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Fetal Care in Focus: Fetal Infection Presentation on Ultrasound Evaluation

By: Katie Francis, MSN, APRN & Amanda Harrison, MSN

During pregnancy, infection in the pregnant person can lead to negative outcomes if the infection passes to the developing fetus. Complications include prematurity, stillbirth, structural anomalies, growth restriction, and severe disease in the newborn. When an infection in a pregnant person passes to the fetus this can be referred to as a "fetal infection" or a "congenital infection". Early detection of fetal infections allows for appropriate management strategies which may include targeted treatments, closer monitoring, and in some cases, delivery planning to optimize neonatal outcomes. In some cases, abnormalities detected on ultrasound examination may prompt providers to order serological testing to look for the presence of certain infectious agents in the blood of the pregnant person. In other cases, a pregnant person may undergo infection screening due to a possible exposure to an infected individual and/or because the pregnant person has symptoms of infection. In this case, targeted ultrasound screening will look for signs of fetal infection. In either situation, fetal ultrasound evaluation is crucial in guiding care or treatment.

Congenital infections can be caused by specific pathogens including bacteria, viruses, and parasites. Although not all infectious agents present in a pregnant person can cross the placenta and infect a developing fetus, some examples of pathogens that can lead to fetal infections include cytomegalovirus (CMV), toxoplasmosis, parvovirus B19, rubella virus, varicella-zoster virus, syphilis, and Zika virus.^{1,2} Each of these pathogens presents distinct signs in affected fetuses undergoing ultrasound evaluation. Refer to Table 1 for markers associated with congenital infections commonly seen during ultrasound evaluation.²

Once fetal infection is suspected, a definitive diagnosis can only be made through diagnostic testing. Amniocentesis can be performed to obtain amniotic fluid, which is comprised of fetal urine, for polymerase chain reaction (PCR) testing. PCR testing can confirm or rule out the presence of specific pathogens in the amniotic fluid. However, a positive result will not occur until 6-8 weeks after the initial infection in the pregnant person occurs. Additionally, fetal urine will not indicate infection until at least 18-20 weeks gestational age. Therefore, it is advised to delay amniocentesis until after 18-20 weeks gestation or until 7 weeks after the initial infection in the pregnant person.²

The earlier a fetus is infected with one of these pathogens during gestation, the more likely it is to be affected. It is important to note that ultrasound evaluation may not always identify evidence of infection in an affected fetus. Even if imaging is normal with a confirmed infection in the pregnant person, an infected fetus could still experience long-term effects from the pathogens, so postnatal follow-up is necessary.^{2,3}

In the case of Syphilis, a sexually transmitted infection caused by the bacteria *Treponema pallidum*, the transmission to the fetus through the placenta can occur at any stage of the pregnant person's disease. As the pregnancy progresses, the likelihood of the infection being passed on to the fetus increases. The risk of vertical transmission from pregnant person to fetus is also higher in the earlier stages of disease in the pregnant person.⁴

Fetal Care in Focus (cont.)

When Syphilis infection in the pregnant person is known, an ultrasound examination after 20 weeks should be performed to look for signs of fetal infection. Fetal abnormalities can only be detected through ultrasound evaluation after 18 weeks of gestation when the fetus becomes immunocompetent. Common findings on ultrasound evaluation of infected fetuses include hepatomegaly (80%), elevated middle cerebral artery (MCA) Dopplers indicating fetal anemia (33%), placentomegaly (27%), polyhydramnios (12%), as well as ascites and/or hydrops (10%). Less common findings include fetal splenomegaly, cardiomegaly, and pericardial effusions. If infection in the pregnant person is not treated, fetal symptoms will persist and worsen. The progression of symptoms begins with early hepatic and placental findings, followed by amniotic fluid infection, hematologic dysfunction, ascites, and eventually the production of fetal immunoglobulin M (IgM).³

After a sonographic diagnosis of congenital syphilis is made, further ultrasound evaluations should be conducted every one to two weeks to monitor fetal health. When the pregnant person is successfully treated with penicillin, it is possible to cure the fetal infection. Fetal transfusions are rarely needed to treat fetal anemia. With treatment to the pregnant person, MCA Doppler abnormalities, ascites, and polyhydramnios should improve within about a month. Placentomegaly will improve next, and hepatomegaly may take months to resolve.⁵

Fetal infections can have serious consequences for both the pregnant person and the fetus if not identified and managed properly. Ultrasound imaging is crucial for early detection and monitoring of these infections. Recognizing the typical signs that can be seen on ultrasound evaluation that are linked to various fetal infections helps healthcare providers take timely action, ultimately improving the outlook for affected pregnancies.

Author Biographies

Katie Francis, MSN, APRN - Author

Katie Francis has been a nurse for 25 years at SSM Health Cardinal Glennon Children’s Hospital, first as a NICU nurse, and then as a pediatric and neonatal transport nurse. Katie was the founding nurse coordinator of the SSM Health St. Louis Fetal Care Institute, where she has served for the last 15 years. She currently works as the program coordinator. She is dedicated to providing comprehensive and compassionate care to every family facing a fetal diagnosis.

Amanda Harrison, MSN, RN - Author

Amanda Harrison has been a nurse for 19 years at SSM Health Cardinal Glennon Children’s Hospital. She started her career as a nurse in the Pediatric Intensive Care Unit and has been a research nurse coordinator for the St. Louis Fetal Care Institute and Division of Neonatology since 2018. Amanda is a founding member and active participant on the hospital’s nursing research and evidence-based practice council. She has a passion for utilizing evidence-based practice and research to provide the best outcomes for patients and families.

Table 1 Ultrasound signs suggestive of congenital infection

<i>Cranial abnormalities</i>	<i>Extracranial abnormalities</i>	<i>Placental/amniotic fluid abnormalities</i>
Ventriculomegaly	Small-for-gestational age	Placentomegaly
Calcifications	Hyperechogenic bowel	Placental calcifications
Intraventricular synechiae	Hepatomegaly	Oligohydramnios/anhydramnios
Cerebellar abnormalities	Splenomegaly	Polyhydramnios
Vermian hypoplasia	Liver calcifications	
Cerebellar hemorrhage	Ascites	
Calcifications	Pericardial effusion	
Cysts	Skin edema	
Periventricular pseudocysts	Hydrops or fetal anemia	
Malformations of cortical development	(MCA-PSV > 1.5 MoM) in absence	
Lissencephaly-pachygyria	of maternal atypical antibodies	
Oligo-/pachygyria		
Polymicrogyria		
Schizencephaly		
Microcephaly		

Signs are listed in approximate order of frequency. Not all ultrasound signs are present in all infections; some tend to be more common in certain infections, depending on pathogen. MCA, middle cerebral artery; MoM, multiples of the median; PSV, peak systolic velocity.

Formulary Facts: Syphilis Treatment

By: Laurie Niewoehner, Pharm D.

Syphilis treatment during pregnancy

Penicillin G benzathine is the standard for treatment for pregnant patients and non-pregnant individuals. Given the extreme penicillin shortage, it should be reserved for pregnant patients as it is the only option for this population. There are other options for non-pregnant patients such as doxycycline. Given on an appropriate timing regimen, penicillin is effective for treating maternal disease, preventing transmission to the fetus and treating established fetal disease. It is also important for the maternal partner to be treated to prevent maternal re-infection.

Maternal treatment

Primary, Secondary, or early Latent Syphilis:

Single dose of Penicillin G Benzathine 2.4 million units IM (1.2 million units in each buttock), some clinicians recommend an additional dose one week following the first.

Late latent, tertiary or disease of unknown duration:

Three doses of Penicillin G Benzathine 2.4 million units IM (1.2 million units in each buttock) at weekly intervals. If dose is missed for more than 14 days, the full three dose regimen needs to be restarted.

Neurosyphilis (ocular syphilis):

Aqueous crystalline penicillin G (intravenous) 3-4 million units IV Q4 hours for 10-14 days. Penicillin G benzathine 2.4 million units IM once per week for up to 3 weeks to be completed after completion of IV penicillin G to provide a comparable total duration of therapy as latent syphilis.

Treatment of Maternal Partner

Doxycycline 100 mg PO BID for two weeks for primary, secondary or early latent syphilis and for four weeks for late latent or syphilis of unknown duration.

Follow patients carefully to be sure treatment is completed and schedule follow-up visits with patients to verify a decline in syphilis non-treponemal titer (RPR)

Potential Complications of Penicillin Treatment

Jarisch-Herxheimer Reaction-

Signs and Symptoms: Acute febrile reaction with headache, myalgia, rash, and hypotension. Usually occurs within 1-2 hours of treatment and resolves within 24-48 hours.

Management: Supportive care – IV fluids and antipyretics

Complications: May precipitate contractions in patients treated in the second half of pregnancy. Some clinicians may choose to continuously monitor the fetal heart rate for 12-24 hours to confirm fetal status when maternal symptoms are consistent with Jarisch-Herxheimer Reaction.^{1,2}

Penicillin allergy-

Pregnant patients with a penicillin allergy should be skin tested, desensitized and treated with Penicillin G Benzathine. This can be done in the inpatient or outpatient setting, depending on the severity of the reaction. Penicillin allergy is reported by 5-10% of patients, but serious reactions are rare. It's important to verify the history of the allergy as some may assume a side effect such as nausea or vomiting to be an allergy. The symptoms of concern are IgE mediated responses such as urticaria, angioedema, anaphylaxis with airway obstruction. Penicillin skin testing helps to evaluate patients who may be at risk of an IgE mediated response if symptoms are unknown. Women who are allergic should be desensitized and receive penicillin.

Follow up after Penicillin treatment

Nontreponemal titers (VDRL, RPR) tend to increase soon after penicillin is given, a follow up serological assay should be obtained no sooner than 2 months after therapy is completed.

The likelihood of inadequate neonatal treatment is increased if treatment was given less than a month prior to birth, the mother had signs of infection at delivery, or the maternal nontreponemal titer is more than 4-fold higher than the pretreatment level.³

Formulary Facts (cont.)

Syphilis treatment for neonates

Best practice is to consult with Pediatric Infectious Disease to determine which category of congenital syphilis best describes the neonate.

Confirmed or Highly Probable Congenital Syphilis

Any neonate with a serum quantitative nontreponemal serologic titer that is fourfold (or greater) higher than the mother's titer at delivery (e.g., maternal titer = 1:2, neonatal titer \geq 1:8 or maternal titer = 1:8, neonatal titer \geq 1:32)

Treatment:

Aqueous crystalline Penicillin G 50,000 units/kg/dose **IV** q12 hours for the first 7 days of life and every 8 hours thereafter for a total of 10 days. Of note, even if neonate received doses of Ampicillin for possible sepsis, the treatment duration with penicillin should remain 10 days.

If more than one day is missed, then the entire course should be restarted. Data is not sufficient for other antimicrobial agents.

Possible Congenital Syphilis

Any neonate who has a normal examination and a serum quantitative nontreponemal serologic titer equal to or less than fourfold of the maternal titer at delivery (e.g., maternal titer = 1:8, neonatal titer \leq 1:16) and one of the following:

- The mother was not treated or inadequately treated.
- The mother was treated with a nonpenicillin regimen.
- The mother received the penicillin regimen less than 30 days prior to delivery.

Treatment:

Aqueous crystalline Penicillin G 50,000 units/kg/dose **IV** q12 hours for the first 7 days of life and every 8 hours thereafter for a total of 10 days.

OR

Benzathine penicillin G – 50,000 units/kg **IM** as a single dose.

Congenital Syphilis Less Likely

Any neonate who has a normal examination and a serum quantitative nontreponemal serologic titer equal or less than fourfold of the maternal titer at delivery (e.g., maternal titer = 1:8, neonatal titer \leq 1:16) and both of the following are true:

- The mother was treated during pregnancy and the treatment regimen was initiated \geq 30 days before delivery.
- The mother has no evidence of reinfection.

Treatment:

Benzathine penicillin G – 50,000 units/kg **IM** as a single dose

Congenital Syphilis Unlikely

Any neonate who has a normal examination and a serum quantitative nontreponemal serologic titer equal to or less than fourfold of the maternal titer at delivery and both of the following are true:

- The mother's treatment was adequate before pregnancy.
- The mother's nontreponemal serologic titer remained low and stable before and during pregnancy and at delivery (e.g., VDRL \leq 1:2 or RPR \leq 1:4).

No treatment is required. Any neonate with reactive nontreponemal tests should be followed serologically to ensure nontreponemal test returns negative. If follow may be uncertain consider giving Benzathine penicillin G – 50,000 units/kg IM x1.

Neonatal Follow up:

All neonates with reactive nontreponemal tests should receive thorough follow-up examinations and serologic testing (i.e., RPR or VDRL) every 2–3 months until the test becomes nonreactive.

Un-treated neonates with congenital syphilis less likely or unlikely:

- Nontreponemal antibody titers should decrease by age 3 months.
- Antibody titers should be nonreactive by age 6 months.
- If the nontreponemal test is nonreactive at 6 months, no further evaluation or treatment is needed.
- If the nontreponemal test is still reactive at 6 months, the infant is likely infected and should be treated.

Treated neonates:

Those who exhibit persistent nontreponemal test titers by age 6–12 months should be reevaluated by infectious disease and consideration of re-treatment with a 10-day course of a penicillin G regimen.^{1,2}

Author Biography

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Laurie Niewoehner is a Clinical Pharmacist, specializing in high-risk obstetrics and neonates at SSM Health St. Mary's Hospital – St Louis for 22 years. She obtained a PharmD from the University of Minnesota and completed a pediatric pharmacy residency at Children's Mercy Hospital in Kansas City, Missouri. Laurie currently serves as a preceptor at the University of Health Sciences and Pharmacy in St. Louis.

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2. [UpToDate: Syphilis in Pregnancy](#)
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The SSM Health Perinatal Outreach Program

The Perinatal Outreach Program is a collaborative effort between SSM Health St. Mary's Hospital – St. Louis, SSM Health Cardinal Glennon Children's Hospital, and Saint Louis University School of Medicine.

It is designed to improve outcomes for mothers and babies through educational programs and quality improvement activities for regional perinatal care providers in Eastern Missouri and Southern Illinois.

SSM Health Cardinal Glennon Children's Hospital and SSM Health St. Mary's Hospital – St. Louis are designated by the Illinois Department of Public Health as the Administrative Perinatal Center for Southern Illinois.

Continuing Education Opportunities

Many continuing education opportunities, including traditional lectures, hands-on skills sessions, as well as online presentations are available for perinatal professionals in eastern Missouri and Southern Illinois. For course calendars or more specific information on programs, please visit ssmhealth.com/perinatal-outreach, call the Perinatal Outreach Program at 314-577-5317, or send an email to:

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