes surgical intervention (Kasai portoenterostomy) to attempt to restore bile flow. If the surgery is performed at 90 or more days after birth, the chances to restore bile flow significantly decrease, and liver transplantation is likely. Therefore, early detection of biliary atresia is essential; persistent jaundice at 2 or 3 weeks after birth should raise concern for cholestasis and a conjugated bilirubin level should be measured.

- The differential diagnosis of jaundice in newborns and young infants is broad.
- The first step in the diagnostic evaluation is to determine whether the cause of jaundice is from unconjugated or conjugated hyperbilirubinemia by analyzing total and conjugated bilirubin levels.

Item C22A. Differential Diagnosis of Jaundice in Newborns and Young Infants.

Unconjugated hyperbilirubinemia

Increased production of bilirubin:

- Physiological jaundice
- Hemolysis: ABO or Rh incompatibility, erythrocyte membrane or enzyme defects, disseminated intravascular coagulopathy
- Polycythemia
- Cephalohematoma

Decreased hepatocellular uptake or conjugation:

- Physiological jaundice
- Prematurity
- Congenital hypothyroidism
- Breast milk jaundice
- Drugs
- Gilbert syndrome and Crigler-Najjar syndrome

Conjugated hyperbilirubinemia

Obstruction of biliary system:

- Biliary atresia
- Choledochal cyst
- Alagille syndrome

Defect of bile acid synthesis or transport:

- Bile acid synthesis defect
- PFIC-1, BESP defect, MDR3 defect

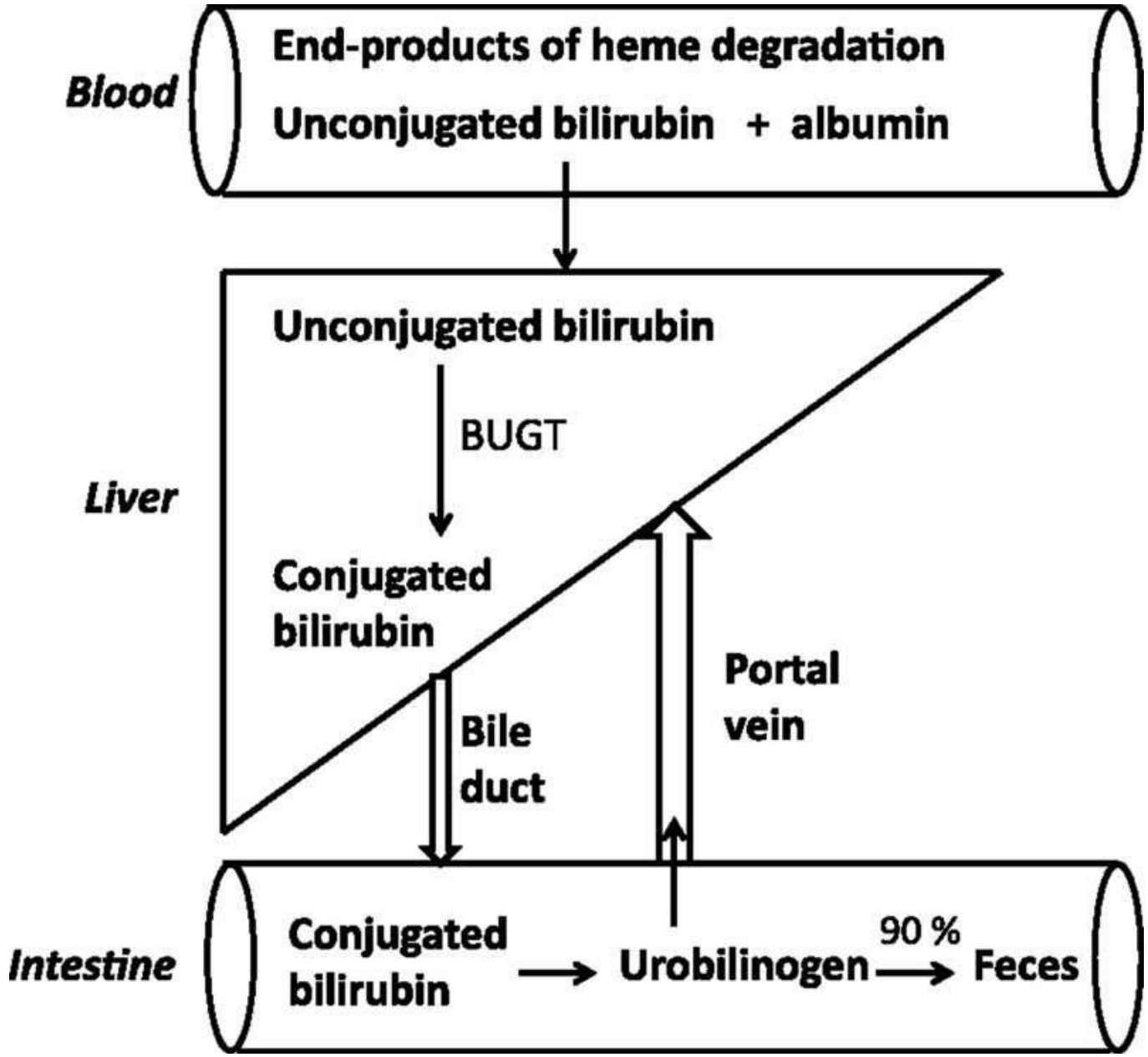
Metabolic liver diseases and systemic conditions:

- Gestational alloimmune liver disease
- Metabolic liver disease: tyrosinemia, α_1-antitrypsin deficiency, galactosemia, mitochondrial hepatopathies
- Infection: TORCH, sepsis, UTI
- Acute liver injury: ischemia, hypoxia, acidosis
- Parenteral nutrition-associated cholestasis

Bilirubin Pathway

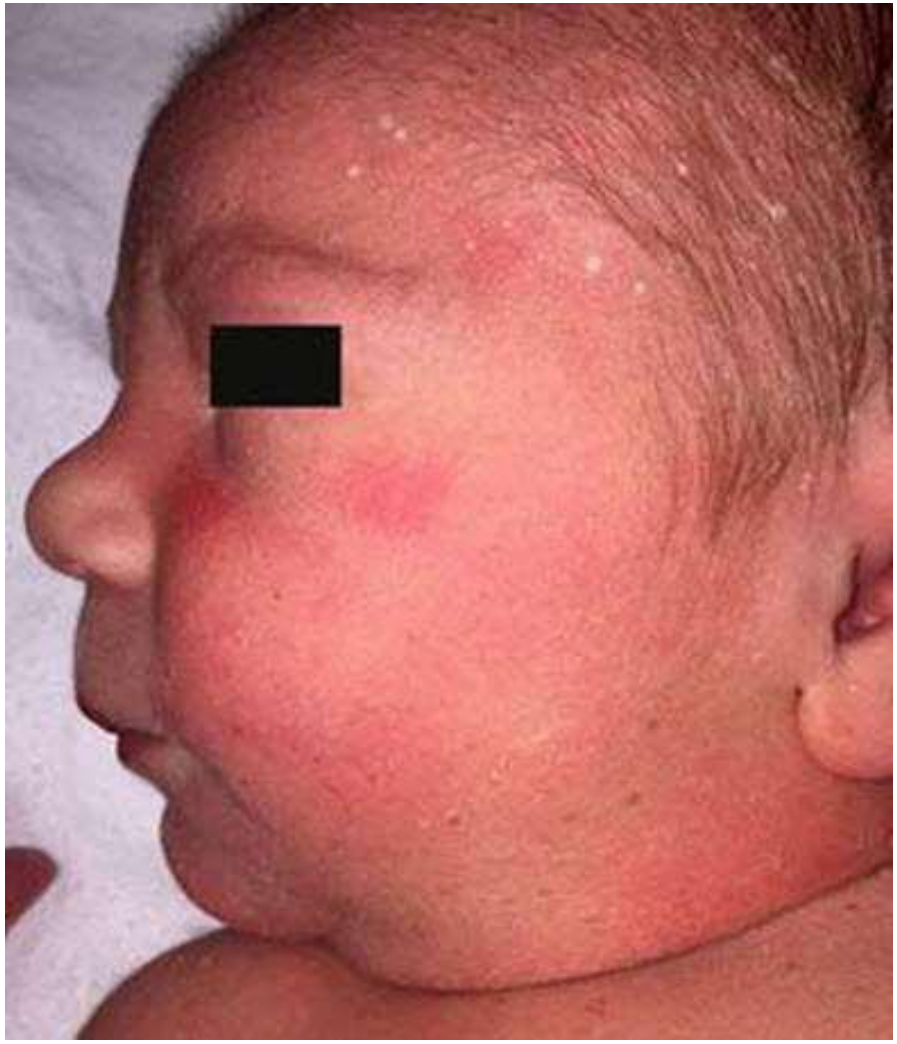
- Bilirubin is produced as a result of heme degradation Unconjugated bilirubin is transported to the liver (generally tightly bound to albumin), where conjugation by bilirubin uridine diphosphate-glucuronosyltransferase (BUGT) occurs, forming conjugated bilirubin.

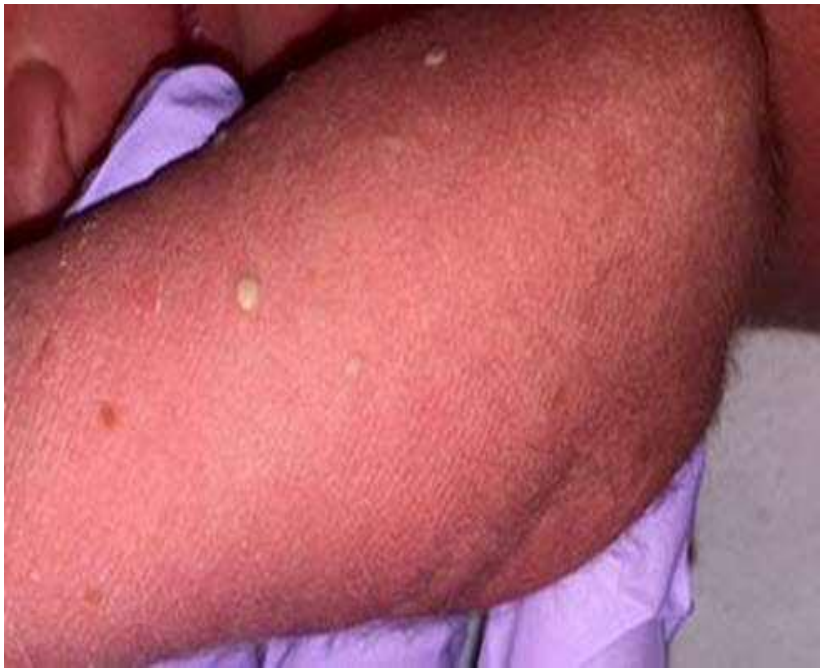
- Conjugated bilirubin is then transported out of the liver and into the bile ducts as a component of bile. As conjugated bilirubin enters the intestine, it is metabolized by bacteria to form urobilinogen, which is then excreted in feces, or deconjugated by bacteria to form unconjugated bilirubin, which can be reabsorbed in the intestine, also known as enterohepatic circulation.


Blood
End-products of heme degradation
Unconjugated bilirubin + albumin
Liver
Unconjugated bilirubin
BUGT
Conjugated bilirubin
Bile duct
Portal vein
Intestine
Conjugated bilirubin
Urobilinogen
90 %
Feces

Q5

- A term neonate who was born with “a rash” is being evaluated. He was the product of an uncomplicated full-term pregnancy, labor, and delivery. The infant has normal vital signs and appears well. The physical examination findings are remarkable only for skin lesions.
- The eruption involves the face, trunk, and extremities





- Of the following, microscopic examination of the contents of the described lesions is MOST likely to demonstrate

  A. eosinophils
  B. gram-positive cocci
  C. multinucleated giant cells
  D. neutrophils

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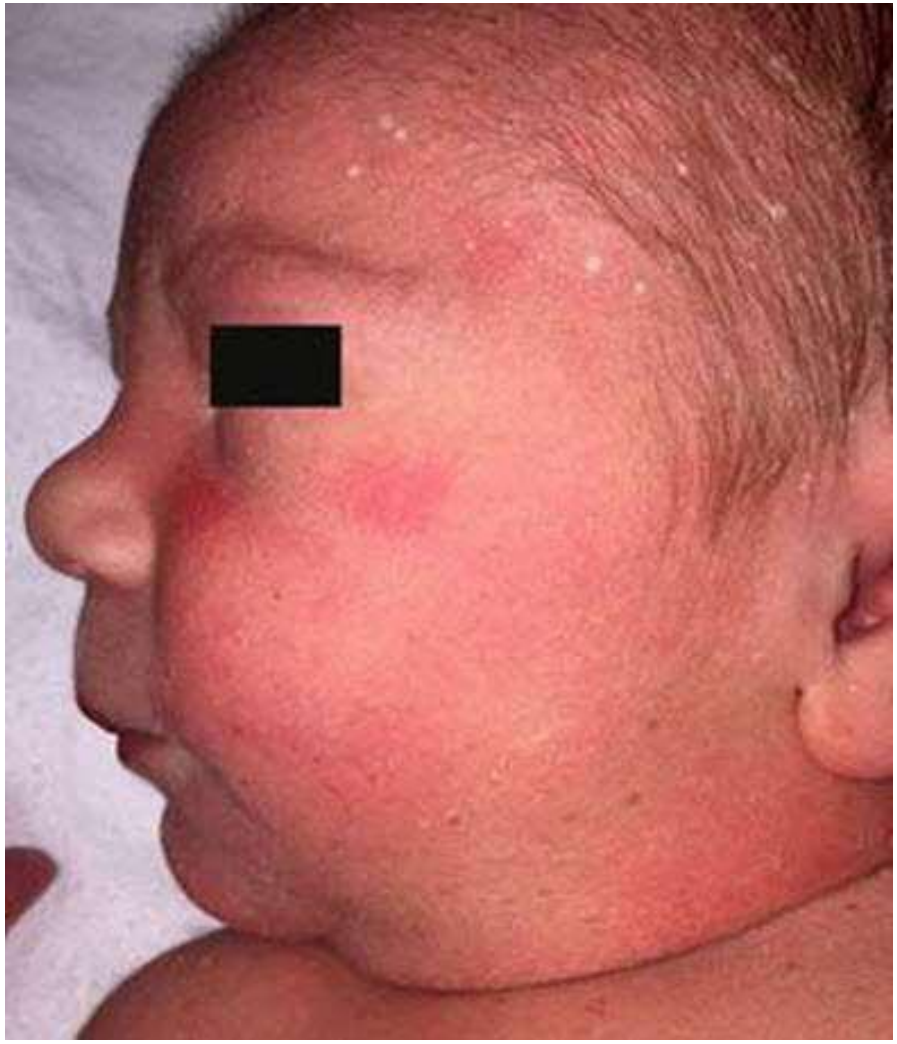
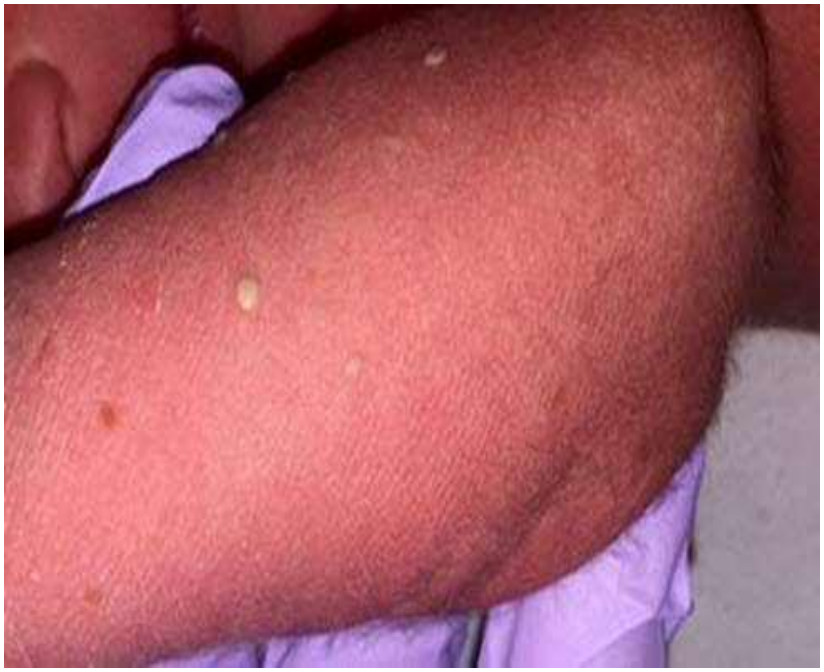




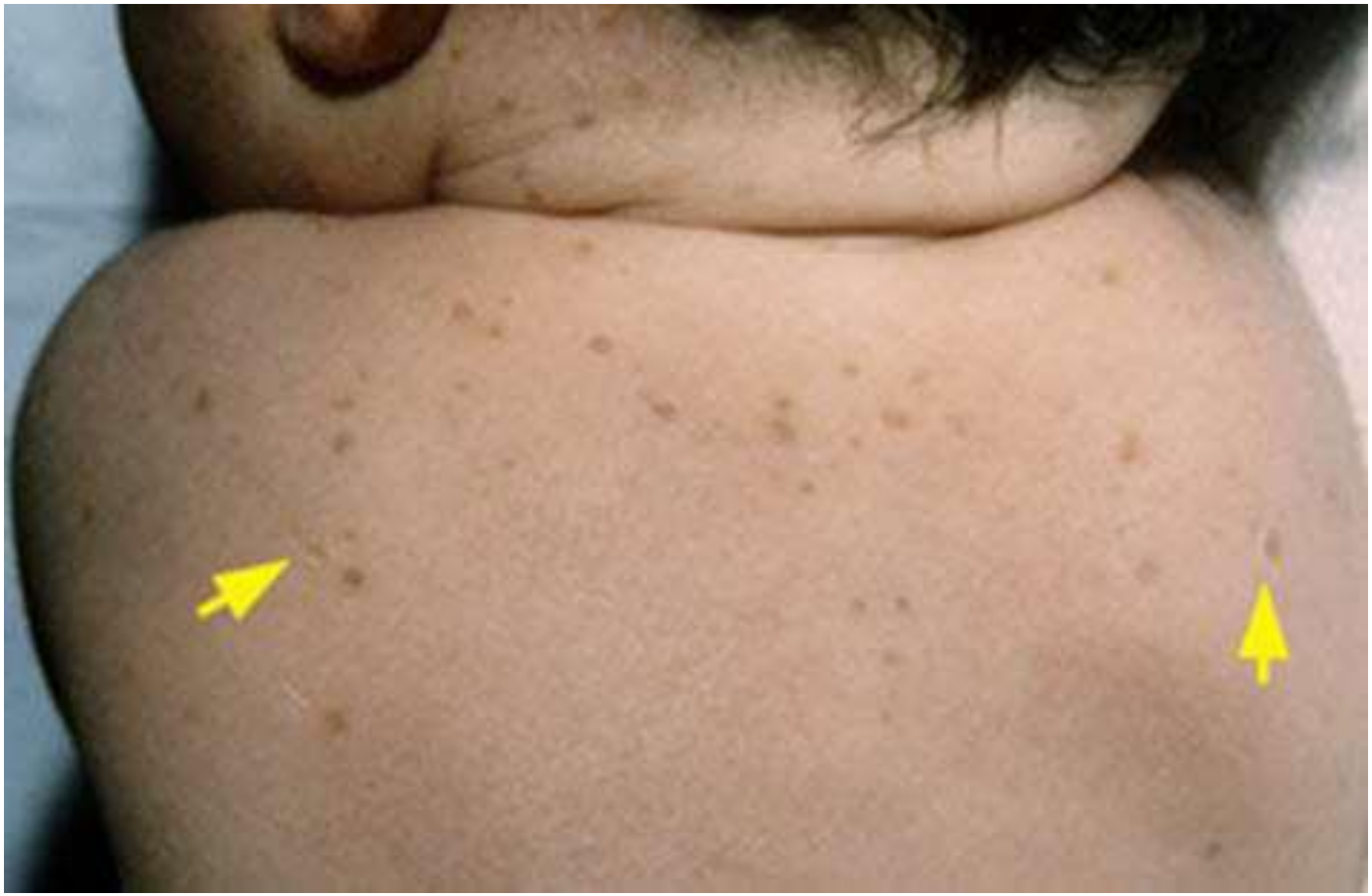
- Of the following, microscopic examination of the contents of the described lesions is MOST likely to demonstrate

  A. eosinophils
  B. gram-positive cocci
  C. multinucleated giant cells
  D. neutrophils

Correct Answer :D

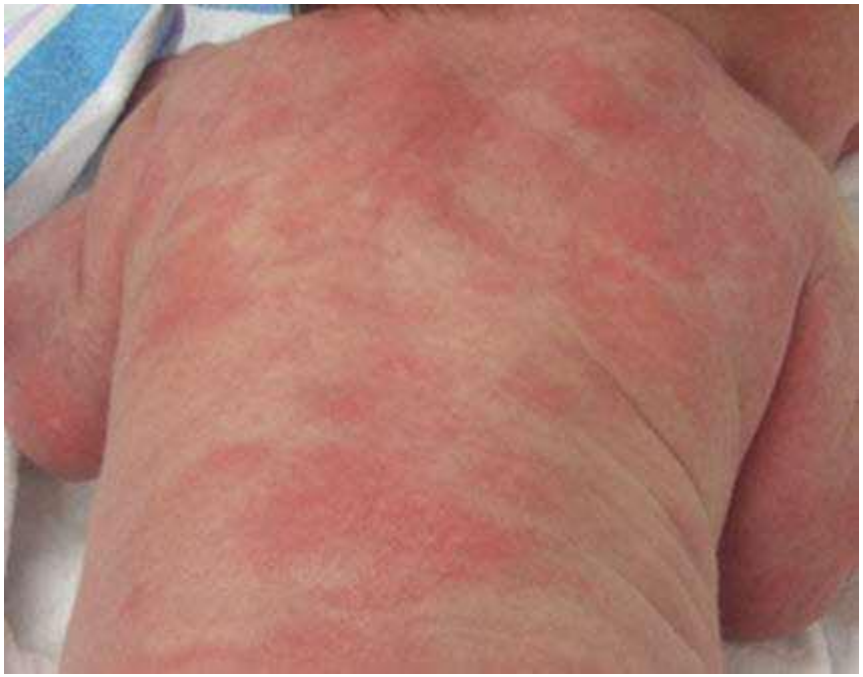
- The infant in the vignette has pustules without surrounding erythema concentrated on the face and extremities and small round hyperpigmented macules, some of which are surrounded by scale. These findings are consistent with a diagnosis of transient neonatal pustular melanosis (TNPM). Microscopic examination of pustule contents would reveal neutrophils but no organisms.

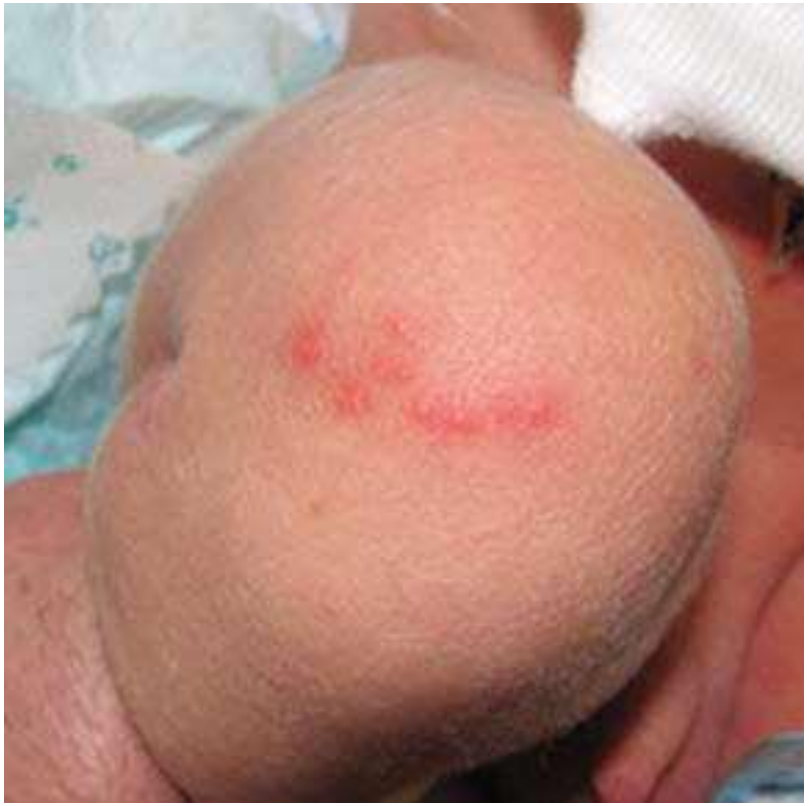
- Transient neonatal pustular melanosis is a self-limited disorder of unknown cause that occurs most often in African American infants. The condition begins in utero as sterile pustules that may rupture or remain intact after delivery. When pustules rupture, the infant is left with round hyperpigmented macules (the bases of pustules) that often are surrounded by a rim or collarette of scale (the remnants of pustule roofs).
- The lesions of TNPM may be widespread but tend to be concentrated on the forehead, chin, neck, lower back, and shins. Pustules resolve 24 to 48 hours after birth and hyperpigmented macules fade in several weeks to months.

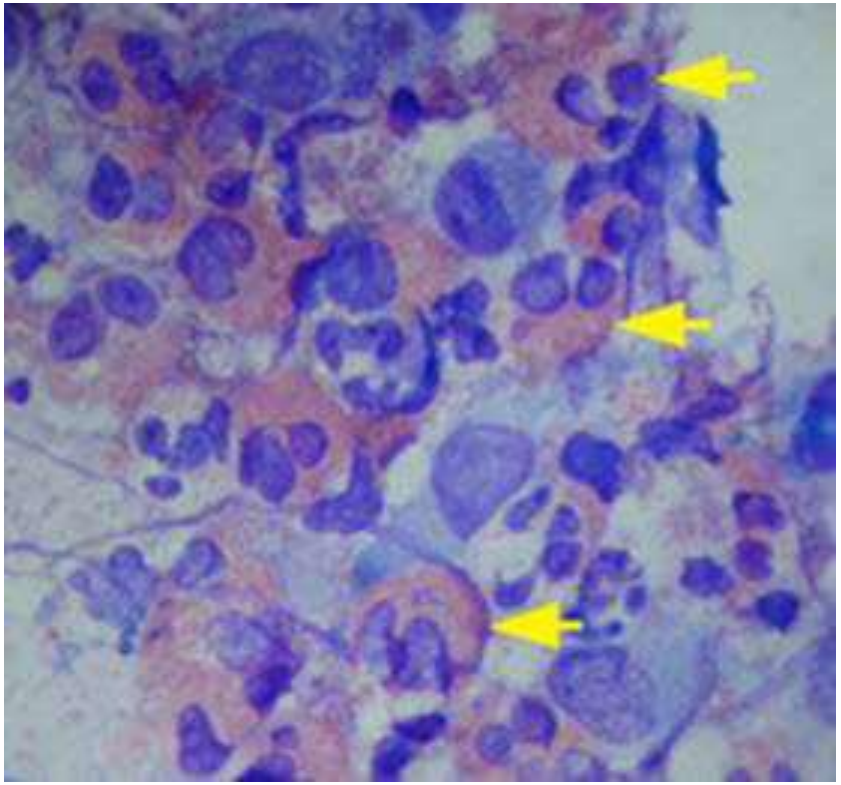


- **The differential diagnosis of vesicular or pustular lesions in a neonate includes a number of disorders, including:**

- • **Erythema toxicum:** A benign, self-limited disorder of unknown cause. It occurs commonly in term infants but is unusual in those who are preterm. The onset is usually at 24 to 48 hours after birth but may be delayed to 10 days after birth. The lesions usually resolve within weeks. Lesions are erythematous macules that develop a yellow or white central papule, vesicle, or pustule Vesicles and pustules contain eosinophils
-

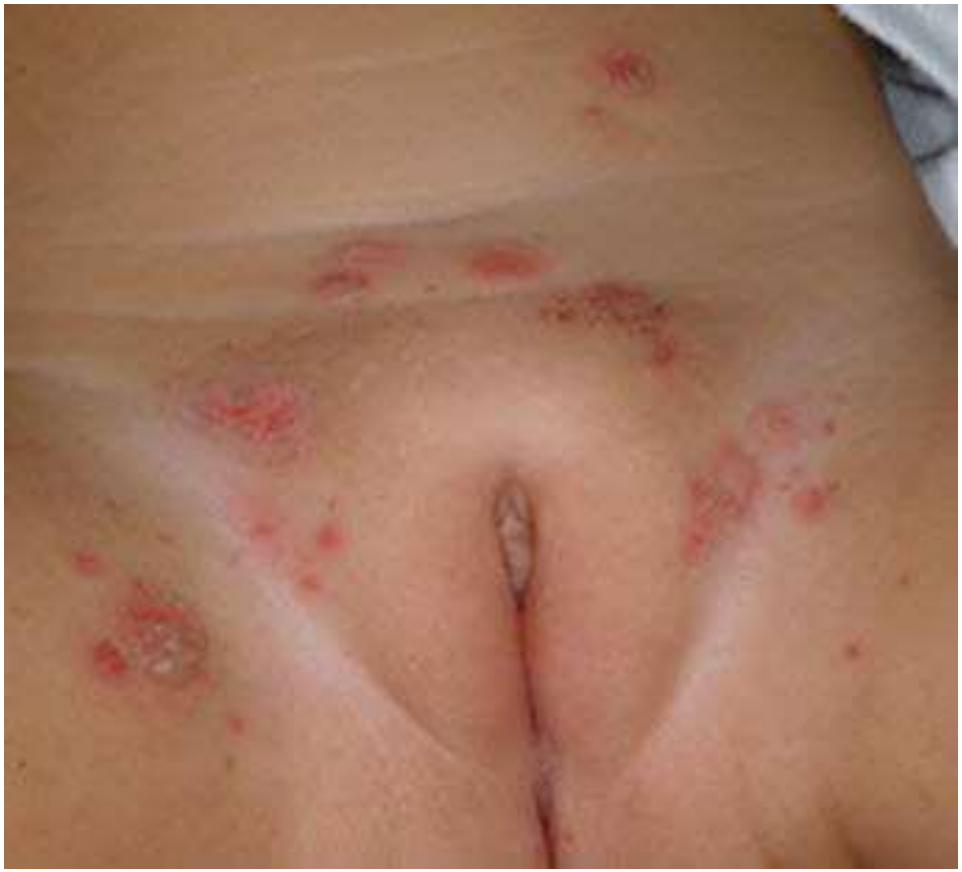






- ***Wright stain of fluid from a vesicle in erythema toxicum demonstrating eosinophils (arrows) containing orange-red granules stained with eosin***

- • **Impetigo neonatorum**: Caused by *Staphylococcus aureus* infection, impetigo neonatorum appears as pustules or bullae on erythematous bases. Lesions are often concentrated in the diaper area, axillae, and neck folds. When lesions rupture, erosions appear, not hyperpigmented macules
- A Gram stain of lesional fluid would reveal gram-positive cocci.



- Neonatal herpes simplex virus infection: Typically, lesions are grouped vesicles on an erythematous base. A Tzanck smear performed on material scraped from the base of a ruptured vesicle would reveal multinucleated giant cells.

Q6

Q6

- A 3-day-old male neonate is admitted to the neonatal intensive care unit (NICU) for hypoglycemia. He was born at 39 weeks of gestation via spontaneous vaginal delivery with a birthweight of 4.4 kg. The pregnancy was uncomplicated; there was no history of gestational diabetes.

- Routine monitoring of blood glucose, because of his large-for-gestational age status, revealed several results in the 20 to 30 mg/dL (1.1-1.7 mmol/L) range that were confirmed on laboratory testing. The neonate initially breastfed vigorously, then became increasingly lethargic.

Q6

- His blood glucose level did not normalize with supplementation of standard infant formula. In the NICU, he has required a glucose infusion rate of 14 mg/kg per minute to maintain normal levels. Significant physical examination findings include generalized macrosomia and increased subcutaneous fat. He has no dysmorphic features, no evidence of any congenital anomalies, and normal male genitalia with bilaterally descended testes.

- Of the following, the MOST likely cause of this neonate's hypoglycemia is (a)

A. fatty acid oxidation disorder

B. glycogen storage disease

C. hyperinsulinism

D. hypopituitarism

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- Of the following, the MOST likely cause of this neonate's hypoglycemia is (a)

A. fatty acid oxidation disorder

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C. hyperinsulinism

D. hypopituitarism

Correct Answer: C

- The **neonate described in the vignette has hyperinsulinism**. Clinical features consistent with hyperinsulinism include his large-for-gestational age size at birth, macrosomia, persistent hypoglycemia despite supplemental formula feedings, and high glucose infusion rate (>8 mg/kg per minute) required to maintain normal glucose levels. The large-for-gestational age size at birth and macrosomia are because of the intrauterine insulin effect on growth.

- This neonate’s presentation is most consistent with congenital hyperinsulinism resulting from a genetic mutation causing abnormally excessive insulin secretion. More common causes of hyperinsulinism include maternal diabetes and perinatal stress. Beckwith-Wiedemann syndrome is also associated with hyperinsulinism.

- Guidelines recommend obtaining a “critical sample” of blood at the time of hypoglycemia (glucose <50 mg/dL [2.8 mmol/L]) to aid in determining the etiology of persistent neonatal hypoglycemia. In addition to confirming the plasma glucose level, measurements of insulin, β- hydroxybutyrate (a ketone body), free fatty acids, growth hormone, and cortisol levels are useful tests to perform.

- Results consistent with hyperinsulinism include a detectable insulin level, low β-hydroxybutyrate and free fatty acid levels, and appropriately high growth hormone and cortisol levels. Insulin, an anabolic hormone, suppresses fatty acid oxidation and ketone body formation.
- Hypoglycemia is a normal stimulus for growth hormone and cortisol secretion.

- The response to glucagon administration at the time of hypoglycemia provides useful diagnostic information. Insulin promotes storage of glucose as glycogen in the liver. Thus, at the time of hypoglycemia resulting from hyperinsulinism, liver glycogen is available for release by glucagon.

- An increase in plasma glucose by more than 30 mg/dL (>1.7 mmol/L) after glucagon administration is consistent with hyperinsulinism. In other causes of hypoglycemia, liver glycogen is depleted, therefore glucagon has a minimal effect on plasma glucose.

- It is important to recognize hyperinsulinism for proper treatment and to avoid the adverse outcomes of persistent hypoglycemia. Immediate treatment of hypoglycemia includes an intravenous bolus of 2 mL/kg of 10% dextrose followed by continuous infusion of dextrose. High glucose infusion rates are usually required in cases of hyperinsulinism.

- Frequent feeding can help maintain normal glucose levels; glucagon can be used as adjunctive therapy. Hyperinsulinism may be transient or permanent. Diazoxide is the first-line medication for longterm management of permanent hyperinsulinism. Surgery (removal of a focal affected area of the pancreas or near-total pancreatectomy for diffuse disease) is indicated for permanent hyperinsulinism not responsive to medical therapy

- Fatty acid oxidation disorders, glycogen storage disease, and hypopituitarism also cause hypoglycemia, but are not associated with large-for-gestational age size at birth, macrosomia, or a requirement for high glucose infusion rates. Fatty acid oxidation disorders usually present after the neonatal period, given the frequency of feedings in neonates.

- A longer fasting period is required before hypoglycemia resulting from a fatty acid oxidation disorder occurs. Glycogen storage disease is usually associated with hepatomegaly. Hypopituitarism may be associated with wandering nystagmus (because of optic nerve hypoplasia), midline defects, and micropenis in boys (resulting from gonadotropin deficiency).

THANK YOU

GOOD LUCK ☺

DON'T FORGET
YOUR MASK!