



TORCH Infections

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Overview

- Toxoplasmosis
- Other (syphilis)
- Rubella
- Cytomegalovirus (CMV)
- Herpes simplex virus (HSV)
- Intrauterine transmission of these infections to the fetus produces multiple symptoms when the child is born
- Maternal risk factors include lapsed immunizations, sexually transmitted infections, and animal exposures during pregnancy.
 - Timing of maternal infection is a key epidemiologic factor because fetal damage usually depends on the gestational age.
 - With the exception of HSV, infections during the first trimester have the worst outcome

Kahoot! - Pretest

- <https://play.kahoot.it/v2/?quizId=6b7139c2-a26c-44f3-bf51-a006c1f8e709>

Case - HPI

- 11 month year old F presenting with fever
- Tmax 104
- No pmhx (vaccines UTD)
- Less enthusiastic to eat or drink, and sleepy, but always easily rousable
- NBNB emesis x1, otherwise eliminating appropriately
- abnormal movements: three discrete abnormal movement episodes, characterized by flailing of the arms/legs in a single lunge type movement lasting < 1 second each
- Birth Hx: Ex-38wk, s/p pCS for failure of descent. ROM 28h, apgars 9/9. No NICU stay, d/c with Bili HIR

Case (cont.) - Exam

- WD/WN/WH female in NAD. Cries at times, but consolable.
- NC/AT. Conjunctiva pink, sclera anicteric. EOMI/PEARL at 4mm. MMM. OP without pharyngeal erythema or exudates. TM pearly gray bilaterally with normal color and contour of bilateral external auditory canals. There is a single small lesion on the R lower lip
- Supple
CTA
- RRR +S1/S2, no S3/S4, no murmurs
- S/NT/ND
- No edema
- Awake. Oriented appropriate per age. Normal tone. CN II-XII intact. Motor 5/5
UE/LE. SILT
- Brisk cr. Good skin turgor without tenting. No rashes

Newborn Screening

- Asymptomatic infants generally are not screened for congenital infections, with the following exceptions:
- Toxoplasmosis – Some European countries and a few select states in the United States have adopted universal newborn screening for toxoplasmosis
- Cytomegalovirus (CMV) – Targeted newborn screening for congenital CMV infection (ie, testing infants who fail the newborn hearing screen) is performed in some institutions.

Screening During Pregnancy

- Initial Visit:
 - Documentation of immunity to rubella and varicella
 - Testing for syphilis, hepatitis B antigen, and chlamydia
 - Opt-out approach to human immunodeficiency virus testing
- Consider repeat STD screen 32-34wk in high risk patients

Organism	Maternal Infection*	Fetal Neonatal Infection* (Attack Rate)	Number of Infected Newborns†	Symptomatic Children† (% of infected)
Toxoplasmosis	2	0.8 (40%)	3,040	700 (23%)
Cytomegalovirus	7.6	3.4 (40%)	11,552	1,906 (16.5%)
Herpes Simplex	7.6	2.3 (30%)	8,740	3,496 (40%)
Hepatitis C	114	5.7 (5%)	5,700	4,560 (80%)
Parvovirus B19	0.9	0.3 (33%)	1,140	38 (3%)
HIV	2	0.5 (25%)	1,900	1,900 (100%)
Syphilis	1.6	0.8 (50%)	304	304 (100%)
GBS sepsis	210	105‡ (50%)	399,000	6,200 (1.5%)

* per 1000 births.

† Based on 3.8 million births per year in the United States.

‡ Colonized only.

Table 1
Worldwide prevalence estimates of selected TORCH infections

	Worldwide Prevalence	US Prevalence of Congenitally Acquired Disease in the United States	Seropositivity in Women of Childbearing Age ^a	
			Low Prevalence (%)	High Prevalence (%)
Toxoplasmosis	201,000 ^b	10–33/100,000 live births	11 (Europe)	77 (South America)
<i>Treponema pallidum</i>	36.4 million	7.8/100,000 live births	0.67 (North America)	10 (Central Africa)
CMV	Unavailable	800/1000,000 live births	30–50 (United States)	>90 (South America)
Hepatitis B	240 million	<0.1/1000,000 US population	1.3 (North America)	8.7 (west sub-Saharan Africa)
Hepatitis C	130–150 million	<0.1/100,000 US population	1.2 (North America)	>10 (Middle East, Eastern Asia)
HIV	35.3 million	162 infants/y, 2010	0.1 (North America, Western Europe)	12 (Southern Africa)

^a Women aged 15–49 y.

^b Congenital toxoplasmosis.

Toxoplasmosis

- **Epidemiology**: 2 to 10 per 1000 births
- **Pathophysiology**: *Toxoplasma gondii* oocysts transmission occurs by ingesting the infected tissue or inhaling the fecal particles. Transplacental transmission causes congenital toxoplasmosis
- **History and Physical Distinguishing Features**: so-called classic triad of congenital toxoplasmosis consists of chorioretinitis, hydrocephalus, and intracranial calcifications
- **Special Work up**:
 - Due to the possibility of ocular involvement, an ophthalmologist should be consulted to assess for possible chorioretinitis
 - Neuroimaging studies should be conducted to assess intracranial calcifications and/or hydrocephalus
 - The most sensitive and specific testing includes a mixture of tests to assess for IgA, IgG, and IgM
- **Prognosis**: Most common late finding is chorioretinitis. there may be findings at birth, such as
 - intracranial calcifications and chorioretinitis at birth may suggest a poor prognosis with seizures and developmental delay likely
 - long-term problems: school dysfunction, hearing and visual issues, and gross motor problems that require close monitoring

Syphilis (Other)

- **Epidemiology**: incidence of congenital syphilis reflects the rate of syphilis in women of childbearing age
- **Pathophysiology**: transmitted through the placenta or vertically in the birth canal
- **History and Physical Distinguishing features**: Most neonates with congenital syphilis are asymptomatic at birth. Overt infection can manifest in the fetus, the newborn, or later in childhood.
- **Special Work Up**: The evaluation of a child with congenital syphilis depends on whether the mother was diagnosed during pregnancy and properly treated or not.
 - All children: rapid plasma reagin (RPR) to be compared to the mother's RPR titer.
 - If a mother is inadequately treated during pregnancy or the child has evidence of an elevated RPR with findings consistent with syphilis, the child needs a thorough evaluation
- **Prognosis**: Patients with syphilis will have good outcomes as long as they are recognized and diagnosed at birth and receive the correct and prompt therapy

Rubella

- **Epidemiology:** rare in developed countries with established rubella immunization programs.
- **Pathophysiology:** transmitted to the mother by aerosols/respiratory droplets and to the fetus through the placenta
- **History and Physical Distinguishing Features:** sensorineural deafness, cataracts, cardiac malformations (eg, patent ductus arteriosus, pulmonary artery hypoplasia), and neurologic and endocrinologic sequelae
- **Special Work Up:**
 - Audiology consultation: hearing loss is very common, hearing tests should be conducted in all patients.
 - Laboratory testing could include attempts to culture the virus from the nasopharynx or the assessment for IgM in the newborn.
- **Prognosis:** Patients with congenital rubella syndrome continue to have a poor prognosis with multiple organ systems impacted to include cardiac malformations, hearing loss, cataracts, and brain anomalies.

CMV, Cytomegalovirus

- **Epidemiology:** CMV has emerged as the most common congenital viral infection.
 - Maternal CMV infection during pregnancy most often results from close contact with young children, particularly children attending daycare centers
- **Pathophysiology:** transmits to the mother by blood transfusion, organ transplants, or most commonly through the mucus membrane exposure.
 - Passes either through the placenta, birth canal, or breast milk to the fetus or neonate
- **History and Physical Distinguishing Features:** Petechiae, jaundice at birth, hepatosplenomegaly, thrombocytopenia, small size for gestational age, microcephaly, intracranial calcifications, sensorineural hearing loss, chorioretinitis, and seizures

CMV, Cytomegalovirus

- **Special Work Up:** Infection is usually confirmed by the isolation of the virus within the first month of life
 - While any sterile site can be used, the urine is the most common source of isolation
 - Ophthalmology (cataracts, chorioretinitis) and audiology (hearing loss) are essential
 - Neuroimaging to assess for the presence or absence of intracranial, periventricular calcifications
- **Prognosis:** Prognosis of patients with congenital cytomegalovirus is variable.
 - If valganciclovir can be administered to symptomatic newborns in a timely manner, it has shown value

Herpes

- **Epidemiology:** Humans are the natural hosts for the herpes virus, and the newborns usually get HSV-2 as it predominantly causes genital infections
- **Pathophysiology:** HSV transmits to the mother by sexual contact and later to the fetus via either ascending infection or exposure during parturition.
 - Maternal primary infection during the third trimester has the highest percentage of neonatal infection
- **History and Physical Distinguishing Features:** Most newborns with perinatally acquired HSV appear normal at birth, although many are born prematurely.
 - Patterns: Localized to the skin, eyes, and mouth, Localized central nervous system (CNS) disease, Disseminated disease involving multiple organs
 - Intrauterine HSV infection is rare and usually results from maternal viremia associated with primary HSV infection during pregnancy. Live-born infants with congenital HSV infection may exhibit a characteristic triad of skin vesicles, ulcerations, or scarring

Herpes

- **Special Work Up:** Any child who presents with a concern for neonatal HSV should be aggressively evaluated.
 - complete sepsis evaluation to include a lumbar puncture.
 - Further evaluation and consultation may include consultation with ophthalmology, neurology, and audiology.
 - Hearing tests must be conducted
- **Prognosis:** Patients with neonatal HSV infections will have an outcome that is dependent on the presentation as well.

Clinical manifestations that are suggestive of specific congenital infections in the neonate

Congenital toxoplasmosis

- Intracranial calcifications (diffuse)
- Hydrocephalus
- Chorioretinitis
- Otherwise unexplained mononuclear CSF pleocytosis or elevated CSF protein

Congenital syphilis

- Skeletal abnormalities (osteochondritis and periostitis)
- Pseudoparalysis
- Persistent rhinitis
- Maculopapular rash (particularly on palms and soles or in diaper area)

Congenital rubella

- Cataracts, congenital glaucoma, pigmentary retinopathy
- Congenital heart disease (most commonly patent ductus arteriosus or peripheral pulmonary artery stenosis)
- Radiolucent bone disease
- Sensorineural hearing loss

Congenital cytomegalovirus

- Thrombocytopenia
- Periventricular intracranial calcifications
- Microcephaly
- Hepatosplenomegaly
- Sensorineural hearing loss

Herpes simplex virus

Perinatally acquired HSV infection

- Mucocutaneous vesicles
- CSF pleocytosis
- Thrombocytopenia
- Elevated liver transaminases
- Conjunctivitis or keratoconjunctivitis

Congenital (in utero) HSV infection (rare)

- Skin vesicles, ulcerations, or scarring
- Eye abnormalities (eg, micro-ophthalmia)
- Brain abnormalities (eg, hydranencephaly, microcephaly)

Congenital varicella

- Cicatricial or vesicular skin lesions
- Microcephaly

Congenital Zika syndrome

- Microcephaly
- Intracranial calcifications
- Arthrogryposis
- Hypertonia/spasticity
- Ocular abnormalities
- Sensorineural hearing loss

Table 2
Clinical findings associated with selected TORCH infections

	Hepatosplenomegaly	Cardiac Lesions	Skin Lesions	Hydrocephalus	Microcephaly	Intracranial Calcifications	Ocular Disease	Hearing Deficits
Toxoplasmosis	+	(-)	Petechiae/purpura, maculopapular rash	++	+	Diffuse intracranial calcifications	Chorioretinitis	(-)
<i>Treponema pallidum</i>	+	(-)	Petechiae/purpura, maculopapular rash	(-)	(-)	(-)	Chorioretinitis, glaucoma	(-)
Rubella	+	Patent ductus arteriosus, pulmonary artery stenosis, myocarditis	Petechiae/purpura	+	(-)	(-)	Chorioretinitis, cataracts, microphthalmia	++
CMV	+	+	Petechiae/purpura	(-)	++	Periventricular calcifications	Chorioretinitis	++
HSV	+	Myocarditis	Petechiae/purpura, vesicles	+	+	(-)	Chorioretinitis, cataracts	+
Parvovirus B19	+	Myocarditis	Subcutaneous edema, petechiae	(-)	(-)	(-)	Microphthalmia, retinal and corneal abnormalities	(-)

Adapted from Remington J, Klein J, Wilson C, et al, editors. Infectious diseases of the fetus and newborn infant. 7th edition. Philadelphia: Elsevier Saunders, 2011; with permission.

Patient Education

- Maternal education and early *in utero* diagnosis is very important
- Regular prenatal care and maternal health are key
- All women of childbearing age should ensure that they have their immunizations up to date
- Safe sexual practices can help eliminate the risk STI (syphilis, HIV, HSV)
- Expectant mothers who have a febrile illness during pregnancy should be sure to report that illness to their physicians
- Safe eating practices such as the avoidance of processed foods (deli meats) and eating thoroughly cooked foods can help prevent the transmission of toxoplasmosis.

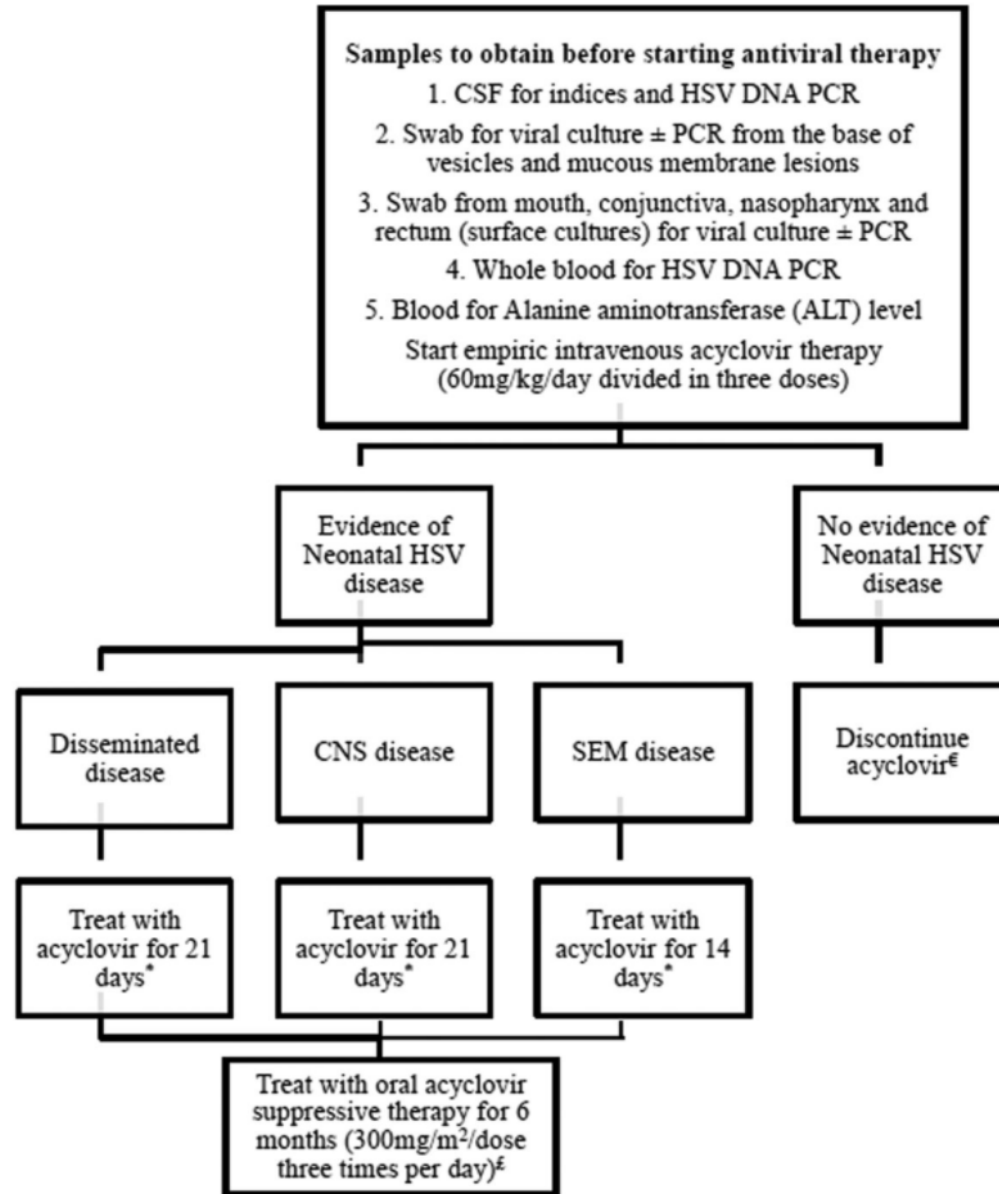
Perinatal Infection	Epidemiologic Risk Factors	Clinical Risk Factors
CMV	High-risk sexual behavior, history of STD, occupational exposure	Immunosuppression, Hepatitis, flu-like syndrome, ultrasound findings
Hepatitis B	High-risk sexual behavior, history of STD, drug abuse, high-risk populations, blood transfusion, occupational exposure	Hepatitis, immunosuppression, Positive screening serology
HIV	High-risk sexual behavior, history of STD, drug abuse, blood transfusion, high-risk populations	Immunosuppression, CD ⁴ count < 200 cells/ml ³ , positive screening serology
Syphilis	High-risk sexual behavior, history of STD, drug abuse, High-risk populations	Immunosuppression, Ulcer, rash, positive screening serology
Herpes simplex	High-risk sexual behavior, history of STD, drug abuse, high-risk populations	Painful ulcers or vesicles
Parvovirus B19	Occupational exposure	Flu-like syndrome, rash, anemia in patients with hemoglobinopathies
Rubella	Rubella nonimmune	Fever, malaise, rash, positive screening serology
Toxoplasmosis	Exposure or consumption of raw meat, failure to wash home garden produce, exposure to a recently weaned out-of-doors kitten or an ill cat	Flu-like syndrome, hepatitis, immunosuppression, Ultrasound findings
Varicella	Contact exposure, occupational exposure	Characteristic vesicular rash

Work Up Review

- Review of maternal history (evidence of rubella immunity, syphilis serology, history of herpes simplex virus [HSV], exposure to cats, etc)
 - Assessment of physical stigmata consistent with various intrauterine infections
 - Complete blood count and platelet count
 - Liver function tests (particularly important in HSV infection)
 - Radiographs of long bones
 - Ophthalmologic evaluation
 - Audiologic evaluation
 - Neuroimaging
 - Lumbar puncture

Case (cont).

- ID was consulted and recommended Acyclovir (10-15mg/kg IV q8) for at least 21 days which was started on 5/14. PICC placed
- Neurology was consulted due to potential seizure activity, and on the night of admission (5/14) she had an overnight vEEG without evidence of seizures. Neurology recommended a MRI brain w/wo contrast on 5/17 which was unremarkable.
- Multiple perioral vesicles were noted which were later swabbed and came back positive for HSV1.
- ENT was also consulted and completed bedside laryngoscope noting vesicular lesions along posterior pharyngeal wall.
- Ophthalmology was consulted and noted no herpetic lesions on 5/15
- Audiology performed a hearing screen under sedation which did not demonstrate any hearing deficits.
- All herpetic lesions resolved before discharge.



Take Away Points

- Many of the clinical syndromes for those viruses that present in the immediate neonatal period overlap with each other.
- They usually cause a rash, which can be maculopapular, petechial (blueberry muffin rash), or purpuric.
- Microcephaly, sensorineural hearing loss (particularly with CMV), and chorioretinitis may be present.
- Hepatosplenomegaly and cardiac anomalies are also frequent findings

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