TORCH Testing for Optimal Management of Perinatal infections

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Clinical Brief

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Perinatal infections account for 2–3% of all congenital anomalies. TORCH infections, which include toxoplasmosis, rubella, cytomegalovirus (CMV), and herpes simplex (HSV), are some of the most common infections associated with congenital anomalies. TORCH infections in pregnancy can cause serious fetal consequences. Therefore, proper diagnosis of maternal disease and fetal monitoring once diagnosed are extremely important. They allow clinicians to properly counsel mothers on the potential for adverse fetal outcomes when these infections are present.[1]

Toxoplasmosis

Toxoplasmosis is a disease that results from infection with *Toxoplasma gondii*, one of the world's most common parasites. Individuals become infected by eating undercooked contaminated meat, exposure to infected cat feces, or mother-to-child transmission during pregnancy.

Most healthy people with toxoplasmosis do not have any signs or symptoms because their immune system prevents illness; some may have flu-like symptoms such as body aches, headache, fever, and fatigue.[2] However, infants and those with weakened immune systems may have serious disease. Infants are most at risk of contracting toxoplasmosis if the mother becomes infected in the third trimester and least at risk if she becomes infected during the first trimester. On the other hand, the earlier in pregnancy the infection occurs, the more serious the outcome for the infant.[3]

Many early infections end in stillbirth or miscarriage. Infants who survive are likely to be born with serious problems, such as:[3]

- Seizures
- An enlarged liver and spleen
- Yellowing of the skin and whites of the eyes (jaundice)
- Severe eye infections

Only a small number of babies who have toxoplasmosis show signs of the disease at birth. Often, even infants who are infected don't develop signs—which may include hearing loss, mental disability, or serious eye infections—until their teens or later.

Preventive measures, including assessing maternal risk and counseling patients how to avoid *T. gondii*, are a primary strategy.[4] Fortunately, treatments that act by limiting parasite multiplication are also available. Medications for toxoplasmosis include pyrimethamine, sulfadiazine, and folinic acid.[4]

Rubella

Rubella, or German measles, is caused by a virus that's passed from person to person. It can spread when an infected person coughs or sneezes or by direct contact with an infected person's respiratory secretions. It can also be passed on from pregnant women to their unborn children via the bloodstream.

Rubella is an acute, self-limiting viral infection. Rubella most often affects children and usually causes mild disease with few symptoms.[5] Women who are infected with rubella may develop arthritis, but the most serious consequence of rubella infection is the risk for birth defects, miscarriage, and congenital rubella syndrome (CRS). Manifestations of CRS may include low birth weight, deafness, eye disease, mental disability, and congenital heart disease.[5]

The highest risk of CRS is in countries where women of childbearing age do not have immunity to the disease (either through vaccination or from having had rubella). Before the introduction of the vaccine, up to 4 babies in every 1000 live births were born with CRS.[6]

To-date, four WHO regions have established goals to eliminate this preventable cause of birth defects. In 2015, the WHO Region of the Americas became the first in the world to be declared free of endemic transmission of rubella.[6]

As with toxoplasmosis, prevention is a primary strategy against rubella; a very effective vaccine is available that produces a 95% seroconversion rate. In the United States and other countries, rubella vaccine is available as part of the measles, mumps, and rubella (MMR) vaccine, which may also include varicella.[7] No specific medication exists to treat rubella; mild symptoms are typically managed with bed rest and medications to manage fever as needed.[5]

Cytomegalovirus

Cytomegalovirus (CMV) is the most common cause of congenital and perinatal infections worldwide. Most people don't know they have CMV, because healthy individuals' immune systems usually prevent the virus from causing illness. But the virus, which remains dormant in the body, can cause complications during pregnancy and in those with a weakened immune system. The virus spreads through bodily fluids, and a pregnant person can pass it on to the unborn baby.[8]

Also known as HCMV, CMV, or human herpesvirus 5 (HHV-5), cytomegalovirus is the most commonly transmitted virus to a developing fetus.

CMV modes of transmission:[9]

- Touching the eyes, inside of the nose, or mouth after coming into contact with the body fluids of an infected person
- Sexual contact with an infected person
- The breast milk of an infected mother
- Organ, bone marrow, or stem cell transplantation or blood transfusions
- Birth. An infected mother can pass the virus to her baby before or during birth. The risk of transmitting the virus to the baby is higher if the mother becomes infected for the first time during pregnancy.

Most CMV infections are asymptomatic, but CMV can cause serious health problems after maternal-fetal transfer, either in utero or via breastfeeding, and in immunocompromised individuals (such as HIV-infected persons and those who have undergone organ transplantation).[8]

At birth, the majority of infected babies are asymptomatic. Some may develop signs of CMV infection over time—months or years later. Hearing loss and developmental delay are common long-occurring conditions. Some may also develop vision problems. Symptoms of CMV in immunocompetent adults can be similar to those of mononucleosis and include fever, sore throat, swollen glands, and fatigue.[8]

Treatment is not usually necessary for immunocompetent people with CMV infection, but when needed, medications to relieve symptoms may be used.[8,10] Antiviral medications, primarily valganciclovir, may be used to treat babies with signs of congenital CMV infection.[8]

Herpes Simplex Virus

Herpes simplex virus (HSV) infection causes recurring episodes of small, painful, fluid-filled blisters on the skin, mouth, lips (cold sores), eyes, or genitals. HSV is very contagious and can be transmitted by direct contact with sores or sometimes contact with an affected area even when no sores are present.

Type 1: HSV-1, or oral herpes, causes cold sores to form on the lips, gums, tongue, and inside of the mouth. In some cases, it can also cause genital herpes. Transmission of HSV-1 can occur through saliva and/or sharing such items as toothbrushes, lipsticks, and eating utensils.

Type 2: HSV-2 causes genital herpes.

HSV causes acute and recurrent infections. It is one of the most common viral infections found in humans. While most cases are mild and self-limiting, as with other TORCH diseases, HSV infection may cause generalized and fatal infection in newborns and immunocompromised people.[11]

Transmission of HSV occurs via contact of mucous membranes (eyes, genitals, or mouth) with a seropositive individual during active viral shedding.[11] The majority of infants (up to 60%) born to mothers with symptoms at time of delivery develop HSV infection.[12] When present in infants, HSV infections often produce very severe disease with high mortality and morbidity.

No current antiviral treatments can eradicate HSV infection, and treatment of a first oral or genital infection does not prevent chronic infection of nerves. However, during recurrences, antiviral drugs such as acyclovir, valacyclovir, and famciclovir may relieve discomfort slightly and help symptoms resolve a day or two sooner. Infants require systemic antiviral medications, usually over a long (6-month) course, to provide sustained viral suppression.[13] Early, effective treatment of HSV infections is critical for infants.[1]

TORCH Testing

TORCH testing is typically performed in women before or as soon as pregnancy is detected. Babies with symptoms consistent with TORCH syndrome may also be tested.[1] TORCH testing screens blood samples for the presence of antibodies to **T**oxoplasmosis, **R**ubella, **C**ytomegalovirus (CMV), and **H**erpes simplex virus (HSV).[14]

How TORCH testing is used, and when clinicians request it

TORCH testing is used to identify when a person has recently had infection (IgM antibodies present), had infection in the past (IgG antibodies present), or has never been exposed to the infectious organisms (neither antibody present).

This testing is often performed in the first trimester of pregnancy.[1] If the suspected exposure or infection was very recent (within a few days), the clinician may repeat TORCH testing to rule out a false-negative result.[14]

Patient history and risk factors guide prenatal and maternal testing for TORCH.

The TORCH test panel is requested if a pregnant woman is suspected of having any of the TORCH infections. Rubella infection during the first 16 weeks of pregnancy presents major risks for the unborn baby. If a pregnant woman has a rash and other symptoms of rubella, laboratory tests are required to make the diagnosis. A physician cannot tell if a person has rubella by their clinical appearance, since other infections may look the same. Women infected with toxoplasma or CMV may have flu-like symptoms that are not easily differentiated from other illnesses. Antibody testing is used to help the physician diagnose an infection that may be harmful to the unborn baby.

The TORCH panel may also be requested for the newborn if the infant shows any signs suggestive of these infections, such as exceptionally small size relative to the gestational age, deafness, mental retardation, seizures, heart defects, cataracts, enlarged liver or spleen, low platelet level, or jaundice.

TORCH test results

TORCH test results are either positive or negative, indicating the presence or absence of IgG and IgM antibodies for each of these infectious agents (toxoplasma, rubella, CMV, and HSV). Any positive results should be validated with additional testing to confirm diagnosis.[14]

TORCH blood tests can determine if the person has had a recent infection, a past infection, or has never been exposed to the virus. Patients who have had a recent infection with one of the TORCH organisms will have IgM antibody to the specific agent, and those with a past infection will have an IgG antibody, which is lifelong. In the case of rubella, it is also possible to be positive for IgG antibody if the person was vaccinated. If neither immunoglobulin is detectable, there has been no infection with these microorganisms. In case of previous immunity of the mother, IgG antibody will always be present in the baby due to passive transfer through the placenta. However, IgM antibodies are too big to pass through the placenta, so their isolation in the baby's blood will indicate a recent (or congenital) infection.

Likewise, the presence of IgM antibody in the pregnant woman suggests a new infection with or active replication of the virus or parasite.[14] IgG antibody in the pregnant woman may be a sign of past infection or vaccination with one of these infectious agents. A positive test does not provide

information about when the infection occurred. By testing a second blood sample drawn 2 weeks later, the level of antibody can be compared. If the second blood draw shows an increase in IgG antibody, it may indicate a recent infection.

Toxoplasmosis Testing

The indirect diagnosis of toxoplasmosis can be made by serologic testing in immunocompetent patients with suspected acute disease.

Diagnosis can also be made by direct observation of the parasite in stained tissue sections, cerebrospinal fluid (CSF), or other biopsy material. These techniques are used less frequently because of the difficulty of obtaining these specimens.

Toxoplasma antibody test interpretation

IgM	IgG	Possible Interpretation
Negative	Positive	Past infection
Negative	Negative	No infection or very early infection; no previous exposure
Positive	Negative	Early infection; in a newborn, indicates congenital infection
Positive	Positive	Current infection; chronic infection; could indicate re-activation; IgM may be positive for several months after the infection resolves

Source: https://www.testing.com/tests/toxoplasmosis-testing

Both Toxo IgM and Toxo IgG assays are available on the ADVIA Centaur® systems and Atellica® IM Analyzer. With their very high sensitivity and specificity, they help ensure result accuracy. The Toxo IgG assay has a wide measuring range of 0.5–700.0 IU/mL, which helps provide clinicians with critical information on the assessment of a patient's immunological response.

Rubella Testing

Antibody detection is the primary laboratory testing method for diagnosis of rubella. Both IgM and IgG antibody tests can be used to differentiate between an acute or recent rubella infection. The IgG antibody test can also be used to assess the immune status of the patient, either from past infection or vaccination, and is often used to determine immunity to rubella in pregnant women.

Rubella antibody test interpretation

Age	IgM	IgG	Interpretation
Adult/Child	Positive	Positive or negative	Recent infection
Adult/Child	—	Positive	Prior infection or vaccination, immune
Newborn	Positive		Recent postnatal or congenital infection
Newborn	—	Positive	Mother has passed antibodies to baby during pregnancy; this passive immunity may last for up to 6-12 months.
Any age	Negative	Negative	No current or prior infection; not immune; no or low immune response due to weakened immune system

Source: https://www.labcorp.com/help/patient-test-info/rubella-test

Rubella IgM and IgG assays are available on the ADVIA Centaur systems and Atellica IM Analyzer offering further consolidation of TORCH testing onto one platform. Good sensitivity, specificity, and precision help ensure result accuracy and consistency.

Cytomegalovirus Testing

In addition to CMV IgM and IgG assays, IgG avidity assays that measure the binding strength between IgG antibodies and virus can help distinguish a primary CMV infection from a past infection. Following primary CMV infection, IgG antibodies first have low binding strength (low avidity) and then over 2–4 months mature to high binding strength (high avidity).[8]

Diagnosis of acute maternal CMV infection by the presence of IgM and low IgG avidity requires confirmation of fetal infection, which is typically performed by CMV polymerase chain reactive (PCR) testing of the amniotic fluid. To diagnose congenital CMV infection, testing should be performed within the first 3 weeks of life, because testing after this period does not differentiate intrauterine from perinatal acquisition of CMV infection. Viral culture of the urine and saliva continue to be the gold standard for diagnosis of congenitally infected infants.[8]

CMV antibody test interpretation

CMV, IgM	CMV, IgG	Possible Interpretation
Negative	Negative	• No current or prior infection; no immunity (person is susceptible to primary infection) • Symptoms due to another cause • OR immune system cannot produce adequate amount of antibody (immunocompromised)
Positive	Negative	• Recent active primary infection • OR re-exposure to CMV • OR reactivation of latent CMV *Result is NOT diagnostic of primary infection
Positive	Positive (with four fold increase in titer between first sample and another collected later (acute and convalescent samples	Likely active primary or reactivated latent infection
Negative	Positive	Past exposure (immunity to primary infection); latent infection

Source: https://www.labcorp.com/help/patient-test-info/cytomegalovirus-cmv-tests)

Unlike tests from other assay manufacturers, the ADVIA Centaur and Atellica IM CMV IgG and CMV IgM assays have no equivocal zone, thereby producing potentially faster results and reducing costs by decreasing the need for repeat testing.

Herpes Simplex Virus Testing

There are various testing options to diagnose HSV infection, depending on patient history and status:[15]

- Antibody tests for HSV (e.g., enzyme immunoassays)
- Viral cultures from the oropharynx, nasopharynx, skin lesions, mucous membrane (eye and mouth) swabs, rectal swabs, blood buffy coat, and CSF
- PCR testing of CSF, skin lesions, mucous membranes, and blood
- Direct immunofluorescent antibody staining of skin lesions

HSV 1 and HSV 2 Antibody Testing

To treat the patient appropriately, it is important to be able to discriminate between HSV-1 and HSV-2. Serological HSV type-specific serology has a number of applications, e.g., to guide duration and dosage of antiviral therapy, allow for stringent epidemiological analyses, evaluate the efficacy of HSV vaccine candidates, and help the clinician during counseling of couples when one has genital herpes.[16]

HSV test interpretation

Clinical Signs	HSV serology		PCR		Interpretation
	HSV-1 IgG	HSV-2 IgG	HSV-1	HSV-2	
Primary genital herpes	N	N	P	N	Acute HSV-1 infection
	N	N	N	P	Acute HSV-2 infection
	P	N	N	P	Acute HSV-2 infection, HSV-1 latency
Recurrent genital herpes	P	N	P	N	Recurrent HSV-1 infection
	P	P	P	N	Recurrent HSV-1 infection, HSV-2 latency
	N	P	N	P	Recurrent HSV-2 infection
	P	P	N	P	Recurrent HSV-2 infection, HSV-1 latency
No genital herpes lesions	N	N	N	N	Susceptibility
	P	N	N	N	Past HSV-1 infection (HSV-1 latency)
	N	P	N	N	Past HSV-2 infection (HSV-2 latency)
	P	P	N	N	Past HSV-1 and HSV-2 infection (HSV-1 and HSV-2 latency)
	P	N	P	N	Asymptomatic shedding of HSV-1, past HSV-1 infection (HSV-1 latency)
	N	P	N	P	Asymptomatic shedding of HSV-2, past HSV-2 infection (HSV-2 latency)
	P	P	P	N	Asymptomatic shedding of HSV-1, past HSV-1 and HSV-2 infection (HSV-1 and HSV-2 latency)
	P	P	N	P	Asymptomatic shedding of HSV-2, past HSV-1 and HSV-2 infection (HSV-1 and HSV-2 latency)

Source: Adapted from Sauerbrei A. Infect Drug Resist. 2016;9:129-4.

The ADVIA Centaur HSV1 and HSV2 assays enable the laboratory to be more efficient. Unlike other automated HSV assays, the Siemens Healthineers assays have no equivocal zone, so all initial results can be reported immediately. Results in the equivocal zone require repeat testing, leading to longer turnaround time, the need for additional resources, and an overall increase in costs.

Early identification of infection and subsequent clinical intervention can dramatically reduce vertical transmission rates, making access to TORCH testing an important component of adequate prenatal care. Screening for common infectious agents using the TORCH panel may help to prevent many potential birth defects, as some of the TORCH infections can be effectively treated if the mother is diagnosed early in her pregnancy.

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We are a team of 66,000 highly dedicated employees across more than 70 countries passionately pushing the boundaries of what's possible in healthcare to help improve people's lives around the world.

Product availability may vary from country to country and is subject to varying regulatory requirements. Please contact your local representative for availability.

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