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Which Infections Increase the Risk of Birth Defects?

***Sonja A. Rasmussen**, Centers for Disease Control and Prevention, Atlanta, Georgia*
***Amelia K. Watson**, University of Florida College of Medicine, Gainesville, Florida*
***Margaret A. Honein**, Centers for Disease Control and Prevention, Atlanta, Georgia*

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The identification of Zika virus as a cause of birth defects has renewed interest in infectious causes of birth defects. Certain infections during pregnancy have long been known to cause birth defects. The effects of rubella during pregnancy were first described in 1941 by Dr. Norman Gregg, an Australian ophthalmologist who identified a particular type of cataract in infants born to women infected with rubella virus (German measles) during pregnancy. The findings in infants whose mothers had been infected with rubella virus during pregnancy were later expanded beyond cataracts to include hearing loss, heart defects, and intellectual disability (termed congenital rubella syndrome). Since then, infections with other pathogens during pregnancy have been identified as causes of adverse pregnancy and birth outcomes, including structural birth defects (Table).

Other infections (e.g., influenza) have not been specifically recognized as a cause of birth defects, but fever, which often occurs with infection, has been associated with an increased risk for certain birth defects, including a doubling in the risk for neural tube defects, including spina bifida and anencephaly. Some infections are suspected to increase the risk for adverse pregnancy outcomes (e.g., Japanese encephalitis virus has been suspected to increase the risk for pregnancy loss, based on evidence from case series), but the increased risk has not been well documented. Some infections pass from mother to infant during pregnancy but have not been found to increase the risk of birth defects (e.g., human immunodeficiency virus [HIV]), although HIV-induced immunosuppression increases the risk of other infections that can increase the risk of birth defects. For most infections, the risk of adverse pregnancy and birth outcomes is unknown because systematic studies have not been performed.

Several different types of adverse pregnancy and birth outcomes, ranging from pregnancy loss to structural birth defects apparent at birth, to developmental disabilities observed after birth, have been associated with infections during pregnancy. Infectious causes of adverse pregnancy and birth outcomes include viruses (cytomegalovirus [CMV], herpes simplex-2 (HSV-2), lymphocytic choriomeningitis virus [LCMV], parvovirus B19, rubella, varicella, Venezuelan equine encephalitis virus, Zika virus), bacteria (*Treponema pallidum, Listeria monocytogenes*), and parasites (*Toxoplasma gondii*). Some infectious pathogens increase the risk for pregnancy loss (e.g., *Listeria monocytogenes and parvovirus B19*), while others increase the risk for birth defects that are evident at birth (e.g., rubella and Zika viruses). Several infectious pathogens increase the risk for defects of the brain and eye, including CMV, LCMV, *Toxoplasma gondii*, and Zika virus. Some infections during pregnancy (e.g., CMV) can cause problems, such as hearing loss, which appear several months after birth in infants with no apparent problems at birth.

As with other teratogenic exposures during pregnancy, the timing of an infection during pregnancy affects the types and frequencies of adverse outcomes observed. For example, the risk of birth defects from first trimester rubella infection may be as high as 100 percent, and includes eye abnormalities, congenital heart defects, defects of the central nervous system, hearing loss and intrauterine growth retardation. Infection in the second trimester poses a lower risk of abnormalities, and the types of abnormalities include hearing loss, retinopathy, microcephaly, and cognitive impairment. Third trimester rubella infection is associated with a much lower risk to the fetus, primarily of intrauterine growth retardation, rather than of birth defects or developmental disabilities.

Infections that cause adverse pregnancy and birth outcomes have different primary routes of transmission, including exposure to infected saliva and urine of infected persons (CMV), fresh urine, droppings, saliva, or nesting materials from infected rodents (LCMV), contaminated foods (Listeria monocytogenes), undercooked foods and cat feces (Toxoplasma gondii), bites of infected mosquitoes (Zika virus), and sexual contact (syphilis and Zika virus). Depending on the type of infection, approaches to prevention differ (Table). For most infections, avoidance of exposure (e.g., avoidance of mosquito bites, rodents, contaminated foods, or contact with infected persons) is the primary prevention strategy. For women who have contracted syphilis during pregnancy, early recognition and treatment can be effective in preventing congenital syphilis. The most successful program for prevention of birth defects that occur after infection during pregnancy is the rubella vaccination program. Following development of a vaccine against rubella and a comprehensive vaccination program, rubella and congenital rubella syndrome have been eliminated from the United States, and progress toward elimination is being made in other countries throughout the world.

Table: Infections that Cause Adverse Pregnancy and Birth Outcomes Following Exposures during Pregnancy

Infection	Pathogen	Most Common Routes of Exposure	Potential Strategies for Pregnant Women to Reduce Risk	Adverse Pregnancy and Birth Outcomes	CDC Website (if available)
Cytomegalovirus (CMV)	Cytomegalovirus – Herpesviridae family	Direct contact with body fluids (e.g., urine, saliva) Sexual contact	Avoid contact with saliva and urine from young children	• Pregnancy loss • Microcephaly • Seizures • Intracerebral (usually periventricular) calcifications • Intellectual disability • Vision loss • Hearing loss (may be present at birth or develop later) • Low birth weight	https://www.cdc.gov/cmv/
Herpes simplex	Herpes simplex virus 2 –	Sexual contact	Avoid sexual contact with infected persons	• Skin, eye, mouth disease – disease	https://www.cdc.gov/std/herpes/

virus 2 (HSV-2)	Herpesviridae family		or use latex condoms Viral suppression of infected partner	localized to skin, eye and mouth • Central nervous system disease • Disseminated disease – involving multiple organs including liver, lungs, and central nervous system	
Listeriosis	*Listeria monocytogenes* - bacterium	Consuming Listeria-contaminated foods	Avoid consuming foods potentially contaminated with Listeria (e.g., soft cheese made with raw milk, raw or lightly cooked sprouts, and hot dogs, lunch meats, cold cuts, other deli meats, or fermented or dry sausages unless they are heated to an internal temperature of 165°F or until steaming hot just before serving)	• Pregnancy loss • Preterm labor	https://www.cdc.gov/listeria/
Lymphocytic Choriomeningitis Virus (LCMV)	Lymphocytic choriomeningitis virus - Arenaviridiae family	Contact with urine, feces, saliva, or blood of infected rodents (common house mouse, hamsters and other pet rodents)	Avoid contact with mice and pet rodents during pregnancy	• Macrocephaly, usually due to noncommunicating hydrocephalus • Microcephaly • Periventricular calcifications and other brain abnormalities • Chorioretinitis, optic atrophy, nystagmus, vitreitis, strabismus, microphthalmia, and cataract	https://www.cdc.gov/vhf/lcm/

Parvovirus B19 (erythema infectiosum, Fifth disease)	Parvovirus B19 - Parvoviridae family	Exposure to respiratory secretions from persons infected with parvovirus B19	Avoid contact with persons infected with Parvovirus B19, if susceptible	• Fetal hydrops • Intrauterine growth restriction • Pleural and pericardial effusions • Fetal death	https://www.cdc.gov/parvovirusb19/fifth-disease.html
Rubella (German measles)	Rubella virus - Togaviridae family	Direct or droplet contact from nasopharyngeal secretions	Vaccinate with rubella-containing vaccine before pregnancy	• Hearing loss • Intellectual disability • Intrauterine growth restriction • Microcephaly • Cataracts, microphthalmia, glaucoma, chorioretinitis, retinopathy • Patent ductus arteriosis, septal defects, pulmonary artery stenosis • Hepatosplenomegaly • Thrombocytopenia, purpura	https://www.cdc.gov/rubella/
Syphilis	*Treponema pallidum* - bacterium	Sexual contact	Avoid sexual contact with infected persons or use latex condoms Routine screening of pregnant women during pregnancy (at first prenatal visit for all women and additional testing at 28 weeks' gestation and again at delivery for those at increased risk), followed by treatment if indicated	• Fetal Hydrops • Preterm birth • Fetal death • Hepatosplenomegaly • Snuffles (copious nasal secretions) • Lymphadenopathy • Mucocutaneous lesions • Pneumonia • Osteochondritis • Pseudoparalysis, edema, rash, • Hemolytic anemia, thrombocytopenia	https://www.cdc.gov/std/syphilis/

				• If untreated, later onset findings: • Interstitial keratitis • Hearing loss • Hutchinson teeth (peg-shaped, notched central incisors) • Anterior bowing of the shins • Frontal bossing • Saddle nose • Symmetric, painless swelling of the knees	
Toxoplasmosis	*Toxoplasma gondii* – protozoan	Consumption of undercooked contaminated meat Exposure to cat feces or contaminated soil	Avoid consumption of undercooked meats Wear gloves during any contact with soil or sand Avoid exposure to cat faces	• Intrauterine growth restriction • Fetal death • Cerebral calcifications • Hydrocephalus • Microcephaly • Chorioretinitis • Seizures • Intellectual disability • Hearing loss	https://www.cdc.gov/parasites/toxoplasmosis/
Varicella (chickenpox)	Varicella-zoster virus – Herpesviridae family	Close contact with a person with varicella or herpes zoster	Vaccinate with varicella vaccine before pregnancy if woman is determined to be susceptible	• Limb hypoplasia • Scarring of skin • Eye abnormalities • Neurologic abnormalities	https://www.cdc.gov/chickenpox/
Venezuelan Equine Encephalitis	Venezuelan Equine Encephalitis virus – Togaviridae family	Bite of infected mosquito	Avoid bites of infected mosquitoes	• Pregnancy loss • Microcephaly • Hydranencephaly • Necrosis of brain tissue • Microphthalmia • Hip dislocation	--

Zika virus	Zika virus – Flaviviridae family	Bite of infected mosquito Sexual transmission	Avoid bites of infected mosquitoes Avoid sexual contact with persons with Zika virus exposure or confirmed infection or use latex condoms Avoid travel to areas with risk of Zika virus	• Severe microcephaly • Misshapen skull consistent with fetal brain disruption sequence • Subcortical calcifications of brain • Hydrocephalus and increased extra-axial fluid • Polymicrogyria • Hypoplasia or absence of brain structures • Microphthalmia, coloboma • Retinal scarring and pigmentary changes • Joint contractures, including clubfoot, hip dislocation	https://www.cdc.gov/zika/

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