# The Term Newborn
## Congenital Infections

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**KEYWORDS**

• Term • Newborn • Congenital • Infection

**KEY POINTS**

- Congenital cytomegalovirus infection is the most common congenital infection worldwide; however, many infants remain undetected because of mild or asymptomatic infection.
- Perinatally acquired human immunodeficiency virus (HIV) infection can largely be prevented through early maternal HIV testing, initiation of effective maternal antiretroviral treatment, prompt initiation of neonatal antiretroviral prophylaxis, and avoidance of maternal breastmilk.
- Recognition, diagnosis, and management of infants with suspected congenital infection can be challenging for newborn care providers, especially when emerging pathogens that are not included in the TORCH pneumonic (toxoplasmosis, rubella, cytomegalovirus, and herpes simplex virus) are being considered.
- Recent advances in diagnostic testing, chemoprophylaxis, and treatment have led to improved outcomes in certain congenital infections.

### INTRODUCTION

Maternal bacterial, viral, and parasitic pathogens can be transmitted across the placenta to the fetus, resulting in congenital infection with sequelae ranging from asymptomatic infection to severe debilitating disease and still birth.[1]

The TORCH pneumonic includes toxoplasmosis, rubella, cytomegalovirus (CMV), and herpes simplex virus; however, it provides a limited description of the expanding list of pathogens associated with congenital infection. Human immunodeficiency virus (HIV), syphilis, enterovirus, parvovirus, varicella virus, Chagas disease, and several emerging pathogens such as Zika virus and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have also been associated with intrauterine transmission and should be considered in infants with suspected congenital infection.[2] Newborn care

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providers frequently deviate from recommendations on the evaluation of infants with congenital infections.[3] Traditionally used tests such as TORCH titer screens and total immunoglobulin (Ig) M for infants with isolated growth restriction or who are small for gestational age have limited value based on current evidence.[4–6]

This article focuses on the evaluation and management of infants with common congenital infections such as CMV, and infections that warrant early diagnosis and treatment to prevent serious complications, such as toxoplasmosis, HIV, and syphilis. Zika virus and Chagas disease remain uncommon and are discussed briefly.

## CONGENITAL CYTOMEGALOVIRUS INFECTION

### *Disease Overview*

CMV is a ubiquitous double-stranded DNA virus that belongs to the herpesvirus family. Similar to varicella zoster virus and herpes simplex virus, CMV establishes latency after primary infection and can reactivate intermittently, including during pregnancy. In high-income countries, congenital CMV is a leading cause of sensorineural hearing loss (SNHL), and is the most common congenital infection, with an estimated incidence of 0.6% to 0.7% of all live births.[7,8] In the absence of universal newborn screening for CMV, most infants with congenital infection remain undetected because almost all remain asymptomatic at birth. Infants with symptomatic infection are important to recognize because recent clinical trials have shown that early antiviral treatment can decrease the risk of serious long-term sequelae such as hearing loss and neurodevelopmental delay.[9]

### *Transmission and Pathogenesis*

CMV is transmitted by direct contact with infected body fluids, including saliva, urine, blood, breastmilk, semen, and genital tract secretions. Women with no prior history of CMV infection are susceptible to primary infection during pregnancy, which may occur after household or occupational exposure to young children or other symptomatic or asymptomatic individuals shedding CMV.[10] Intrauterine CMV transmission occurs when CMV crosses the placenta to infect the fetus during a primary or nonprimary maternal CMV infection.

The rate of CMV transmission to the fetus and the risk of symptomatic disease in infected infants is higher after primary maternal CMV infection compared with nonprimary infection.[7,11] Infants infected in the first trimester (<13 weeks) after primary maternal CMV infection have a much higher risk of SNHL (24%) and other long-term neurologic sequelae (32%) compared with infants infected later in pregnancy.[12] Because of the challenges in diagnosing nonprimary maternal CMV infection, it is unclear whether the timing of nonprimary infection during pregnancy is associated with risk of symptomatic disease or SNHL in infected infants.

Although the risk of vertical transmission following primary maternal CMV infection is high (30%–35%), the proportion of infants with congenital CMV infection attributable to primary maternal infection is low (22.6%). This difference occurs because only 1% to 4% of CMV seronegative women develop primary CMV infection during pregnancy. Furthermore, most women of reproductive age are CMV seropositive and therefore not susceptible to primary CMV infection.[13,14]

### *Epidemiology*

CMV infection is common among women of reproductive age worldwide, with seroprevalence approaching 100% in some resource-limited countries.[15] Rates of infection vary widely by age, race, and socioeconomic factors.[16] In a large study of the

**Table 1**
**Estimated burden of congenital infection attributable to type of maternal cytomegalovirus infection and rate of cytomegalovirus transmission**

| Type of Maternal CMV Infection | Description | Rate of Transmission to Fetus (%) | Proportion of All Congenital CMV Infections Attributable to Type of Maternal Infection in the United States (%) |
|---|---|---|---|
| Primary | CMV infection in women without prior CMV infection and with no preexisting immunity | 30–35 | 22.6 |
| Nonprimary | Reactivation of latent CMV infection or reinfection with a new strain of CMV in women with prior CMV infection and preexisting immunity | 0.1–1.7 | 77.4 |

US population, the overall age-adjusted CMV seroprevalence for girls and women aged 6 to 49 years was estimated to be 55.5%. CMV seropositivity was associated with older age, non-Hispanic black race, Mexican American ethnicity, foreign place of birth, low household income and education level, and high crowding index. Although most non-Hispanic black women and Mexican American women develop primary CMV infection during the peak reproductive years between adolescence and their 30s, almost all infants with congenital CMV infection are born to CMV-seropositive women who develop nonprimary infections during pregnancy (Table 1).[16] As the mean age of primiparous mothers increases in the United States, a higher proportion will be CMV seropositive during pregnancy.[17] This point is important to consider because efforts to prevent primary maternal CMV infection through vaccines or behavioral measures may have a limited impact in older mothers who have already had CMV infection.

### *Clinical Presentation*

Approximately 85 to 90% of infants with congenital CMV infection are asymptomatic at birth; however, approximately 13.5% of these infants may develop long-term complications. In symptomatic infants the risk is much higher with 40% to 58% developing permanent sequelae.[7,8] The clinical features and laboratory and imaging findings of infants with symptomatic infection are summarized in Table 2.[18] Infants with isolated hearing loss have been characterized as both symptomatic and asymptomatic subjects in clinical trials and are now considered a distinct cohort by many experts.

The overall mortality associated with congenital CMV infection is estimated to be 4%, with the highest mortality in infants who present with severe or fulminant disease at birth.[19]

### *Diagnosis*

A significant challenge for health care providers is knowing which infants to test for evidence of congenital CMV infection. In infants with mild disease or nonspecific signs

**Table 2**
**Clinical, laboratory, and imaging findings in symptomatic congenital cytomegalovirus infection**

| | |
|---|---|
| Clinical Features | Prematurity<br>Small for gestational age (≤2 SD for gestational age)<br>Microcephaly (≤2 SD for gestational age)<br>Petechiae or purpura, blueberry muffin rash<br>Jaundice<br>Hepatosplenomegaly<br>Lethargy, hypotonia, seizures, poor sucking reflex |
| Laboratory Abnormalities | Anemia<br>Thrombocytopenia<br>Leukopenia, isolated neutropenia<br>Hepatitis (increased liver aminotransferase or bilirubin level)<br>CSF abnormalities such as increased protein levels |
| Neuroimaging Abnormalities[a] | Intracranial calcifications, periventricular cysts, ventriculomegaly, white matter abnormalities, cortical atrophy, migration disorders, cerebellar hypoplasia, lenticulostriatal vasculopathy |
| Hearing Evaluation | SNHL affecting 1 or both ears |
| Ophthalmologic Examination | Chorioretinitis<br>Retinal hemorrhage, optic atrophy, strabismus |

*Abbreviation:* CSF, cerebrospinal fluid; SD, standard deviation.
[a] Head ultrasonography, magnetic resonance imaging or computed tomography.

and symptoms, a high index of suspicion is required. The following indications should prompt testing for CMV infection[18]:

- Infants born to women with a history of suspected or confirmed primary CMV infection during pregnancy
- Infants with signs and symptoms consistent with congenital CMV infection (**Table 2**)
- Infants with confirmed SNHL. Some experts recommend CMV testing in infants with suspected SNHL if a formal audiologic evaluation cannot be done before 3 weeks of life
- Infants with prenatal or postnatal neuroimaging findings consistent with congenital CMV infection

Infants with congenital CMV infection shed large amounts of virus in urine and saliva for prolonged periods. Historically, the gold-standard technique for establishing a diagnosis was standard or rapid (shell vial) viral culture of urine or saliva. However, recent clinical studies have shown that polymerase chain reaction (PCR) is more sensitive than viral culture and has lower costs and much shorter turnaround time.[20] In high-income countries, testing for congenital CMV by urine or saliva PCR is therefore preferred and should be done before the first 2 to 3 weeks of life, because detection of CMV beyond this period cannot reliably distinguish postnatal from congenital infection (**Table 3**). When congenital CMV infection is suspected in infants older than 3 weeks, a PCR assay can be performed on newborn dried blood samples (Guthrie cards) if available; however, a negative result does not rule out CMV infection because the sensitivity is much lower compared with PCR of urine or saliva.[21]

Although false-positive results are uncommon, all infants with a positive urine or saliva PCR or rapid viral culture result should have a confirmatory PCR test performed

**Table 3**
**Diagnosis of congenital cytomegalovirus infection**

| Sample | Sample Method | Test Method | Sensitivity (%) | Specificity (%) | Advantages | Disadvantages |
|---|---|---|---|---|---|---|
| Saliva | Use a sterile swab to collect saliva from the inside of an infant's mouth between the cheek and lower gum before breastfeeding, or >1 h after breastfeeding. Place swab in a dry storage tube or transport medium | PCR | 97.4–100 | 99.9 | Sample collection is noninvasive, quick and can easily be performed at the bedside | False-positive results can occur when infant saliva is contaminated with maternal breast milk or maternal genital tract secretions during delivery |
| Urine | Use a sterile urine collection bag or place sterile cotton balls in the diaper[a] | PCR | 93–100 | 99–100 | — | Urine collection can be challenging, especially in preterm infants |
| Blood | CMV antigen<br>CMV serology (IgG, IgM)<br>Dried blood spot PCR<br>Whole-blood or plasma quantitative CMV PCR[b] | Not routinely recommended for the diagnosis of congenital CMV | | | | |

[a] Urine obtained from sterile cotton balls placed in the diaper was reported to be less sensitive when rapid CMV culture was compared with PCR.
[b] Blood CMV PCR should not be used to rule out early CMV infection because not all infants with symptomatic disease have detectable viremia.

on either urine or saliva. A single negative urine CMV PCR result is sufficient to exclude congenital CMV infection.[18]

### *Management of Infants with Congenital Cytomegalovirus Infection*

Asymptomatic infants with congenital CMV infection often do not require antiviral treatment or additional supportive care. A clinical trial is being conducted to determine whether antiviral treatment of asymptomatic neonates without hearing loss decreases the risk of delayed-onset hearing loss during the first 18 months of life (https://clinicaltrials.gov/ct2/show/NCT03301415).

The optimal management of asymptomatic infants with isolated hearing loss remains unclear; however, clinical trials are being conducted to evaluate the effectiveness of antiviral treatment on hearing and developmental outcomes (https://clinicaltrials.gov/ct2/show/NCT03107871). With little evidence to recommend routine antiviral treatment of asymptomatic infants, health care providers should discuss the risks and potential benefits of antiviral treatment with parents and caregivers.

Infants with symptomatic disease should have a comprehensive evaluation for associated complications, as summarized in **Table 4**.

Health care providers should observe universal or standard precautions when caring for infants with congenital CMV infection. Gloves should be worn with any potential exposure to blood, urine, saliva, or other body fluids. Although transmission of CMV from breast milk can lead to postnatal CMV infection in infants without congenital infection, maternal breastfeeding of infants with congenital CMV infection is not contraindicated. In infants who already have CMV infection, postnatal exposure to maternal CMV virus in breast milk is unlikely to lead to a new infection or worse outcome.

**Table 4**
**Management of symptomatic infants with congenital cytomegalovirus infection**

| | |
|---|---|
| Physical Examination | Evaluate for clinical features of infection (Table2) |
| Laboratory Tests | CBCd<br>LFTs<br>Creatinine, BUN<br>Blood CMV PCR viral load at baseline has been associated with adverse CNS Outcomes; however, routine monitoring is not recommended |
| Hearing Assessment | Evaluate with brain stem auditory evoked response to detect SNHL |
| Ophthalmologic Evaluation | Obtain ophthalmology eye examination to evaluate for chorioretinitis |
| Neuroimaging | Obtain head ultrasonography. MRI or computed tomography imaging is recommended when there are abnormalities on ultrasonography or when there are clinical features suggestive of CNS disease, such as microcephaly or seizures |
| Antiviral Treatment | Intravenous ganciclovir or oral valganciclovir |
| Supportive Care | Treatment of CNS complications such as seizures with antiepileptic drugs<br>Management of hematologic abnormalities such as thrombocytopenia |

*Abbreviations:* BUN, blood urea nitrogen; CBCd, complete blood count with differential; CNS, central nervous system; LFTs, liver function tests.

### *Antiviral treatment and monitoring*

Infants with symptomatic congenital CMV should receive treatment with either intravenous ganciclovir or oral valganciclovir (**Table 5**) as soon as the diagnosis is confirmed and ideally before 30 days of life. Randomized controlled trials have shown that antiviral treatment improves hearing and neurodevelopmental outcomes up to 24 months of age, and that 6 months of treatment with oral valganciclovir is more effective than 6 weeks of the antiviral treatment.[9,22,23] Adverse effects associated with antiviral treatment are mostly hematologic and include neutropenia and thrombocytopenia. Increased levels of liver transaminases may also be observed.

### *Follow-up care of infants infected with cytomegalovirus*

All symptomatic and asymptomatic infants with congenital CMV infection should have periodic hearing assessments performed because hearing loss can worsen or emerge during infancy and early childhood. Formal hearing assessments performed by an audiologist are recommended every 3 to 6 months in the first year, then every 6 months until 3 years of age, and then every 12 months until 6 years of age.[18] Follow-up with an ophthalmologist, an ear, nose, and throat specialist, and a developmental specialist may also be indicated based on disease severity.

Symptomatic infants who are discharged on oral valganciclovir treatment require follow-up with a pediatric infectious disease specialist for monitoring of physical growth and development and for management of valganciclovir dosing and treatment-related adverse effects.

## PERINATAL HUMAN IMMUNODEFICIENCY VIRUS EXPOSURE AND INFECTION

### *Disease Overview*

HIV-1 and HIV-2 are enveloped RNA retroviruses that are transmitted predominantly through contact with body fluids, such as blood, semen, vaginal secretions, and breast milk. In 2019, the World Health Organization (WHO) estimated that 38 million people worldwide were living with HIV infection, including approximately 1.8 million children less than 15 years of age.[24] High-income countries such as the United States have a much lower prevalence of HIV infection, with an estimated 1.2 million people living with HIV at the end of 2018,[25] including approximately 1918 children less than 13 years of age.[26]

The development of safe and effective antiretroviral (ARV) drugs for HIV treatment and prophylaxis, and improvements in access to HIV testing and treatment, have led to significant decreases in new HIV infections, HIV-related deaths, and in the rates of mother-to-child transmission (MTCT) worldwide.[24] HIV-2 infection is uncommon outside of western Africa and is not discussed further in this article.

### *Transmission and Pathogenesis*

Infants can acquire HIV-1 infection from the mother during pregnancy (in utero), during labor and delivery, or postnatally through breastfeeding. Without interventions to prevent transmission, the risk of MTCT is approximately 25% to 30%, with higher rates up to 42% reported in resource-limited countries.[27] Most MTCT transmission occurred during pregnancy and labor (15%–30%), whereas 10% to 20% was attributed to breastfeeding.[27] In the United States and many high-income countries, the risk of MTCT has been reduced to approximately 1% to 2%.

Most Perinatal HIV transmission occurs during labor and delivery when infant mucosal surfaces are exposed to maternal blood and vaginal secretions containing HIV. In a large clinical trial conducted in resource-limited countries, the initiation of maternal ARV treatment during pregnancy reduced perinatal HIV transmission rates

**Table 5**
**Antiviral treatment of symptomatic congenital cytomegalovirus infection**

| Antiviral Drug | Indication | Dose | Duration | Adverse Effects | Monitoring |
|---|---|---|---|---|---|
| Valganciclovir (oral suspension) | Mild disease | 16 mg/kg/dose twice daily | 6 mo | Neutropenia<br>Thrombocytopenia<br>Increased levels of transaminases | Obtain CBCd, LFTs, BUN, creatinine before treatment; then weekly for first 4 wk, then monthly until treatment completion |
| Ganciclovir (IV)[a] | Severe or life-threatening disease or when oral absorption is suboptimal | 6 mg/kg/dose every 12 h | Up to 6 wk; may switch to oral valganciclovir once condition improves and oral feeds are tolerated | Neutropenia<br>Thrombocytopenia<br>Hepatotoxicity | |

[a] Ganciclovir should be administered intravenously through a central venous catheter.

to less tthan 0.5% through the first week of life, underscoring the impact of early maternal HIV testing and effective ARV treatment on pregnancy outcomes.

The risk of HIV transmission through breastfeeding seems to be highest in the first few months of life and is associated with maternal viral load, degree of maternal immune suppression, presence of mastitis, and duration of breastfeeding. HIV-infected cells and cell-free virus can be detected in human breast milk. Although breastfeeding is discouraged in high-income countries, the risk of postnatal HIV transmission in breastfed infants in resource-limited countries can be reduced to less than 1% when effective antepartum ARV treatment is coupled with either prolonged infant ARV prophylaxis or extended maternal ARV treatment.

### *Epidemiology*

The number of women living with HIV infection who give birth each year in the United States has gradually declined from approximately 8700 in 2006, to recent estimates of 5000 per year.[28] Although fewer women with HIV infection give birth each year, most of the reduction in MTCT has been attributed to several prenatal (universal HIV antibody testing of pregnant women, maternal antiretroviral treatment during pregnancy), intrapartum (antiretroviral treatment, elective cesarean section for women with high risk of HIV transmission), and postnatal (infant antiretroviral prophylaxis, avoidance of maternal breastfeeding) interventions.[29] It is estimated that the implementation of these measures resulted in 22,000 fewer cases of perinatal HIV transmission in the United States between the years 1994 and 2010.[30] Recent data indicate that, of the approximately 37,968 individuals newly diagnosed with HIV infection in the United States in 2018, only 65 (<1%) were attributed to infants with perinatally acquired HIV infection.[26] Although HIV infection occurs among all racial and ethnic groups, black/African American individuals are disproportionately affected in the United States, accounting for approximately 65% of perinatal HIV infections and 57% of new HIV infections in adults and adolescents in 2018.[26]

### *Clinical Presentation*

Most infants with perinatal HIV exposure or infection remain asymptomatic at birth and have normal physical examinations during the neonatal period. Adverse pregnancy outcomes such as preterm birth and low birth weight have been associated with maternal HIV infection and use of combination ARVs during pregnancy.[31] Opportunistic infections such as disseminated candidiasis or *Pneumocystis jiroveci* pneumonia, and other clinical and laboratory abnormalities associated with HIV infection such as lymphadenopathy, hepatosplenomegaly, delayed developmental milestones, anemia, and leukopenia, tend to occur later in infancy.

### *Diagnosis*

Newborn care providers have an important role in ensuring that every infant born to a mother with an unknown HIV status undergoes prompt maternal or infant testing with a US Food and Drug Administration (FDA)–approved rapid HIV antigen/antibody immunoassay that detects HIV-1 and HIV-2 antibodies, and HIV-1 p24 antigen. These tests are reported to have sensitivities and specificities that range from 99% to 100%.[32] In high-income countries, a positive rapid test result should lead to the initiation of infant antiretroviral prophylaxis as soon as possible, and to delayed maternal breastfeeding while confirmatory HIV testing is done.

All infants with known perinatal HIV exposure should have HIV RNA or HIV DNA nucleic acid tests (NATs) performed during the first few weeks of life (**Tables 6 and 7**).[33] Infants with higher risk of perinatal HIV transmission may require earlier and

**Table 6**
**Perinatal human immunodeficiency virus transmission risk, timing of human immunodeficiency virus diagnostic testing, and selection of antiretroviral regimen**

| Risk Category | HIV Diagnostic Tests [a,b] | ARV Treatment Regimen | Duration of Treatment |
|---|---|---|---|
| Low risk of perinatal HIV transmission:<br>• Infants born to mothers who received antiretroviral therapy during pregnancy and had sustained viral suppression at the time of delivery (HIV RNA level <50 copies/mL) | HIV RNA or DNA NATs should be obtained at the following ages:<br>• 14–21 d<br>• 1–2 mo<br>• 4–6 mo | Single drug treatment with ZDV | 4 wk |
| Higher risk of perinatal HIV transmission:<br>• Mothers who received neither antepartum nor intrapartum ARV drugs<br>• Mothers who received only intrapartum ARV drugs<br>• Mothers who received antepartum and intrapartum ARV drugs but who have detectable viral loads near delivery, particularly when delivery was vaginal<br>• Mothers with acute or primary HIV infection during pregnancy<br>• Mothers with unconfirmed HIV status who have a positive HIV antibody test at delivery or postpartum | HIV RNA or HIV DNA NATs should be performed at the following ages:<br>• Birth<br>• 14–21 d<br>• 1–2 mo<br>• 2–6 wk after ARV prophylaxis is discontinued<br>• 4–6 mo | Three-drug regimen: ZDV, lamivudine plus (nevirapine or raltegravir) | Consultation with a pediatric HIV expert is recommended |

[a] Positive HIV NAT results should be confirmed with a repeat NAT as soon as possible.
[b] The exclusion of HIV infection in infants who are not breastfed requires 2 or more negative HIV NATs obtained at age greater than or equal to 1 month and age greater than or equal to 4 months respectively, or 2 negative HIV antibody tests obtained separately at age greater than or equal to 6 months.

**Table 7**
**Antiretroviral drug dosages by gestational age at birth**

| Antiretroviral Drug (ARV) | Dosage |
|---|---|
| ZDV<br>• Oral solution is available in 10 mg/mL | Oral:<br>• GA ≥ 35 wk: 4 mg/kg/dose every 12 h<br>• GA ≥ 30 to <35 wk: 2 mg/kg/dose every 12 h; increase to 3 mg/kg/dose every 12 h at PNA 15 d<br>• GA<30 wk: 2 mg/kg/dose every 12 h<br>Intravenous (75% of oral dose):<br>• GA ≥ 35 wk: 3 mg/kg/dose every 12 h<br>• GA ≥ 30 to <35 wk: 1.5 mg/kg/dose every 12 h; increase to 2.3 mg/kg/dose every 12 h at PNA 15 d<br>• GA<30 wk: 1.5 mg/kg/dose every 12 h |
| Lamivudine (3TC)<br>• Oral solution is available in 2 concentrations (10 mg/mL and 5 mg/mL) | Oral:<br>• GA ≥ 32 wk: 2 mg/kg/dose twice daily; increase to 4 mg/kg/dose twice daily at 4 wk of age |
| Nevirapine<br>• Oral solution available in 10 mg/mL | Oral:<br>• GA ≥ 37 wk: 6 mg/kg/dose twice daily; increase to 200 mg/m$^2$ of BSA per dose twice daily at age >4 wk for infants with confirmed HIV infection<br>• GA ≥ 34 to <37 wk: 4 mg/kg/dose twice daily during the first week of life; increase to 6 mg/kg/dose twice daily for age 1–4 wk; increase to 200 mg/m$^2$ of BSA per dose twice daily at age >4 wk for infants with confirmed HIV infection |
| Raltegravir<br>• One packet can be used to prepare a suspension with a final concentration of 10 mg/mL | Oral:<br>GA ≥ 37 wk and weight ≥2 kg:<br>• Birth to 1 wk: 1.5 mg/kg/dose once daily<br>Fixed dosing:<br>2 to <3 kg: 0.4 mL (4 mg) once daily<br>3to <4 kg: 0.5 mL (5 mg) once daily<br>4 to <5 kg: 0.7 mL (7 mg) once daily<br>• 1–4 wk: 3 mg/kg/dose twice daily<br>Fixed dosing:<br>2 to <3 kg: 0.8 mL (8 mg) twice daily<br>3 to <4 kg: 1 mL (10 mg) twice daily<br>4 to <5 kg: 1.5 mL (15 mg) twice daily<br>• 4–6 wk: 6 mg/kg/dose twice daily<br>Fixed dosing:<br>3 to <4 kg: 2.5 mL (25 mg) twice daily<br>4 to <6 kg: 3 mL (30 mg) twice daily<br>6 to <8 kg: 4 mL (40 mg) twice daily |

*Abbreviations:* BSA, body surface area; GA, gestational age; PNA, postnatal age.

more frequent HIV testing.[33] The specificity of HIV RNA and DNA NATs approaches 100%, whereas the sensitivities range from 20% at birth to 100% by age 3 months.[34] A positive infant NAT result at or earlier than 48 hours of life suggests an intrauterine HIV infection, whereas infants with negative initial NATs who subsequently test positive likely developed an intrapartum HIV infection.

HIV antibody tests are not recommended for the diagnosis of HIV infection in infants less than 18 months of age because of transplacental transfer of maternal HIV antibodies. Umbilical cord blood should not be used for infant HIV testing because of the risk of contamination of the sample with maternal blood.

### *Management of Neonates with Perinatal Human Immunodeficiency Virus Exposure or Infection*

All newborns with perinatal HIV exposure ideally should be treated with antiretroviral drugs within 6 to 12 hours of delivery.[33] The selection of a specific ARV regimen and dose should be determined by the gestational age of the infant and maternal and infant risk factors for HIV transmission (see **Table 6**). There is little evidence to guide changes in bathing practices or timing of circumcision for newborns with perinatal HIV exposure.[33]

Hepatitis B vaccine and all age-appropriate and weight-appropriate immunizations should be administered to infants with perinatal HIV exposure. Live, attenuated oral rotavirus vaccine can be safely administered to infants with HIV infection.

Women with HIV infection may be at increased risk of other sexually transmitted or opportunistic infections, such as hepatitis C, hepatitis B, syphilis, gonorrhea, chlamydia, toxoplasmosis, tuberculosis, or herpes simplex virus. A detailed maternal and obstetric history should be obtained and maternal test results for coinfections should be reviewed if available. Infants born to women with other infections should undergo appropriate diagnostic evaluations and may require additional treatment.

Universal or standard precautions should be observed when caring for infants with perinatal HIV exposure.[35] Gloves should be worn when handling newborns during and after birth and with any potential exposure to blood or body fluids.

#### *Antiretroviral treatment and monitoring*

Infants at low risk of MTCT should be treated with a 4-week course of oral or intravenous zidovudine (ZDV) prophylaxis (see **Table 6**). Infants with higher risk of MTCT or those with confirmed HIV infection may require treatment with a 3-drug ARV regimen recommended by a pediatric HIV expert.

A complete blood count with differential should be obtained before initiating antiretroviral drugs and after 4 weeks of treatment to evaluate for abnormalities such as anemia and neutropenia, which have been associated with ARV use in infants.

## BREASTFEEDING AND FEEDING PRACTICES

In countries where safe water and affordable feeding alternatives such as infant formula are widely available, woman with HIV infection are strongly discouraged from breastfeeding their infants, regardless of maternal viral load. Although infant and maternal prophylaxis with antiretroviral drugs reduces the risk of postnatal HIV transmission, complete avoidance of maternal breast milk is the only effective way to prevent HIV transmission from breast milk to infants. Donor breast milk that has been pasteurized and adequately screened for infection may be a safe alternative for women who wish to feed their infants human breast milk. Occasionally, women with HIV infection on effective antiretroviral therapy and with undetectable viral loads may choose to breastfeed their infants, despite the risk of HIV transmission. In these

circumstances, adult and pediatric HIV experts should be consulted to help minimize the risk of HIV transmission.[33]

Parents and caregivers with HIV infection should be advised to avoid feeding infants premasticated (prechewed or prewarmed) solid food, because this practice has been associated with HIV transmission.[36]

### PROPHYLAXIS AGAINST *PNEUMOCYSTIS JIROVECI*

To prevent *P jiroveci* pneumonia, all infants with perinatal HIV exposure should begin trimethoprim-sulfamethoxazole prophylaxis at age 4 to 6 weeks, after completing infant ARV prophylaxis, unless HIV infection has been excluded presumptively with 2 or more negative NATs obtained at ages greater than or equal to 2 weeks and age greater than or equal to 4 weeks.

### FOLLOW-UP OF INFANTS EXPOSED TO OR INFECTED WITH HUMAN IMMUNODEFICIENCY VIRUS

Infants with perinatal HIV exposure or infection may require additional HIV diagnostic testing and treatment and should follow up with a pediatric HIV expert after hospital discharge.

### HELPFUL RESOURCES

In the United States, the http://nccc.ucsf.edu/clinician-consultation/perinatal-hiv-aids/ National Clinician Consultation Center provides consultations on the management of perinatal HIV infection (1-888-448-8765; 24 hours a day, 7 days a week).

## SYPHILIS

### *Disease Overview*

Congenital syphilis (CS) occurs when a mother with syphilis transmits the infection to the fetus. CS should always be considered in the evaluation of an infant with suspected congenital infection because the clinical presentation is highly variable, with significant overlap with other diseases.[2,37,38] CS is a preventable disease and is treatable if diagnosed early in the newborn period.

### *Epidemiology*

CS incidence tends to follow trends of increasing primary and secondary syphilis cases in the adult population.[39] The United States and several other countries have reported marked increases in reported cases of CS in recent years. In the United States, the rate of reported CS cases was 33.1 cases per 100,000 live births in 2018 and this reflects a 185.3% increase compared with 2014 rates.[39] The increasing trend of adult syphilis cases is expected to continue, and reversing this increased incidence may not be possible without significant biomedical advancements or a vaccine.[40]

### *Transmission/Pathogenesis*

CS occurs when the spirochete *Treponema pallidum* is transmitted from mother through the placenta to infect the fetus. Maternal primary and secondary syphilis infections are associated with higher rates of fetal and congenital infection than latent-stage syphilis.

Risk factors for transmission include:

- Limited prenatal care

- High treponemal titers
- Late or no maternal treatment

### *Clinical Presentation*

CS presents with varying degrees of severity in fetuses and newborns, from asymptomatic infection to in utero demise, hydrops fetalis, and preterm birth (**Table 8**).[41,42,46] Undiagnosed and untreated infants with no apparent clinical signs at birth remain at risk for later sequelae and morbidity. Hepatomegaly is the most common fetal and postnatal clinical finding with CS.[38,43]

### *Diagnosis*

The diagnosis of CS may be challenging in asymptomatic infants and is often first suspected after a detailed review of the maternal and prenatal history. Maternal treponemal and nontreponemal syphilis screening test results obtained during the pregnancy should be reviewed on all infants before discharge from the birth hospital.[44] Women who are at high risk for syphilis infection may benefit from repeat syphilis testing during the third trimester and at delivery because infections acquired later in pregnancy may be missed by first-trimester syphilis screening tests. A history of treated or untreated syphilis in the mother or a history of abnormal syphilis screening

**Table 8**
**Clinical, laboratory, and radiographic features of congenital syphilis**

| | |
|---|---|
| Clinical Pearls | 1. Most infants with CS have no clinical signs at birth<br>2. Most common signs: hepatomegaly, syphilitic rhinitis (snuffles) jaundice, rash, lymphadenopathy, skeletal findings<br>3. Radiographic findings may be the only apparent feature, are commonly present at birth, and are usually bilateral and symmetric |
| Fetal[41–43] | In utero demise, IUGR, ascites, nonimmune hydrops fetalis, hepatomegaly, intrahepatic calcifications, increased middle cerebral artery dopplers, placentomegaly |
| Newborn Examination[37,38,44] | Fever, small for GA, rash, syphilitic rhinitis, cranial nerve palsies,<br>seizure, hepatomegaly, splenomegaly, lymphadenopathy (may be generalized; palpable epitrochlear nodes) mucous patch, condylomata lata, pseudoparalysis of Parrot (presents as immobile extremity caused by pain), rectal bleeding |
| Ophthalmic[45] | Chorioretinitis, cataracts, glaucoma |
| Laboratory[38] | Hemolytic anemia, leukopenia, leukocytosis, thrombocytopenia, hypoglycemia, CSF pleocytosis, increased CSF protein level,<br>increased liver transaminase levels, direct hyperbilirubinemia |
| Radiographic[44] | Periostitis, osteochondritis |
| Other | Pneumonia alba, nephrotic syndrome, pancreatitis, myocarditis, gastrointestinal malabsorption, hypopituitarism,<br>diabetes insipidus |

*Abbreviation:* IUGR, intrauterine growth restriction.

test results during pregnancy should prompt further evaluation in the infant. This evaluation may include a detailed physical examination, nontreponemal blood tests such as reactive plasma regain (RPR) or venereal disease research laboratory (VDRL), and other laboratory and imaging studies based on risk of infection (**Table 9**).

### *Treatment*

The evaluation, diagnosis, and treatment of CS is determined by the risk and severity of syphilis infection based on 4 categories of infection: proved or highly probable; possible; less likely; or unlikely[44] (see **Table 9**). Parenteral penicillin G is the only effective treatment of CS.[47,48]

### *Prevention*

Preventing CS involves syphilis prevention for women and their partners as well as timely identification and treatment of pregnant women with syphilis. The WHO launched a global campaign for the elimination of CS in 2007, but several challenges have prevented significant reductions.[49,50]

Missed opportunities for prevention include limited prenatal care but also lack of adequate testing and inadequate or no treatment in some cases.[51] Repeat syphilis screening tests during the third trimester and at delivery can detect newly acquired infections in high-risk women.[39]

## TOXOPLASMOSIS

### *Disease Overview*

Congenital toxoplasmosis (CT) occurs when the obligate intracellular parasite, *Toxoplasma gondii*, is transmitted from mother to fetus. This infection is frequently asymptomatic in both mothers and newborns. Diagnosis may require testing at specialized laboratories, and treatment often includes agents unfamiliar to most newborn health care providers.[52]

### *Transmission and Pathogenesis*

Cats are the definitive hosts, whereas humans and other animals serve as intermediate hosts. Humans become infected after ingestion of undercooked or raw meat, unpasteurized raw milk, and soil or water contaminated with oocytes from cat feces. Infection may also occur via blood transfusion and organ transplant.[52] The risk of maternal to fetal transmission varies greatly by region and country.[53]

Transmission of *T gondii* from mother to fetus may occur in 3 different scenarios of maternal infection:

1. Immunocompetent and seronegative mother who acquires acute primary infection 3 months before conception or during pregnancy
2. Pregnant mother who is immune to one strain and becomes infected with a new more virulent strain
3. Severely immunocompromised mother with reactivation of toxoplasmosis during pregnancy

### *Clinical Presentation*

The presentation of congenital toxoplasmosis varies significantly, and different regions seem to have distinct clinical signs and severity that may reflect strain-related differences in phenotype. CT disease in the United States has been reported to be more severe than European disease.[54] Asymptomatic neonates are at risk of developing significant later sequelae.[55,56] **Table 10** describes the clinical features of CT.

**Table 9**
**Evaluation and treatment of neonates born to women with reactive syphilis tests during pregnancy**

| Category | Clinical and Laboratory Findings | Evaluation | Treatment |
|---|---|---|---|
| Proven, highly probable CS | Abnormal physical examination<br>Or<br>Serum quantitative nontreponemal serologic titer, 4-fold higher than the mother's titer[a]<br>Or<br>A positive darkfield test or PCR assay of lesions or body fluids | CSF analysis (CSF VDRL, cell count, and protein)<br>CBC with differential and platelet count<br>Other tests (as clinically indicated):<br>Long-bone radiographs, chest radiography, transaminases, neuroimaging, ophthalmologic examination, auditory brain stem response | Preferred treatment: Aqueous crystalline penicillin G, 50,000 U/kg, intravenously, every 12 h (during the first 7 d) then every 8 h (for infants older than 7 d) for a total of 10 d of therapy<br>Or<br>Alternative treatment: procaine penicillin G, 50,000 U/kg, IM in a single daily dose for 10 d |
| Possible CS | Normal examination<br>And<br>A serum quantitative nontreponemal serologic titer, $\leq$4-fold the maternal titer<br>And one of the following:<br>Mother was not treated, was inadequately treated, or had no documentation of receiving treatment<br>Or<br>Mother was treated with erythromycin or another nonrecommended regimen (ie a nonpenicillin regimen)<br>Or<br>Mother received recommended treatment <4 wk before delivery | CSF analysis (CSF VDRL, CBC count, and protein)<br>CBC including differential and platelet count<br>Long-bone radiography<br>These evaluations may not be necessary if 10 d of parenteral therapy is administered | Preferred treatment: aqueous crystalline penicillin G, 50,000 U/kg, intravenously, every 12 h (1 wk or younger), then every 8 h for infants older than 1 wk, for a total of 10 d of therapy (preferred)<br>Or<br>Alternative treatment:<br>Procaine penicillin G, 50,000 U/kg, IM (single daily dose for 10 d)<br>Or<br>Alternative treatment in select cases: benzathine penicillin G, 50,000 U/kg, IM, single dose (recommended by some experts, but only if all components of the evaluation are obtained and are normal, including normal CSF results and follow-up is certain) |

| | | | |
|---|---|---|---|
| CS less likely | Normal examination<br>And<br>A serum quantitative nontreponemal serologic titer equal to or less than 4-fold the maternal titer<br>And<br>Mother was treated during pregnancy (treatment was appropriate for stage of infection, and treatment was administered >4 wk before delivery)<br>And<br>Mother has no evidence of reinfection or relapse | No evaluation | Benzathine penicillin G, 50,000 U/kg, IM, single dose<br>Alternative strategy[b]:<br>Infants whose mother's nontreponemal titers decreased at least 4-fold after appropriate therapy for early syphilis or remained stable at low titer (eg, VDRL $\leq$ 1:2; RPR $\leq$ 1:4) may be followed every 2–3 mo without treatment until the nontreponemal test becomes nonreactive |
| CS is unlikely | Normal infant examination<br>And<br>A serum quantitative nontreponemal serologic titer equal to or less than 4-fold the maternal titer<br>And<br>Mother was treated adequately before pregnancy<br>And<br>Mother's nontreponemal serologic titer remained low and stable before and during pregnancy and at delivery (eg, VDRL $\leq$ 1:2; RPR $\leq$ 1:4) | — | No treatment required, but infants with reactive nontreponemal tests should be followed serologically to ensure test result returns to negative<br>Recommended by some experts: benzathine penicillin G, 50,000 U/kg, IM, single dose can be considered if follow-up is uncertain and infant has a reactive test<br>Neonates with a negative nontreponemal test result at birth and whose mothers were seroreactive at delivery should be retested at 3 months to rule out serologically negative incubating CS at the time of birth |

*Abbreviations:* CBC, complete blood count; IM, intramuscularly.

[a] Absence of a 4-fold or greater title does not exclude CS.

[b] Nontreponemal antibody titers should decrease by 3 months of age and should be nonreactive by 6 mo of age whether the infant was infected and adequately treated or was not infected and initially seropositive because of transplacentally acquired maternal antibody. Patients with increasing titers or with persistent stable titers 6 to 12 months after initial treatment should be reevaluated. This evaluation should include a CSF examination. Treatment should include a 10-day course of parenteral penicillin G, even if they were treated previously.

*Data from* Centers for Disease Control and Prevention. Sexually Transmitted Diseases Treatment Guidelines. Congenital Syphilis. 2015; https://www.cdc.gov/std/tg2015/congenital.htm. and Kimberlin DW BM, Jackson MA, Long SS. *Red Book: 2018 Report of the Committee on Infectious Diseases*: American Academy of Pediatrics; 2018:773-788.

**Table 10**
**Clinical features of congenital toxoplasmosis**

| | |
|---|---|
| Fetal | Fetal demise, hydrocephalus, intracranial calcifications/densities, intrahepatic calcifications, IUGR, ascites, pericardial effusions, increased placental thickness and placental densities, echogenic bowel |
| Neurologic | Hypotonia, macrocephaly or microcephaly, palsies, spasticity, seizures, CSF abnormalities, encephalopathy, intracranial calcifications, hydrocephalus, brain masses<br>Nystagmus, cataracts, amblyopia, strabismus, optic nerve atrophy, amblyopia, chorioretinitis, microphthalmia, microcornea, pneumonitis |
| Ophthalmic | — |
| Other | Temperature instability, myocarditis, anemia, sepsislike syndrome, rash, hepatitis, jaundice, thrombocytopenia, hepatomegaly, splenomegaly, lymphadenopathy |

Data from Maldonado YA, Read JS. Diagnosis, Treatment, and Prevention of Congenital Toxoplasmosis in the United States. *Pediatrics.* 2017;139(2):e20163860 and Feigin and Cherry's textbook of pediatric infectious diseases/[edited by] James D. Cherry, Gail J. Harrison, Sheldon L. Kaplan, William J. Steinbach, Peter J. Hotez. Eighth edition. ed. Philadelphia, PA: Elsevier; 2018.

## DIAGNOSIS AND TREATMENT

Diagnosis of congenital toxoplasmosis is challenging because most women with toxoplasmosis remain asymptomatic. When maternal infection is suspected, early diagnosis, treatment, and evaluation of the fetus may help reduce the risks of infection and fetal complications. Evaluation of infants for CT should include multidisciplinary consultation with infectious disease specialists, retinal specialists, and neurologists. In 2017, Maldonado and colleagues[52] published a technical report with detailed

**Table 11**
**Clinical and imaging findings associated with congenital Zika infection**

| | |
|---|---|
| Clinical Neurologic Signs | Severe microcephaly; hypertonia, dysphagia, hearing deficits |
| Neuroradiologic Signs | Lenticulostriate vasculopathy and germinolytic cysts; subcortical calcifications; ventriculomegaly, thin cortical mantle;<br>fetal brain disruption sequence; brainstem hypoplasia |
| Eye | Microphthalmia; cataract; intraocular calcifications; coloboma,<br>posterior ocular findings; focal macular pigment mottling,<br>chorioretinal atrophy with a predilection for the macular area,<br>congenital glaucoma and optical nerve hypoplasia, and optic disc abnormalities |
| Musculoskeletal | Arthrogryposis, clubfoot |
| Urologic | Cryptorchidism, hypospadias |
| Other | Craniofacial anomalies |

Data from[45,66–68]

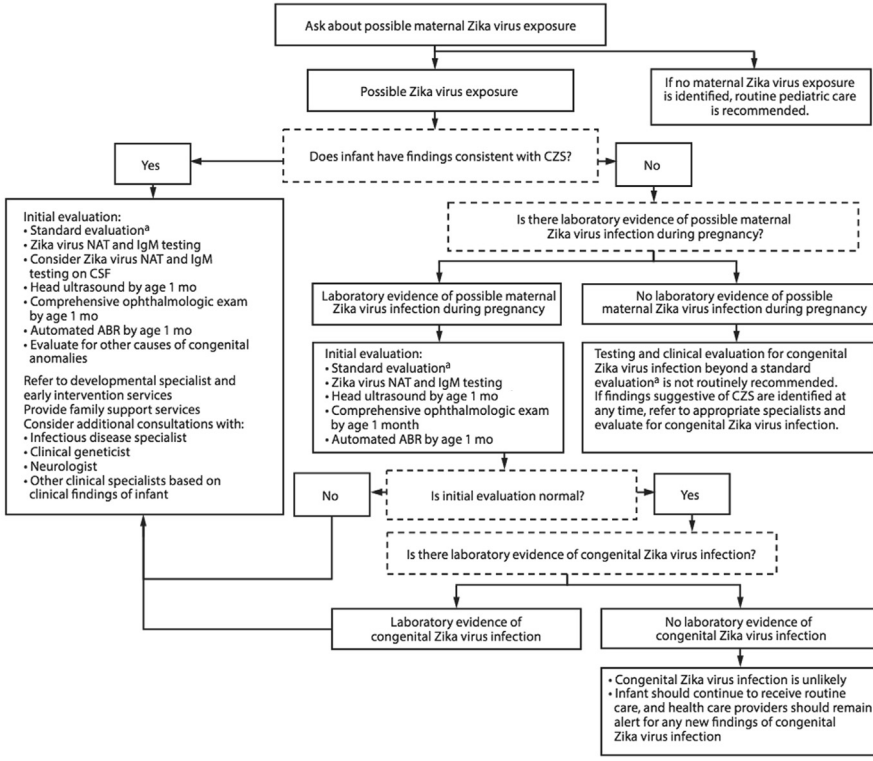


**Fig. 1.** Recommendations for the evaluation of infants with possible congenital Zika virus infection based on infant clinical findings,[a,b] maternal testing results,[c,d] and infant testing results[e,f] (United States, October 2017).[a] All infants should receive a standard evaluation at birth and at each subsequent well-child visit by their health care providers including (1) comprehensive physical examination, including growth parameters, and (2) age-appropriate vision screening and developmental monitoring and screening using validated tools. Infants should receive a standard newborn hearing screen at birth, preferably using auditory brainstem response. [b]Automated auditory brainstem response (ABR) by age 1 month if newborn hearing screen passed but performed with otoacoustic emission methodology. [c]Laboratory evidence of possible Zika virus infection during pregnancy is defined as (1) Zika virus infection detected by a Zika virus RNA NAT on any maternal, placental, or fetal specimen (referred to as NAT-confirmed); or (2) diagnosis of Zika virus infection, timing of infection cannot be determined or unspecified flavivirus infection, timing of infection cannot be determined by serologic tests on a maternal specimen (ie, positive/equivocal Zika virus IgM and Zika virus plaque reduction neutralization test [PRNT] titer $\geq$10, regardless of dengue virus PRNT value; or negative Zika virus IgM, and positive or equivocal dengue virus IgM, and Zika virus PRNT titer $\geq$10, regardless of dengue virus PRNT titer). The use of PRNT for confirmation of Zika virus infection, including in pregnant women, is not routinely recommended in Puerto Rico (https://www.cdc.gov/zika/laboratories/lab-guidance.html). [d]This group includes women who were never tested during pregnancy as well as those whose test results were negative because of issues related to timing or sensitivity and specificity of the test. Because the latter issues are not easily discerned, all mothers with possible exposure to Zika virus during pregnancy who do not have laboratory evidence of possible Zika virus infection, including those who tested negative with currently available technology, should be considered in this group. [e]Laboratory testing of infants for Zika virus should be performed as early as possible, preferably within the first few days after birth, and

recommendations on the evaluation, diagnosis, and treatment of CT. Clinicians evaluating infants for CT may consult toxoplasmosis reference centers for consultation (helpful resources are provided later).

Treatment recommendations vary by region, and comparative studies are not available. In the United States, recommended treatment includes pyrimethamine, sulfadiazine, and folinic acid for up to 12 months.[52]

### *Helpful Resources*

(1) Palo Alto Medical Foundation Toxoplasma Serology Laboratory, Palo Alto, CA: www.pamf.org/serology; e-mail: toxolab@pamf.org.
(2) Toxoplasmosis Center at the University of Chicago (Center of the National Collaborative Chicago-based Congenital Toxoplasmosis Study): telephone, (773) 834-4130.

## CONGENITAL ZIKA VIRUS

### *Transmission and Pathogenesis*

Zika virus is transmitted to humans through the bite of the *Aedes* mosquito. Zika can also be acquired through sexual transmission and blood transfusions.[57] Infection during pregnancy can result in congenital Zika virus (CZ) infection.

As of July 2019, 87 countries and territories have had evidence of local mosquito-borne Zika infection.[58] In the United States, the last reported local mosquito-borne infections were noted in Florida and Texas in 2017. Since 2018, there have been no reported cases of locally transmitted Zika in the Unites States. Cases continue to be reported in US territories, but have significantly declined each year since 2017.[59]

### *Clinical Presentation*

CZ can result in a range of clinical signs in the newborn.[60–64] Early reports describing CZ focused on microcephaly, but later studies revealed a wide range of associated anomalies in addition to microcephaly.[60] Clinicians should be aware that many newborns with CZ may have no clinical signs, including normal head circumference.[64] Exposed neonates without signs of CZ are still at risk for later neurodevelopmental delays and/or deficits despite normal clinical and imaging findings at birth.[65] Clinical and neuroimaging features of CZ are listed in **Table 11**.

### *Diagnosis and Treatment*

The ideal strategy for laboratory evaluation and timing of diagnostic testing is unclear. Infants with signs of CZ have been noted to have negative laboratory evaluations.[60,67]

**Fig. 1** provides guidance on evaluation of infants with possible CZ.[66]

includes concurrent Zika virus NAT in infant serum and urine, and Zika virus IgM testing in serum. If CSF is obtained for other purposes, Zika virus NAT and Zika virus IgM testing should be performed on CSF. [f]Laboratory evidence of congenital Zika virus infection includes a positive Zika virus NAT or a nonnegative Zika virus IgM with confirmatory neutralizing antibody testing, if PRNT confirmation is performed. CZS, congenital Zika syndrome. (From Adebanjo T, Godfred-Cato S, Viens L, et al. Update: Interim Guidance for the Diagnosis, Evaluation, and Management of Infants with Possible Congenital Zika Virus Infection - United States, October 2017. MMWR Morb Mortal Wkly Rep. 2017;66(41):1089-1099.)

**Table 12**
**Clinical signs and features of congenital Chagas**

| | |
|---|---|
| More Common | Low birth weight<br>Respiratory distress<br>Hepatomegaly<br>Splenomegaly |
| Less Common | Prematurity<br>Cardiomyopathy/heart failure<br>Sepsis<br>Meningoencephalitis<br>Petechiae<br>Anemia |

Data from[72–76]

No treatment is available for Zika virus and future epidemics are expected to expand into previously unaffected populations because of climate change, population growth, and population movement.[69,70]

### *Helpful Resources*

1) Centers for Disease Control and Prevention (CDC) recommendations with detailed laboratory specimen guidance can be found at: https://www.cdc.gov/zika/hc-providers/test-specimens-at-time-of-birth.html

## CHAGAS DISEASE

### *Transmission and Pathogenesis*

Chagas disease, or American trypanosomiasis, is caused by infection with the protozoan parasite *Trypanosoma cruzi*. The parasite can be passed from mother to fetus, resulting in congenital infection. The prevalence of Chagas and congenital Chagas (CC) varies widely, and it is most prevalent in Mexico, Central America, and South America.[71]

Chagas is an underappreciated health concern in the United States, with 40,000 women of childbearing age estimated to have chronic Chagas disease. In the United States, it is estimated that up to 300 infants are born with CC each year.[71]

The CDC includes Chagas disease on its list of neglected parasitic infections, which includes parasitic disease based on numbers of infected individuals, disease severity, and ability to prevent and treat.[72]

### *Clinical Presentation, Diagnosis, Treatment, and Prevention*

Women at risk for Chagas should be screened for infection before and during pregnancy.[71] Approximately half of infants with CC have no clinical signs. When clinical signs are present, they are similar to the nonspecific signs commonly associated with other congenital infections (**Table 12**). Both benznidazole and nifurtimox are used to treat infants with CC disease.[73,77] Early treatment of CC is well tolerated and is curative in 90% of cases.[77–79]

## SUMMARY

Infants with congenital infections are often asymptomatic at birth or present with mild, nonspecific signs and symptoms, making diagnosis challenging. Newborn care

providers should be aware of the wide range of traditional (TORCH) and emerging fetal and neonatal pathogens that can cause congenital infection. With the advancements in molecular and other diagnostic testing, a targeted, disease-specific evaluation for congenital infection is preferred rather than a broad search for infectious agents with comprehensive antibody panels. Although newborn care providers are critical in suspecting, diagnosing, and initiating early treatment, coordination among obstetric, perinatal, and pediatric infectious disease and other specialties is often required for the optimal diagnosis and management of infants with congenital infection.

## WHAT ARE THE CURRENT BEST PRACTICES FOR CONGENITAL INFECTIONS RELATED TO HIV,CMV, TOXOPLASMOSIS, ZIKA, AND CHAGAS?

1. Optimal communication among obstetric and newborn care providers regarding maternal exposure, risk associated with congenital infections, and prenatal laboratory documentation.
2. Targeted disease-specific testing instead of TORCH titer screens and/or total IgM is the ideal approach to laboratory evaluation.
3. Urine or saliva PCR are the optimal tests for diagnosis of CMV because of superior sensitivity and rapid turnaround time. The tests should be performed before 2 to 3 weeks of age.
4. Infants with symptomatic CMV infection should be treated promptly with antiviral treatment to decrease the risk of long-term sequelae.
5. Mothers with unknown HIV status and their infants should have prompt testing with an FDA-approved rapid HIV antigen/antibody immunoassay that detects HIV-1 and HIV-2 antibodies, and HIV-1 p24 antigen.
6. Repeat syphilis screening should occur during the third trimester and at the time of delivery for high-risk mothers to adequately rule out congenital infection.
7. Consultation with toxoplasmosis reference centers and laboratories should be considered for optimal evaluation and management of congenital toxoplasmosis.
8. Newborn care providers should ask about the mother's potential Zika exposure for every newborn, because changes in interim guidance for maternal care may lead to lower numbers of mothers being tested.
9. Women at risk for Chagas disease should be screened for infection before and during pregnancy.

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