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INTRAUTERINE INFECTIONS IN CHILDREN

Educational and methodical manual

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Educational and methodological manual for students of the center for retraining and improving the quality of teachers of medical universities TSMU

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The following topics will be covered:

1. Definition and Relevance

- Concept of intrauterine (congenital) infection
- Global and local epidemiology
- Impact on perinatal morbidity and mortality

2. Etiology and Pathogens

- TORCH complex (Toxoplasmosis, Other [syphilis, HIV, parvovirus B19, Zika], Rubella, Cytomegalovirus, Herpes)
- Additional agents (Hepatitis viruses, Enteroviruses, SARS-CoV-2, Listeria, Group B Streptococcus, Candida)

3. Pathogenesis and Mechanisms of Transmission

- Transplacental transmission
- Ascending infection from maternal genital tract
- Perinatal/intrapartum infection
- Iatrogenic causes

4. Risk Factors

- Maternal infections during pregnancy
- Premature rupture of membranes, chorioamnionitis
- Immunological status of mother and fetus
- Socioeconomic and environmental factors

5. Classification of Intrauterine Infections

- By pathogen (viral, bacterial, parasitic, fungal)
- By timing (early vs. late congenital infections)
- By clinical presentation (symptomatic vs. asymptomatic)

6. Clinical Manifestations

- General features: prematurity, low birth weight, intrauterine growth restriction (IUGR)
- Severe outcomes: hydrops fetalis, intrauterine death

7. Diagnostic Approaches

- Maternal screening (serology, PCR, ultrasound markers)

- Neonatal diagnostic tools (IgM/IgG antibodies, PCR, cultures)
- Imaging: ultrasound, MRI, CT in congenital infections
- Histopathology and placental studies

8. Management and Treatment

- Antimicrobial and antiviral therapy in neonates
- Supportive therapy (sepsis management, respiratory support, nutrition)
- Role of immunoglobulins and antiviral prophylaxis

Introduction. Intrauterine infections in children.

Intrauterine infection (IUI) in children is one of the most important problems in modern neonatology and perinatal medicine. These infections develop when the fetus is exposed to infectious agents during pregnancy, either through transplacental transmission, ascending spread from the maternal genital tract, or, less commonly, iatrogenic interventions. The consequences of such infections may range from subclinical manifestations to severe systemic disease, congenital malformations, or even intrauterine death.

The relevance of this topic is explained by the high frequency of intrauterine infections and their significant contribution to perinatal morbidity and mortality. According to international studies, congenital infections account for up to 10–15% of neonatal deaths and remain a major cause of long-term neurological and developmental disabilities in children. Timely recognition and prevention are therefore central tasks for neonatologists, pediatricians, and obstetricians.

The classical group of pathogens associated with intrauterine infections is summarized in the well-known acronym TORCH (Toxoplasmosis, “Other” infections such as syphilis, HIV, parvovirus B19, and Zika virus, Rubella, Cytomegalovirus, and Herpes simplex virus). However, recent years have expanded this list to include pathogens such as hepatitis viruses, enteroviruses, and emerging infections like SARS-CoV-2, which may also adversely affect fetal development.

Clinical manifestations of intrauterine infections are diverse. They may include intrauterine growth restriction, prematurity, low birth weight, hepatosplenomegaly, jaundice, anemia, congenital malformations, neurological deficits, hearing or vision impairment, and systemic inflammatory responses. Some infections, such as cytomegalovirus, can remain latent and later manifest as delayed neurocognitive development.

The study of intrauterine infections is essential for medical students because it illustrates the close interconnection between maternal health, fetal development, and neonatal outcomes. A clear understanding of the mechanisms of vertical transmission, diagnostic approaches (serology, PCR, ultrasound, histopathology), and preventive measures (vaccination, antenatal screening, maternal treatment) provides the foundation for reducing the burden of these conditions.

In this manual, particular attention is given to the pathogenesis, diagnostic methods, clinical manifestations, and strategies for prevention and treatment of intrauterine infections. This knowledge will not only improve the competence of future physicians in managing affected neonates but also contribute to the broader public health goal of reducing congenital and perinatal morbidity.

1. Definition and Relevance

TORCH Syndromes – Key Features

Infection	Key Features in Infant	Mnemonic / Clue
T – Toxoplasmosis	Hydrocephalus, Intracranial calcifications, Chorioretinitis, Seizures	"TIC" → Toxoplasma = Intracranial calcifications + Chorioretinitis
O – Others (Syphilis, HIV, Varicella, Parvovirus B19)	Syphilis: Snuffles, Hutchinson teeth, Saddle nose, Saber shins, Rash on palms/soles Varicella: Cicatricial scars, Limb hypoplasia, CNS defects Parvovirus B19: Severe fetal anemia, Hydrops fetalis	"Syphilis = Snuffles & Shins"
R – Rubella	Congenital cataracts, Sensorineural deafness, PDA (heart defect), Microcephaly, Hepatosplenomegaly	"Rubella = Cataracts + PDA + Deafness"
C – Cytomegalovirus (CMV)	Periventricular calcifications, Microcephaly, Chorioretinitis, Sensorineural hearing loss, Growth restriction	"CMV = C for Calcifications (Periventricular)"
H – Herpes simplex virus (HSV)	Vesicular skin lesions, Keratoconjunctivitis, Encephalitis, Disseminated sepsis-like illness	"Herpes = vesicles + encephalitis"

Quick Student Mnemonic:

"ToRCH" →

- T = Toxoplasma → Brain + Eye
- R = Rubella → Cataracts + PDA + Deafness
- C = CMV → Periventricular calcifications
- H = HSV → Vesicles + CNS

Intrauterine infections are infection that can affect the fetus and result in significant fetal consequences.

These are:

- T – Toxoplasma
- – Others (Syphilis, HIV)
- R – Rubella
- C – Cytomegalovirus
- H – Herpes group i.e. Varicella

TORCH – When to suspect?

Infant with unexplained:

- Failure to thrive
- Anaemia, Thrombocytopenia
- Rash
- Hepatosplenomegaly
- Cholestasis

TORCH infections are mostly asymptomatic

TORCH – Diagnosis

- Serology:
  - IgM: Diagnostic
  - IgG: Persisting @ 6–9 months OR titre ↑ with time
- PCR

This means:

- IgM → indicates recent/active infection (diagnostic in neonates).
- IgG → if still positive after 6–9 months or rising titres → suggests congenital infection (otherwise, maternal IgG wanes).
- PCR → highly sensitive, confirms infection (e.g., CMV PCR from urine/saliva within 3 weeks of birth).

The World Health Organization (WHO) estimates that congenital infections account for 2–3% of all neonatal deaths and up to 5–10% of perinatal morbidity globally.

- Cytomegalovirus (CMV) is the most frequent congenital viral infection (0.2–2.4% of live births), followed by Toxoplasmosis, Rubella, and Syphilis.
- The highest prevalence is observed in low- and middle-income countries, particularly in regions with limited antenatal screening and vaccination coverage.

o In endemic regions, congenital syphilis alone is responsible for approximately 200,000 stillbirths and neonatal deaths annually.

o Local (Regional) Perspective:

o In Central Asia and Uzbekistan, seroprevalence studies report CMV IgG positivity exceeding 90% among women of childbearing age, indicating widespread exposure.

o Rubella incidence has declined markedly following national immunization programs, yet sporadic congenital rubella cases still occur in unvaccinated populations.

o HIV, hepatitis B, and syphilis remain significant perinatal risks, emphasizing the importance of universal antenatal screening and maternal prophylaxis.

Impact on Perinatal Morbidity and Mortality

Intrauterine infections profoundly affect fetal growth, organogenesis, and neonatal outcomes, depending on the timing of maternal infection and pathogen virulence.

First Trimester:

o Highest teratogenic potential → structural anomalies (e.g., microcephaly, cataracts, congenital heart disease).

o Leads to spontaneous abortion or severe congenital malformations (e.g., Congenital Rubella Syndrome, Varicella Embryopathy).

o Second and Third Trimester:

o Associated with growth restriction, preterm delivery, hepatosplenomegaly, anemia, and thrombocytopenia.

o CMV and Zika infections can cause neurodevelopmental delay, sensorineural hearing loss, and microcephaly even in asymptomatic neonates.

o Overall Outcomes:

o Intrauterine infections account for up to 10–15% of all perinatal deaths and a significant proportion of long-term neurological and sensory disabilities in survivors.

o Early maternal screening, vaccination (Rubella, Varicella, Hepatitis B), and prophylactic measures (VZIg, ART for HIV, penicillin for syphilis) dramatically reduce morbidity and mortality.

2. Etiology and Pathogens

Intrauterine infections arise from a wide spectrum of viral, bacterial, parasitic, and fungal agents capable of crossing the placental barrier and infecting the developing fetus. The resulting damage depends on the pathogen, gestational age at infection, and maternal immune status.

Classical TORCH Complex Pathogens

The TORCH group represents the most well-established causes of congenital and perinatal infections:

Pathogen	Transmission Route	Key Fetal Manifestations
T – Toxoplasma gondii	Transplacental (from raw meat or cat feces exposure)	Hydrocephalus, chorioretinitis, intracranial calcifications
O – Others		
Syphilis (Treponema pallidum)	Transplacental or during birth	Snuffles, rash, hepatosplenomegaly, Hutchinson's triad
HIV	Transplacental, peripartum, or via breast milk	Immunodeficiency, failure to thrive, recurrent infections
Parvovirus B19	Transplacental	Fetal anemia, hydrops fetalis, spontaneous abortion
Zika virus	Transplacental	Microcephaly, cortical atrophy, ventriculomegaly
R – Rubella virus	Transplacental	Cataract, PDA, sensorineural deafness (Congenital Rubella Syndrome)
C – Cytomegalovirus (CMV)	Transplacental, perinatal	Periventricular calcifications, hepatosplenomegaly, SNHL
H – Herpes simplex virus (HSV)	Intrapartum (birth canal)	Vesicular skin lesions, encephalitis, disseminated infection

Additional and Emerging Pathogens

Beyond the TORCH group, several additional infectious agents have been implicated in intrauterine and perinatal disease:

Pathogen	Type	Fetal/Neonatal Effects
Hepatitis B, C, D, E viruses	Viral	Chronic hepatitis, cirrhosis, neonatal jaundice, stillbirth (HBV, HCV)
Enteroviruses (Coxsackie, Echo, Polio)	Viral	Myocarditis, meningoencephalitis, neonatal sepsis-like illness
SARS-CoV-2	Viral	Preterm birth, fetal distress, rare vertical transmission, placental inflammation
Listeria monocytogenes	Bacterial	Chorioamnionitis, granulomatosis infantiseptica, sepsis
Group B Streptococcus (GBS)	Bacterial	Early-onset sepsis, meningitis, pneumonia
Candida species	Fungal	Congenital cutaneous candidiasis, disseminated candidiasis in preterm infants
Mycoplasma / Ureaplasma	Bacterial	Chronic chorioamnionitis, bronchopulmonary dysplasia (in preterm infants)

3. Pathogenesis and Mechanisms of Transmission

Pathophysiology in TORCH

- Intrauterine TORCH infection in the first trimester↓
- Seemingly mild infection in mother with low grade fever ± rash↓
- Crosses placenta and affects organogenesis in fetus↓
- Causes multiple congenital anomalies and at times IUD

If TORCH infection (Toxoplasmosis, Others, Rubella, CMV, HSV) occurs in the 1st trimester:

- Even if the mother has only mild symptoms (low-grade fever, rash), the infection can cross the placenta.
- Since organogenesis happens in the 1st trimester, the infection can disrupt development → congenital anomalies (e.g., heart defects, cataracts, microcephaly).
- In severe cases, it may lead to IUD (Intrauterine Death).

If infection happens later (2nd or 3rd trimester):

- Organogenesis is mostly complete, so the risk of congenital malformations is lower.
- But infection can still cause growth restriction, hepatosplenomegaly, chorioretinitis, or neurologic issues in the fetus.

It highlights:

- Week 0 (LMP) → pregnancy dating starts
- Week 2 (Conception)
- Week 4–5 (UPT positive)
- Week 13 (End of 1st trimester)
- TORCH infection risk highest during this period → congenital anomalies/IUD
- Timeline diagram showing pregnancy stages and TORCH infection risk:
- LMP (Week 0) → starting point of pregnancy calculation
- Conception (~Week 2) → actual fertilization
- UPT Positive (~Week 4–5) → when pregnancy is usually detected
- 1st Trimester (0–13 weeks) → highest risk for TORCH infections → congenital anomalies / IUD
- Pathophysiological Mechanisms
- Transplacental (hematogenous) — most common for TORCH pathogens.
- Ascending infection — from maternal genital tract (e.g., GBS, Candida).
- Perinatal transmission — during passage through infected birth canal (e.g., HSV, GBS).
- Postnatal infection — through breastfeeding or close contact (e.g., HIV, CMV).

Pathogenesis and Mechanisms of Fetal Damage in Intrauterine Infections

The pathogenesis of intrauterine infections involves a complex interaction between the infectious agent, placental barrier integrity, and the developing fetal

immune system. The severity and nature of fetal injury depend primarily on the gestational age at exposure, type of pathogen, and duration of infection.

Routes of Fetal Infection

Route	Mechanism	Examples
1. Transplacental (hematogenous)	Pathogen crosses placenta via maternal bloodstream	Rubella, CMV, Toxoplasma, Syphilis, Parvovirus B19, Zika
2. Ascending infection from genital tract	Organisms ascend through cervix and amniotic fluid	Group B Streptococcus, Listeria, Candida
3. Intrapartum infection (during delivery)	Exposure to infected maternal secretions or blood	HSV, HIV, HBV, Chlamydia, Gonococcus
4. Postnatal transmission	Via breast milk or close contact	CMV, HIV, HSV, HBV

Pathophysiological Mechanisms of Fetal Damage

1. Direct cytopathic injury

- Pathogens invade fetal cells, leading to necrosis, apoptosis, and inflammatory destruction.
- Example: CMV and Zika virus infect neural progenitor cells → microcephaly, cortical atrophy, and ventriculomegaly.

2. Vasculitis and placental insufficiency

- Infection of placental vasculature causes ischemia, infarction, and hypoxia, resulting in intrauterine growth restriction (IUGR) or stillbirth.
- Example: Syphilis, Listeriosis, and Parvovirus B19.

3. Immune-mediated injury

- Maternal immune response and cytokine release induce inflammatory damage in fetal tissues.
- Example: Zika and SARS-CoV-2 trigger placental villitis and chronic inflammation.

4. Interference with organogenesis

- Infection during early embryogenesis (first trimester) leads to teratogenic malformations, as seen in:
  - Rubella → congenital heart disease, cataract, deafness
  - Varicella embryopathy → limb hypoplasia, optic atrophy

5. Persistent infection and latency

- Some agents establish latency, causing delayed manifestations months or years later.
- Example: Congenital CMV → progressive sensorineural hearing loss and neurodevelopmental delay.

Gestational Timing and Outcomes

Trimester of Infection	Predominant Effect	Examples
First trimester	Teratogenic malformations, miscarriage	Rubella, CMV, Varicella
Second trimester	Growth retardation, anemia, hepatosplenomegaly	Syphilis, Toxoplasmosis
Third trimester	Preterm labor, sepsis-like illness, neonatal infection	HSV, GBS, Listeria

Placental Pathology

Common histopathological features include:

- Chronic villitis (CMV, Zika, Rubella)
- Granulomatous inflammation (Toxoplasmosis, Listeria)
- Perivillous fibrin deposition and infarction (Syphilis, Parvovirus B19)
- Calcifications and viral inclusions in trophoblasts (CMV)

HIV in Infants

- < 1 yr: Infants can't make IgM or IgA against HIV.
- Maternal IgG against HIV can persist in baby till 24 months.
- Diagnosis in < 2 yrs child:

Meaning:

- HIV serology (IgG) is not reliable in infants <18–24 months, because maternal antibodies cross the placenta and stay in baby's blood.
- For diagnosis in infants <2 years → need virological tests:
  - HIV DNA PCR (preferred)
  - HIV RNA PCR

p24 antigen (less commonly used).

Pathogenesis and Mechanisms of Transmission of Intrauterine Infection in Children

The pathogenesis of intrauterine infection depends on how the pathogen enters the intrauterine environment and interacts with the placenta, fetal membranes, and fetal tissues. The mechanism of transmission determines the timing, severity, and clinical presentation of fetal or neonatal disease.

Transplacental (Hematogenous) Transmission

Mechanism:

- Pathogens present in the maternal bloodstream cross the placental barrier and enter the fetal circulation via the chorionic villi.
- This is the most common route for viral and protozoal infections.

Typical pathogens:

- Viral: Rubella, Cytomegalovirus (CMV), Zika virus, Parvovirus B19, Varicella-Zoster virus
- Parasitic: *Toxoplasma gondii*
- Bacterial: *Treponema pallidum* (syphilis), *Listeria monocytogenes*

Pathogenesis:

- Maternal viremia or bacteremia → placental infection → inflammation (villitis, intervillositis) → entry into fetal blood.
- Results in teratogenic effects, growth restriction, or fetal death depending on gestational age.

Example: Rubella infection during the first trimester → congenital heart disease, cataract, and deafness (Congenital Rubella Syndrome).

Ascending Infection from Maternal Genital Tract

Mechanism:

- Microorganisms from the vagina or cervix ascend through the cervical canal into the uterine cavity, infecting the amniotic fluid, fetal membranes, and ultimately the fetus.
- Occurs especially with premature rupture of membranes (PROM) or prolonged labor.

Typical pathogens:

- *Group B Streptococcus (GBS)*
- *Escherichia coli*
- *Ureaplasma urealyticum*, *Mycoplasma hominis*
- *Candida albicans*

Pathogenesis:

- Causes chorioamnionitis and amniotic fluid contamination.

- The fetus becomes infected by inhalation or swallowing of infected amniotic fluid, leading to pneumonia, sepsis, or meningitis after birth.

Example: GBS colonization in the maternal genital tract → neonatal sepsis and pneumonia.

Perinatal / Intrapartum Transmission

Mechanism:

- Infection occurs during delivery, when the neonate passes through an infected birth canal or is exposed to maternal blood and secretions.

Typical pathogens:

- Viruses: Herpes simplex virus (HSV-2), Hepatitis B, HIV, Human papillomavirus (HPV)
- Bacteria: Group B Streptococcus, Neisseria gonorrhoeae, Chlamydia trachomatis

Pathogenesis:

- Direct mucocutaneous exposure → infection of eyes, skin, respiratory tract, or bloodstream.
- May result in neonatal conjunctivitis, encephalitis, or disseminated infection.

Example: Neonatal HSV acquired intrapartum causes vesicular rash and encephalitis within the first 2 weeks of life.

Iatrogenic (Medical) Transmission

Mechanism:

- Fetal infection acquired through medical procedures that breach the uterine or placental barrier.

Examples:

- Amniocentesis, chorionic villus sampling, or fetal transfusion performed during maternal viremia or bacteremia.
- Blood transfusion or organ transplantation from infected donors in the perinatal period.

Typical pathogens:

- CMV, HBV, HIV, Parvovirus B19, and bacterial contaminants.

Pathogenesis:

- Direct inoculation of pathogens into fetal tissues → systemic fetal infection.
- Preventable with strict aseptic techniques and maternal infection screening before invasive procedures.

4. Risk Factors

The occurrence and severity of intrauterine infection are influenced by multiple maternal, fetal, environmental, and procedural factors. These risk factors determine the likelihood of pathogen transmission across the placenta and the extent of fetal injury.

A. Maternal Infections During Pregnancy

1. Primary maternal infection

- First-time exposure during pregnancy carries the highest risk of vertical transmission because the mother lacks preexisting immunity.
- Example: *Primary CMV, Rubella, or Toxoplasma* infection in early gestation → severe congenital disease.

2. Reactivation or reinfection

- Even in immune mothers, latent infections (e.g., CMV, HSV) may reactivate, especially in immunocompromised conditions.
- Usually milder but may still affect the fetus if maternal viremia occurs.

3. Untreated or late-treated maternal diseases

- Delayed diagnosis of syphilis, HIV, or hepatitis B increases perinatal transmission risk.
- Co-infections (e.g., HIV + syphilis) further amplify the risk.

Key insight: Early prenatal screening and vaccination (rubella, hepatitis B, varicella) significantly reduce infection rates.

B. Premature Rupture of Membranes (PROM) and Chorioamnionitis

1. PROM and prolonged labor

- Breach of the amniotic sac allows ascending infection from the maternal genital tract into the uterine cavity.
- The risk increases when the membranes are ruptured >18 hours before delivery.

2. Chorioamnionitis

- Bacterial infection of the fetal membranes and amniotic fluid caused by *GBS, E. coli, Ureaplasma*, or *Mycoplasma*.
- Leads to preterm birth, neonatal sepsis, pneumonia, and meningitis.

3. Invasive obstetric procedures

- Repeated vaginal examinations, intrauterine catheterization, or amniocentesis during labor increase the risk of ascending infection.

Example: Group B Streptococcus colonization + PROM → early-onset neonatal sepsis within 72 hours of birth.

C. Immunological Status of Mother and Fetus

1. Maternal immune suppression

- Conditions such as HIV infection, diabetes, malnutrition, corticosteroid therapy, or immunosuppressive drugs compromise maternal defense.
- Reduced clearance of pathogens enhances vertical transmission risk.

2. Immaturity of fetal immune system

- The fetal immune system is functionally incomplete, with low IgM/IgA production and reduced cell-mediated immunity.
- Even minor infections can become systemic and destructive in utero.

3. Lack of maternal antibody transfer

- Premature infants or maternal infections occurring late in pregnancy may not receive adequate IgG antibodies through the placenta.

D. Socioeconomic and Environmental Factors

1. Poor maternal health and hygiene

- Lack of access to prenatal care, unsafe food or water, and exposure to zoonotic sources (cats, undercooked meat) increase risk of toxoplasmosis and Listeria.

2. Low socioeconomic status

- Associated with limited vaccination coverage, delayed healthcare access, and higher infection rates (syphilis, CMV, hepatitis B).

3. Environmental exposure

- Tropical climates favor vector-borne infections such as Zika virus.
- Overcrowded or unsanitary living conditions contribute to bacterial transmission.

4. Occupational exposure

- Healthcare and laboratory workers face increased risk of hepatitis B, CMV, and parvovirus B19 infections.

5. Classification of Intrauterine Infections

Intrauterine (congenital) infections can be classified according to the causative agent, the timing of infection, and the clinical presentation in the fetus or newborn. This classification aids in clinical diagnosis, prognosis, and therapeutic planning.

Classification by Pathogen

Group	Examples of Pathogens	Typical Features in Fetus/Newborn
1. Viral	Rubella virus, Cytomegalovirus (CMV), Herpes simplex virus (HSV), Varicella-zoster virus, Parvovirus B19, Zika virus, HIV, Hepatitis B and C	Microcephaly, cataracts, hepatosplenomegaly, rash, sensorineural deafness, cardiac defects
2. Bacterial	*Treponema pallidum* (Syphilis), *Listeria monocytogenes*, *Group B Streptococcus*, *Mycoplasma*, *Chlamydia trachomatis*	Pneumonia, sepsis, osteochondritis, hepatomegaly, rash, stillbirth
3. Parasitic	*Toxoplasma gondii*, *Plasmodium falciparum*, *Trypanosoma cruzi*	Hydrocephalus, chorioretinitis, intracranial calcifications, anemia
4. Fungal	*Candida albicans*, *Aspergillus spp.*	Congenital cutaneous candidiasis, disseminated fungal sepsis in preterm infants

Note: The classical TORCH complex represents the main infectious group (Toxoplasmosis, Other [Syphilis, HIV, Parvovirus B19, Zika], Rubella, CMV, Herpes)

Classification by Timing of Infection

Timing	Definition	Pathogenesis & Outcomes
Early (embryonic or first trimester)	Infection occurs during organogenesis (≤12–14 weeks gestation)	→ High risk of teratogenesis, miscarriage, or severe congenital malformations (e.g., rubella, varicella, CMV)
Late (fetal or third trimester)	Infection after organogenesis (>20 weeks gestation)	→ Functional organ damage, growth restriction, preterm birth, or neonatal sepsis (e.g., CMV, syphilis, HSV, GBS)

Example:

- Early rubella infection → Congenital Rubella Syndrome (heart + eye + ear defects).
- Late CMV infection → Hepatosplenomegaly, anemia, sensorineural hearing loss.

Classification by Clinical Presentation

Category	Description	Examples
1. Symptomatic infection	Manifestations evident at or soon after birth; may include structural anomalies or systemic illness	Congenital Rubella Syndrome, Neonatal Herpes, Cytomegalovirus infection with jaundice and hepatomegaly
2. Asymptomatic infection	No obvious clinical signs at birth but later complications (neurologic, auditory, visual)	Congenital CMV (asymptomatic at birth, later SNHL), Toxoplasmosis (delayed chorioretinitis)

Clinical significance:

Even asymptomatic congenital infections can cause late-onset developmental, sensory, or neurological deficits — highlighting the need for long-term follow-up and early screening.

6. Clinical Manifestations

TORCH Infections in Pregnancy – Master Comparison

Feature	Toxoplasma gondii (Protozoa)	Rubella virus (Togaviridae)	Cytomegalovirus (CMV) (Herpesviridae)	Herpes Simplex Virus (HSV)	Syphilis (*Treponema pallidum*)
Agent	Protozoan parasite (*T. gondii*)	RNA virus (*Rubella virus*)	DNA virus (*Cytomegalovirus*)	DNA virus (*Herpesviridae*)	Spirochete bacterium (*T. pallidum*)
Transmission to Mother	- Ingestion (cat feces, raw meat, unwashed veg)	- Respiratory route	- Body fluids (saliva, urine, sexual, droplets)	- Sexual contact - Vertical (intrapartum, via birth canal)	- Sexual contact - Vertical (transplacental)
Maternal Illness	Usually asymptomatic or mild flu	Mild fever, rash, lymphadenopathy, arthritis	Often asymptomatic, flu-like	Primary infection: fever, malaise, painful vesicles	Often asymptomatic; chancre or rash if symptomatic
Trimester Risk	1st → severe anomalies, IUD 2nd → neuro deficits 3rd → subclinical but high transmission	1st → 85% CRS risk Later → risk declines	Primary infection → 33% fetal transmission Reinfection → ~1.4%	1st → miscarriage, IUGR 3rd (esp. peripartum) → neonatal HSV	Any trimester → high risk of transmission if untreated
Fetal / Neonatal Outcomes	- Hydrocephalus, intracranial calcifications, chorioretinitis - Hearing loss,	CRS triad: cataracts, deafness, congenital heart	- Microcephaly, seizures, hearing loss, blueberry muffin rash -	- Neonatal herpes: disseminated sepsis-like illness,	- Stillbirth, prematurity - Congenital syphilis: snuffles,

Feature	Toxoplasma gondii (Protozoa)	Rubella virus (Togaviridae)	Cytomegalovirus (CMV) (Herpesviridae)	Herpes Simplex Virus (HSV)	Syphilis (*Treponema pallidum*)
	hepatosplenomegaly	disease Growth retardation	Hepatosplenomegaly, anemia	encephalitis, vesicular rash, high mortality	rash, Hutchinson's teeth, saddle nose, saber shins
Investigations	IgM, IgG, PCR (amniotic fluid)	IgM, IgG serology	Maternal IgM, IgG avidity Culture from urine/stool in neonates	Viral culture, PCR, serology	VDRL, RPR, confirm with FTA-ABS or TPHA
Management	Spiramycin, Pyrimethamine (cautious use)	No antiviral; supportive care only	No effective antiviral in pregnancy; supportive neonatal care	Acyclovir (maternal & neonatal)	Penicillin (safe & effective in pregnancy)
Prevention	Avoid raw meat, cat litter, unwashed veg	MMR vaccination before pregnancy	Maternal hygiene, no sharing utensils, handwashing	C-section if active lesions Safe sexual practices	Prenatal screening & penicillin treatment

CONGENITAL SYPHILIS

Risk highest if the mother has primary or secondary syphilis (spirochetemia stage). Transmission risk falls in latent syphilis.

Congenital Syphilis

- Early (within 2 yrs of life)
- Late (≥ 2 yrs of life)

Early Congenital Syphilis

(within the first 2 years of life)

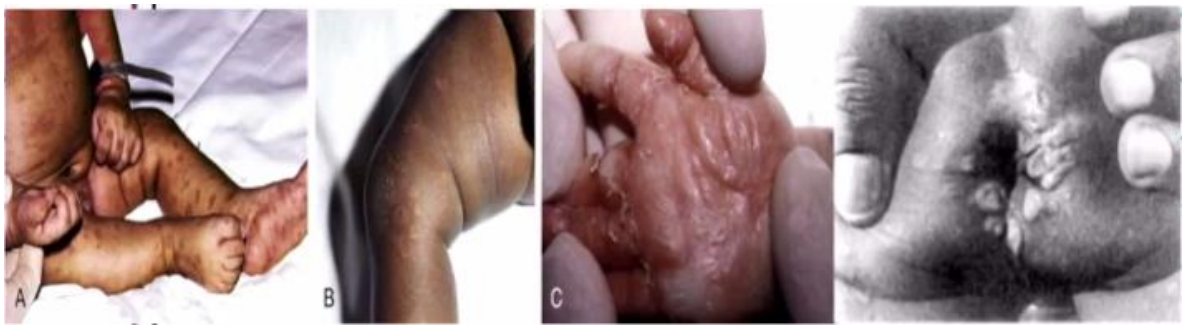
Clinical features:

- Snuffles (profuse mucopurulent rhinitis, highly infectious)
- Maculopapular rash (palms & soles)
- Hepatosplenomegaly
- Lymphadenopathy
- Jaundice, anemia, thrombocytopenia
- Skeletal abnormalities (periostitis, metaphysitis, osteochondritis → "saber shins")
- Pseudoparalysis of Parrot (painful limb immobility)
- Condyloma lata (moist, wart-like lesions)
- Renal lesions (glomerulonephritis, nephrotic syndrome)

- glaucoma

"Pseudoparalysis" = the infant doesn't move a limb, not because of true paralysis (nerve damage), but due to pain, bone/joint disease, or metabolic issues.

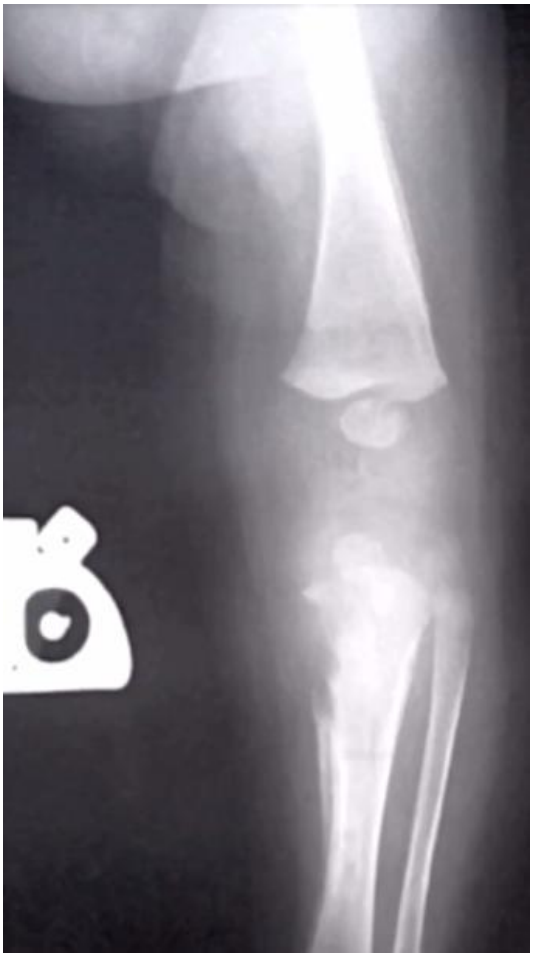
- Early congenital syphilis → Parrot's pseudoparalysis (due to painful periostitis/osteochondritis).
- Scurvy → subperiosteal hemorrhage causes pain → refusal to move limb – "generalized tenderness".
- Septic arthritis / Osteomyelitis → pain and swelling.
- Hypokalemia → muscle weakness, hypotonia, mimicking paralysis.



A,B-papulosquamous rashes on the trunk

C-Palms and soles rashes

D-perianal condyloma



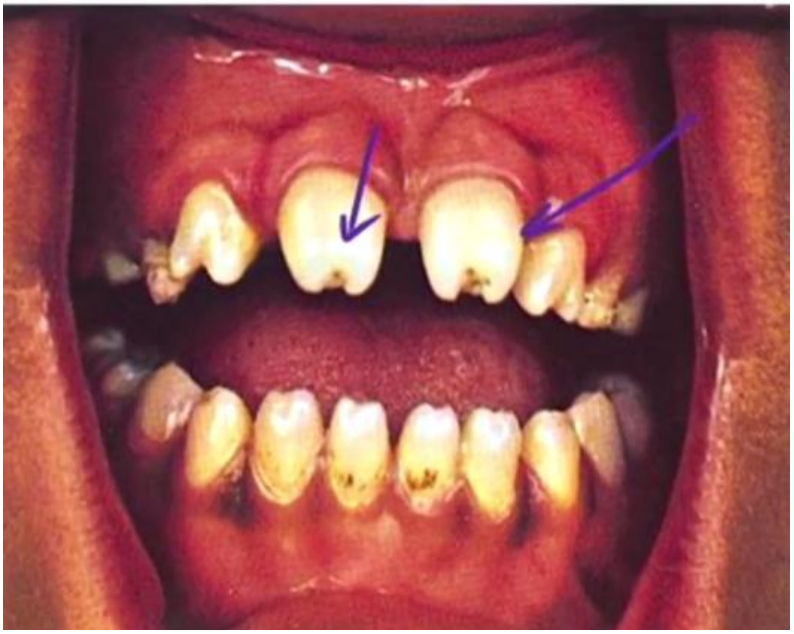
Metaphysitis, periostitis

Late Congenital Syphilis

(after 2 years of life)

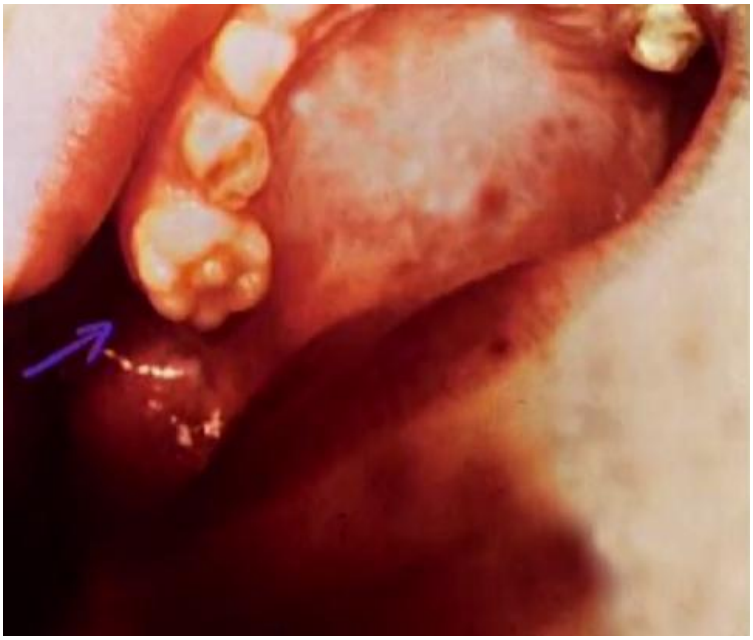
Hutchinson's Triad (classic):

1. Interstitial keratitis (corneal scarring → blindness)
2. SNHL (Sensorineural Hearing Loss)
3. Hutchinson's teeth (notched, peg-shaped incisors)

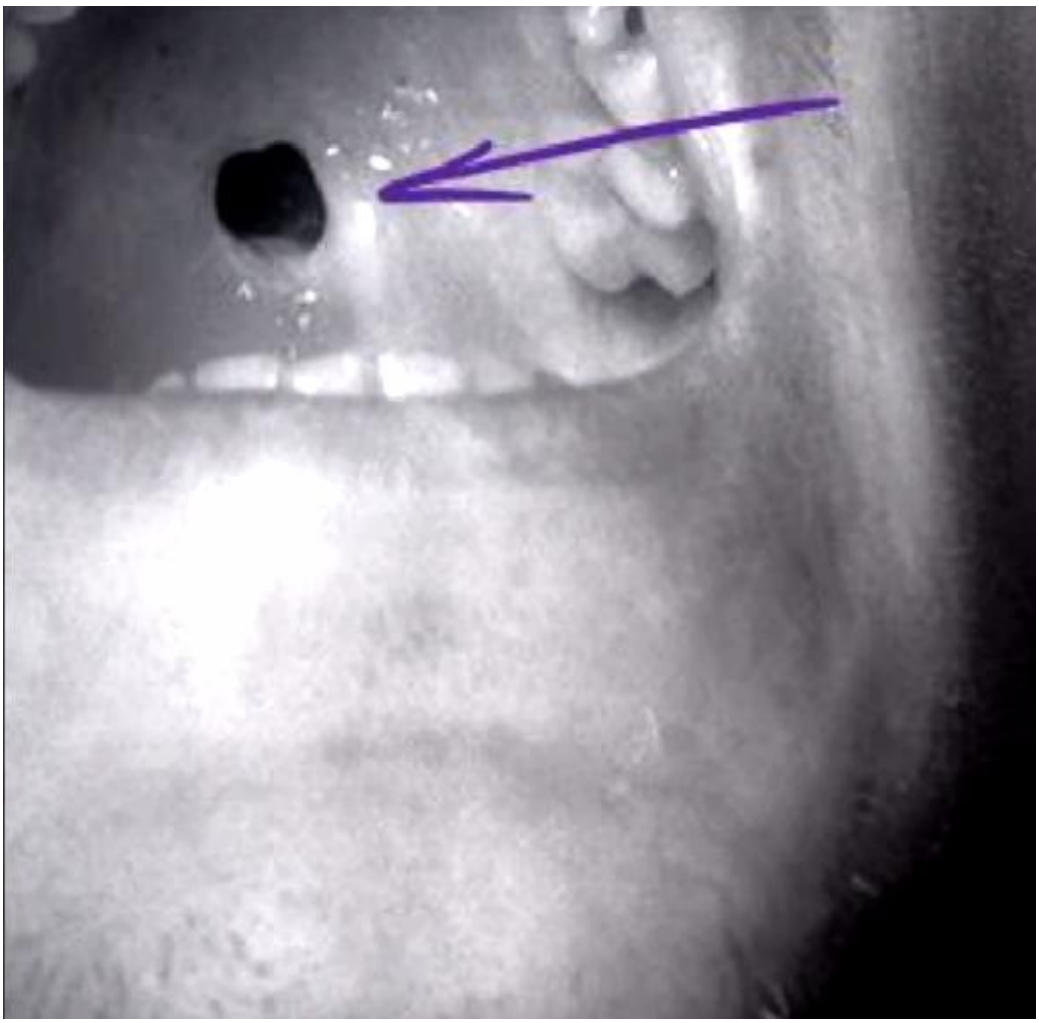


Hutchinson's teeth

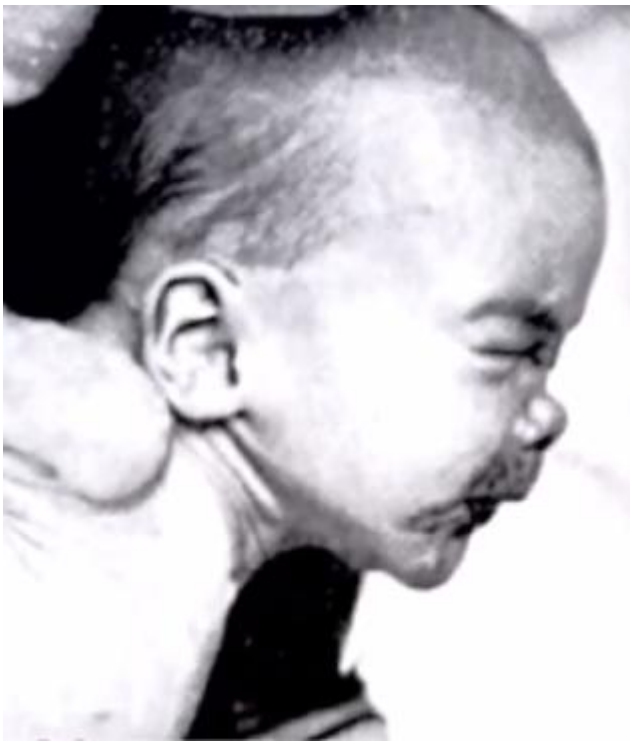
- widely spaced,
- Notched
- Incisors



Mulbery molars



Palate perforation



Saddle nose

Olympian’s brow

Higoumenaki sign (prominence of the sternoclavicular joint)

Rhagades (cracks at the angle of the joint and the chin)

Other late features:

- Mulberry molars
- Frontal bossing
- Saddle nose deformity
- Clutton's joints (painless synovitis of knees)
- High-arched palate (Perforation of palate)
- Saber shins (due to chronic periostitis)
- Higoumenaki's sign *(prominence of sternoclavicular joint)*
- Olympian's brow

Congenital Syphilis: Diagnosis & Treatment Algorithm

1. Screening (Maternal & Neonatal)

- Maternal serology: VDRL / RPR (non-treponemal) + TPHA / FTA-ABS (treponemal).
- Neonate screening if:
  - Mother untreated / inadequately treated,
  - Four-fold higher neonatal VDRL titer than maternal,
  - Clinical suspicion (rash, snuffles, hepatosplenomegaly).

2. Clinical Examination of Neonate

- Snuffles, rash (palms/soles), hepatosplenomegaly, lymphadenopathy, bone tenderness.
- Signs of early syphilis (within 2 yrs) vs late syphilis (>2 yrs).

3. Laboratory & Confirmatory Tests

- Serological test: Neonatal non-treponemal titer ≥4× maternal = diagnostic.
- Direct detection: Dark-field microscopy / fluorescent antibody from placenta, umbilical cord, skin lesions.
- CSF (if neurosyphilis suspected): VDRL, cell count, protein.
- Other supportive tests: X-ray (periostitis, metaphysitis).

4. Treatment

Proven or highly suspected disease:

- Aqueous crystalline Penicillin G IV:
  - 50,000 U/kg/dose every 12 hr (first 7 days of life),
  - then every 8 hr (after 7 days),
  - for 10 days.

Alternative (if IV not feasible):

- Procaine Penicillin G IM: 50,000 U/kg/dose once daily × 10 days.

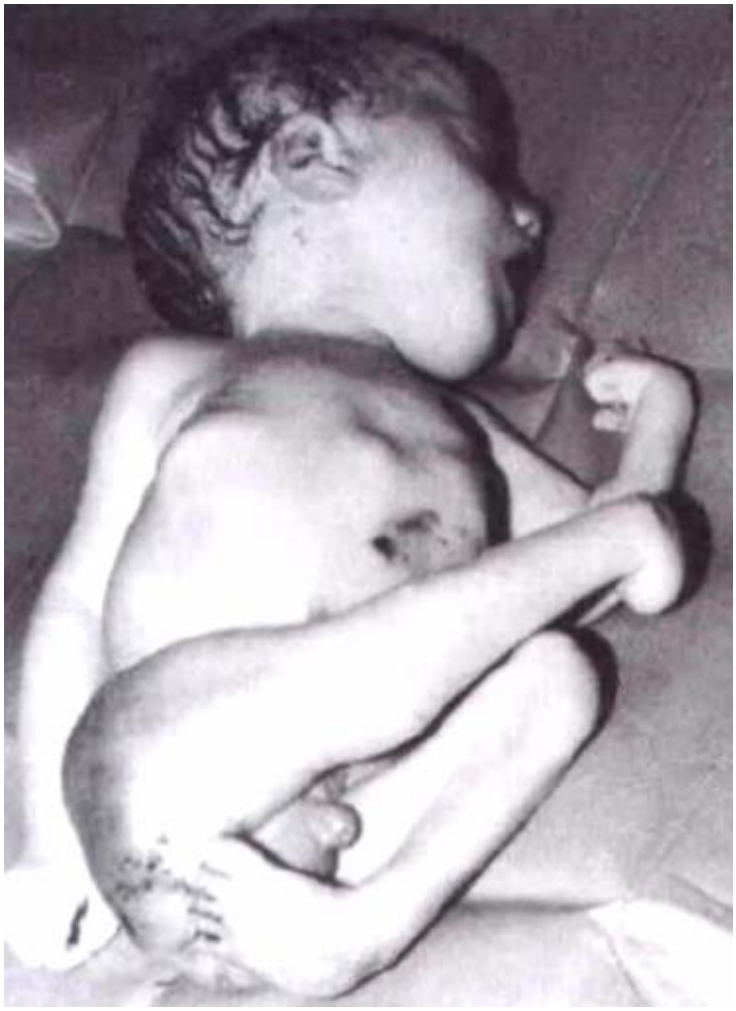
5. Follow-Up

- Repeat serology at 3, 6, 12 months → titers should fall ≥4-fold.
- Persistent or rising titers → retreatment.
- Monitor for late complications (Hutchinson's triad, Clutton's joints).

VARICELLA IN PREGNANCY & NEONATES

1. Congenital Varicella Syndrome (CVS)

- Timing: Maternal infection at 13–20 weeks gestation (highest teratogenic risk).
- Clinical features:
  - Eye: Optic atrophy / hypoplasia
  - Limbs: Aplasia / hypoplasia (esp. L-S plexus involvement)
  - Skin: Cicatricial scarring in dermatomal distribution
  - CNS: Cortical atrophy, seizures, developmental delay
  - Growth restriction



Varicella embryopathy (hypoplastic limb and a scaring rash) – mother got chickenpox during pregnancy

Highest risk: 13–20 wks

Eyes: optic atrophy / hypoplasia

L-S plexus: limb aplasia / hypoplasia

Skin: cicatricial scarring

CNS: atrophy (cortical)

2. Neonatal Varicella

- Timing: Maternal varicella within 5 days before delivery to 2 days after delivery
- Pathophysiology:
  - Virus transmitted, but maternal antibodies not yet formed → newborn lacks passive immunity.
  - Leads to severe disseminated neonatal varicella (high mortality).

Management of Neonatal Varicella (Perinatal Exposure)

1. Risk Window

- Maternal chickenpox 5 days before delivery → 2 days after delivery
- Highest risk: severe disseminated neonatal varicella (high mortality), because maternal antibodies haven't been formed and transferred.

2. Management

At Birth:

- Isolate baby (to prevent spread).
- Give Varicella-Zoster Immunoglobulin (VZIg)
  - Dose: 125 units IM (≤2 kg → 62.5 U; 2–10 kg → 125 U; >10 kg higher doses).
  - Must be given within 96 hours (best <48 hrs).

If Symptomatic:

- Start IV Acyclovir (30 mg/kg/day in 3 divided doses × 10 days).
- Supportive care.

If Mother develops varicella >5 days before delivery:

- Baby usually gets protective maternal IgG antibodies.
- No need for VZIg, only observation ± Acyclovir if symptomatic.

3. Follow-Up

- Monitor for fever, rash, respiratory distress.
- Parents educated on early signs of varicella complications (pneumonia, hepatitis, encephalitis).

Neonatal Varicella – Timing, Risk & Management

Timing of maternal chickenpox rash	Risk to baby	Management
> 5 days before delivery	Baby receives protective maternal antibodies	Observe; Acyclovir SOS if symptomatic
Within 5 days before delivery → 2 days after delivery	Highest risk – severe disseminated neonatal varicella (no maternal antibodies yet)	Isolation + VZIg (within 96 hrs) ± Acyclovir if symptomatic
> 2 days after delivery	Postnatal exposure (infectious contact after birth)	Isolation + Acyclovir SOS

Herpes – Varicella (VZV) Summary Table

Aspect	Details
Agent	Varicella-Zoster Virus (*Herpesviridae*)
Maternal Illness	Always clinical (fever, vesicular rash); not subclinical
Pathogenesis	- 1st trimester: Congenital Varicella Syndrome (neurological + dermatomal defects) - Late pregnancy: Neonatal zoster
Perinatal Transmission	Highest risk if maternal infection occurs 5 days before to 2 days after delivery (no maternal Abs yet)
Congenital Varicella Syndrome	- Skin defects: cicatricial scars - Limb hypoplasia - CNS involvement
Neonatal Infection	- Encephalitis (→ sequelae) - Disseminated varicella infection - Classic vesicular rash - Can cause neonatal death if untreated
Investigations	- Clinical + maternal history - PCR from vesicular lesions - Varicella IgM (may be negative if tested early)
Treatment	- Acyclovir for neonatal/perinatal varicella - Varicella immunoglobulin (VZIG) for all exposed neonates - Prognosis is poor if encephalitis develops
Prevention	- Varicella vaccination (before pregnancy) - Avoid exposure during pregnancy

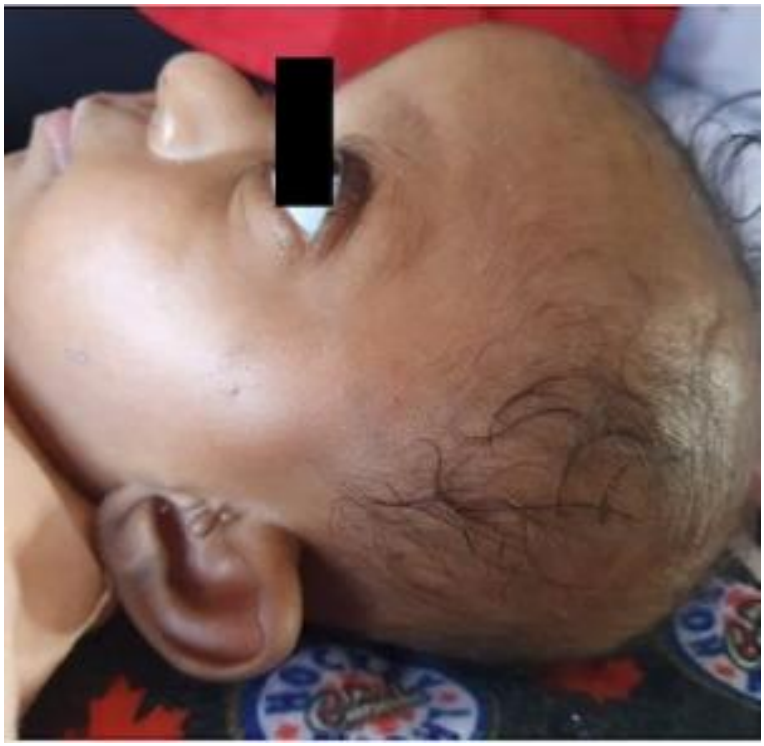
TOXOPLASMA

Agent: Toxoplasma gondii

- Common parasitic infection in humans from cat (host)
- ROT: Mother acquires infection feco-orally and can be asymptomatic or have a mild illness with fever, transmission occurs in all trimesters, however organogenesis in 1st trimester is maximally affected.

Clinical Features:

1. Subclinical infection when later trimesters are affected
2. Intrauterine death, Prematurity and spontaneous abortions
3. Developmental delay along with classic intracranial calcifications
4. Convulsions
5. Chorioretinitis
6. Microcephaly or hydrocephalus
7. Jaundice with hepatosplenomegaly (hepatitis)
8. Sensorineural hearing loss
9. Acute infection can have hepatitis, myocarditis, pneumonitis, thrombocytopenia and maculopapular rash
10. Low set ear



Toxoplasmosis in Pregnancy — Risk vs Severity

Trimester	Transmission Risk	Severity of Fetal Damage	Typical Outcomes
1st (0–13 wks)	Low	High	Severe congenital anomalies, IUD, spontaneous abortion
2nd (14–26 wks)	Medium	Medium	Neurological deficits, hepatosplenomegaly, some subclinical
3rd (27–40 wks)	High	Low	Mostly subclinical at birth, late manifestations (chorioretinitis, learning disability)

Toxoplasmosis in Pregnancy: Investigations, Management & Prevention

Category	Details
Investigations	Clinical syndrome is often the basis of diagnosis Serology: Toxoplasma IgM antibodies (acute infection) IgG avidity testing → distinguishes recent vs. past infection PCR (amniotic fluid / cord blood): detects fetal infection
Management	Prevention is the best option (since treatment in pregnancy is difficult) Pyrimethamine: limited use (crosses placenta, risk to fetus) Spiramycin: used in some cases to reduce maternal–fetal transmission Supportive care: manage complications in the neonate
Prevention	Avoid undercooked meat (especially pork, lamb) - Wash fruits & vegetables thoroughly Avoid contact with cat litter / soil (Toxoplasma oocysts) Practice good kitchen hygiene No transmission through breast milk and human milk banking (safe for feeding)

Rubella in Pregnancy

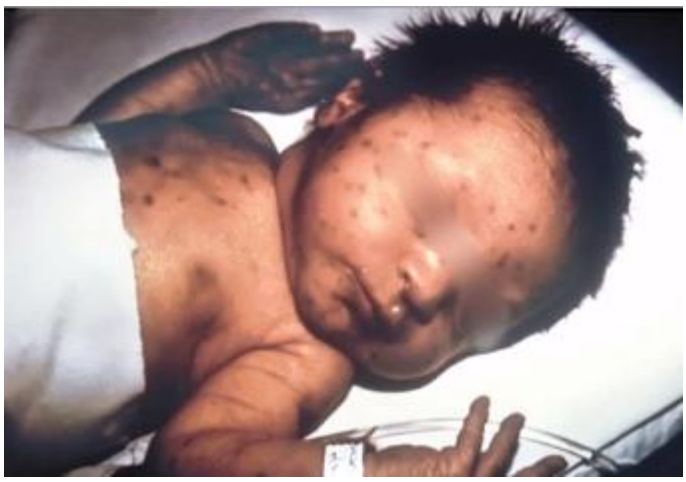
Category	Details
Agent	*Rubella virus* (family Togaviridae)
Epidemiology	- Previously common in childhood - Now reduced due to MMR vaccination - Still present in unvaccinated mothers/adolescents
Transmission	- Respiratory route (droplet infection) - Maternal illness: mild fever, rash, tender lymphadenopathy, arthritis
Risk in Pregnancy	- Highest in 1st trimester → up to 85% risk of Congenital Rubella Syndrome (CRS) - Risk decreases in 2nd and 3rd trimesters
Fetal Outcomes (CRS)	- Classic CRS triad: cataracts, deafness, congenital heart disease - Growth retardation - Developmental delay
Investigations	- Clinical spectrum in child (key clue) - Rubella IgM (confirms recent infection) - IgG positivity after 4 weeks supports diagnosis
Management	- No specific antiviral treatment during pregnancy - Supportive care for affected child
Prevention	- Best option: immunization - MMR vaccine at ~9 months + booster - Vaccinate unvaccinated adolescents & women of childbearing age - Vaccination before conception is crucial

Comparison: Toxoplasma vs Rubella in Pregnancy

Feature	Toxoplasma gondii	Rubella virus
Agent	Protozoan parasite (*Toxoplasma gondii*)	RNA virus (*Togaviridae*)
Transmission to Mother	- Ingestion of oocysts (cat feces, soil) - Undercooked meat, unwashed vegetables	- Respiratory route (droplet infection)
Maternal Symptoms	- Often asymptomatic or mild flu-like illness	- Mild fever, rash, lymphadenopathy, arthritis
Trimester Risk	- 1st trimester: Severe anomalies, IUD, spontaneous abortion - 2nd: Neuro deficits, hepatosplenomegaly - 3rd: High transmission, often subclinical at birth	- 1st trimester: 85% risk of Congenital Rubella Syndrome (CRS) - Risk declines in later trimesters
Fetal Outcomes	- Hydrocephalus, intracranial calcifications, chorioretinitis - Hearing loss, hepatosplenomegaly, prematurity	- CRS triad: Cataracts, deafness, congenital heart disease - Growth retardation
Prevention	- Avoid cat litter, undercooked meat, unwashed fruits/vegetables - Good hygiene - No breast milk transmission	- MMR vaccination before pregnancy (9 months + booster) - Immunize women of childbearing age
Treatment	- Limited: Spiramycin (↓ transmission), Pyrimethamine (limited use in pregnancy)	- No specific antiviral treatment available

CYTOMEGALOVIRUS IN PREGNANCY

Category	Details
Agent	*Cytomegalovirus (Herpesviridae family)*
Transmission	- Contact with infected body fluids (saliva, urine, sexual, droplets)
Epidemiology	- 90% seroprevalence among women of reproductive age in India - 1.4% of seropositive women transmit CMV during pregnancy - 33% of newly infected mothers transmit to fetus
Clinical Features	- Spontaneous abortion, prematurity, fetal growth retardation - Polyhydramnios - Developmental delay, microcephaly, convulsions - Vision loss (squint, cataract, chorioretinitis) - Sensorineural hearing loss (commonest sequelae) - Neonatal hepatitis, hepatosplenomegaly, bleeding - Anemia, thrombocytopenia - “Blueberry muffin” rash in neonates
Diagnosis	- Mainly clinical - CMV culture (urine, stool) in neonates - Maternal CMV IgM antibodies - IgG avidity (recent vs past infection)
Management	- No effective curative treatment during pregnancy - Prevention only option → maternal education & hygiene - Avoid exposure to infected saliva/urine (esp. toddlers) - Supportive care for affected neonate
Prevention	- Hand hygiene, avoid sharing utensils with young children - No vaccine available (unlike Rubella)



Management of Infants Born to HBV-Positive Mothers

1. Risk of Transmission

- Highest risk if mother is HBsAg + and HBeAg + (up to 90% → chronic infection in infant).
- Lower risk if HBsAg + and HBeAg – (≈10%).
- Transmission occurs perinatally (during delivery) > transplacental.

2. Immediate Postnatal Management

- Within 12 hours of birth:
- Hepatitis B vaccine (birth dose) – intramuscular
- HBIG (Hepatitis B Immunoglobulin) – different site from vaccine

Both must be given within 12 hours (latest 24 hours).

3. Vaccination Schedule

- Standard 3-dose schedule:
  - Birth dose (within 12–24 hrs)
  - 6 weeks
  - 10 weeks
  - 14 weeks (or per local schedule: 0, 1, 6 months)

4. Follow-Up Testing

- At 9–12 months of age (or 1–2 months after last vaccine dose):
  - HBsAg and anti-HBs checked.

Interpretation:

- HBsAg negative + Anti-HBs ≥10 mIU/mL → Protected
- HBsAg negative + Anti-HBs <10 mIU/mL → Non-responder → revaccination needed
- HBsAg positive → Infant infected → needs long-term follow-up

5. If HBIG not available

- Give Hepatitis B vaccine alone within 24 hours
- Protection lower, but still reduces transmission risk significantly

6. Breastfeeding

- Not contraindicated, even if mother is HBsAg +, provided infant has received HBV vaccine ± HBIG.

Fetal Alcohol Syndrome

→ Features:

- Skin folds at corner of eye
- Low nasal bridge
- Short nose
- Indistinct philtrum
- Microcephaly
- Small eye opening
- Small midface
- Thin upper lip
- Maxillary / midface hypoplasia

(diagram showing typical facies: low nasal bridge, epicanthal folds, short palpebral fissures, flat midface, thin upper lip, indistinct philtrum, micrognathia, short nose)

- Alcohol is never safe in pregnancy.
- Most common heart disease: VSD / PDA
- CNS & Behaviour: 70% patients → most common = ADHD

7. Diagnostic Approaches

Intrauterine (congenital) infections require a multidisciplinary diagnostic approach integrating maternal, fetal, and neonatal assessments. Early and accurate detection is crucial for preventing severe developmental sequelae and guiding targeted therapy.

A. Maternal Screening

Maternal screening identifies women at risk during pregnancy and helps prevent vertical transmission.

Diagnostic Tool	Purpose / Detection	Examples / Interpretation
1. Serological tests (IgM, IgG)	Detect current or past infection	- Rubella IgM → acute infection - CMV IgG avidity → distinguishes recent (<12 wk) vs. past infection
2. PCR (Polymerase Chain Reaction)	Detect pathogen DNA/RNA in maternal blood, urine, or amniotic fluid	High-sensitivity test for CMV, Toxoplasma, Parvovirus B19, Zika, HIV
3. Ultrasound markers of fetal infection	Identify structural or functional abnormalities suggesting congenital disease	- IUGR - Ventriculomegaly, intracranial calcifications - Hepatosplenomegaly, ascites - Hydrops fetalis
4. Amniocentesis / Chorionic villus sampling	Direct fetal sample for PCR or culture	Used when maternal serology positive or ultrasound abnormalities detected

*Example:*Detection of high CMV viral load in amniotic fluid by PCR after 21 weeks confirms congenital CMV infection.

B. Neonatal Diagnostic Tools

Method	Target / Purpose	Interpretation / Key Points
1. Serology (IgM, IgG)	Detect fetal immune response	- IgM in cord blood or neonatal serum → diagnostic (since it does not cross placenta). - Persistent IgG after 6–9 months → congenital infection.
2. PCR assays	Detect viral or parasitic DNA/RNA directly from neonatal blood, urine, or saliva	- CMV PCR within 3 weeks after birth = confirmatory test. - HIV DNA/RNA PCR used in infants <18 months.
3. Microbial cultures	Isolation of bacteria or fungi	- *Listeria*, *GBS*, *Candida* from blood or CSF cultures.
4. Newborn screening tests	Dried blood spot (DBS) testing for HIV, CMV, or metabolic indicators	Enables large-scale population screening in endemic regions.

Note: A combination of serological and molecular tests improves diagnostic accuracy, particularly for TORCH pathogens.

C. Imaging Techniques

Modality	Indications	Findings Suggestive of Infection
Prenatal Ultrasound	Routine screening of fetal anatomy	- Intracranial or hepatic calcifications - Hydrocephalus - Ascites, placentomegaly
Fetal MRI	When ultrasound findings are inconclusive	- Cortical atrophy (CMV, Zika) - White matter lesions, cerebellar hypoplasia
Postnatal MRI / CT	Evaluation of CNS damage in neonate	- Periventricular calcifications (CMV) - Diffuse brain loss (Zika) - Hydrocephalus (Toxoplasmosis)

D. Histopathology and Placental Studies

Specimen	Findings / Diagnostic Value
Placenta	Villitis, intervillositis, fibrin deposition, infarction, or viral inclusion bodies (CMV, Rubella)
Umbilical cord / membranes	Inflammatory infiltrates (chorioamnionitis) in bacterial infections
Fetal tissue (autopsy / biopsy)	Granulomas (*Listeria*, *Toxoplasma*), necrosis, calcifications
Immunohistochemistry / In situ hybridization	Localizes specific pathogens in placental or fetal tissue

*Example:*Detection of cytomegalic inclusion cells with “owl’s eye” nuclei in the placenta strongly supports congenital CMV infection.

8. Management and Treatment

The management of intrauterine infections is multidimensional, involving targeted antimicrobial or antiviral therapy, supportive neonatal care, and preventive immunological strategies. Early diagnosis and treatment are essential to reduce perinatal morbidity, mortality, and long-term developmental sequelae.

A. Antimicrobial and Antiviral Therapy in Neonates

1. Targeted Antimicrobial Therapy (Bacterial & Parasitic Infections)

Pathogen	Recommended Drug(s)	Notes / Duration
Syphilis (*Treponema pallidum*)	Aqueous crystalline Penicillin G IV (50,000 U/kg every 12h for 10 days)	Drug of choice; prevents neurosyphilis & late complications
Listeria monocytogenes	Ampicillin + Gentamicin	Duration: 10–14 days for mild, 21 days for meningitis
Toxoplasma gondii	Pyrimethamine + Sulfadiazine + Folinic acid	Long-term therapy (up to 1 year) to prevent relapse
Group B Streptococcus (GBS)	Ampicillin + Gentamicin	Early-onset sepsis; maternal prophylaxis reduces risk

2. Antiviral Therapy

Viral Infection	First-Line Drug(s)	Dosage / Duration / Notes
Cytomegalovirus (CMV)	Ganciclovir or Valganciclovir	6 months therapy; improves hearing and neurodevelopmental outcomes
Herpes Simplex Virus (HSV)	Acyclovir IV (60 mg/kg/day ÷ 3 doses for 14–21 days)	Start immediately on suspicion; essential for encephalitis
Varicella-Zoster Virus (VZV)	Acyclovir IV (30 mg/kg/day for 10 days)	For congenital/neonatal varicella; add VZIg if high-risk exposure
HIV	Zidovudine (AZT) prophylaxis ± combination ART	Begin within 6–12 hrs after birth; continue 4–6 weeks
Hepatitis B Virus (HBV)	HBV vaccine + HBIG within 12 hrs of life	Prevents vertical transmission; highly effective (>90%)

Key insight: Early initiation of antiviral therapy (within the first 2–3 weeks) significantly reduces long-term neurological damage in congenital CMV and HSV infections.

B. Supportive Therapy

In addition to pathogen-specific treatment, comprehensive supportive care is vital for neonatal stabilization and prevention of secondary complications.

System	Supportive Measures	Purpose
Sepsis management	Intravenous fluids, vasopressors, and broad-spectrum antibiotics until culture results	Stabilize circulation and prevent multi-organ failure
Respiratory support	Oxygen therapy, CPAP, or mechanical ventilation	Manage pneumonia, respiratory distress, or pulmonary edema
Nutritional support	Parenteral or nasogastric feeding; breast milk if maternal infection controlled	Prevent growth restriction and optimize immunity
Hematologic support	Transfusion for anemia, platelet concentrates for thrombocytopenia	Restore normal hematologic parameters
Neurodevelopmental follow-up	Regular hearing, vision, and developmental screening	Early detection of sequelae (SNHL, microcephaly, motor delay)

Clinical note: Many congenital infections (CMV, Zika, Toxoplasma) require long-term multidisciplinary follow-up — involving neonatologists, neurologists, ophthalmologists, and audiologists.

C. Role of Immunoglobulins and Antiviral Prophylaxis

1. Immunoglobulin Therapy

Indication	Type of Immunoglobulin	Use
Varicella exposure in neonates or pregnant women	Varicella-Zoster Immunoglobulin (VZIg)	Given within 96 hrs of exposure to prevent severe disease
Hepatitis B prevention	HBIG + HBV vaccine	Given within 12 hrs of birth to infants of HBsAg+ mothers
Cytomegalovirus prevention (select cases)	CMV hyperimmune globulin (experimental/adjunctive)	Reduces transmission in high-risk pregnancies

2. Antiviral and Antimicrobial Prophylaxis

- HIV: Maternal ART during pregnancy + infant zidovudine prophylaxis.
- Syphilis: Routine antenatal screening and maternal penicillin treatment before 28 weeks gestation.
- GBS: Intrapartum antibiotic prophylaxis (IAP) in colonized mothers prevents early-onset neonatal sepsis.
- Toxoplasmosis: Spiramycin in pregnant women with acute infection reduces transplacental transmission.
- Varicella: Vaccination of seronegative women before pregnancy.

TESTS

1. In which cases can intrauterine infection in newborns occur?
A. When the mother contracts various infections during pregnancy*
B. If the mother has heart disease
C. If the mother does not follow hygiene rules
D. If the umbilical cord is long
E. If healthcare workers violate aseptic and antiseptic rules
2. Congenital syphilis can be suspected by the following signs:
A. Vesicles on palms and soles, rhinitis, splenomegaly*
B. Signs of active encephalitis
C. Myocarditis
D. Hemorrhagic syndrome
E. Interstitial nephritis
3. In congenital rubella, the pathogen is isolated from which fluid?
A. Blood*
B. Urine
C. Cerebrospinal fluid
D. Meconium
E. Saliva
4. Which drug is used in the treatment of cytomegaly?
A. Cytotek*
B. Vitamins
C. Chloroquine
D. Ampicillin
E. Erythromycin
5. Hepatitis B virus is transmitted by which route?
A. Hematogenous*
B. Contact
C. Alimentary
D. Through the birth canal
E. Contaminated medical instruments
6. Diagnosis of congenital syphilis is confirmed by:
A. Wassermann reaction*
B. Coombs test
C. Sabin-Feldman test
D. Detection of antiviral antibodies

E. Tuberculin test

7. Treatment of congenital syphilis includes:

A. Penicillin*

B. Carbamazepine

C. Doxycycline

D. Tetracycline

E. Amphotericin

8. In intrauterine infection, diagnosis is confirmed if IgG in the mother's blood is increased compared to the child's blood by:

A. 3 times*

B. 2 times

C. 4 times

D. 5 times

E. 6 times

9. The most common etiology of intrauterine infections is:

A. Virus + viral association*

B. Bacterial

C. Viral

D. Fungal

E. Virus + bacterial association

10. What is the lethality rate in generalized intrauterine infection?

A. 70–80%*

B. 40–50%

C. 20–30%

D. 50–60%

E. 10–20%

11. In neonatal candidiasis, which system is affected?

A. Skin and mucous membranes*

B. Lungs

C. Heart

D. Kidneys

E. Liver

12. If infection occurs during the blastogenesis stage of the fetus, which clinical signs are observed?

A. Embryonic death, miscarriage*

B. No changes

C. Dysplasia
D. Intrauterine growth retardation
E. Hypoplasia of internal organs
13. What is included in the classic triad of toxoplasmosis?
A. Hydrocephalus, chorioretinitis, intracranial calcifications*
B. Microcephaly, hepatomegaly, urethritis
C. Chorioretinitis, hydrocephalus, splenomegaly
D. Hepatomegaly, urethritis, heart defects
E. Hydrocephalus, chorioretinitis, cataract
14. Which drugs are used in the treatment of toxoplasmosis?
A. Chloroquine, folic acid*
B. Folic acid, ampicillin
C. Vitamin C, folic acid
D. Streptomycin, Hofitol
E. Tavegyl, Vitamin B6
15. In rubella infection, Gregg's triad in newborns includes:
A. Congenital heart defect, eye damage, hearing loss*
B. Kidney damage, congenital heart defect, eye damage
C. Lung damage, congenital heart defect, eye damage
D. Eye damage, hearing loss, cardiomegaly
E. Lung damage, congenital heart defect, hepatomegaly
16. Treatment of mycoplasmal pneumonia in newborns:
A. Erythromycin*
B. Ampicillin
C. Ceftriaxone
D. Sulfacamphocaine
E. Gentamicin
17. Which tests are performed in the diagnosis of intrauterine infections?
A. ELISA method*
B. Complete blood count
C. Urinalysis
D. Ultrasound
E. ECG
18. Which viral serotypes play the main role in the pathogenesis of neonatal herpes?
A. HSV-1 and HSV-2*
B. Influenza, parainfluenza

C. HSV-3 and HSV-4
D. Adenovirus, influenza
E. HSV-5 and HSV-6
19. Clinical signs characteristic of neonatal herpes:
A. Localized vesicular rash, fever*
B. Fever, pneumonia
C. Localized vesicular rash, carditis
D. Fever, pyelonephritis
E. Localized vesicular rash, arthritis
20. Treatment of chlamydial pneumonia in newborns:
A. Clarithromycin*
B. Ampicillin
C. Ceftriaxone
D. Sulfacamphocaine
E. Gentamicin

CASE STUDIES

Clinical case №1.

A 3 month old infant comes with a white area in the eye. On examination child has no social smile, no head control, microcephaly is present. The mother says she had a history of fever with rash during her pregnancy. Child has a weight of 3.9 kgs and length of 55 cms, having a birth weight of 2.1 kgs.

What is the most probable cardiac finding in this child?

A. Tetralogy of Fallot

B. Double outlet right ventricle

C. Atrial septal defect

D. Patent Ductus Arteriosus

Answer – congenital rubella syndrome - D. Patent Ductus Arteriosus. In the child: White spot in the eye → congenital cataract, no social smile, no head control → developmental delay, Microcephaly, Mother had fever with rash during pregnancy → suspicion of Congenital Rubella Syndrome (CRS). The classical triad of Congenital Rubella Syndrome includes: Cataract, Deafness, Congenital heart disease.

Clinical case №2.

A mother develops acute varicella 3 days before her delivery. What is the neonatal disease that can occur?

A. Disseminated neonatal varicella

B. Neonatal zoster

C. Asymptomatic as maternal antibodies will be transferred

D. Congenital varicella syndrome

Answer – A. Disseminated neonatal varicella. If the mother develops acute varicella within 5 days before delivery or up to 2 days after delivery, the newborn is at very high risk of developing disseminated neonatal varicella. This is because the mother has not yet had time to produce protective IgG antibodies and transfer them to the fetus across the placenta. Therefore, the infant is exposed to the virus without passive immunity, leading to severe, often life-threatening generalized infection. Congenital varicella syndrome occurs only if the mother is infected during the first or early second trimester (before 20 weeks), and presents with limb hypoplasia, cicatricial skin lesions, ocular defects, and neurologic abnormalities. Neonatal zoster happens when a child who was exposed in utero develops shingles later in childhood, not immediately after birth. Option C is incorrect because maternal antibodies are not yet available at this stage.

Clinical case №3.

In the CMV infection late during the pregnancy, what is the common isolated manifestation that can occur?

A. Isolated PDA

B. Sensorineural Hearing loss

C. Cataract

D. Microcephaly

Correct Answer: B. Sensorineural Hearing Loss. Cytomegalovirus (CMV) is the most common congenital viral infection. When infection occurs late in pregnancy, the baby is usually not severely affected systemically, but can develop isolated sensorineural hearing loss. CMV is in fact the leading non-genetic cause of sensorineural hearing loss in newborns and children.

Clinical case №4.

The treatment of neonatal varicella acquired during the perinatal period is done using all EXCEPT

A. Acyclovir

B. IV Immunoglobulin

C. Foscarnet

D. Varicella Zoster immunoglobulin

Correct Answer: C. Foscarnet. Management of neonatal varicella includes: IV Acyclovir (first-line antiviral treatment), Varicella-Zoster Immune Globulin (VZIG) for prophylaxis or early disease, IV Immunoglobulin (IVIG) may be considered in severe cases, Foscarnet is not used in the treatment of neonatal varicella. It is typically reserved for resistant CMV or acyclovir-resistant HSV infections, not for VZV in neonates.

Clinical case №5.

Which of the following is true about congenital CMV?

a. It is most common intrauterine infection, second to syphilis

b. Blood PCR is best to diagnose within 2–3 weeks of life

c. Asymptomatic patients have risk of SNHL

d. 30–40% are symptomatic at birth

Correct Answer: *Asymptomatic patients have risk of SNHL (Sensorineural Hearing Loss).* Congenital CMV is actually the most common congenital infection (more common than syphilis). Diagnosis: CMV PCR in blood or urine, but it must be performed within the first 3 weeks of life to distinguish congenital from postnatal infection. 90% of infected newborns are asymptomatic at birth, but about 10–15%

of them may later develop sensorineural hearing loss (SNHL) or neurodevelopmental delay. Only 10% of congenitally infected infants are symptomatic at birth (not 30–40%).

Clinical case №6. A 4-month-old child, who is born to HIV-positive mother, has recurrent diarrhoea. What should be done next?

A) Stop breast feed & start ART

B) HIV dried blood spot PCR

C) HIV Antibodies detection

D) IgM for Giardiasis and antibodies

Correct Answer: B. HIV dried blood spot PCR. In children <18 months, antibody testing is not reliable (maternal IgG persists up to 24 months). Diagnosis requires virological tests (HIV DNA PCR, HIV RNA PCR, or dried blood spot PCR). In this scenario (4 months + recurrent diarrhea in an HIV-exposed infant) → the next step is HIV virological testing, not antibody detection. Stopping breastfeeding and starting ART immediately (Option A) is incorrect until diagnosis is confirmed.

Assessment Criteria

№	Mastery (%) / Score	Grade	Level of Student Knowledge
1.	90–100	Excellent “5”	Makes correct decisions and conclusions based on the situation. Uses additional literature (in native and English languages) when preparing for practical classes. Knows neonatal anatomy, physiology, and hygiene, explains clearly. Independently analyzes intrauterine diseases. Conducts patient examination independently, makes the correct diagnosis, and recommends treatment and prevention plans. Actively participates in interactive games. Correctly solves case studies, fully justifies the answers. Actively participates in TMI discussions, asks questions, and adds comments. Performs practical skills clearly and correctly, understands the purpose. Has good knowledge of sanitary and preventive measures of diseases.
2.	70–89	Good “4”	Actively participates in interactive games. Correctly solves case studies but does not prescribe full treatment and does not know the exact dosage of medications. Knows neonatal AFH and explains clearly. Has complete knowledge of etiology, pathogenesis, and clinical features of intrauterine diseases, performs differential diagnosis, prescribes treatment, but cannot provide prevention. Performs practical skills step by step. Collects anamnesis correctly, knows how to examine the patient, makes a presumptive diagnosis. Can analyze laboratory tests. Actively participates in TMI discussions. Correctly solves case studies, makes a diagnosis, but cannot prescribe treatment and prevention.
3.	60–69	Satisfactory “3”	Correctly solves case studies but cannot justify the diagnosis. Knows respiratory system AFH and explains clearly. Has complete knowledge of the etiology, pathogenesis, and clinical features of bronchitis, but cannot perform differential diagnosis or prescribe treatment. Performs practical skills step by step, but makes mistakes. Collects anamnesis correctly, knows how to examine the patient, but cannot determine the severity of the disease. Partially analyzes laboratory tests. Actively participates in TMI discussions.
	59 and below	Unsatisfactory “2”	Attends classes in uniform, has a notebook and stethoscope, but is unprepared for the lesson.

Assessment of student knowledge and control criteria
Forms of current assessment (CA) of practical training in "Outpatient polyclinic pediatrics".

Grade	Appropriation (%) and in points	The student's level of knowledge

Main literature:

Review of Pediatrics & Neonatology 6th EDition 2020

Additional literature:

Comprehensive review series "CRS PAEDIATRICS"Active Recall Based Integrated Edition 2021

Internet sites:

Amboss.com

Lecturio.com

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13 noyabr 2025 yil. **9372-son**

Toshkentdavlat tibbiyot universiteti Ilmiy kengashining 2025-yil

29-oktyabrdagi 4-sonli bayonnomasidan ko‘chirma

Ilmiy kengash raisi: t.f.d., professor Sh.A.Boymuradov

Ilmiy kotib: t.f.d., professor G.A.Ismailova

Qatnashdilar: kengash a’zolari (118 kishi)

Kun tartibi:

4. O‘quv, o‘quv-uslubiy qo‘llanmalar, monografiya va uslubiy tavsiyanomalar tasdig‘i.

ESHITILDI:

Toshkent davlat tibbiyot universiteti O‘quv-uslubiy departamentning O‘quv-metodik ta’minot bo‘limi boshlig‘i J.A.Anvarov so‘zga chiqib, Oilaviy tibbiyotda bolalar kasalliklari kafedrasi xodimlari G.A.Yusupova, N.A.Israilova, G.X.Iskanova, D.R.Dinmuxammadiyevalar tomonidan ingliz tilida tayyorlagan “Intrauterine infection in children” nomli o‘quv uslubiy qo‘llanma bilan Ilmiy kengash a’zolarini tanishtirdi va tasdiqlash uchun ovozga qo‘ydi.

QAROR QILINDI:

Toshkent davlat tibbiyot universiteti Oilaviy tibbiyotda bolalar kasalliklari kafedrasi xodimlari G.A.Yusupova, N.A.Israilova, G.X.Iskanova, D.R.Dinmuxammadiyevalar tomonidan ingliz tilida tayyorlagan “Intrauterine infection in children” nomli o‘quv uslubiy qo‘llanmasi tasdiqlansin.

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