

A term infant develops marked jaundice after extensive bruising at delivery. Which additional history most strongly increases concern for severe hyperbilirubinemia?

- A. A sibling who required treatment for significant neonatal jaundice
- B. An older sibling with isolated eczema
- C. Maternal history of seasonal rhinitis
- D. A paternal history of migraine
- E. An uncomplicated vertex delivery without bruising

ORIGINAL SOURCE TABLE | Table 137.1 | PDF p. 1119 | printed p. 1107

Table 137.1	Risk Factors for Severe Neonatal Hyperbilirubinemia
GENETIC FACTORS	
• Gilbert syndrome • Crigler-Najjar syndrome • Alagille syndrome • β thalassemia • Glucose-6-phosphate dehydrogenase deficiency • Bilirubin glucuronosyltransferase polymorphism • Pyruvate kinase deficiency • Erythrocyte structural defects (including hereditary spherocytosis and elliptocytosis) • Galactosemia	
MATERNAL FACTORS	
• Family history of severe jaundice, splenectomy, or cholecystectomy • Primiparity • Teenage pregnancy • Diabetes • Rhesus incompatibility • ABO incompatibility • Other blood group isoimmunization • Use of drugs during labor (including oxytocin, promethazine, and bupivacaine) • Exclusive breastfeeding	
PERINATAL FACTORS	
• Mode of deliver (breech vs vertex, instrumentation) • Birth trauma (cephalohematoma or substantial bruising, extravasation) • Birth asphyxia • Congenital infections (including cytomegalovirus and syphilis) • Sepsis	
NEONATAL FACTORS	
• Male sex • Prematurity or low birthweight and small-for-gestational age • Hypothyroidism • Polycythemia • Hypoglycemia • Low intake of breast milk, dehydration, or weight loss • Breast milk jaundice • Jaundice in the first day of life • Trisomy 21 • Infant of diabetic mother • Cephalohematoma, other bruising	
OTHER RISK FACTORS AND MARKERS	
• Previous sibling received phototherapy or exchange transfusion • PredischARGE total serum bilirubin or transcutaneous bilirubin concentration in the high zone • Use of hemolytic agents (e.g., naphthalene or menthol-based products) in glucose-6-phosphate dehydrogenase deficient population groups • Folate deficiency • Aflatoxins • Hypothermia • Birth outside of a healthcare facility	

Modified from Olusanya BO, Kaplan M, Hansen TWR. Neonatal hyperbilirubinaemia: a global perspective. *Lancet Child Adolesc.* 2018;2:610–618. Panel 2, p. 612.

A newborn is visibly jaundiced during the first 18 hours of life. Which initial investigation set best follows the evaluation table?

- A. CBC and smear, total and direct bilirubin, blood type and direct antiglobulin test
- B. Serum transaminases alone
- C. Urine culture alone
- D. A hearing screen and thyroid ultrasonography
- E. Stool occult blood testing alone

ORIGINAL SOURCE TABLE | Table 137.2 | PDF p. 1119 | printed p. 1107

Table 137.2 Evaluation of the Neonate with Significant Jaundice		
CONCERN	POSSIBLE DIAGNOSIS	INITIAL LABORATORY TESTS
Jaundice on day 1	Hemolysis* TORCH/sepsis Hepatic failure syndromes† Internal hemorrhage	CBC, smear Total and direct bilirubin Blood type and Coombs test
Jaundice requiring phototherapy	Hemolysis* TORCH/sepsis	As above
Direct/ conjugated hyperbilirubinemia	TORCH/sepsis Biliary atresia Other causes of cholestasis‡ Hepatic failure syndromes†	Hepatic enzymes, INR, check newborn screen for metabolic disease, blood glucose, blood ammonia and lactate, urine and blood cultures, CMV and HSV PCR

*Hemolysis may be immune or nonimmune (RBC membrane or enzyme defects).

†Hepatic failure syndromes: HSV, CMV, gestational alloimmune liver disease, mitochondrial liver disease, familial hemophagocytic syndrome.

‡See Chapter 404.

A neonate becomes jaundiced during the first 24 hours, with a rapidly rising predominantly indirect bilirubin level. Which category in the diagnostic table best fits?

- A. Hemolytic state or enclosed hematoma
- B. Physiologic jaundice of a term infant
- C. Isolated breast milk jaundice at 3 weeks
- D. Uncomplicated transient physiologic adaptation
- E. Primary conjugated cholestasis with pale stools

ORIGINAL SOURCE TABLE | Table 137.3 | PDF p. 1120 | printed p. 1108

Table 137.3 Diagnostic Features of the Various Types of Neonatal Jaundice							
DIAGNOSIS	VAN DEN BERGH REACTION	JAUNDICE		PEAK BILIRUBIN CONCENTRATION		BILIRUBIN RATE OF ACCUMULATION (mg/dL/day)	COMMENTS
		APPEARS	DISAPPEARS	MG/DL	AGE IN DAYS		
Physiologic jaundice"							Usually relates to degree of maturity
Full-term	Indirect	2-3 days	4-5 days	10-12	2-3	<5	
Preterm	Indirect	3-4 days	7-9 days	15	6-8	<5	
Hyperbilirubinemia caused by metabolic factors							Metabolic factors: hypoxia, respiratory distress, lack of carbohydrate
Full-term	Indirect	2-3 days	Variable	>12	First wk	<5	Hormonal influences: hypothyroidism, hormones, Gilbert syndrome
Preterm	Indirect	3-4 days	Variable	>15	First wk	<5	Genetic factors: Crigler-Najjar syndrome, Gilbert syndrome
Hemolytic states and hematoma	Indirect	May appear in first 24 hr	Variable	Unlimited	Variable	Usually >5	Erythroblastosis: Rh, ABO, Kell congenital hemolytic states: spherocytic, nonspherocytic Infantile pyknocytosis Drug: vitamin K Enclosed hemorrhage—hematoma
Mixed hemolytic and hepatotoxic factors	Indirect and direct	May appear in first 24 hr	Variable	Unlimited	Variable	Usually >5	Infection: bacterial sepsis, pyelonephritis, hepatitis, toxoplasmosis CMV HSV Rubella, syphilis
Hepatocellular damage	Indirect and direct	Usually 2-3 days; may appear by second wk	Variable	Unlimited	Variable	Variable, can be >5	Biliary atresia; paucity of bile ducts, familial cholestasis, galactosemia; hepatitis, infection, hepatic failure syndromes*

*Congenital: neonatal alloimmune liver disease, hemophagocytic lymphocytosis, mitochondrial hepatic disorders, inborn errors of metabolism
†V, Cytomegalovirus; HSV, herpes simplex virus.
‡From Brown AK. Neonatal jaundice. *Pediatr Clin North Am.* 1962;9:575–603.

A neonate has liver failure with marked hyperferritinemia and elevated triglycerides. Which diagnosis in the laboratory comparison is most strongly suggested?

- A. Hemophagocytic lymphohistiocytosis
- B. Gestational alloimmune liver disease
- C. Ischemic liver injury
- D. Mitochondrial hepatopathy
- E. An isolated physiologic bilirubin rise

ORIGINAL SOURCE TABLE | Table 137.4 | PDF p. 1121 | printed p. 1109

Table 137.4	Typical Laboratory Findings in Neonatal Liver Failure				
	GALD	HLH	MITOCHONDRIAL	VIRAL	ISCHEMIC
Transaminase levels (IU/L)	Normal/mild increase <100	Moderate/significant increase (>1,000)	Moderate increase (100-500)	Significant increase (>1,000)	Significant increase (>1,000-6,000)
INR	Significant increase	Moderate/significant increase	Moderate/significant increase	Moderate/significant increase	Moderate/significant increase
Ferritin level (ng/mL)	800-7,000	Significant increase (>20,000)	Variable	Significant increase (>20,000)	Variable depending on underlying cause of ischemia
Triglyceride levels	Normal	Increased	Normal	Normal	Normal
Hypoglycemia	Yes	Often	Yes	Often	Variable
Lactic acidosis	Normal	Normal	Increased	Normal	Often
α-Fetoprotein level (for age)	Increased	Normal	Normal/increased	Normal	Normal
Cholestasis	Progressive after birth	Moderate/significant	Moderate	None/mild at presentation	Mild/moderate

HLH, Hemophagocytic lymphohistiocytosis; GALD, gestational alloimmune liver disease; INR, international normalized ratio.
From Larson-Nath C, Vitola BE. Neonatal acute liver failure. *Clin Perinatol*. 2020;47:25–39. Table 2 with data from Sundaram SS, Alonso EM, Narkewicz, MR, et al. *J Pediatr* 2011;159:813–818; Taylor SA, Whittington, PF. *Liver Transpl*. 2016;22(5):677–685; Bitar R, Thwaites R, Davison S, et al. *J Pediatr Gastroenterol Nutr*. 2017;64(1):70–75; Fellman V, Koti H. *Semin Fetal Neonatal Med*. 2011;16(4):222–228.

An infant with severe unconjugated hyperbilirubinemia develops extensor hypertonia, retrocollis, and opisthotonos during the first week. Which phase is represented?

- A. The second phase of acute bilirubin encephalopathy
- B. The first phase of acute bilirubin encephalopathy
- C. The chronic form after the first year
- D. The first year of the chronic form
- E. An uncomplicated physiologic response

ORIGINAL SOURCE TABLE | Table 137.5 | PDF p. 1123 | printed p. 1111

Table 137.5	Clinical Features of Kernicterus
ACUTE FORM	
Phase 1 (first 1-2 days): poor suck, stupor, hypotonia, seizures	
Phase 2 (middle of first week): hypertonia of extensor muscles, opisthotonos, retrocollis, fever	
Phase 3 (after the first week): hypertonia	
CHRONIC FORM	
First year: hypotonia, active deep tendon reflexes, obligatory tonic neck reflexes, delayed motor skills	
After first year: movement disorders (choreoathetosis, ballismus, tremor), upward gaze, sensorineural hearing loss	

From Dennery PA, Seidman DS, Stevenson DK. Neonatal hyperbilirubinemia. *N Engl J Med* 2001;344:581–590.

A newborn has anemia after a difficult delivery and evidence of a large fetomaternal hemorrhage. Which mechanism in the differential table accounts for the anemia?

- A. Blood loss
- B. Immune-mediated red-cell destruction
- C. Red-cell enzyme deficiency
- D. Reduced erythropoiesis from parvovirus
- E. Physiologic anemia of prematurity

ORIGINAL SOURCE TABLE | Table 139.1 | PDF p. 1130 | printed p. 1118

Table 139.1 Differential Diagnosis of Neonatal Anemia		
BLOOD LOSS • Iatrogenic blood loss (phlebotomy) • Placental hemorrhage • Placental previa • Injury of umbilical or placental vessels • Fetomaternal transfusion • Fetoplacental transfusion • Twin-twin transfusion • Acute perinatal hemorrhage (e.g., cesarean birth, other obstetric trauma) • Chronic in utero blood loss	↑ RBC DESTRUCTION <i>Immune-Mediated Hemolysis</i> • Rh incompatibility • ABO incompatibility • Minor antigen incompatibility <i>RBC Membrane Disorders</i> • Hereditary spherocytosis • Hereditary elliptocytosis • Hereditary pyropoikilocytosis • Hereditary stomatocytosis <i>RBC Enzyme Disorders</i> • G6PD deficiency • Pyruvate kinase deficiency	↓ RBC PRODUCTION • Physiologic anemia and anemia of prematurity • Infection (rubella, CMV, parvovirus B19) • Bone marrow suppression (acute stress in perinatal period) • Hemoglobinopathy (γ-globin mutation, unstable β-hemoglobinopathy, α-thalassemia major) • Bone marrow suppression (CMV, EBV) • Diamond-Blackfan anemia • Schwachman-Diamond syndrome • Congenital dyserythropoietic anemia • Fanconi anemia • Pearson syndrome • Congenital leukemia

CMV, Cytomegalovirus, EBV, Epstein-Barr virus; G6PD, glucose-6-phosphate dehydrogenase.

A jaundiced neonate has persistent microspherocytes, a negative direct antiglobulin test, and a positive eosin-5-maleimide flow test. Which diagnosis best fits the table?

- A. Hereditary spherocytosis
- B. ABO hemolytic disease
- C. G6PD deficiency
- D. Pyruvate kinase deficiency
- E. Hereditary elliptocytosis

ORIGINAL SOURCE TABLE | Table 139.2 | PDF p. 1133 | printed p. 1121

Table 139.2 Morphologic Abnormalities of Erythrocytes in Neonates with Jaundice			
ABNORMAL ERYTHROCYTE MORPHOLOGY	MOST LIKELY CAUSES	SUGGESTED LABORATORY TESTING/FINDINGS	OTHER FEATURES
Microspherocytes	Hereditary spherocytosis	DAT (–) EMA flow (+) Persistent spherocytosis Reticulocytosis	MCHC/MCV elevated (>36, likely >40)
	ABO hemolytic disease	DAT (+) Transient spherocytosis Reticulocytosis	MCHC/MCV normal (<36, likely <34)
Elliptocytes	Hereditary elliptocytosis	DAT (–)	MCHC normal MCV normal
Bite and blister cells	G6PD deficiency Unstable hemoglobin	G6PD enzyme activity Heinz body preparation	Typically affects males, but rare females are also affected Ethnicity of equatorial origin
Echinocytes	PK deficiency Other glycolytic enzyme deficiency	PK enzyme activity Quantify activity of other glycolytic enzymes	Autosomal recessive, likely to have no family history
Schistocytes	DIC and/or perinatal asphyxia	Low levels of FV and FVIII, elevated levels of D-dimers	Low or falling platelet count Normal to high IPF
	Heinz body HA	Positive result of Heinz body preparation	Normal to high MPV DIC, perinatal asphyxia
	ADAMTS-13 deficiency (TTP)	Severely decreased ADAMTS-13 activity (<0.1 U/mL) high levels of LDH	ADAMTS-13 deficiency, early neonatal HUS, and giant hemangiomas all involve platelet consumption from endothelial injury and all have similar neonatal presentation
	Neonatal hemolytic-uremic syndrome	Acute renal failure	
	Homozygous protein C deficiency	Severely decreased functional protein C activity (<1%)	
	Giant hemangioma	May be internal or external	

DAT, Direct antiglobulin test; DIC, disseminated intravascular coagulation; EMA, eosin 5-maleimide; FV, factor V; FVIII, factor VIII; G6PD, glucose-6-phosphate dehydrogenase; HA, hemolytic anemia; HUS, hemolytic uremic syndrome; IPF, immature platelet fraction; LDH, lactic dehydrogenase; MCHC, mean corpuscular hemoglobin concentration; MCV, mean corpuscular volume; MPV, mean platelet volume; PK, pyruvate kinase; TTP, thrombotic thrombocytopenic purpura.

From Christensen RD, Yaish HM. Hemolytic disorders causing severe neonatal hyperbilirubinemia. *Clin Perinatol*. 2015;42:515–527. Table 3.

An infant has congenital hyporegenerative anemia that later becomes macrocytic and responds to corticosteroids. Which syndrome in the table is most compatible?

- A. Diamond-Blackfan syndrome
- B. Congenital dyserythropoietic anemia type II
- C. Dyskeratosis congenita
- D. Adenosine deaminase deficiency
- E. Hereditary spherocytosis

ORIGINAL SOURCE TABLE | Table 139.3 | PDF p. 1133 | printed p. 1121

Table 139.3 Syndromes Associated with Congenital Hyporegenerative Anemia		
SYNDROME	PHENOTYPIC FEATURES	GENOTYPIC FEATURES
Adenosine deaminase deficiency	Autoimmune hemolytic anemia, reduced erythrocyte adenosine deaminase activity	AR, 20q13.11
Congenital dyserythropoietic anemias	<i>Type I (rare):</i> megaloblastoid erythroid hyperplasia and nuclear chromatin bridges between nuclei <i>Type II (most common):</i> hereditary erythroblastic multinuclearity with positive acidified serum test result, increased lysis to anti-I antibodies <i>Type III:</i> erythroblastic multinuclearity ("gigantoblasts"), macrocytosis	<i>Type I:</i> 15q15.1-q15.3 <i>Type II:</i> 20q11.2 <i>Type III:</i> 15q21
Diamond-Blackfan syndrome	Steroid-responsive hypoplastic anemia, often macrocytic after 5 mo of age	AR; sporadic gene variants and AD inheritance described; 19q13.2, 8p23.3-p22
Dyskeratosis congenita	Hypoproliferative anemia usually presenting between 5 and 15yr of age	X-linked recessive, locus on Xq28; some cases with AD inheritance
Fanconi syndrome	Steroid-responsive hypoplastic anemia, reticulocytopenia, some macrocytic RBCs, shortened RBC life span Cells are hypersensitive to DNA cross-linked agents	AR, multiple genes: complementation group A 16q24.3; group B Xp22.3; group C 9q22.3; group D2 3p25.3; group E 6p22-p21; group F 11p15; group G 9p13
Osler hemorrhagic telangiectasia syndrome	Hemorrhagic anemia	AD, 9q34.1
Osteopetrosis	Hypoplastic anemia from marrow compression; extramedullary erythropoiesis	AR, 16p13, 11q13.4-q13.5; AD, 1p21; lethal, reduced levels of osteoclast
Pearson syndrome	Hypoplastic sideroblastic anemia, marrow cell vacuolization	Pleioplasmatic rearrangement of mitochondrial DNA; X-linked or AR
Peutz-Jeghers syndrome	Iron-deficiency anemia from chronic blood loss	AD, 19p13.3
ATR-X and ATR-16 syndromes	ATR-X: hypochromic, microcytic anemia; mild form of hemoglobin H disease ATR-16: more significant hemoglobin H disease and anemia are present	ATR-16, 16p13.3, deletions of α -globin locus

AD, Autosomal dominant; AR, autosomal recessive; ATR-16, chromosome 16-related α -thalassemia/mental retardation; ATR-X, X-linked α -thalassemia/mental retardation. From Christensen RD. Neonatal erythrocyte disorders. In: Gleason CA, Juul SE, eds. *Avery's Diseases of the Newborn*. 10th ed. Philadelphia: Elsevier; 2018: Table 81-2.

A firstborn infant of a group-O mother and group-A infant develops immune jaundice, while severe fetal anemia is uncommon. Which incompatibility pattern is most consistent?

- A. ABO hemolytic disease
- B. RhD hemolytic disease
- C. Kell alloimmunization
- D. An inherited red-cell enzyme defect
- E. Fetomaternal hemorrhage

ORIGINAL SOURCE TABLE | Table 140.1 | PDF p. 1135 | printed p. 1123

Table 140.1 Etiologies of Hemolytic Disease of the Fetus and Newborn			
	Rh	ABO	KELL
BLOOD GROUPS			
Mother	Rh-negative	O (occasionally B)	K1-negative
Infant	Rh-positive (D is most common)	A (sometimes B)	K1-positive
CLINICAL FEATURES			
Occurrence in firstborn	5%	40–50%	Rare
Severity in subsequent pregnancies:	Predictable	Difficult to predict	Somewhat predictable
Stillbirth/hydrops	Frequent (less with Rh-immunoglobulin use)	Rare	10%
Severe anemia	Frequent	Rare	Frequent
Jaundice	Prominent, severe	Mild-moderate	Mild
LABORATORY TESTS			
Direct antiglobulin test (infant)	Positive	Positive or negative	Positive or negative
Reticulocyte count	Elevated	Elevated	Variable
RBC antibodies (mother)	Usually detectable Antibody titers may help predict severity of fetal disease	May not be detectable Antibody titers may not correlate with fetal disease	Usually detectable Antibody titers may not correlate with fetal disease; fetus can be affected at titers lower than for Rh-mediated hemolysis

A pregnant patient has clinically significant anti-K antibodies. Which severity grouping in the red-cell-antigen table includes the K antigen?

- A. Severe hemolytic disease of the fetus and newborn
- B. Only mild postnatal jaundice
- C. Only moderate disease requiring phototherapy
- D. No recognized fetal hemolytic disease
- E. A nonimmune cause of hydrops

ORIGINAL SOURCE TABLE | Table 140.2 | PDF p. 1137 | printed p. 1125

Table 140.2 Red Cell Antigens That Cause Hemolytic Disease of the Fetus and Newborn (HDFN)		
MILD HDFN	MODERATE HDFN	SEVERE HDFN
ABO (A, B)	Rh (EW, hrs, Tar, Rh32, HrBE, Hr _o)	Rh (D, c, f, Ce, C ^w , cE)
Rh (C, e, C ^x , VS, CE, Be ^a , JAL)	Diego (Di ^a , Di ^b , Wr ^a , ELO)	Kell (K, k, Ku, Js ^b)
Kell (Kp ^a , Js ^a , Ul ^a)	Duffy (Fy ^a)	Globoside (PP ₁ P _k)
Junior (Jra)	Gerbich (Ge3)	MNSs (Vw, Mur, MUT)
Kidd (Jk ^a , Jk ^b , Jk3)	H (H)	Mittenberger (Mi ^a)
Duffy (Fy ^b)	Kell (K, k, Ku, Js ^b)	MNSs (Vw, Mur, MUT)
Langereis (Lan)	MNSs (U, Ss S, s, Mt ^a , M ^v)	Gerbich (PP1Pk)
MNSs (M, N, Hil, Or)	Colton (Co ^a)	(HJK)
Colton (Co ^b , Co ³)	(Kg)	—
Scianna (Rd, SC2)	(Sara)	—
Xg (Xg ^a)	—	—
(At ^a)	—	—

Mild HDFN, published reports of needing phototherapy for postnatal jaundice; *moderate HDFN*, published reports of needing postnatal exchange transfusion; *severe HDFN*, published reports of hydrops fetalis or intrauterine transfusions.

Note that some antigens have no system as per International Society of Blood Transfusion classification.

From Jackson ME, Baker JM. Hemolytic disease of the fetus and newborn. *Clin Lab Med.* 2021;41:133–151. Table 1.

A 6-week-old exclusively breastfed infant without vitamin K prophylaxis presents with intracranial hemorrhage. Which form of vitamin K deficiency bleeding best fits?

- A. Late-onset disease
- B. Classic disease
- C. Early-onset disease
- D. Birth-trauma hemorrhage alone
- E. Hemolytic disease of the newborn

ORIGINAL SOURCE TABLE | Table 142.1 | PDF p. 1140 | printed p. 1128

Table 142.1 Vitamin K Deficiency Bleeding (Hemorrhagic Disease of the Newborn)			
	EARLY-ONSET DISEASE	CLASSIC DISEASE	LATE-ONSET DISEASE
Age	0-24 hr	2-7 days	1-6 mo
Potential sites of hemorrhage	Cephalohematoma Subgaleal Intracranial Gastrointestinal Umbilicus Intraabdominal	Gastrointestinal Ear-nose-throat-mucosal Intracranial Post circumcision Cutaneous Injection sites	Intracranial Gastrointestinal Cutaneous Ear-nose-throat-mucosal Injection sites Thoracic
Etiology/risks	Maternal drugs (phenobarbital, phenytoin, warfarin, rifampin, isoniazid) that interfere with vitamin K levels or absorption Inherited coagulopathy	Vitamin K deficiency Exclusive breastfeeding	Cholestasis: malabsorption of vitamin K (biliary atresia, cystic fibrosis, hepatitis) Abetalipoprotein deficiency Idiopathic in Asian breastfed infants Warfarin ingestion
Prevention	Avoidance of high-risk medication Possibly antenatal vitamin K to treatment of mother (20 mg) before birth and postnatal administration to infant soon after birth	Prevented by parenteral vitamin K at birth Oral vitamin K regimens require repeated dosing	Prevented by parenteral and high dose oral vitamin K during period of malabsorption or cholestasis
Incidence	Very rare	~2% if infant not given vitamin K soon after birth	Dependent on primary disease

Infants who present with hemorrhage should be given 1-5 mg of vitamin K.

Prompt recognition of infants who do present with bleeding from vitamin K deficiency is important.

A fetus with nonimmune hydrops has persistent supraventricular tachycardia. Which etiologic category in the table contains this finding?

- A. Cardiovascular disease and arrhythmia
- B. Hematologic disease only
- C. Thoracic lymphatic malformation only
- D. Chromosomal disease only
- E. Maternal diabetes alone

ORIGINAL SOURCE TABLE | Table 143.1 | PDF p. 1142 | printed p. 1130

Table 143.1 Principal Diagnoses Associated with Nonimmune Hydrops Fetalis		
CARDIOVASCULAR (21%) STRUCTURAL - Hypoplasias (left or right heart) - AV canal defect - Single ventricle - Transposition of great arteries - Septal defects (VSD/ASD) - Tetralogy of Fallot - Ebstein anomaly - Ductus arteriosus closure - Truncus arteriosus - Valvular (stenosis/insufficiency) ARRYTHMIAS - Atrial (flutter/tachyarrhythmia) - Wolff-Parkinson-White - Supraventricular tachycardia - Long QT interval - Heart block CARDIOMYOPATHY - Tumors - Neoplasias - Myopathies - Cardiosplenic syndromes - Hereditary cardiomyopathies INFECTION (6.7%) - Cytomegalovirus - Parvovirus B19 - Syphilis - Herpes simplex - Rubella - Coxsackievirus - Leptospirosis <i>Trypanosoma cruzi</i> INBORN STORAGE DISEASE (1.1%) - Gaucher disease - GM1 gangliosidosis - Sialidosis - MPS IVA and VII - Mucopolysaccharidosis type I+II - Galactosialidosis - Niemann-Pick type C TTTS-PLACENTAL (5.6%) <i>Twin</i> - TTTS - Acardiac twin <i>Placental</i> - Umbilical vein thrombosis - Umbilical cord angiomatosis - True cord knot - Chorionic vein thrombosis - Rare placenta disorders	THORACIC/EXTRATHORACIC MASS/LYMPHATIC (12.4%) <i>Mass Effect</i> - Diaphragmatic hernia - Congenital pulmonary adenomatoid malformation - Intrathoracic mass - Pulmonary sequestration - Chylothorax - Airway obstruction - Pulmonary lymphangiectasia - Bronchogenic cyst <i>Other</i> - Milroy syndrome - Generalized lymphatic dysplasia - Lymphedema-distichiasis syndrome <i>Skeletal Dysplasias</i> - Thanatophoric dysplasia - Short rib polydactyly - Hypophosphatasia - Osteogenesis imperfecta chondrogenesis - Campomelic dysplasia - Lethal achondroplasia - Nager syndrome IDIOPATHIC (17.8%) CHROMOSOMAL (13.4%) TRISOMY 21 18 13 MONOSOMY 45, X 45, X (mosaic) DUPLICATIONS 18 q + 11p DELETIONS 13 q - 17 q - TRIPLOIDY	HEMATOLOGIC (10.4%) - Alpha-thalassemia - Hereditary stomatocytosis - Fetomaternal hemorrhage - Glucose-6-phosphate deficiency - Leukemia - Pyruvate kinase deficiency - Red blood cell aplasia - Diamond-Blackfan syndrome GASTROINTESTINAL (0.5%) - Duodenal atresia - Duodenal diverticulum - Jejunoleal atresia - Volvulus - Imperforate anus - Meconium peritonitis - Intestinal malrotation - Intestinal duplication - Hepatic fibrosis - Cholestasis - Biliary atresia - Hepatic vascular malformations - Hepatitis - Hepatic necrosis - Liver tumor or cysts SYNDROMIC/MISCELLANEOUS (8.1%) - Noonan syndrome and other RASopathies - Arthrogryposis - Multiple pterygium syndrome - Neu-Laxova syndrome - Pena-Shokeir syndrome - Myotonic dystrophy - Saldino-Noonan syndrome - Francois syndrome, type III - Familial nuchal bleb - Elejalde syndrome - Thoracoabdominal syndrome URINARY TRACT MALFORMATION (2.3%) - Urethral stenosis - Urethral atresia - Posterior urethral valve - Finnish type nephrosis - Edwards (prune belly) syndrome OTHER - HLH - IPEX - Nemaline myopathy - Multiple pterygium syndrome - Hyper IgE syndrome

ASD, Atrial septal defect; AV, arteriovenous; HLH, hemophagocytic lymphohistiocytosis; IPEX, immune dysregulation polyendocrinopathy enteropathy X-linked; MPS, mucopolysaccharide; TTTS, twin-twin transfusion syndrome; VSD, ventricular septal defect.

Modified from Martin RJ, Fanaroff AA, Walsh MC, eds. *Fanaroff & Martin's Neonatal-Perinatal Medicine Diseases of the Fetus and Infant*, 11th ed. Philadelphia: Elsevier; 2020: Tab 23.4, p 381.

An opioid-exposed newborn is assessed with the Eat, Sleep, Console approach. Which observed behavior meets the table's sleep concern?

- A. Sleeping less than 1 hour after a feed
- B. Sleeping 2 hours after a feed
- C. Coordinating feeding in less than 10 minutes
- D. Remaining consoled for at least 10 minutes
- E. Taking at least 10 mL per feed

ORIGINAL SOURCE TABLE | Table 145.1 | PDF p. 1146 | printed p. 1134

Table 145.1	Eat, Sleep, Console (ESC) Assessment Approach to Neonatal Opioid Withdrawl
EATS Takes > 10 min to coordinate feeding with hunger cues < 10 min for breastfeeds < 10 mL of a feed	
SLEEPS < 1 hr after a feed	
CONSOLES Takes > 10 min to be consoled Cannot stay consoled for 10 min	
Nonpharmacologic interventions include rooming in, caregiver presence, skin to skin contact, holding/cuddling, safe swaddling (avoid face), feed on demand after hunger cues, breastfeeding, non-nutritive sucking, quiet low stimulation low-light environment, rhythmic motion, additional caregiver support, minimal disruptions in environment, cluster care to awake times, safe sleep, caregiver self-care and rest.	

These parameters suggest withdrawl.
Data from Amin A, Frazie M, Thompson S, Patel A. Assessing the Eat, Sleep, Console model for neonatal abstinence syndrome management at a regional referral center. *J Perinatol*. 2023 Apr 25:1–7; Blount T, Painter A, Freeman E, et al. Reduction in length

A neonate with withdrawal requires pharmacologic treatment with a short-acting opioid listed in the table. Which agent is given every 3 hours initially?

- A. Morphine
- B. Methadone
- C. Buprenorphine
- D. Phenobarbital
- E. Clonidine

ORIGINAL SOURCE TABLE | Table 145.2 | PDF p. 1147 | printed p. 1135

Table 145.2	Medications Used in Pharmacologic Treatment of Neonatal Abstinence Syndrome			
DRUG	INITIAL DOSING	DOSING INCREASES	WEANING SCHEDULE	ADD ADJUVANT THERAPY
Morphine	0.05 mg/kg/dose q3h	Increase dose 10–20%	10% of stabilizing dose q24h	>1 mg/kg/day of morphine Unable to wean for 2 days
Methadone	0.1 mg/kg/dose q6h for 4 doses	Increase to q4h if unable to capture	0.7 mg/kg/dose q12h × 2 doses, then 0.05 mg/kg/dose q12h × 2 0.04 mg/kg/dose q12h × 2 0.03 mg/kg/dose q12h × 2 0.02 mg/kg/dose q12h × 2 0.01 mg/kg/dose q12h × 2 0.01 mg/kg/dose q24h × 1	Unable to wean for 2 days
Buprenorphine	4 µg/kg q8h	2 µg/kg until maximum of 15 µg/kg	3 µg/kg/dose q8h × 3 doses 2 µg/kg/dose q8h × 3 2 µg/kg/dose q8h × 2 2 µg/kg/dose q24h × 1	Unable to wean for 2 days
Phenobarbital	20 mg/kg	—	5 mg/kg daily	N/A
Clonidine	1.5 µg/kg/dose q3h	25% dose escalation q24h	10% every day	N/A

N/A, Not available; q24h, every 24 hours.

A child has characteristic facial features, growth deficiency, and impaired brain growth, but prenatal alcohol exposure cannot be confirmed. Which statement about the table's fetal alcohol syndrome criteria is correct?

- A. The diagnosis may still be considered when all required features are present
- B. Documented exposure is mandatory in every case
- C. Facial features alone are sufficient
- D. Normal growth is required
- E. A confirmed pathogenic chromosome variant is required

ORIGINAL SOURCE TABLE | Table 146.1 | PDF p. 1151 | printed p. 1139

Table 146.1	Diagnostic Criteria for Fetal Alcohol Syndrome
At least 2 of the following, with or without documented prenatal alcohol exposure: • Facial features (Hoyme system requires two or more, 4-Digit Diagnostic Code requires all three): • Palpebral fissures ≤ 10th percentile (Hoyme system) or ≤ 3rd percentile (4-Digit code) • Thin upper lip (ranking of 4 or 5 on racially normed Lip-Philtrum Guide*) • Smooth philtrum (ranking of 4 or 5 on racially normed Lip-Philtrum Guide*) • Prenatal and/or postnatal growth deficiency: • Height and/or weight $\leq 10\%$ for age and sex at any point of time (prenatal or postnatal) • Adjust for gestational age if preterm. (4-Digit Diagnostic Code puts emphasis on short stature) • Deficient brain growth, abnormal brain formation or neurophysiology: one or more of following: • Head circumference ≤ 10th % (Hoyme system) or ≤ 3rd percentile (4-Digit Diagnostic Code) • Structural brain abnormalities • Recurrent nonfebrile seizures with other causes excluded (Hoyme system) • Neurobehavioral impairment: • For children < 3 y/o: Developmental delay ≥ 1.5 SD below the mean • For children 3 y/o or older (either of the following): • Cognitive impairment: Scores ≥ 1.5 SD below mean (Hoyme) or ≥ 2 SD below mean (4-Digit Diagnostic Code) either for global abilities or for at least one neurobehavioral domain (executive function, specific learning impairment, memory impairment, or visual-spatial impairment). The Hoyme system defines impairment domain as normal or abnormal. The 4-Digit Diagnostic Code has three domains defined: normal, moderate, severe. • Behavioral impairment without cognitive impairment: ≥ 1.5SD below mean in self-regulation (mood or behavioral regulation), attention deficit, or impulse control.	

*Hoyme system and the 4-Digit Diagnostic Code have different Lip-Philtrum guides.
SD = standard deviation.

A child has documented prenatal alcohol exposure, at least two characteristic facial features, and neurobehavioral impairment but no growth deficiency. Which table-based diagnosis is most compatible?

- A. Partial fetal alcohol syndrome
- B. Full fetal alcohol syndrome by facial findings alone
- C. Alcohol-related birth defects without malformations
- D. Neurobehavioral disorder with no exposure
- E. Uncomplicated normal variation

ORIGINAL SOURCE TABLE | Table 146.2 | PDF p. 1152 | printed p. 1140

Table 146.2	Diagnostic Criteria for Partial Fetal Alcohol Syndrome
• WITH documented prenatal alcohol exposure (requires A and B): A. Facial features (at least two of three) B. Neurobehavioral impairment (same as for FAS), i.e., leaves out brain abnormalities and growth deficiency • WITHOUT documented prenatal alcohol exposure (requires A, B, and C): A. Facial features (at least two of three) B. Growth deficiency OR deficient brain growth/structural brain abnormalities/recurrent seizures (at least one of these) C. Neurobehavioral impairment (same as for FAS), i.e., same as FAS except it is EITHER growth deficiency OR brain growth/structural brain abnormalities/recurrent seizures (does not require both)	

Note that the diagnosis of FAS and pFAS are the only FASDs that can be diagnosed in the absence of a confirmed maternal history of PAE.
FAS, Fetal alcohol syndrome; FASD, fetal alcohol spectrum disorder; pFAS, partial fetal alcohol syndrome.

A 2-year-old with documented prenatal alcohol exposure has behavioral concerns. Which limitation does the alcohol-related neurodevelopmental disorder table specify?

- A. A definitive diagnosis cannot be made before age 3 years
- B. Documented prenatal exposure is irrelevant
- C. A congenital cardiac defect is mandatory
- D. Facial dysmorphism is mandatory
- E. One isolated attention problem is sufficient

ORIGINAL SOURCE TABLE | Table 146.3 | PDF p. 1152 | printed p. 1140

Table 146.3	Diagnostic Criteria for Alcohol-Related Neurodevelopmental Disorder
Requires A and B: Note: Cannot be diagnosed definitively in children <3 yr old	
A. Documented prenatal alcohol exposure	
B. Neurobehavioral impairment:	
• WITH cognitive impairment: Global delay OR deficit in at least TWO neurobehavioral domains (executive function, specific learning impairment, memory impairment, visual-spatial impairment) • WITHOUT cognitive impairment: Behavioral deficit in at least TWO domains (behavioral regulation, attention, impulse control)	

A school-age child exposed to alcohol before birth has impaired neurocognition and self-regulation. Which additional pattern is specified for neurobehavioral disorder associated with prenatal alcohol exposure?

A. At least two adaptive-function deficits, including communication or social communication

B. Isolated growth failure without functional impairment

C. A single abnormal serum transaminase result

D. One major cardiac malformation without behavioral findings

E. Normal adaptation in all settings

ORIGINAL SOURCE TABLE | Table 146.4 | PDF p. 1152 | printed p. 1140

Table 146.4	Diagnostic Criteria for Neurobehavioral Disorder Associated with Prenatal Alcohol Exposure
ND-PAE is a mental health disorder (rather than a medical disorder) included in the DSM-5 (2013) as a “new clarifying term” that encompasses the range of developmental disabilities associated with PAE that affect function and are not due to other conditions. This diagnosis requires: • ≥1 deficit in neurocognition • ≥2 deficits in adaptive functioning (at least one in communication or social communication and interaction) • ≥1 deficit in self-regulation • History of maternal consumption of more than 13 alcoholic drinks in any 30-day period of the pregnancy or more than 2 alcoholic drinks in one sitting • Onset of the disorder in childhood • The findings cause clinically significant distress or impairment in important areas of functioning and are not better explained by other causes (medication, medical conditions, genetic disorders, or environmental neglect)	

Although the diagnosis of ND-PAE overlaps with ARND, ND-PAE aims to describe the *behavioral and mental health effects* on an individual with PAE. Unlike ARND, a diagnosis of ND-PAE can be given with or without the physical characteristics of FAS (ARND does not include physical characteristics) and the diagnosis of ND-PAE can be

A child with documented prenatal alcohol exposure has radioulnar synostosis. Which diagnostic grouping lists this skeletal malformation?

- A. Alcohol-related birth defects
- B. Alcohol-related neurodevelopmental disorder alone
- C. Neonatal opioid withdrawal
- D. Classic vitamin K deficiency bleeding
- E. Physiologic neonatal jaundice

ORIGINAL SOURCE TABLE | Table 146.5 | PDF p. 1152 | printed p. 1140

Table 146.5	Alcohol-Related Birth Defects
This diagnosis refers to a pattern of structural birth defects and other congenital abnormalities that can be characteristic of FASD. Requires both A and B A. Documented prenatal alcohol exposure B. One or more specific major malformations found to be the result of prenatal alcohol exposure: • Cardiac: ASD, VSD, aberrant great vessels, conotruncal heart defects • Skeletal: radioulnar synostosis, vertebral segmentation defects, large joint contractures, scoliosis • Renal: kidney/ureteral malformations • Eyes: strabismus, ptosis, retinal vascular abnormalities, optic nerve hypoplasia • Ears: conductive or neurosensory hearing loss	

ASD, Atrial septal defect; FASD, fetal alcohol spectrum disorder; VSD, ventricular septal defect.

An infant of a mother with diabetes develops respiratory distress and a thickened interventricular septum. Which morbidity listed in the table accounts for the cardiac finding?

- A. Septal hypertrophy associated with maternal diabetes
- B. Isolated congenital heart block
- C. Hereditary long-QT syndrome
- D. Infective endocarditis
- E. Primary pulmonary valve atresia

ORIGINAL SOURCE TABLE | Table 147.1 | PDF p. 1154 | printed p. 1142

Table 147.1	Morbidity in Infants of Diabetic Mothers
Congenital anomalies	
Heart failure and septal hypertrophy of heart	
Surfactant deficiency, respiratory distress syndrome, transient tachypnea of the newborn, persistent pulmonary hypertension	
Hyperbilirubinemia	
Hypoglycemia, hypocalcemia, hypomagnesemia	
Macrosomia, nerve injury related to birth trauma	
Renal vein thrombosis	
Small left colon	
Unexplained intrauterine demise	
Polycythemia	
Visceromegaly	
Predisposition to later-life obesity, insulin resistance, and diabetes	

From Devaskar SU, Garg M. Disorders of carbohydrate metabolism in the neonate. In: Martin RJ, Fanaroff AA, Walsh MC, eds. *Fanaroff & Martin’s Neonatal-Perinatal Medicine*, 10th ed. Philadelphia: Elsevier; 2015: Box 95-3.

A ventilated preterm neonate develops new pneumonia after a prolonged hospital stay. Which acquisition category in the table includes catheter- and ventilation-associated pathogens?

- A. Postnatal acquisition
- B. Transplacental acquisition
- C. Intrapartum acquisition only
- D. A noninfectious genetic syndrome
- E. Congenital immune hemolysis

ORIGINAL SOURCE TABLE | Table 148.3 | PDF p. 1158 | printed p. 1146

Table 148.3 Etiologic Agents of Neonatal Pneumonia According to Timing of Acquisition	
TRANSPLACENTAL Cytomegalovirus (CMV) Herpes simplex virus (HSV) <i>Mycobacterium tuberculosis</i> Rubella virus <i>Treponema pallidum</i> Varicella-zoster virus (VZV) <i>Listeria monocytogenes</i> PERINATAL Anaerobic bacteria Chlamydia CMV Enteric bacteria Group B <i>Streptococci</i> <i>Haemophilus influenzae</i> HSV <i>Listeria monocytogenes</i> <i>Mycoplasma</i>	POSTNATAL Adenovirus <i>Candida</i> spp.* Coagulase-negative staphylococci CMV Enteric bacteria* Enteroviruses Influenza viruses A, B Parainfluenza <i>Pseudomonas</i>* Respiratory syncytial virus (RSV) <i>Staphylococcus aureus</i> <i>Mycobacterium tuberculosis</i> <i>Legionella</i>

*More likely with mechanical ventilation or indwelling catheters, or after abdominal surgery.

A newborn develops infection shortly after birth and cultures grow group B Streptococcus. In which timing category does the table list this organism?

- A. Early-onset infection
- B. Only congenital transplacental infection
- C. Only late-onset infection
- D. Only infection after adolescence
- E. A noninfectious inflammatory syndrome

ORIGINAL SOURCE TABLE | Table 148.2 | PDF p. 1158 | printed p. 1146

Table 148.2 Most Common Pathogens Causing Neonatal Infections, Grouped by Timing of Infection	
CONGENITAL/PERINATAL • Toxoplasmosis • <i>Treponema pallidum</i> (syphilis) • Rubella • Cytomegalovirus • Herpes simplex virus • Hepatitis B and C • Human immunodeficiency virus • Varicella • Parvovirus B19 • Tuberculosis • Zika virus EARLY-ONSET • Group B Streptococcus • <i>Escherichia coli</i> • <i>Haemophilus</i> species • <i>Staphylococcus aureus</i> • <i>Klebsiella</i> species • <i>Enterococcus</i> species • Herpes simplex virus • <i>Streptococcus anginosus</i> • <i>Listeria monocytogenes</i>	• <i>Enterobacter</i> species • <i>Citrobacter</i> species • <i>Streptococcus pneumoniae</i> • <i>Morganella morganii</i> • <i>Pseudomonas</i> species • <i>Serratia</i> species • <i>Bacteroides</i> species LATE-ONSET • Coagulase-negative staphylococci • <i>Staphylococcus aureus</i> • <i>Escherichia coli</i> • <i>Candida</i> species • <i>Enterococcus</i> species • Group B Streptococcus • <i>Klebsiella</i> species • <i>Enterobacter</i> species • <i>Pseudomonas</i> species • Respiratory syncytial virus • Herpes simplex virus • Enteroviruses • <i>Listeria monocytogenes</i>

A newborn with poor feeding and temperature instability develops apnea but has no fever. Which interpretation is best supported by the table?

- A. These can be initial manifestations of neonatal infection
- B. Absence of fever excludes neonatal infection
- C. Apnea is confined to neurologic birth injury
- D. Feeding change is unrelated to infection
- E. Temperature instability occurs only with hypoglycemia

ORIGINAL SOURCE TABLE | Table 148.4 | PDF p. 1159 | printed p. 1147

Table 148.4 Initial Signs and Symptoms of Infection in Newborn Infants	
GENERAL Fever, temperature instability Hypothermia “Not doing well” Poor feeding Icteric	CARDIOVASCULAR Pallor; mottling; cold, clammy skin Tachycardia Hypotension Bradycardia
GASTROINTESTINAL Abdominal distention Vomiting Diarrhea Splenomegaly	CENTRAL NERVOUS Irritability, lethargy Tremors, seizures Hyporeflexia, hypotonia Abnormal Moro reflex Irregular respirations Full fontanel High-pitched cry
RESPIRATORY Apnea, dyspnea Cyanosis, retractions Grunting, grunting Pneumothorax	HEMATOLOGIC Jaundice Splenomegaly Pallor Petechiae, purpura Bleeding

A sick newborn has abdominal distension, shock, and findings suggestive of intestinal necrosis. Which noninfectious mimic of neonatal sepsis appears in the differential?

- A. Necrotizing enterocolitis
- B. Physiologic reflux
- C. Uncomplicated neonatal acne
- D. Benign transient breast enlargement
- E. An isolated neonatal nevus

ORIGINAL SOURCE TABLE | Table 148.6 | PDF p. 1160 | printed p. 1148

Table 148.6	Serious Systemic Illness in Newborns: Differential Diagnosis of Neonatal Sepsis
CARDIAC Congenital: hypoplastic left heart syndrome, other structural disease, persistent pulmonary hypertension of the newborn (PPHN) Acquired: myocarditis, hypovolemic or cardiogenic shock, PPHN	
GASTROINTESTINAL Necrotizing enterocolitis Spontaneous gastrointestinal perforation Midgut volvulus Hepatic failure (inborn errors of metabolism, neonatal iron storage disease)	
HEMATOLOGIC Neonatal purpura fulminans Immune-mediated thrombocytopenia Immune-mediated neutropenia Severe anemia Malignancies (congenital leukemia) Langerhans cell histiocytosis Hereditary clotting disorders Familial hemophagocytic lymphohistiocytosis	
METABOLIC Hypoglycemia Adrenal disorders: adrenal hemorrhage, adrenal insufficiency, congenital adrenal hyperplasia Inborn errors of metabolism: organic acidurias, lactic acidoses, urea cycle disorders, galactosemia	
NEUROLOGIC Intracranial hemorrhage: spontaneous, caused by child abuse Hypoxic-ischemic encephalopathy Neonatal seizures Infant botulism	
RESPIRATORY Respiratory distress syndrome Aspiration pneumonia: amniotic fluid, meconium, or gastric contents Lung hypoplasia Tracheoesophageal fistula Transient tachypnea of the newborn	

In an international clinical assessment of a sick newborn, which finding is a table-listed respiratory danger sign of severe infection?

- A. Severe chest indrawing with grunting
- B. Normal quiet breathing
- C. A normal respiratory rate with no effort
- D. Isolated occasional hiccups
- E. A normal oxygen saturation while asleep

ORIGINAL SOURCE TABLE | Table 148.5 | PDF p. 1160 | printed p. 1148

Table 148.5	Clinical Criteria for the Diagnosis of Sepsis in the International Setting: IMCI and WHO Criteria for Severe Infections in Children
• <i>Neurologic</i>: Convulsions, drowsy or unconscious, decreased activity, bulging fontanel • <i>Respiratory</i>: Respiratory rate >60 breaths/min, grunting, severe chest indrawing, central cyanosis • <i>Cardiac</i>: Poor perfusion, rapid and weak pulse • <i>Gastrointestinal</i>: Jaundice, poor feeding, abdominal distention • <i>Dermatologic</i>: Skin pustules, periumbilical erythema or purulence • <i>Musculoskeletal</i>: Edema or erythema overlying bones or joints • <i>Other</i>: Temperature >37.7°C (99.9°F; or feels hot) or <35.5°C (95.9°F; or feels cold)	

IMCI, Integrated Management of Childhood Illness; WHO, World Health Organization. Adapted from WHO. *Pocket Book Of Hospital Care for Children: Guidelines for the Management of Common Childhood Illnesses*. 2nd ed. Geneva: WHO. 2013. p 45–69. http://www.who.int/maternal_child_adolescent/documents/child_hospital_care/en/.

A neonate with possible sepsis is being assessed. Which perinatal factor in the evaluation table raises concern?

- A. Prolonged duration of membrane rupture
- B. An uncomplicated elective delivery before labor
- C. A documented negative maternal GBS screen
- D. Intact membranes until delivery
- E. An uneventful prenatal course without infection

ORIGINAL SOURCE TABLE | Table 148.8 | PDF p. 1162 | printed p. 1150

Table 148.8	Evaluation of a Newborn for Infection or Sepsis
HISTORY (SPECIFIC RISK FACTORS)	
Maternal infection during gestation or at parturition (type and duration of antimicrobial therapy):	
Urinary tract infection	
Chorioamnionitis	
Maternal colonization with group B <i>Streptococci</i> , <i>Neisseria gonorrhoeae</i> , herpes simplex	
Low gestational age/birthweight	
Multiple birth	
Duration of membrane rupture	
Complicated delivery	
Fetal tachycardia (distress)	
Age at onset (in utero, birth, early postnatal, late)	
Location at onset (hospital, community)	
Medical intervention:	
Vascular access	
Endotracheal intubation	
Parenteral nutrition	
Surgery	
EVIDENCE OF OTHER DISEASES*	
Congenital malformations (heart disease, neural tube defect)	
Respiratory tract disease (respiratory distress syndrome, aspiration)	
Necrotizing enterocolitis	
Metabolic disease (e.g., galactosemia)	
EVIDENCE OF FOCAL OR SYSTEMIC DISEASE	
General appearance, neurologic status	
Abnormal vital signs	
Organ system disease	
Feeding, stools, urine output, extremity movement	
LABORATORY STUDIES	
<i>Evidence of Infection</i>	
Culture from a normally sterile site (blood, CSF, other)	
Demonstration of a microorganism in tissue or fluid	
Molecular detection (blood, urine, CSF) by specific PCR and/or 16S ribosomal DNA	
Maternal or neonatal serology (syphilis, toxoplasmosis)	
<i>Evidence of Inflammation</i>	
Leukocytosis, increased immature/total neutrophil count ratio	
Acute-phase reactants: C-reactive protein, erythrocyte sedimentation rate, procalcitonin, ferritin	
Cytokines: interleukin-6, interleukin-B, tumor necrosis factor	
Pleocytosis in CSF or synovial or pleural fluid	
Disseminated intravascular coagulation: fibrin degradation products, D-dimer	
<i>Evidence of Multiorgan System Disease</i>	
Metabolic acidosis: pH, Pco ₂	
Pulmonary function: Po ₂ , Pco ₂	
Renal function: blood urea nitrogen, creatinine	
Hepatic injury/function: bilirubin, alanine transaminase, aspartate transaminase, ammonia, prothrombin time, partial thromboplastin time	
Bone marrow function: neutropenia, anemia, thrombocytopenia	

*Diseases that increase the risk of infection or may overlap with signs of sepsis.
CSF, Cerebrospinal fluid; PCR, polymerase chain reaction.

A 5-day-old infant is evaluated for suspected late-onset sepsis. Which culture study is listed as useful after 72 hours of life but not for early-onset sepsis evaluation?

- A. Urine culture
- B. Tracheal aspirate culture in every infant
- C. Routine skin swab culture
- D. Cord-blood fungal culture
- E. Stool culture in every infant

ORIGINAL SOURCE TABLE | Table 148.9 | PDF p. 1163 | printed p. 1151

Table 148.9 Culture-Based and Non–Culture-Based Diagnostics for Neonatal Sepsis			
CATEGORY	PARAMETER	OPTIMAL TIMING, VOLUME OF SPECIMEN, ROUTINE/INVESTIGATIONAL*	APPLICABILITY FOR NEONATAL SEPSIS
CULTURE BASED			
Blood	Culture	>1 mL of whole blood, from two sites	Gold standard for bacteremia
CSF	Culture	When clinically feasible	Gold standard for bacterial meningitis
Urine	Culture	>72 hr of life	Not useful for EOS; indicated for LOS evaluation
Tracheal aspirate	Culture	Neonates with endotracheal tube in place and signs of progressive respiratory distress	Usually reflects colonization
NON–CULTURE BASED			
Neutrophil indices	Neutropenia Absolute neutrophil count Absolute immature neutrophil count	After 12 hr of life Consider GA, delivery mode, altitude, arterial versus venous sampling, time since birth	Neutropenia better predictor for sepsis than leukocytosis
Neutrophil markers	CD64	Elevated for 24 hr after infection Requires 50 μ L blood Results within hours Investigational	Cut points between 2.38 and 3.62 optimal sensitivity, specificity, and NPV for EOS
Platelet count	Thrombocytopenia and thrombocytosis	Late findings; slow to respond	Thrombocytopenia associated with fungal infection
CSF cell count	CSF WBC	Uninfected neonates: mean 10 cells/mm ³ ; range up to 20 cells/mm ³	Does not predict culture-proven meningitis
CSF chemistries	CSF protein CSF glucose	Term <100 mg/dL Preterm higher; 70–80% of serum glucose	Elevated in fungal meningitis Low glucose specific for bacterial meningitis
Acute phase reactants	CRP Procalcitonin	8–24 hr after infection 2–12 hr after infection	Good NPV Better sensitivity but less specificity than CRP

*Investigational refers to an assay or parameter that is undergoing evaluation for clinical use and applicability.

CSF, Cerebrospinal fluid; EOS, early-onset sepsis; GA, gestational age; LOS, late-onset sepsis; MHC II, major histocompatibility complex class II; NPV, negative predictive value; TNF, tumor necrosis factor; WBC, white blood cell count.

From Shane AL, Stoll BJ. Recent developments and current issues in the epidemiology, diagnosis, and management of bacterial and fungal neonatal sepsis. *Am J Perinatol*.

A pregnant patient previously delivered an infant with invasive group B streptococcal disease. Which approach to intrapartum GBS prophylaxis is supported by the table?

- A. Provide intrapartum prophylaxis in the current pregnancy
- B. Withhold prophylaxis unless the newborn develops fever
- C. Provide prophylaxis only after neonatal blood cultures result
- D. Use only a previous pregnancy's negative screening test
- E. Defer prophylaxis until after delivery

ORIGINAL SOURCE TABLE | Table 148.11 | PDF p. 1164 | printed p. 1152

Table 148.11 Indications for Intrapartum Antibiotic Prophylaxis to Prevent Early-Onset Group B <i>Streptococcus</i> Disease	
INTRAPARTUM GBS PROPHYLAXIS INDICATED	INTRAPARTUM GBS PROPHYLAXIS NOT INDICATED
Previous infant with invasive GBS disease	Colonization with GBS during a previous pregnancy (unless an indication for GBS prophylaxis is present for current pregnancy)
GBS bacteriuria during any trimester of the current pregnancy	GBS bacteriuria during previous pregnancy (unless another indication for GBS prophylaxis is present for current pregnancy)
Positive GBS screening culture during current pregnancy (unless a cesarean delivery is performed before onset of labor or amniotic membrane rupture)	Cesarean delivery before onset of labor or amniotic membrane rupture regardless of GBS colonization status or gestational age
Unknown GBS status at the onset of labor (culture not done, incomplete, or results unknown) and any of the following: Delivery at <37 weeks' gestation* Amniotic membrane rupture ≥18 hr Intrapartum temperature ≥38.0°C (100.4°F) [†] Intrapartum NAAT [‡] positive for GBS	Negative vaginal and rectal GBS screening culture in late gestation during the current pregnancy, regardless of intrapartum risk factors

*Recommendations for the use of intrapartum antibiotics for prevention of early-onset GBS disease in the setting of threatened preterm delivery are presented in Chapter 230.

[†]If amnionitis is suspected, broad-spectrum antibiotic therapy that includes an agent known to be active against GBS should replace GBS prophylaxis.

[‡]If intrapartum NAAT is negative for GBS but any other intrapartum risk factor (delivery at <37 wk gestation, amniotic membrane rupture ≥18 hr, or temperature ≥38.0°C/100.4°F) present, intrapartum antibiotic prophylaxis is indicated.

A pregnant patient cares for a toddler who attends day care and asks how to reduce the risk of congenital cytomegalovirus infection. Which prevention approach is listed?

- A. Avoid direct contact with toddler urine and saliva through hygiene practices
- B. Give routine maternal CMV vaccination during pregnancy
- C. Treat all household contacts with antiviral medication
- D. Eliminate all maternal dairy products
- E. Give the newborn antibiotics before delivery

ORIGINAL SOURCE TABLE | Table 149.2 | PDF p. 1167 | printed p. 1155

Table 149.2	Prevention Strategies for Congenital and Perinatal Infections
PATHOGEN	PREVENTION STRATEGY
CMV	Hygienic education to avoid direct contact with toddler urine/saliva, avoid new sexual partners
HSV	Prevention of maternal STI near delivery and exposure of newborn to active maternal lesions
VZV	Vaccination of nonpregnant women of childbearing age with a negative varicella history or vaccine immunity
Rubella virus	Vaccination of nonpregnant women of childbearing age with no immunization history
HIV	Safe sex practices; maternal treatment with HAART on infection
SARS-CoV-2	Prenatal and maternal vaccination, masking, and social distancing
Zika virus	Prevention of mosquito bites and safe sex practices with persons who have recently traveled to endemic areas
<i>Toxoplasma gondii</i>	Avoiding undercooked meat, avoiding unpasteurized goat milk, avoiding raw mollusks, avoid contact with litter or soil potentially contaminated with cat feces
<i>Treponema pallidum</i>	Safe sex practices; screening in nonpregnant populations

HSV, Herpes simplex virus; CMV, cytomegalovirus; VZV, varicella-zoster virus; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; STI, sexually transmitted infection; HAART, highly active antiretroviral therapy.
From Auriti C, De Rose DU, Santisi A, et al. Pregnancy and viral infections: Mechanisms

A neonate has hydrocephalus, diffuse intracranial calcifications, and chorioretinitis. Which congenital infection best matches the syndrome table?

- A. Toxoplasma gondii
- B. Rubella virus
- C. Treponema pallidum
- D. Congenital HIV infection
- E. Group B streptococcal sepsis

ORIGINAL SOURCE TABLE | Table 149.4 | PDF p. 1168 | printed p. 1156

Table 149.4 Syndromes in the Neonate Caused by Congenital Infections	
ORGANISM	SIGNS
Toxoplasma gondii	Hydrocephalus, diffuse intracranial calcification, chorioretinitis
Rubella virus	Cardiac defects, sensorineural hearing loss, cataracts, microcephaly, “blueberry muffin” skin lesions, hepatomegaly, interstitial pneumonitis, myocarditis, disturbances in bone growth, intrauterine growth restriction
CMV	Microcephaly, periventricular calcifications, jaundice, petechiae or purpura, hepatosplenomegaly, intrauterine growth restriction, sensorineural hearing loss
HSV	Skin vesicles or scarring, eye scarring, microcephaly or hydranencephaly, vesicular skin rash, keratoconjunctivitis, meningoencephalitis, sepsis with hepatic failure
Treponema pallidum	Bullous, macular, or eczematous skin lesions involving palms and soles; rhinorrhea; dactylitis and other signs of osteochondritis and periostitis; hepatosplenomegaly; lymphadenopathy
VZV	Limb hypoplasia, cicatricial skin lesions, ocular abnormalities, cortical atrophy
Parvovirus B19	Nonimmune hydrops fetalis
HIV	Severe thrush, failure to thrive, recurrent bacterial infections, calcification of basal ganglia
Zika virus	Microcephaly, lissencephaly, cerebellar hypoplasia, akinesia syndrome, macular scarring, retinal mottling, subcortical calcifications, hypertonia

HSV, Herpes simplex virus; CMV, cytomegalovirus; VZV, varicella-zoster virus.
From Maldonado YA, Nizet V, Klein JO, et al. Current concepts of infections of the fetus and newborn infant. In Wilson CB, Nizet V, Maldonado Y, et al., eds. Remington and Klein: Infectious Diseases of the Fetus and Newborn, 8th ed. Philadelphia: Elsevier; 2016: Tables 1–7.

Answer key and teaching notes

01. A | Table 137.1 | PDF p. 1119, printed p. 1107

Why: The table lists a family history of severe jaundice and birth trauma among risk factors.
Closest distractor: Seasonal rhinitis is unrelated to the listed bilirubin risk factors.

02. A | Table 137.2 | PDF p. 1119, printed p. 1107

Why: Day-1 jaundice prompts evaluation for hemolysis and other serious causes with bilirubin fractions, blood count/smear, and blood-group testing.
Closest distractor: Transaminases alone do not assess the major hemolytic concerns.

03. A | Table 137.3 | PDF p. 1120, printed p. 1108

Why: The table places hemolytic states and hematoma among causes that may appear during the first 24 hours and produce indirect hyperbilirubinemia.
Closest distractor: Physiologic jaundice in the table typically begins on day 2 or 3.

04. A | Table 137.4 | PDF p. 1121, printed p. 1109

Why: The HLH column combines a very high ferritin concentration with increased triglycerides.
Closest distractor: Gestational alloimmune liver disease may raise ferritin but the table lists triglycerides as normal.

05. A | Table 137.5 | PDF p. 1123, printed p. 1111

Why: The second acute phase includes extensor hypertonia, opisthotonos, retrocollis, and fever.
Closest distractor: The first acute phase emphasizes poor suck, stupor, hypotonia, and seizures.

06. A | Table 139.1 | PDF p. 1130, printed p. 1118

Why: Fetomaternal transfusion is listed under blood loss.
Closest distractor: Immune hemolysis destroys circulating red cells and is a separate category.

07. A | Table 139.2 | PDF p. 1133, printed p. 1121

Why: The table links persistent microspherocytes, DAT negativity, and positive EMA flow with hereditary spherocytosis.
Closest distractor: ABO disease can also show spherocytes but more often has a positive DAT and transient morphology.

08. A | Table 139.3 | PDF p. 1133, printed p. 1121

Why: The table describes steroid-responsive hypoplastic, often macrocytic anemia in Diamond-Blackfan syndrome.
Closest distractor: Congenital dyserythropoietic anemia type II has a distinct erythroblast morphology rather than this characteristic steroid-responsive hypoplasia.

09. A | Table 140.1 | PDF p. 1135, printed p. 1123

Why: The ABO column notes frequent involvement of a firstborn infant, usually milder jaundice, and rare severe anemia.
Closest distractor: Rh disease is less likely in a firstborn and more often produces severe anemia.

10. A | Table 140.2 | PDF p. 1137, printed p. 1125

Why: The table places Kell K among antigens associated with severe HDFN, including reports of hydrops or intrauterine transfusion.
Closest distractor: The mild category does not capture the documented severe potential of K antigen.

11. A | Table 142.1 | PDF p. 1140, printed p. 1128

Why: Late-onset VKDB occurs from 1 to 6 months and commonly involves intracranial bleeding, with exclusive breastfeeding among risks.
Closest distractor: Classic VKDB occurs at 2 to 7 days.

12. A | Table 143.1 | PDF p. 1142, printed p. 1130

Why: The cardiovascular section explicitly includes supraventricular tachycardia among arrhythmias associated with hydrops.
Closest distractor: A hematologic mechanism is a separate category and does not describe the documented rhythm disturbance.

13. A | Table 145.1 | PDF p. 1146, printed p. 1134

Why: The table lists sleep of less than 1 hour after a feed as a withdrawal concern.
Closest distractor: The other listed feeding and consolation observations do not meet these concern thresholds.

14. A | Table 145.2 | PDF p. 1147, printed p. 1135

Why: The table lists morphine as an initial every-3-hour opioid regimen.
Closest distractor: Methadone has a different initial interval in this table.

15. A | Table 146.1 | PDF p. 1151, printed p. 1139

Why: The table states that all specified features can establish FAS with or without documented prenatal exposure.
Closest distractor: Exposure history is valuable but is not mandatory under this table's FAS criteria.

Answer key and teaching notes

16. A | Table 146.2 | PDF p. 1152, printed p. 1140

Why: With documented exposure, the partial FAS table requires facial features and neurobehavioral impairment without requiring growth deficiency.
Closest distractor: Full FAS has additional specified growth and brain criteria.

17. A | Table 146.3 | PDF p. 1152, printed p. 1140

Why: The table explicitly states ARND cannot be diagnosed definitively before age 3 years.
Closest distractor: One isolated behavioral symptom does not meet its multidomain impairment criteria.

18. A | Table 146.4 | PDF p. 1152, printed p. 1140

Why: The ND-PAE criteria include two or more adaptive deficits, at least one involving communication or social communication, along with other domains.
Closest distractor: A structural malformation alone does not satisfy the neurobehavioral criteria.

19. A | Table 146.5 | PDF p. 1152, printed p. 1140

Why: The alcohol-related birth-defects table includes radioulnar synostosis among skeletal malformations.
Closest distractor: ARND focuses on neurobehavioral deficits rather than the listed structural defect.

20. A | Table 147.1 | PDF p. 1154, printed p. 1142

Why: The table includes heart failure and septal hypertrophy among morbidities of infants of diabetic mothers.
Closest distractor: Heart block is not the listed explanation for the structural septal thickening.

21. A | Table 148.3 | PDF p. 1158, printed p. 1146

Why: The postnatal column includes organisms marked as more likely with mechanical ventilation or indwelling catheters.
Closest distractor: Transplacental infection precedes birth and does not explain this hospital-onset exposure pattern.

22. A | Table 148.2 | PDF p. 1158, printed p. 1146

Why: Group B Streptococcus appears under early-onset pathogens in the timing table.
Closest distractor: It is not confined to the late-onset category.

23. A | Table 148.4 | PDF p. 1159, printed p. 1147

Why: The table lists poor feeding, temperature instability, and apnea among early signs of neonatal infection.
Closest distractor: Neonatal infection may present without fever, so its absence is not exclusionary.

24. A | Table 148.6 | PDF p. 1160, printed p. 1148

Why: Necrotizing enterocolitis is listed under gastrointestinal illnesses that can resemble systemic sepsis.
Closest distractor: Physiologic reflux does not account for shock and intestinal necrosis.

25. A | Table 148.5 | PDF p. 1160, printed p. 1148

Why: The IMCI/WHO criteria table includes grunting and severe chest indrawing among respiratory signs.
Closest distractor: Quiet breathing without increased effort is not a listed respiratory danger sign.

26. A | Table 148.8 | PDF p. 1162, printed p. 1150

Why: The table includes duration of membrane rupture among maternal and delivery risk factors.
Closest distractor: An elective delivery before labor does not represent the membrane-rupture exposure in the table.

27. A | Table 148.9 | PDF p. 1163, printed p. 1151

Why: The table lists urine culture after 72 hours as indicated in late-onset evaluation but not useful for early-onset sepsis.
Closest distractor: Tracheal aspirates are restricted to intubated infants with respiratory deterioration and often reflect colonization.

28. A | Table 148.11 | PDF p. 1164, printed p. 1152

Why: A prior infant with invasive GBS disease is a listed indication for prophylaxis in a subsequent delivery.
Closest distractor: Waiting for neonatal illness defeats the intrapartum prevention strategy.

29. A | Table 149.2 | PDF p. 1167, printed p. 1155

Why: The CMV row emphasizes hygiene to reduce direct exposure to young children's urine and saliva.
Closest distractor: A routine maternal CMV vaccine is not the strategy listed in this table.

30. A | Table 149.4 | PDF p. 1168, printed p. 1156

Why: The congenital-infection table lists this combination for toxoplasmosis.
Closest distractor: Rubella is more strongly associated with cataracts, hearing loss, and cardiac defects in the table.

Table selection log

- 01. Table 137.1 | PDF p. 1119 | printed p. 1107 | Completed
- 02. Table 137.2 | PDF p. 1119 | printed p. 1107 | Completed
- 03. Table 137.3 | PDF p. 1120 | printed p. 1108 | Completed
- 04. Table 137.4 | PDF p. 1121 | printed p. 1109 | Completed
- 05. Table 137.5 | PDF p. 1123 | printed p. 1111 | Completed
- 06. Table 139.1 | PDF p. 1130 | printed p. 1118 | Completed
- 07. Table 139.2 | PDF p. 1133 | printed p. 1121 | Completed
- 08. Table 139.3 | PDF p. 1133 | printed p. 1121 | Completed
- 09. Table 140.1 | PDF p. 1135 | printed p. 1123 | Completed
- 10. Table 140.2 | PDF p. 1137 | printed p. 1125 | Completed
- 11. Table 142.1 | PDF p. 1140 | printed p. 1128 | Completed
- 12. Table 143.1 | PDF p. 1142 | printed p. 1130 | Completed
- 13. Table 145.1 | PDF p. 1146 | printed p. 1134 | Completed
- 14. Table 145.2 | PDF p. 1147 | printed p. 1135 | Completed
- 15. Table 146.1 | PDF p. 1151 | printed p. 1139 | Completed
- 16. Table 146.2 | PDF p. 1152 | printed p. 1140 | Completed
- 17. Table 146.3 | PDF p. 1152 | printed p. 1140 | Completed
- 18. Table 146.4 | PDF p. 1152 | printed p. 1140 | Completed
- 19. Table 146.5 | PDF p. 1152 | printed p. 1140 | Completed
- 20. Table 147.1 | PDF p. 1154 | printed p. 1142 | Completed
- 21. Table 148.3 | PDF p. 1158 | printed p. 1146 | Completed
- 22. Table 148.2 | PDF p. 1158 | printed p. 1146 | Completed
- 23. Table 148.4 | PDF p. 1159 | printed p. 1147 | Completed
- 24. Table 148.6 | PDF p. 1160 | printed p. 1148 | Completed
- 25. Table 148.5 | PDF p. 1160 | printed p. 1148 | Completed
- 26. Table 148.8 | PDF p. 1162 | printed p. 1150 | Completed
- 27. Table 148.9 | PDF p. 1163 | printed p. 1151 | Completed
- 28. Table 148.11 | PDF p. 1164 | printed p. 1152 | Completed
- 29. Table 149.2 | PDF p. 1167 | printed p. 1155 | Completed
- 30. Table 149.4 | PDF p. 1168 | printed p. 1156 | Completed

Skipped within this span: Table 137.6 (historical bilirubin threshold); 139.4 (transfusion threshold); 148.1 (incidence statistics); 148.7 (historical SIRS definitions); 148.10 (treatment regimen review).

Last completed: Table 149.4, PDF p. 1168, printed p. 1156. Next search begins after Table 149.4.

Review note: Table 148.5 cites WHO 2013 clinical criteria; WHO published updated guidance in 2024: <https://www.who.int/publications/i/item/9789240102903/>

Table 145.2 lists source-book dosing; current opioid-withdrawal care emphasizes nonpharmacologic measures first: <https://publications.aap.org/pediatrics/article/154/1/e2023063635/197513/>