

# Placental Infections

Mechanisms, morphology, and fetal consequences

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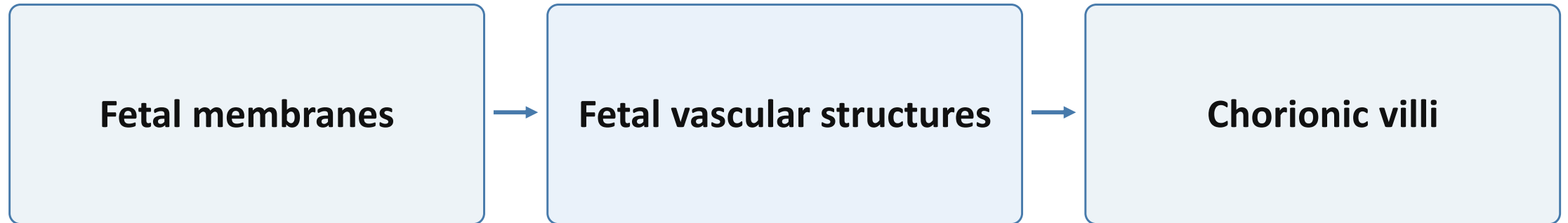
## What the pathology should explain

- Distinguish ascending infection from hematogenous transplacental spread.
- Localize inflammation to membranes, fetal vessels, or chorionic villi.
- Connect maternal and fetal inflammatory patterns with clinically relevant outcomes.
- Interpret TORCH-associated villitis without assuming an organism from morphology alone.

## Why examine the infected placenta?

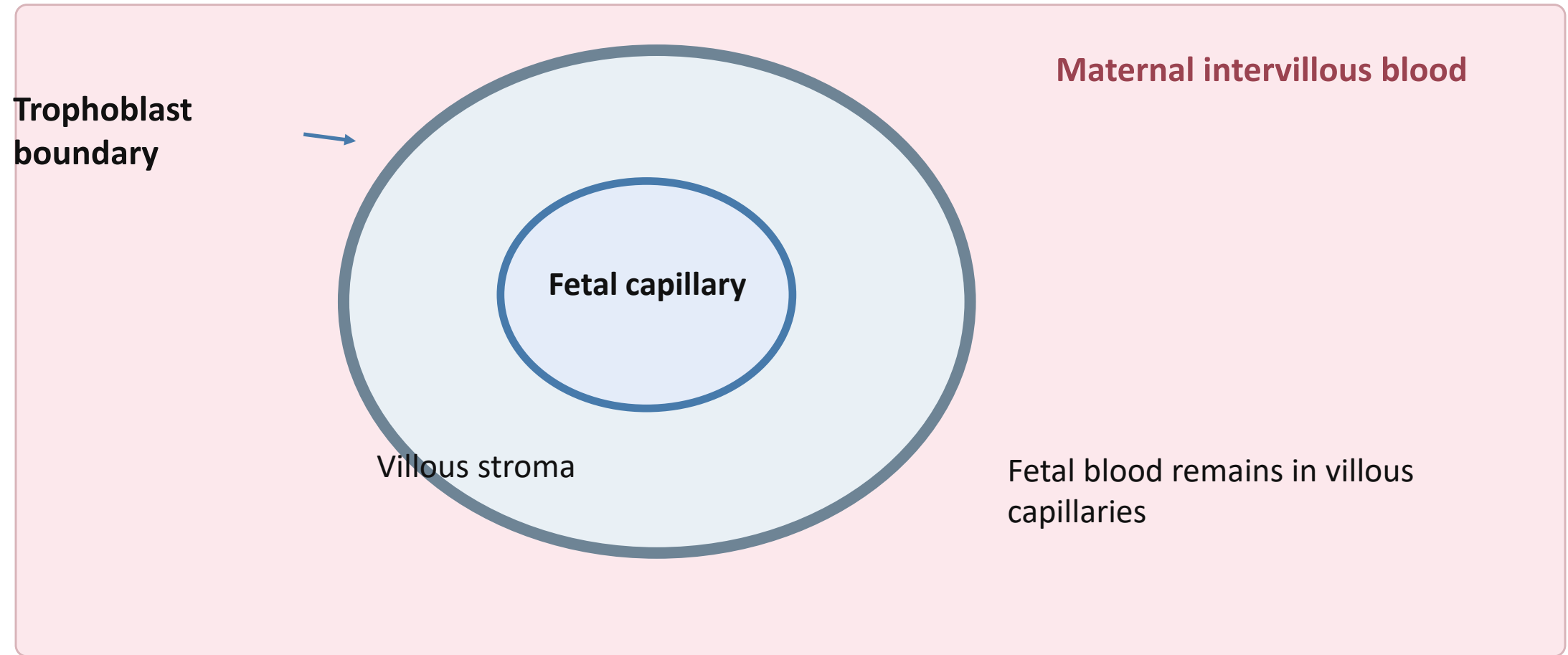
- Placental pathology can help explain adverse pregnancy or perinatal outcomes.
- The distribution of inflammation provides information about how an infection reached the placenta.
- Maternal and fetal responses are anatomically distinct and should be separately described.
- An inflammatory lesion is not, by itself, proof of a particular pathogen or outcome.

## Three placental compartments to recognize



Membranes favor an ascending process; Fetal vessels record a fetal response; Villitis points toward villous inflammation.

# Chorionic villi are the exchange surface



## Trophoblast separates blood compartments

- Syncytiotrophoblast and cytotrophoblast cover chorionic villi.
- Fetal capillaries lie within villous stroma.
- Maternal blood bathes the outside of the villi in the intervillous space.
- This interface normally permits exchange without extensive direct mixing of fetal and maternal blood.

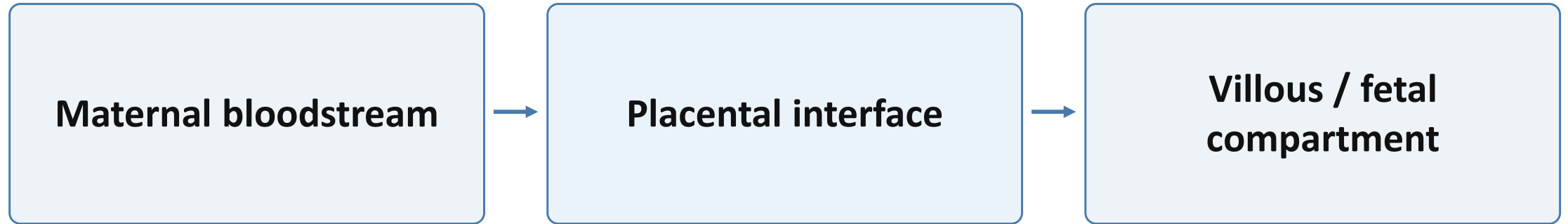
# Maternal and fetal circulations follow different paths



Exchange occurs across the villous boundary; The two bloodstreams do not normally mix freely.

*Schematic circulation map — anatomy is simplified.*

## An exchange barrier is not an absolute infection barrier

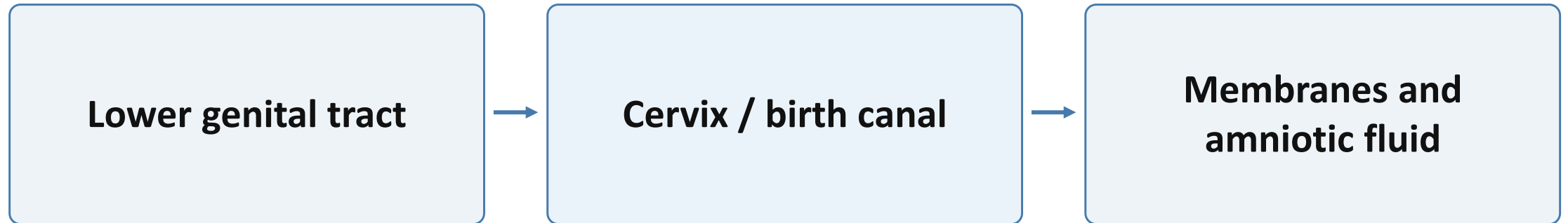


Hematogenous infection may reach the placental exchange structures despite normal separation of circulating blood.

## Two major pathways of placental infection

| Feature                             | Ascending                                    | Hematogenous                                                     |
|-------------------------------------|----------------------------------------------|------------------------------------------------------------------|
| Initial source                      | Birth canal / lower genital tract            | Maternal blood during sepsis, viremia, or parasitemia            |
| Typical early location              | Membranes and amniotic compartment           | Chorionic villi                                                  |
| Characteristic inflammatory pattern | Acute maternal neutrophilic chorioamnionitis | Often chronic villitis; some bacterial cases show acute villitis |

## Ascending infection begins below the membranes



This as the more common route of placental infection.

## Why ascending infections are usually bacterial

- The typical ascending route is through the birth canal.
- Ascending placental infections are virtually always bacterial.
- The organism reaches membranes locally rather than requiring maternal bloodstream dissemination.
- Pattern recognition should begin with route and site—not with a presumed species.

# Membrane anatomy determines the first lesion

**Amniotic surface**

**Amnion**

**Chorion**

**Maternal decidual side**

*Simplified anatomic schematic; Colored layers do not represent H&E staining.*

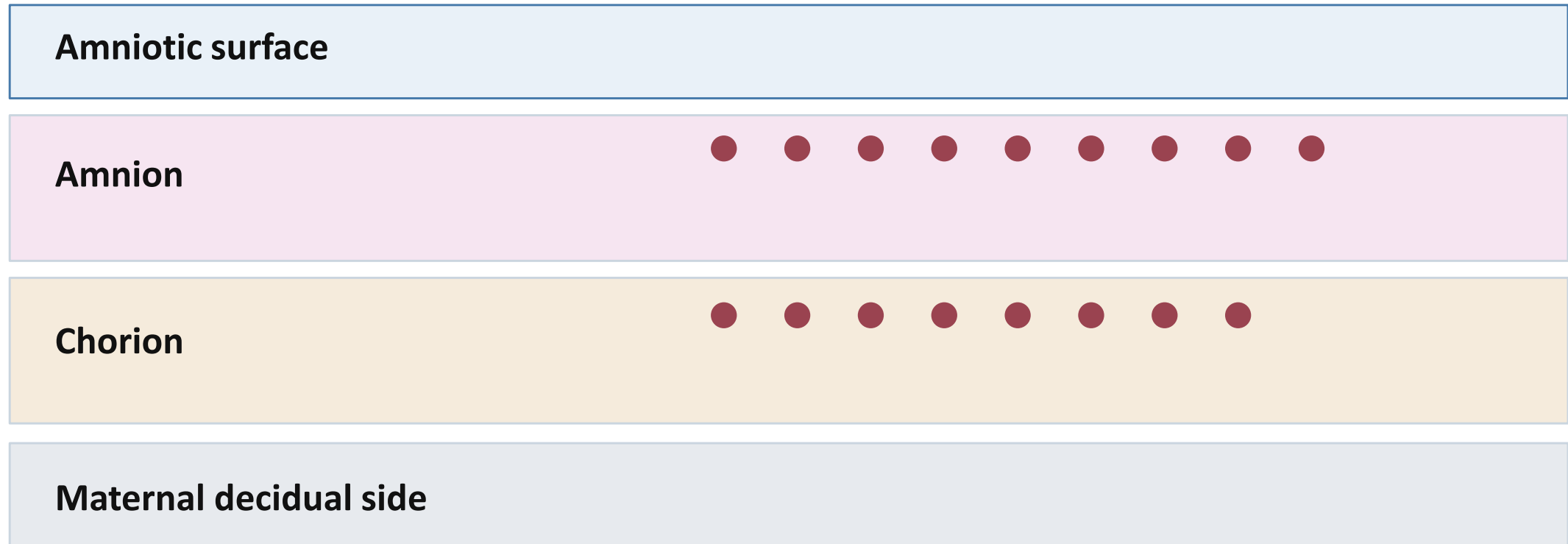
## Acute chorioamnionitis: The maternal lesion

- Acute chorioamnionitis involves inflammatory cells in chorion and amnion.
- The inflammatory cells emphasized by Robbins are maternal neutrophils.
- Inflammation may be appreciable in the membranes even without a demonstrable organism on routine sections.
- The tissue compartment determines whether an observation describes maternal or fetal response.

## Cloudy fluid and exudate: Gross correlates

- Cloudy amniotic fluid with a purulent exudate.
- Gross abnormalities are helpful clues but are not a complete microscopic diagnosis.
- Correlate the gross appearance with the membrane histology.
- Record what is observed rather than inferring a specific microbial cause from discoloration.

# Neutrophils in the membranes: Schematic topography



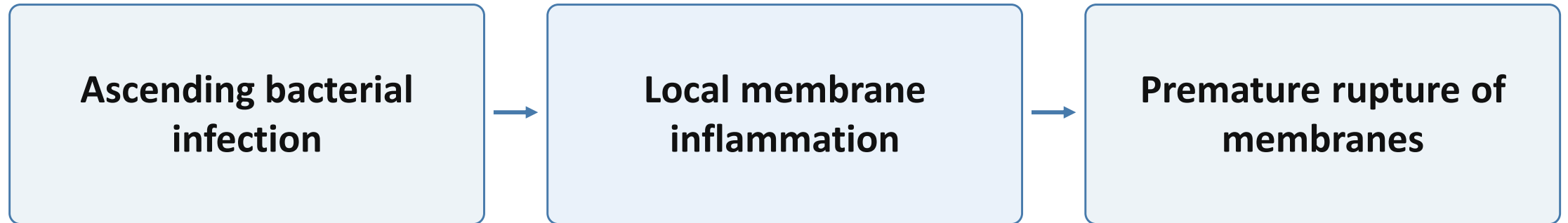
Neutrophils within fetal membranes

*Simplified anatomic schematic; Colored layers do not represent H&E staining.*

## Maternal inflammatory response is defined by origin

- The maternal response is an acute neutrophilic infiltrate in the chorion–amnion.
- It reflects inflammation at the membranes after ascending exposure.
- It is anatomically different from neutrophilic inflammation of fetal vessels.
- Do not equate the presence of maternal inflammation with confirmed fetal inflammatory involvement.

## From membrane infection to membrane rupture



Premature membrane rupture as an important consequence in many ascending infections.

# From membrane infection to preterm delivery

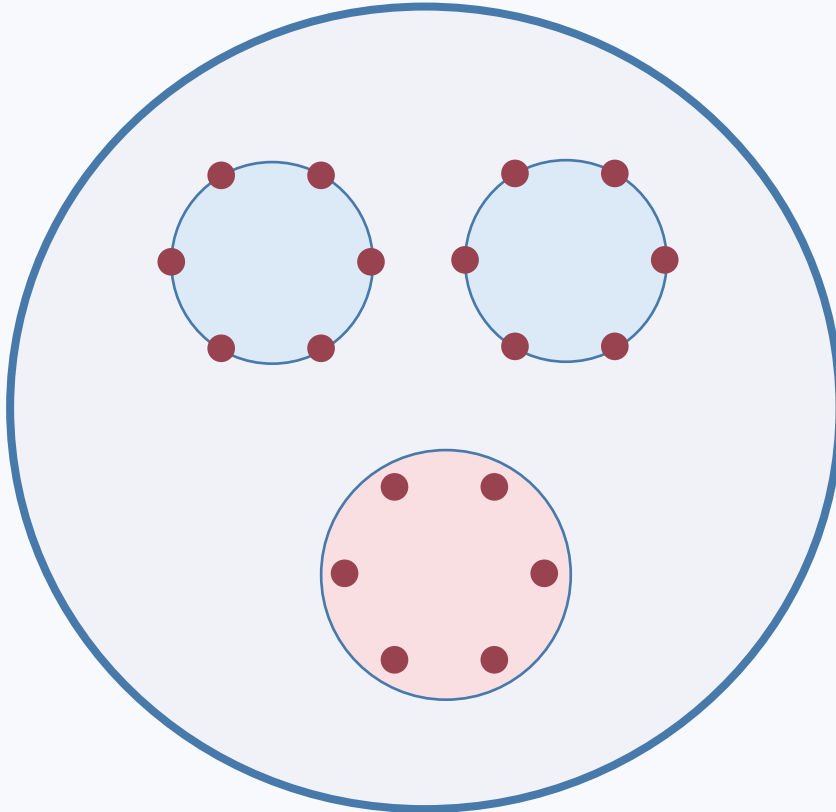


Infection-associated preterm birth is a clinically important pathway, but the route does not determine the outcome in every case.

## Maternal response and fetal response are not synonyms

| Feature               | Maternal inflammatory response    | Fetal inflammatory response                                        |
|-----------------------|-----------------------------------|--------------------------------------------------------------------|
| Principal compartment | Chorion and amnion                | Umbilical cord and/or chorionic plate fetal vessels                |
| Cells emphasized      | Maternal neutrophils              | Inflammation of fetal vascular walls                               |
| Interpretive role     | Evidence of membrane inflammation | Evidence that inflammation involves the fetal vascular compartment |

# Umbilical vasculitis records a fetal response



**Two umbilical arteries**

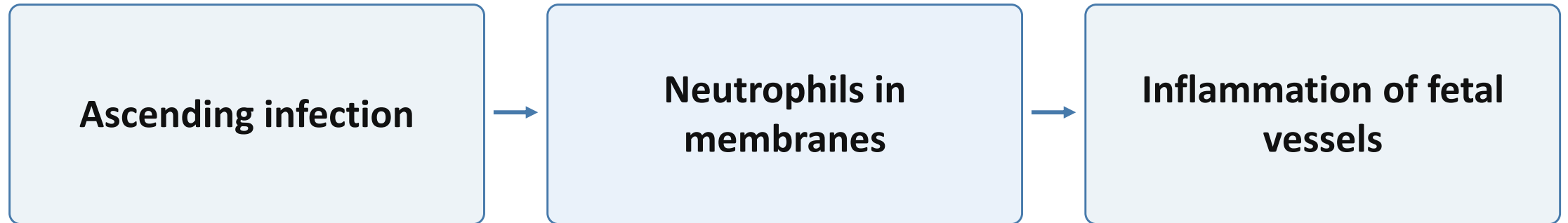
**One umbilical vein**

Inflammatory cells involving fetal vessel walls → fetal inflammatory response

## Chorionic plate vessels can also respond

- Fetal chorionic plate vessels are part of the fetal placental circulation.
- Their involvement is a second site of the fetal vascular inflammatory response.
- The fetal response may be seen in the umbilical vessels, chorionic plate vessels, or both.
- The location of an inflammatory infiltrate must be explicitly reported.

## How the two responses can coexist



This is a conceptual progression, not a mandatory sequence for every affected placenta.

## Clinical significance of intense fetal inflammation

- Intense fetal inflammatory responses with increased perinatal morbidity.
- An increased risk of later cerebral palsy is also noted.
- This is a risk association—not proof that any individual placental lesion caused cerebral palsy.
- Severity and fetal involvement should be interpreted alongside the clinical course.

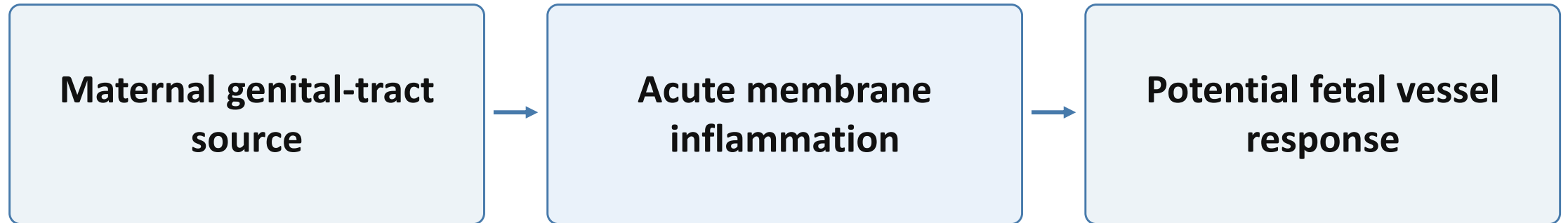
## Why association is not individual-level causation

| What placental histology supports                 | What it does not establish alone                               |
|---------------------------------------------------|----------------------------------------------------------------|
| A documented fetal vascular inflammatory response | A specific neurologic outcome in an individual infant          |
| A pattern associated with elevated perinatal risk | That infection was the only contributor to morbidity           |
| Anatomic evidence of inflammation                 | The precise species without appropriate microbiologic evidence |

## One bacterium named in the broader source: Group B streptococcus

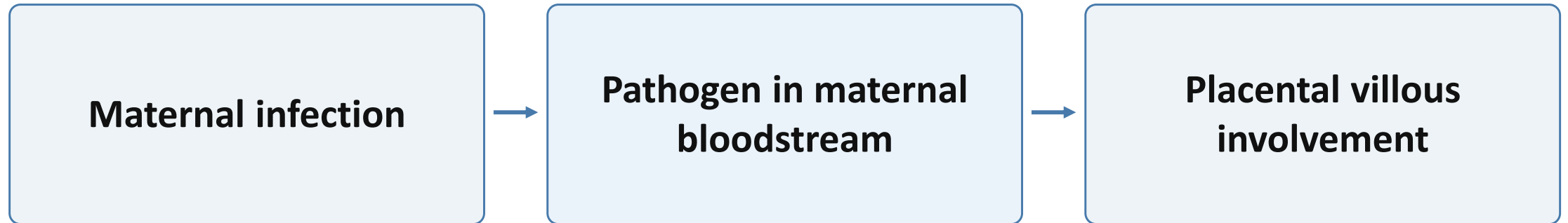
- *Streptococcus agalactiae* (group B streptococcus) can colonize the female genital tract.
- It is a cause of chorioamnionitis during pregnancy.
- Group B streptococcal infection is also an important cause of neonatal sepsis and meningitis.
- The organism is context for the ascending pathway; Histology alone does not identify group B streptococcus.

## Ascending pattern: An integrated interpretation



Look for paired but separately described maternal and fetal inflammatory lesions.

# Hematogenous infection starts with systemic maternal infection

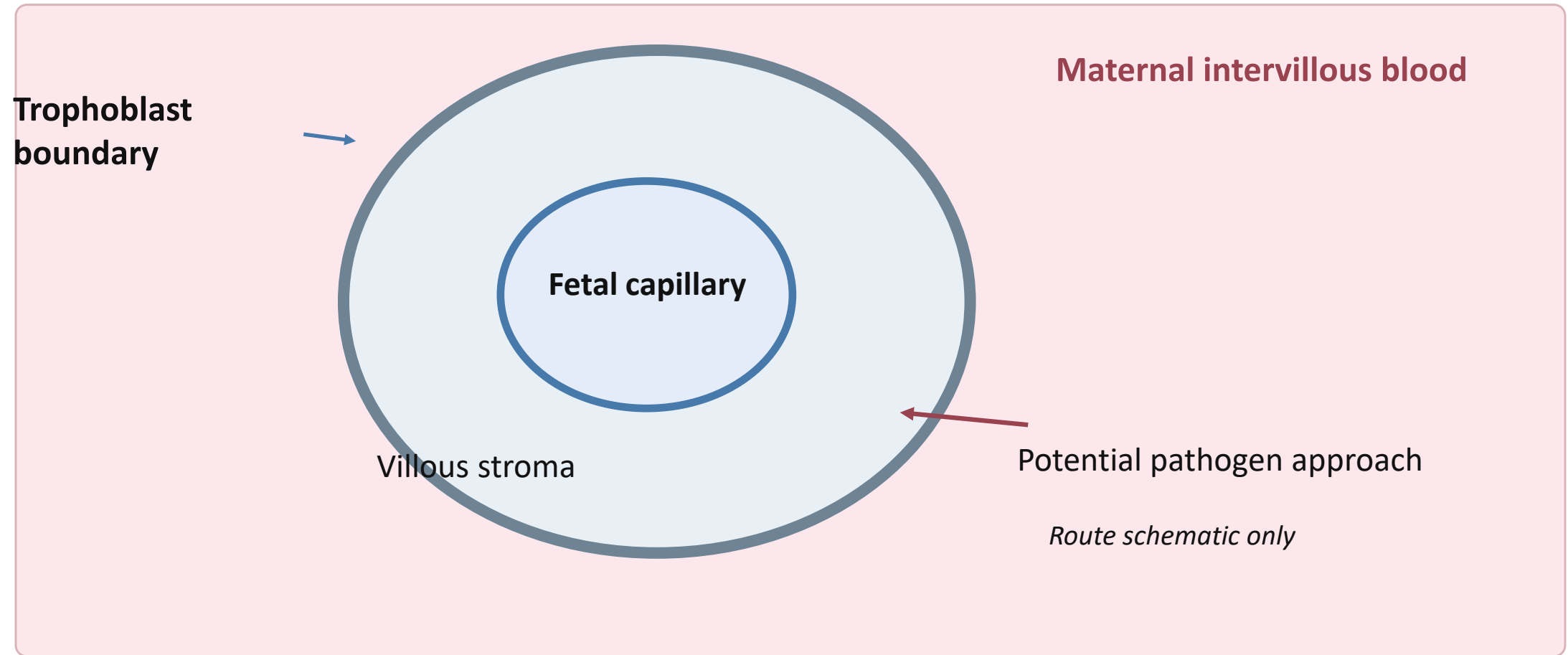


The source specifies maternal sepsis, viremia, and parasitemia as routes into the placenta.

## Three systemic contexts for transplacental spread

| Maternal systemic process | Potential placental exposure                    |
|---------------------------|-------------------------------------------------|
| Sepsis / bacteremia       | Bacterial organisms in maternal blood           |
| Viremia                   | Viruses circulating during maternal infection   |
| Parasitemia               | Parasites circulating during maternal infection |

# Why the villus is a target in blood-borne infection



## Acute villitis can occur after bacterial hematogenous spread

- Bacteria can uncommonly reach the placenta by the hematogenous route.
- This can produce acute inflammatory changes in chorionic villi.
- A villous lesion must be distinguished from inflammation confined to extra-villous membranes.
- An acute villous pattern does not identify the causative organism by itself.

## Chronic villitis is the dominant TORCH-type pattern

- Chronic inflammatory cell infiltrates within chorionic villi.
- This is the usual morphologic response to several hematogenously transmitted TORCH infections.
- Chronic villitis concerns the villous parenchyma rather than only the chorion and amnion.
- The morphologic category is broader than any single microbial diagnosis.

## Villitis and chorioamnionitis are different locations

| Feature                 | Chorioamnionitis                    | Villitis                               |
|-------------------------|-------------------------------------|----------------------------------------|
| Tissue targeted         | Fetal membranes: chorion and amnion | Chorionic villi                        |
| Common route in Robbins | Ascending infection                 | Hematogenous infection                 |
| Cell pattern emphasized | Maternal acute neutrophils          | Often chronic inflammatory infiltrates |
| Principal inference     | Membrane-centered process           | Villous-parenchymal process            |

# Chronic villitis and fetal growth restriction



The Robbins section reports this association; No numerical risk estimate is provided in the supplied section.

## TORCH: The group identified

- T: Toxoplasma infection.
- O: Other infections, including syphilis, tuberculosis, and listeriosis in this section.
- R: Rubella; C: Cytomegalovirus; H: Herpes simplex.
- The mnemonic groups congenital pathogens; It does not imply identical histology or clinical behavior.

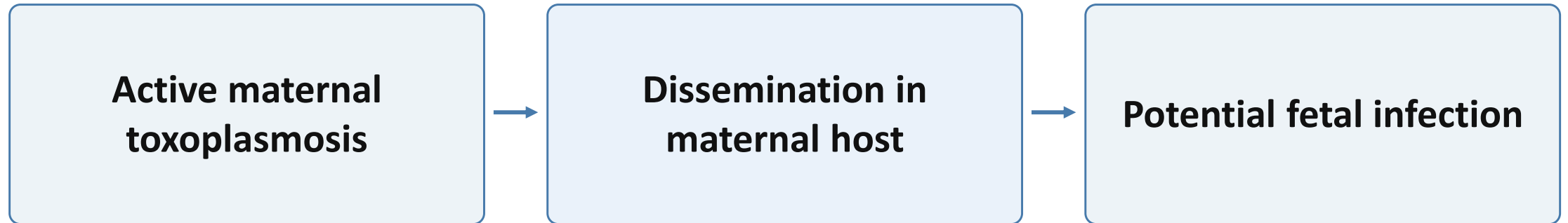
## TORCH agents have a shared route, not identical lesions

| Shared feature                                   | Important limitation                                                  |
|--------------------------------------------------|-----------------------------------------------------------------------|
| Maternal hematogenous spread can infect placenta | Microbial route does not guarantee the same pattern in all infections |
| Chronic villitis may be encountered              | An individual villitis specimen may remain etiologically unclassified |
| Fetal growth restriction may accompany infection | No single outcome is inevitable                                       |

## Toxoplasma: Maternal infection can be vertically transmitted

- *Toxoplasma gondii* is a parasitic protozoan.
- Transmission to offspring can occur during active maternal infection in pregnancy.
- Maternal infection can follow contaminated foods, water, soil, or oocyst exposure.
- The placental lesion is transplacental passage from maternal infection—not a membrane-first bacterial process.

## Toxoplasma: Hematogenous pathway



The route is source-based; The diagram does not prescribe a fixed sequence of histologic events.

## Congenital toxoplasmosis: Potential fetal effects

- Fetal death or pregnancy loss as possible consequences.
- Reported congenital manifestations include hydrocephalus and microcephaly.
- Cerebral calcifications and chorioretinitis are further classic manifestations.
- Clinical recognition may be delayed after birth.

## Syphilis: Transplacental infection

- *Treponema pallidum* can cause congenital infection.
- Congenital syphilis is most frequent in the setting of maternal primary or secondary disease.
- The organisms circulate during these maternal disease stages.
- It belongs to the “other” category of the TORCH grouping used by Robbins.

## Syphilis: Possible loss and infant disease

- Untreated congenital syphilis may cause intrauterine or perinatal death.
- Infantile manifestations include snuffles and desquamating or bullous rashes.
- Hepatomegaly and skeletal abnormalities are described.
- The placenta contributes to the diagnostic picture but does not replace organism-specific assessment.

## Syphilis: Diagnostic evidence must be specific

| Placental pathology                             | Organism-specific laboratory evidence               |
|-------------------------------------------------|-----------------------------------------------------|
| Can document inflammatory placental involvement | Syphilis diagnosis uses serologic testing           |
| Does not uniquely identify <i>T. pallidum</i>   | Nontreponemal tests include RPR and VDRL            |
| Requires clinical correlation                   | Treponemal tests provide specific antibody evidence |

## Rubella: Congenital infection and embryopathy

- Rubella is included in the TORCH group within the placental infection section.
- Robbins also identifies rubella as an environmental infectious cause of congenital malformations.
- Maternal vaccination has markedly reduced rubella embryopathy in high-resource settings.
- The supplied placenta subsection does not specify a rubella-specific microscopic placental hallmark.

## Rubella: Separate fetal effects from villous morphology

| What the source establishes                | What it does not establish here                        |
|--------------------------------------------|--------------------------------------------------------|
| Rubella can be transmitted congenitally    | An exclusive pathognomonic placental pattern           |
| Congenital rubella may produce embryopathy | A diagnostic cell inclusion in every infected placenta |
| The organism is in the TORCH grouping      | A specific histologic sensitivity or specificity       |

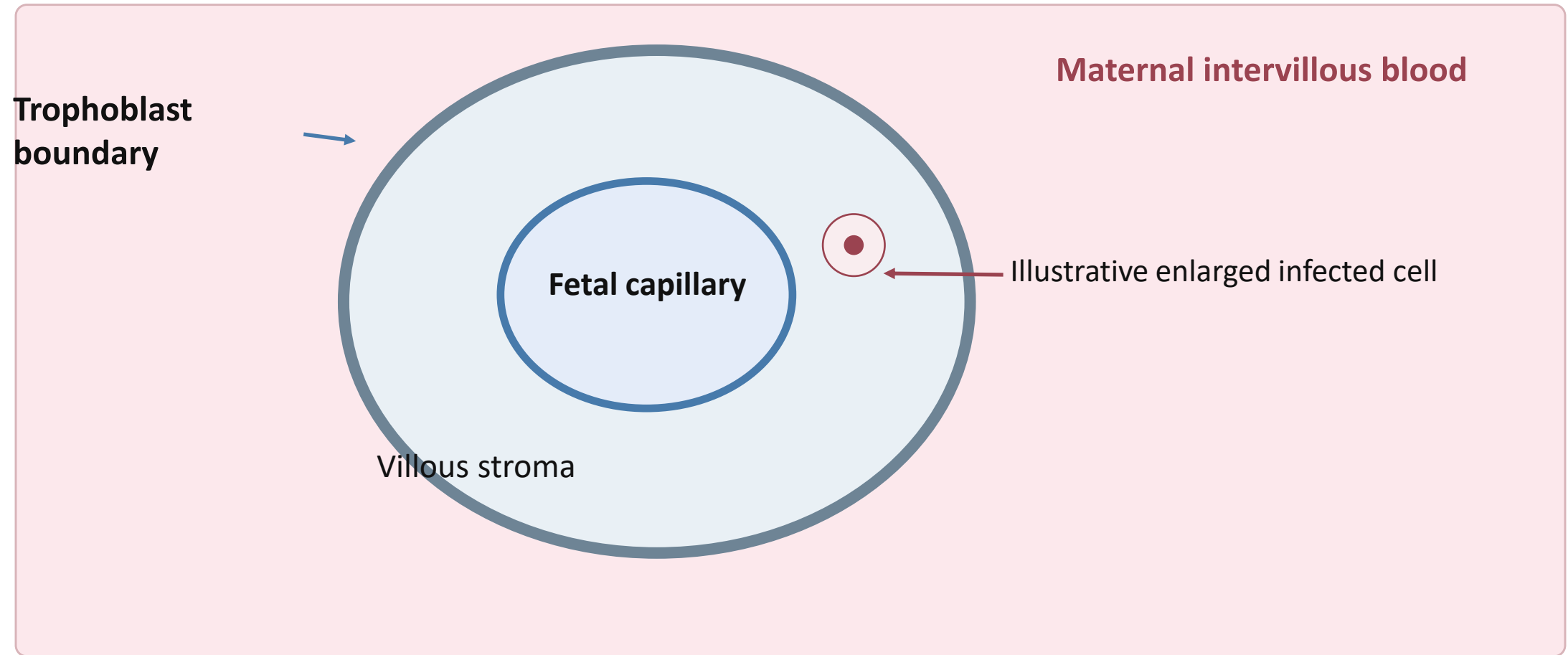
## CMV: Transplacental infection can affect fetal development

- Cytomegalovirus is one of the named TORCH pathogens.
- Congenital infection occurs after infection acquired in utero.
- A spectrum from asymptomatic infection to cytomegalic inclusion disease.
- Placental villitis and viral cytopathic changes can provide morphologic clues.

## CMV: Characteristic cytopathic morphology

- CMV-infected cells may become enlarged.
- Large basophilic intranuclear inclusions with a surrounding clear halo are characteristic.
- Smaller cytoplasmic inclusions may also be seen.
- These are organism-associated cytopathic changes; Generic chronic villitis is less specific.

## CMV within a villus: Site and cell change



## Congenital CMV: Early clinical manifestations

- Affected newborns may show growth restriction and jaundice.
- Hepatosplenomegaly, anemia, and thrombocytopenia-associated bleeding are described.
- Brain abnormalities can include microcephaly and focal calcification in severe cases.
- The neonatal syndrome is not required for placental infection to be present.

## Congenital CMV: Later consequences

- Hearing loss and neurologic impairment may persist among affected survivors.
- Some congenital infections are initially clinically silent.
- Delayed neurologic sequelae may become apparent months or years later.
- Placental findings and neonatal evaluation answer related but different questions.

## Congenital versus perinatal CMV

| Congenital infection                         | Perinatal infection                                            |
|----------------------------------------------|----------------------------------------------------------------|
| Acquired in utero                            | Acquired during passage through birth canal or via breast milk |
| May cause fetal growth/developmental effects | Usually asymptomatic in the setting described by Robbins       |
| Prenatal pathology may be relevant           | Transmission may occur after placental development             |

## HSV: TORCH membership without a specified placental signature

- Herpes simplex is named in the TORCH grouping.
- The supplied placental subsection presents the hematogenous infection framework.
- It does not describe a distinct, pathognomonic HSV placental lesion.
- Do not diagnose HSV from nonspecific chronic villitis alone.

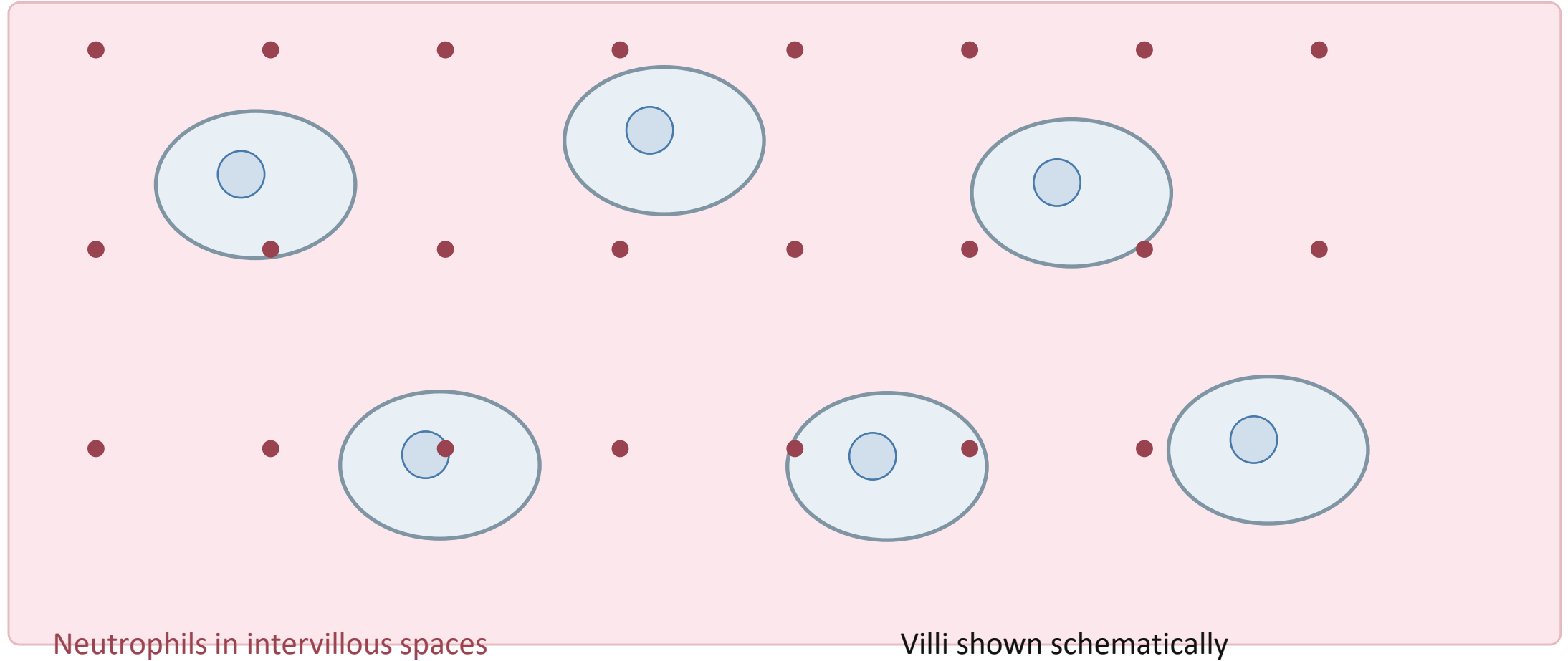
## Listeria: A significant bacterial exception

- *Listeria monocytogenes* is a gram-positive, facultatively intracellular bacillus.
- Pregnancy is a setting of increased vulnerability to serious listeriosis.
- *Listeria* can involve the placenta through a systemic maternal infection.
- The named organism illustrates why hematogenous spread is not restricted to viruses or parasites.

## Listeriosis in pregnancy: Consequences

- Maternal listeriosis is often food-borne.
- Pregnancy-associated listeriosis with amnionitis.
- Reported complications include pregnancy loss, stillbirth, and neonatal sepsis.
- Placental inflammation should be interpreted with maternal and neonatal microbiology.

# Listeria: Acute necrotizing intervillitis



*Conceptual intervillitis schematic — not a microscopy image.*

## Intervillositis differs from villitis

| Intervillositis                                          | Villitis                                     |
|----------------------------------------------------------|----------------------------------------------|
| Intervillous space between villi                         | Inside the villous tissue                    |
| Inflammatory cells occupy maternal blood space           | Inflammatory cells infiltrate villous stroma |
| Listeria figure illustrates an acute necrotizing example | TORCH section emphasizes chronic villitis    |

## Pathogen and lesion: A discriminating comparison

| Infectious context                         | Source-described placental pattern                              |
|--------------------------------------------|-----------------------------------------------------------------|
| Typical ascending bacterial infection      | Acute neutrophilic membrane inflammation $\pm$ fetal vasculitis |
| Common TORCH-type blood-borne infection    | Chronic villitis                                                |
| Occasional blood-borne bacterial infection | Acute villitis                                                  |
| Listeria example in figure 22.50           | Acute necrotizing intervillitis                                 |
| CMV example in figure 22.50                | Villous cells with viral inclusions                             |

## Start an interpretation with anatomic localization



Anatomic localization precedes etiologic attribution, because many infectious processes share inflammatory patterns.

## What the pathology report can legitimately state

- The lesion and its distribution: Membranes, cord vessels, chorionic plate, villi, or intervillous space.
- Whether the findings represent maternal inflammation, fetal inflammation, or both.
- Whether a distinctive cytopathic clue such as CMV inclusion is visible.
- The need for clinical and microbiologic correlation when morphology is nonspecific.

## What the histology cannot safely decide alone

- A unique pathogen identity in every case of acute inflammation.
- That TORCH-type chronic villitis automatically establishes a congenital infection.
- The precise probability of growth restriction or neurologic injury from an individual lesion.
- Whether maternal and infant clinical manifestations share one confirmed organism without direct evidence.

## Case application: Acute inflammation in fetal membranes

### *Illustrative teaching vignette*

A preterm delivery follows premature membrane rupture. The placenta shows neutrophils in the chorion and amnion.

**Which route and inflammatory compartment are most strongly suggested?**

## Case interpretation: Membrane-centered inflammation

- An ascending process is most consistent with the membrane-centered distribution.
- Maternal neutrophils support an acute maternal inflammatory response.
- The described lesion does not establish fetal vessel inflammation unless it is observed.
- No specific bacterial species can be concluded from the morphology alone.

## Case application: Fetal vascular inflammation

### *Illustrative teaching vignette*

A placenta shows acute chorioamnionitis and inflammatory infiltrates involving umbilical vessel walls.

**Which additional inflammatory response is present, and what clinical caveat applies?**

## Case interpretation: Fetal response

- Umbilical vessel vasculitis supports a fetal inflammatory response.
- It is distinct from the maternal neutrophilic response in membranes.
- Intense fetal inflammation is associated with perinatal morbidity and elevated cerebral palsy risk.
- Risk association is not individual proof of neurologic causation.

## Case application: Chronic villitis and growth restriction

### *Illustrative teaching vignette*

A placenta from a pregnancy affected by fetal growth restriction contains chronic inflammatory infiltrates in chorionic villi.

**Which broad infection route is relevant, and what should not be concluded from villitis alone?**

## Case interpretation: Villitis requires etiologic correlation

- The distribution raises consideration of hematogenous infection.
- Several TORCH-type agents may be associated with chronic villitis and growth restriction.
- Chronic villitis is not specific for any one TORCH organism.
- Additional history, clinical testing, and direct evidence are needed for etiologic diagnosis.

## A diagnostic synthesis: Location, cells, and consequence

| Finding                                         | Interpretive implication                                              |
|-------------------------------------------------|-----------------------------------------------------------------------|
| Membrane neutrophils                            | Maternal acute response; usually ascending                            |
| Fetal vessel inflammation                       | Fetal inflammatory response                                           |
| Chronic villous infiltrates                     | Consider blood-borne TORCH-type process                               |
| Intranuclear CMV-type inclusions                | Specific viral cytopathic clue                                        |
| Neutrophilic intervillitis and villous necrosis | Compatible with described Listeria example; not etiologic proof alone |

## Four principles to retain

- Route matters: Ascending infections are most common; Hematogenous infections have a different initial source.
- Location matters: Membranes, fetal vessels, villi, and intervillous spaces are not interchangeable.
- Morphology matters: Acute neutrophilic inflammation, chronic villitis, and viral cytopathic changes convey different information.
- Inference has limits: Clinical correlation and organism-specific evidence remain essential.

# Primary sources and visual provenance

- Robbins, Cotran & Kumar. Pathologic Basis of Disease. 11th ed. (2026). Ch 22, “Gestational and Placental Disorders,” pp 934 and 937.
- Same textbook, Ch 8: CMV (pp 323–324), group B streptococcus (p 327), listeriosis (p 329), congenital syphilis (p 343), toxoplasmosis (pp 360–361).
- Same textbook, Ch 10: congenital anomalies / congenital rubella (pp 413–414).
- All visuals in this presentation are original editable conceptual schematics; they are not histologic specimens or reproduced textbook figures.