

Transplacental (Hematologic) Infections

Maternal bloodstream → placenta → fetal organs

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Learning objectives

- Distinguish hematogenous transplacental spread from ascending perinatal infection.
- Relate gestational timing and organism to fetal injury patterns.
- Explain parvovirus B19–related erythroid aplasia and nonimmune hydrops.
- Recognize selected Robbins-described congenital infection syndromes and morphologic clues.

The focus is route, fetal pathology, and clinicopathologic interpretation.

Two dominant routes of fetal acquisition

Ascending (transcervical)

Organisms move from the cervicovaginal tract; Fetal exposure may occur before or during delivery.

Transplacental (hematogenous)

Maternal bloodborne organisms cross via chorionic villi and enter the fetal bloodstream.

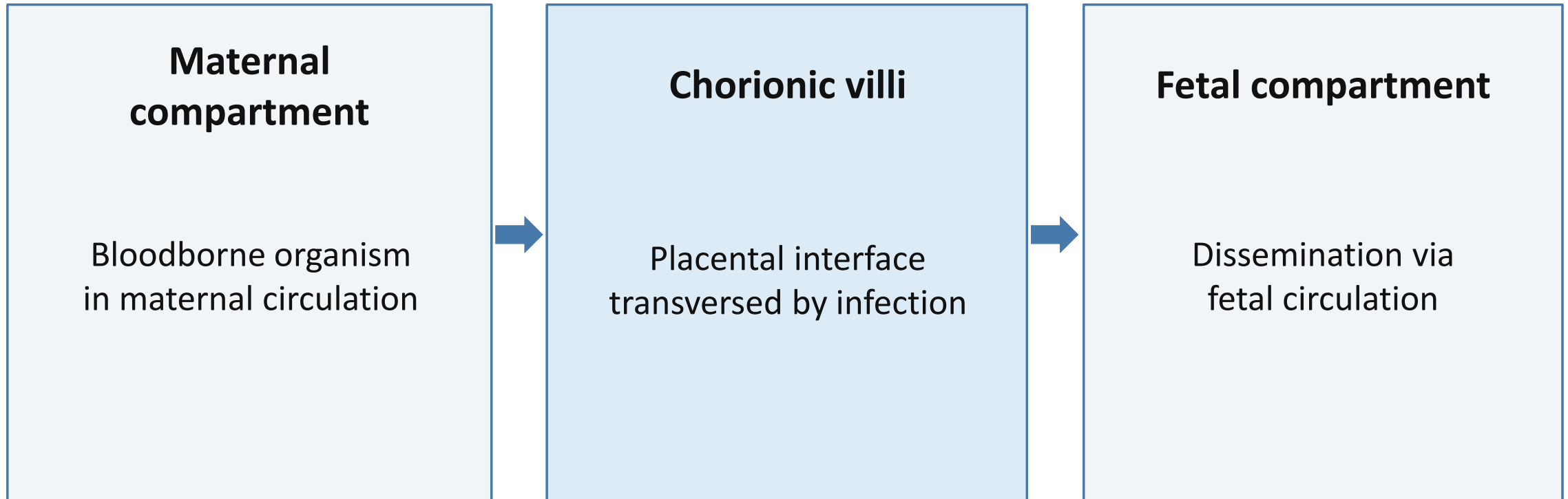
The pathways can coexist, but neither requires passage through the other.

“Hematologic” describes the route—not the phenotype

- Maternal bloodstream provides access to chorionic villi and ultimately fetal blood.
- Some infections injure the fetal hematopoietic system; Many primarily involve other organs.
- A transplacental infection may present with neurologic, ocular, hepatic, cardiac, or systemic findings.

Do not equate transplacental transmission with hemolytic disease.

Transplacental access through the chorionic villi



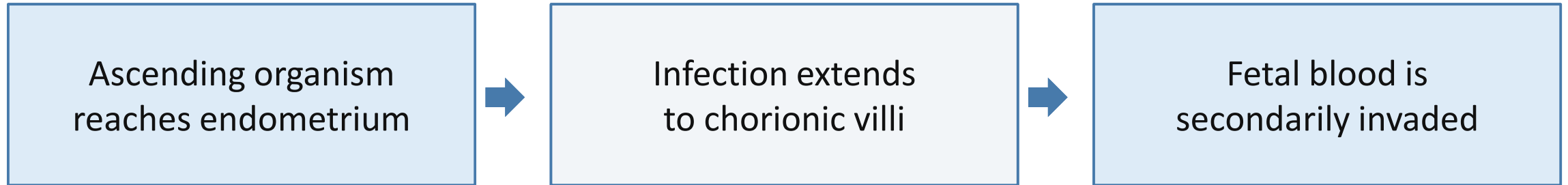
Schematic: Bloodborne spread can occur throughout gestation.

Ascending versus transplacental infection

Ascending (transcervical)	Transplacental (hematogenous)
Microorganisms ascend from the cervix or vagina.	Organisms disseminate through maternal blood and chorionic villi.
Inhalation of infected amniotic fluid or birth-canal exposure.	Fetal bloodstream is directly exposed after crossing the placental interface.
Pneumonia, sepsis, meningitis may follow.	Pattern depends strongly on fetal age and organism.

Route of acquisition influences, but does not determine, clinical presentation.

Mixed pathways can occur



- The source explicitly describes acquisition through both routes in some cases.
- Route attribution may be difficult when placental inflammation and fetal infection coexist.

Organisms transmitted hematogenously

Parasitic

Toxoplasma and malaria are textbook examples.

Viral

Many viral pathogens can cross the placenta; Parvovirus B19 is highlighted.

Bacterial

Listeria and Treponema are notable examples, despite most bacteria favoring ascending spread.

The examples illustrate categories; This is not an exhaustive organism list.

Two determinants of fetal phenotype

Gestational timing

The stage of fetal development changes vulnerability and the type of long-term injury.

Microorganism

Cell tropism, tissue distribution and pathogenesis shape the distinctive organ lesions.

Together, timing and pathogen determine clinical and morphologic expression.

Gestation changes the consequences of infection

Earlier exposure

Risk of persistent developmental consequences.

During gestation

Bloodstream spread may occur at any stage.

Near delivery

Selected infections may also transmit through maternal–fetal blood exchange.

- An early insult can have effects that are not clinically obvious until childhood.

Transmission can also occur during delivery

- Transplacental hematogenous spread is not confined to a single trimester.
- Hepatitis B and HIV are examples of organisms that may be acquired through maternal-to-fetal transfusion during delivery.
- An infection detected neonatally is not, by itself, proof of prenatal acquisition.

Separate the time of detection from the time and route of transmission.

Infection is not synonymous with clinical disease

Evidence of infection

Organism reaches and infects fetal or neonatal tissues.

Some infected infants remain asymptomatic initially.

Transmission route may be known or uncertain.

Manifest disease or sequelae

Inflammatory, destructive, or developmental injury becomes evident.

Clinical expression may be immediate or delayed.

Severity varies with agent and gestational age.

TORCH: A clinical-pathologic grouping

T — Toxoplasmosis

A parasitic congenital infection with ocular and neurologic consequences.

O — Other infections

Includes organisms such as congenital syphilis.

R — Rubella

Included in the source definition of TORCH.

C — Cytomegalovirus

A congenital viral infection with multisystem manifestations.

H — Herpesviruses

Included in TORCH; Route of acquisition may also be ascending.

TORCH is a syndrome-oriented mnemonic, not a single pathogen or transmission mechanism.

Overlapping manifestations in the TORCH group

Organ system	Examples in Robbins
Systemic	Fever
Central nervous system	Encephalitis
Eye	Chorioretinitis
Liver / spleen	Hepatosplenomegaly
Heart / lung	Myocarditis or pneumonitis
Hematologic / skin	Hemolytic anemia; vesicular or hemorrhagic lesions

Overlapping syndromes demand agent-specific interpretation and confirmation.

Neurologic involvement can dominate the phenotype

- Encephalitis is one of the shared presentations explicitly listed for TORCH infections.
- Neurologic impairment after intrauterine infection may be delayed rather than evident at birth.
- Congenital CMV and toxoplasmosis have additional source-described central nervous system findings.

Neurologic findings are clinically important, but not pathogen-specific.

Ocular disease: Chorioretinitis and its context

- Chorioretinitis occurs among the shared TORCH presentations.
- Congenital toxoplasmosis can produce chorioretinitis together with cerebral abnormalities.
- Ocular findings should be interpreted together with neurologic, systemic, and laboratory evidence.

The anatomical site of ocular injury provides a clue—not a unique diagnosis.

Visceral manifestations of congenital infection

Hepatosplenomegaly

Part of the shared TORCH phenotype; Also described in congenital CMV.

Pneumonitis

Included among overlapping TORCH manifestations.

Myocarditis

Can occur in the multisystem TORCH syndrome.

Encephalitis

May coexist with visceral disease and systemic illness.

Why hematologic findings matter

- The TORCH clinical-pathologic group can include hemolytic anemia.
- Congenital CMV can present with anemia and bleeding from thrombocytopenia.
- Parvovirus B19 instead preferentially damages erythroid progenitors and may cause red cell aplasia.

Anemia from destruction and anemia from impaired production are mechanistically different.

Skin clues in congenital infections

Vesicular lesions

Included among possible TORCH manifestations.

Hemorrhagic lesions

Included among TORCH presentations and can signal multisystem involvement.

Listerial papules

Red papular rash of extremities described in neonatal listeriosis.

Congenital syphilis

Desquamating or bullous eruption, often involving palms and soles.

Skin patterns are clues to investigate, not standalone confirmation.

Early gestational infection: Lasting consequences

Early infection

Disturbance while organs are developing.

Fetal effect

Growth restriction or congenital organ abnormalities.

Later recognition

Intellectual disability and other long-term impairments.

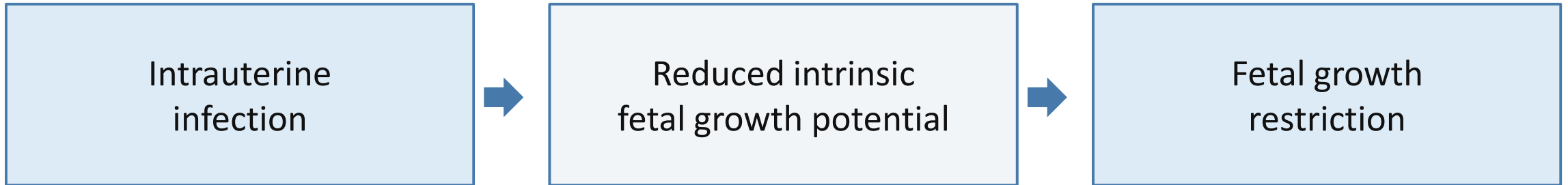
- Cataracts, cardiac defects, and bone defects among possible long-term consequences.

Congenital sequelae

Domain	Examples of long-term consequence
Growth	Growth retardation
Neurodevelopment	Intellectual disability
Ocular	Cataracts
Cardiovascular	Congenital cardiac anomalies
Skeletal	Bone defects

These findings are collective TORCH possibilities; They are not universal for each agent.

Congenital infections within the FGR differential



- Congenital infection among fetal causes of small-for-gestational-age infants.
- The TORCH group is specifically highlighted among infections associated with FGR.

FGR etiologies: Avoid prematurely assuming infection

Fetal causes	Alternative maternal / placental causes
Congenital infections	Reduced placental blood flow in maternal vascular disease
Chromosomal abnormalities	Placental vascular disorders or thrombosis
Congenital anomalies	Maternal malnutrition or exposures

Growth restriction alone cannot establish a congenital infection.

The meaning of symmetric growth restriction

- Fetal-factor growth restriction as often symmetric or proportionate.
- In symmetric FGR, multiple organ systems are similarly affected.
- Congenital infection belongs in the fetal-factor differential alongside chromosomal disease and congenital anomalies.

Symmetry supports a broad fetal-growth assessment; It does not identify a specific pathogen.

Pattern recognition has limits

Shared phenotype

Hepatosplenomegaly, skin lesions, anemia, and neurologic injury may occur with more than one agent.

Different mechanisms

Aplastic erythropoiesis differs from hemolysis or thrombocytopenia.

Timing matters

A delayed clinical finding may originate from infection in utero.

Integrate organism, timing, clinical pattern and corroborating tests.

Parvovirus B19: The hematopoietic prototype

- B19 causes erythema infectiosum (“fifth disease”) in immunocompetent older children.
- In the fetus, its distinctive pathology is preferential infection of erythroid precursor cells.
- Consequent failure of red cell production can contribute to severe fetal anemia and hydrops.

Parvovirus B19 infection during pregnancy

Population / outcome	Robbins statement
Nonimmune pregnant females	Approximately 1–5% acquire B19 infection.
Overall prognosis	Vast majority of affected pregnancies have normal outcomes.
Adverse outcome	Spontaneous abortion, especially in the second trimester.
Other adverse outcomes	Stillbirth, nonimmune hydrops or congenital anemia.

The 1–5% figure refers to infection of seronegative pregnant females, not to fetal loss.

Possible fetal outcomes after maternal B19 infection

Normal outcome

Most pregnancies after maternal infection remain uncomplicated.

Pregnancy loss

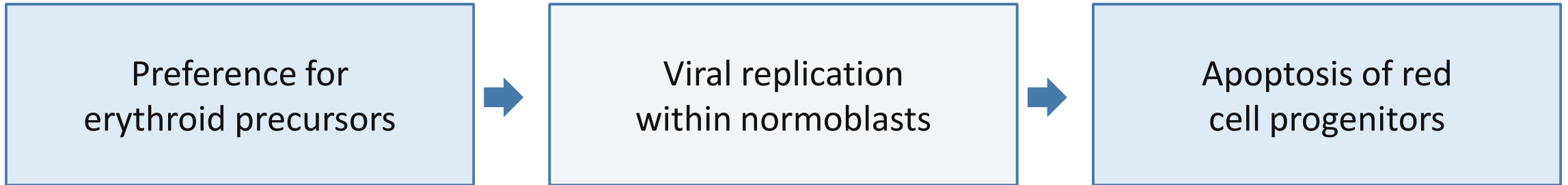
Spontaneous abortion or stillbirth in a minority of affected pregnancies.

Hematologic illness

Congenital anemia and potentially nonimmune hydrops fetalis.

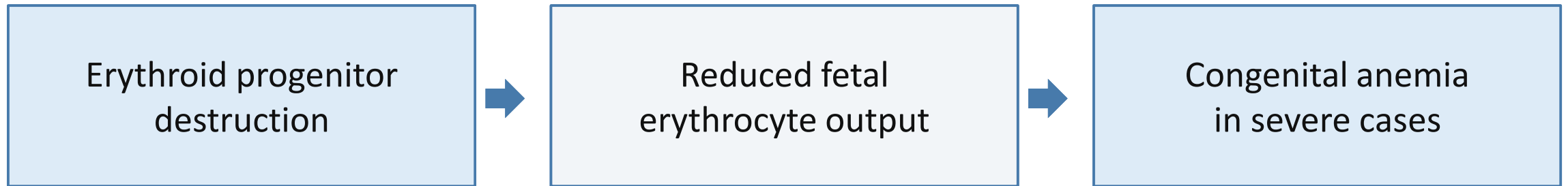
Do not interpret maternal B19 infection as inevitable fetal injury.

Why B19 targets fetal erythropoiesis



- The adjacent fetal-hydrops section specifically identifies progenitor apoptosis.
- Loss of the precursor population causes red cell aplasia.

Red cell aplasia: The key mechanistic lesion



- The major lesion is impaired cell production, not primarily immune red cell hemolysis.
- The degree of fetal compromise depends on how severe the anemia becomes.

Two mechanisms that produce fetal anemia

Reduced production: B19

Viral injury to erythroid precursors.

Red cell aplasia is a central mechanism.

May lead to nonimmune hydrops.

Increased destruction: Immune hemolysis

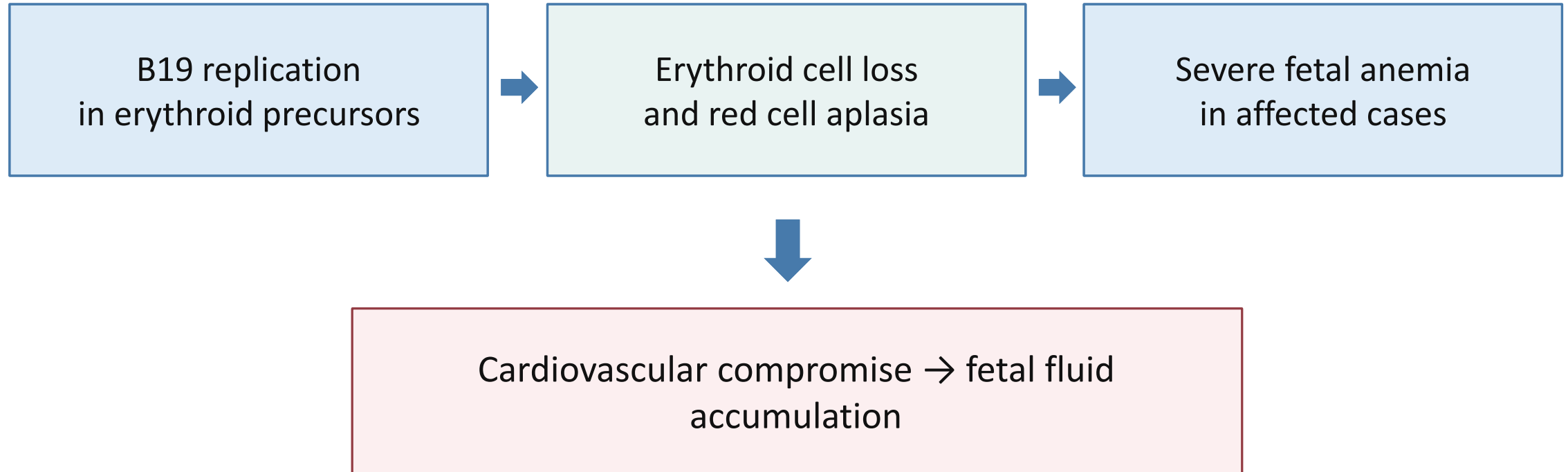
Maternal antibodies react with fetal red cell antigens.

Peripheral red cell destruction is the central mechanism.

May lead to immune hydrops and neonatal jaundice.

Both may culminate in anemia-associated hydrops despite different initiating lesions.

Parvovirus B19: An anemia-to-hydrops pathway



Mechanistic integration; Not every fetal B19 infection causes anemia or hydrops.

Hydrops fetalis: Recognize the morphologic endpoint

- Fetal hydrops describes abnormal accumulation of edema fluid during intrauterine life.
- The most generalized form is severe widespread fetal edema (hydrops fetalis).
- Fluid may also collect in pleural or peritoneal spaces or postnuchal soft tissues.

Hydrops is a phenotype with multiple causes—not a diagnosis of viral infection.

Causes of nonimmune hydrops in the source

Cardiovascular

Structural defects and arrhythmias can cause fetal heart failure.

Chromosomal

Selected aneuploidies and Turner syndrome may be associated.

Fetal anemia

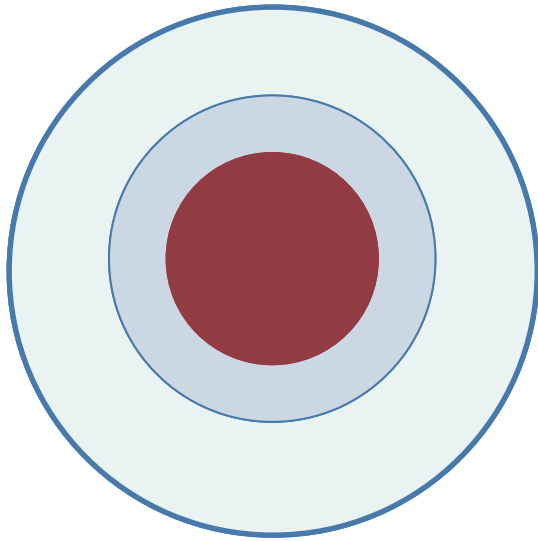
Alpha-thalassemia and parvovirus B19 are named examples.

Other

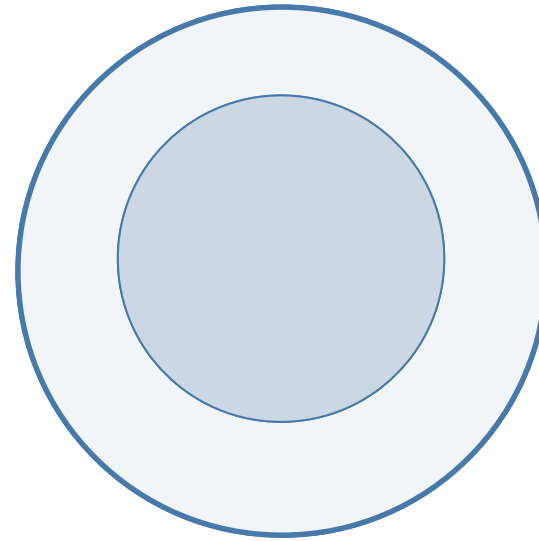
Twin-to-twin transfusion and unexplained cases also occur.

Parvovirus B19 belongs within, not outside, the broader differential.

Parvovirus B19: Identifying erythroid inclusions



Infected erythroid
precursor



Uninfected precursor
for comparison

Schematic only—not an H&E specimen. Fig. 10.9, inclusions are large and homogeneous, with a peripheral chromatin rim.

Inclusion bodies: B19 versus CMV

Parvovirus B19	Cytomegalovirus
Early erythroid precursors / normoblasts.	Enlarged infected cells across many tissues.
Large, homogeneous intranuclear inclusion.	Large basophilic intranuclear inclusion with a clear halo.
Rim of residual peripheral chromatin.	“Owl’s eye” nuclear appearance; Cytoplasmic inclusions can occur.

These descriptions are morphological principles, not a substitute for genuine stained material.

Case: Fetal anemia following maternal viral illness

A pregnancy is complicated by maternal viral infection. Subsequent assessment suggests severe fetal anemia and generalized fluid accumulation. Erythroid precursors contain large homogeneous intranuclear inclusions.

1. Which infection best fits the hematopoietic morphology?

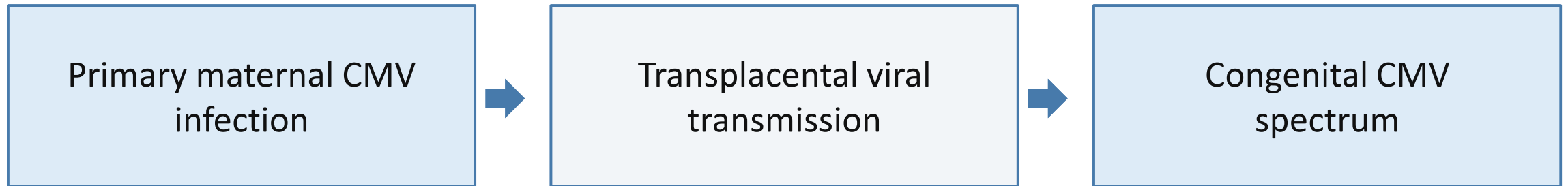
2. What mechanism connects the infection to hydrops?

Case resolution: Parvovirus B19

- The described erythroid inclusion pattern supports parvovirus B19.
- Replication and apoptosis of erythroid precursors produce red cell aplasia.
- Severe anemia can contribute to nonimmune fetal hydrops.
- The outcome cannot be assumed in all maternal infections; Most have a normal pregnancy outcome.

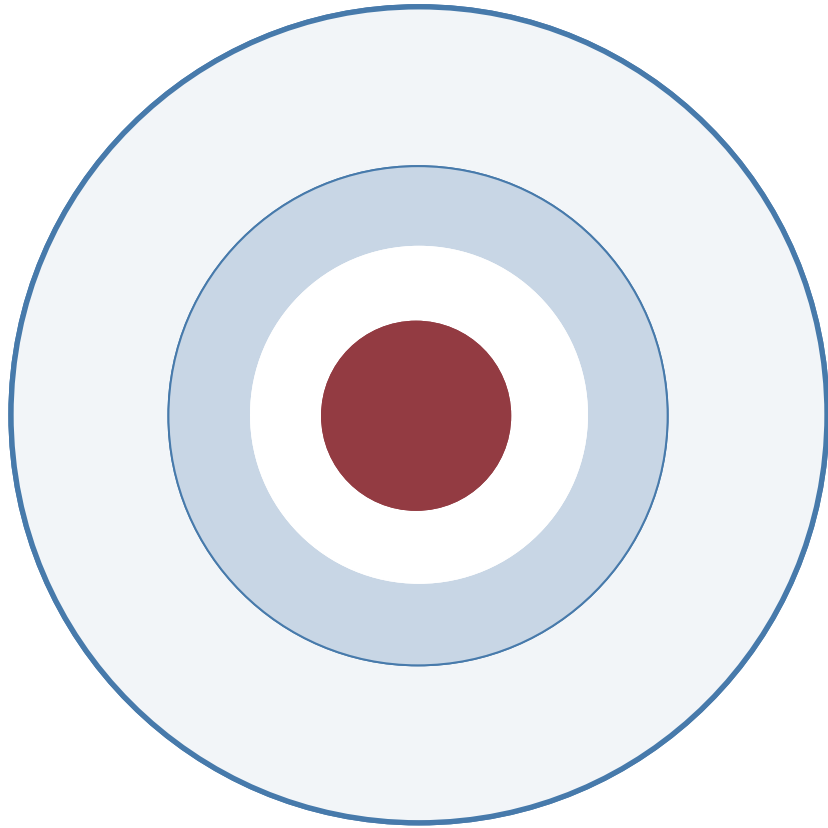
Distinctive cell tropism explains the hematologic phenotype.

Congenital CMV: Route and timing



- Congenital (in utero) CMV from perinatal acquisition at birth or via breast milk.
- Congenital disease may be severe, mild, or asymptomatic initially.

CMV cytopathic morphology: The “owl’s eye” pattern



- Enlargement of the infected cell and nucleus
- Basophilic intranuclear inclusion with a surrounding clear halo
- Additional smaller cytoplasmic inclusions may be present

Schematic—not a diagnostic micrograph. Diagnosis requires appropriate testing and context.

Congenital CMV: Major injury patterns

Growth

Intrauterine growth restriction may occur.

Visceral

Jaundice and hepatosplenomegaly.

Hematologic

Anemia and thrombocytopenia-associated bleeding.

CNS

Encephalitis; Microcephaly and cerebral calcifications in severe cases.

CMV can involve blood, liver, brain and multiple other tissues.

Congenital CMV: Delayed neurologic sequelae

- Survivors may have permanent hearing loss, intellectual disability, or other neurologic impairment.
- Some infants without obvious illness at birth develop deficits later.
- A mild neonatal clinical presentation does not completely exclude long-term consequences.

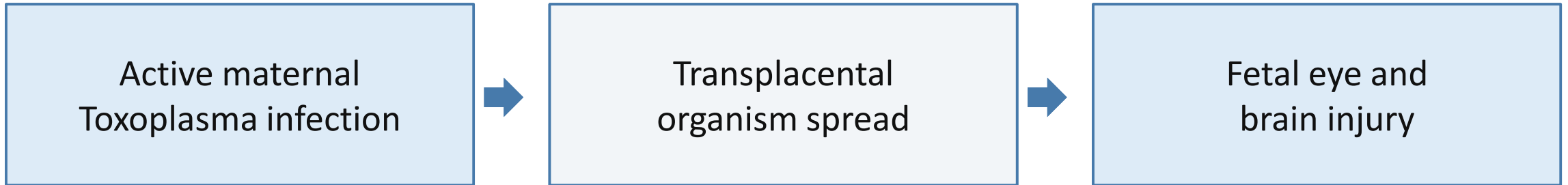
Congenital infection can have a delayed disease phenotype.

Congenital CMV: Diagnostic clue

- Congenital CMV is usually diagnosed by PCR detection of CMV DNA in neonatal urine or saliva.
- Cytomegalic inclusions describe a morphologic effect but are not required to appear in every clinical sample.
- Differentiate congenital acquisition from infection acquired through birth canal secretions or breast milk.

Interpret test results with sampling time and clinical acquisition context.

Congenital toxoplasmosis: Chain of transmission



- Vertical transmission in pregnancy and frequent delayed recognition.
- The organism is an intracellular protozoan.

Congenital toxoplasmosis: Source-described findings

Eye

Chorioretinitis; Congenital ocular disease may be bilateral.

Cerebral fluid spaces

Hydrocephalus may occur.

Brain

Microcephaly, cerebral calcifications and neurocognitive deficits.

Pregnancy

Fetal death or abortion in severe cases.

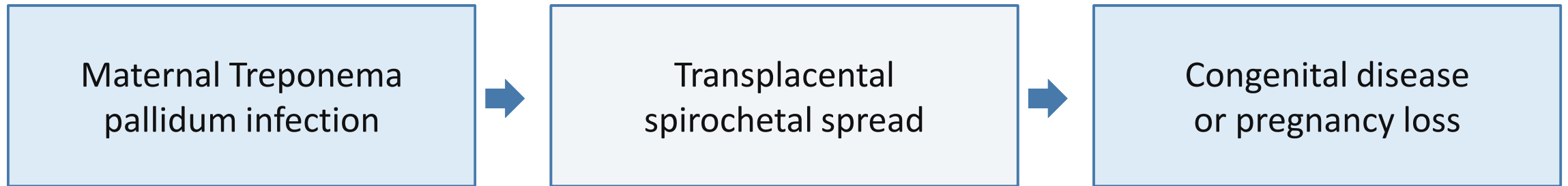
Combine ocular and central nervous system findings rather than assigning an isolated symptom.

Toxoplasmosis may declare itself after birth

- Infants with congenital toxoplasmosis may not become symptomatic until months or years later.
- Serologic diagnosis and PCR of blood or cerebrospinal fluid as diagnostic approaches.
- Congenital manifestations should be distinguished from later-acquired ocular toxoplasmosis.

Absence of a neonatal symptom does not conclusively exclude congenital infection.

Congenital syphilis: Maternal-to-fetal spread



- Greater congenital transmission burden during untreated early maternal disease when organisms are numerous.
- Infantile and tardive clinical syndromes differ.

Infantile congenital syphilis

- Manifestations in the first two years include nasal congestion and discharge (“snuffles”).
- Desquamating or bullous eruptions can involve palms, soles and periorificial skin.
- Hepatomegaly and skeletal abnormalities are frequent findings.

Skin, upper airway, visceral and bone disease may coexist.

Congenital syphilis: Structural pathology

Bone

Osteochondritis and periostitis; Bowing of tibiae may occur.

Liver

Diffuse fibrosis, lymphoplasmacytic inflammation and vascular changes.

Lung

Interstitial fibrosis; Severe stillborn cases may show pneumonia alba.

Multiorgan

Spirochetemia can evoke interstitial inflammation in many tissues.

Tardive congenital syphilis: Classical triad

Interstitial keratitis

Corneal inflammation is a classical late consequence.

Hutchinson teeth

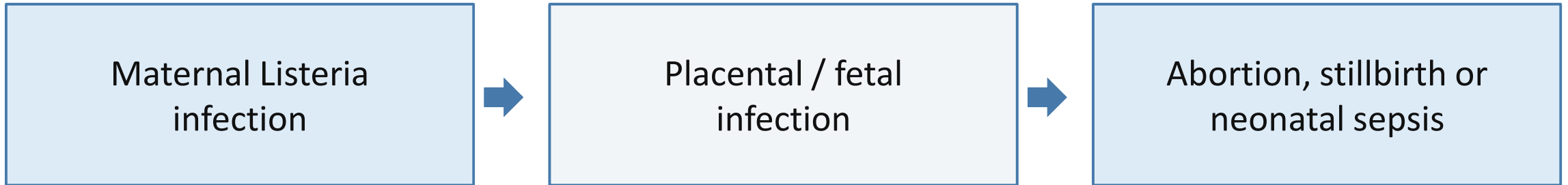
Characteristic small notched or peg-like incisors.

Eighth-nerve deafness

Hearing deficit associated with later congenital disease.

Late signs represent sequelae of congenital infection, not necessarily new acquisition.

Listeriosis: Pregnancy-to-neonate spectrum



- Pregnant patients and neonates are especially susceptible to severe infection.
- The pathogen is a gram-positive, facultatively intracellular bacillus.

Neonatal listeriosis: Morphology and presentation

Dissemination

Granulomatosis infantiseptica may involve many organs.

Inflammation

Acute exudative lesions, abscesses and necrotic nodules.

Placenta

Listerial abscesses may be present.

Clinical

Sepsis, meningitis, and sometimes a red papular extremity rash.

Listeria illustrates why bacterial transplacental infections cannot be overlooked.

Different pathogens, different dominant clues

Agent	Textbook-highlighted pathology	Clinical association
B19	Inclusions in erythroid precursors	Red cell aplasia, anemia, nonimmune hydrops
CMV	Cytomegalic cells with “owl’s eye” inclusion	FGR, CNS, hematologic, hearing effects
T. gondii	Protozoal tissue cysts / tachyzoites	Chorioretinitis, cerebral lesions
T. pallidum	Interstitial visceral and osseous lesions	Early rash; late keratitis, teeth, deafness
Listeria	Abscesses and exudative inflammation	Maternal loss, neonatal sepsis or meningitis

These are discriminating examples, not exhaustive criteria.

Why congenital infection and perinatal sepsis overlap

Congenital hematogenous infection

The organism reaches fetal blood during gestation.

May cause fetal injury and congenital anomalies.

Some manifestations arise months or years later.

Perinatal sepsis syndrome

Clinical illness may emerge around or after delivery.

Pneumonia, sepsis and meningitis can dominate presentation.

Age at onset is useful but does not alone define the route.

Time of illness does not uniquely determine the place of acquisition.

Perinatal sepsis: Terminology

Syndrome	Timing in source	Emphasis
Early onset	First 7 days of life	Often acquired at or shortly before delivery
Late onset	7 days to 3 months	Listeria and Candida may have longer latent intervals

This is clinical sepsis terminology; It is not a classification of congenital malformations.

Source-based testing and morphology clues

Agent	Example clue documented by Robbins
Parvovirus B19	Distinctive intranuclear inclusions in early erythroid precursors
CMV	Viral DNA PCR using neonatal urine or saliva
Toxoplasma	Serologic testing; PCR of blood or CSF in appropriate settings
Syphilis	Treponemal and nontreponemal serologic algorithms
Listeria	Gram-positive bacilli may be seen in CSF or neonatal meconium smear

These are source-derived diagnostic examples, not a complete neonatal investigation guideline.

Integrated case: Growth restriction and multisystem disease

A growth-restricted neonate has jaundice, hepatosplenomegaly, anemia and signs of neurologic injury. The maternal history is incomplete; The timing of acquisition is unknown.

1. Which congenital infections enter the differential based on the source?

2. What additional observations would help discriminate the agents?

Integrated case: Do not force a single diagnosis

- Congenital CMV specifically links FGR, jaundice, hepatosplenomegaly, anemia and neurologic disease.
- The shared TORCH spectrum means toxoplasmosis, syphilis and other pathogens remain part of the broader consideration.
- Look for agent-specific patterns and source-supported tests instead of treating the constellation as pathognomonic.

CMV is a strong source-based pattern match, not a diagnosis without corroboration.

Integrating pathology across organ systems

Mechanism

Ask how the agent reaches fetal tissues and what cells it targets.

Morphology

Locate the characteristic cellular or tissue lesion where one is described.

Phenotype

Connect the lesion to anemia, organ dysfunction, growth failure or malformation.

Time course

Separate prenatal fetal injury from late expression of consequences.

High-yield synthesis

- Transplacental hematogenous infection reaches fetal blood through chorionic villi; Ascending infection is a separate but potentially overlapping route.
- Organism identity and gestational timing govern the fetal clinical-pathologic pattern.
- Parvovirus B19 is distinctive for erythroid progenitor injury, red cell aplasia and possible nonimmune hydrops.
- TORCH presentations overlap; Morphology, timing and agent-directed evaluation refine the diagnosis.

Hematologic route, specific cell tropism, fetal development and phenotype belong in one explanation.

Principal references

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026). Chapter 10: Perinatal Infections; Fetal Hydrops; Fetal Growth Restriction.
- Robbins, Cotran & Kumar. 11th ed. Chapter 8: Cytomegalovirus; Toxoplasmosis; Syphilis; Listeriosis.
- Illustrative pathways and comparisons are original editable teaching schematics based on these source sections.