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Infections and Vaccinations in Pregnancy: Measles, Mumps, Rubella, and Chicken Pox

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Many physicians and pregnant women have made inquiries to the Illinois Teratogen Information Service concerning exposures to measles, mumps, rubella, and chicken pox or regarding their associated vaccines. The focus of this issue of RISK||NEWSLETTER will be on the possible effects of prenatal exposure to these infections or vaccines.

MEASLES

Measles is a highly communicable disease caused by the paramyxovirus. Symptoms of measles include fever, coryza, conjunctivitis, cough, and a maculopapular rash. The interval between exposure and onset of first symptoms is approximately 10 days. About 12-14 days usually elapse before the onset of a rash. The disease is spread chiefly via droplets and in urban areas predominantly infects children between the ages of 2- 6 years. The use of a live attenuated vaccine since 1963 has decreased the incidence of measles to 1% of its former incidence. Measles occurs less frequently in pregnant women than chicken pox or mumps. Before the introduction of the vaccine this incidence was .4-.6/10,000 pregnancies.

It has been suggested that measles can potentially damage the fetus due to the observation that there is a high frequency of chromosome breaks in in-vitro leukocyte metaphase preparations. This teratogenic potential has neither been proved nor refuted due to the rarity of measles infection during pregnancy. In addition, no particular pattern of abnormalities has been found in infants born to women who had measles during their pregnancy. An increased risk of prematurity and spontaneous abortion in pregnancies following measles infection has been found. In addition, congenital measles has been found to vary in severity from a mild to fatal disease.

Passive immunization is recommended for the prevention of measles in exposed, susceptible pregnant women. Therapy with intramuscular immunoglobulin (Ig) should be started as soon as possible. A dose of .25 ml/kg within 72 hours of exposure is a reliable means of prevention of clinical measles, although Ig given up to 7 days after exposure or in smaller doses may also prevent or at least modify the infection. It is also recommended that passive prophylaxis be followed in 8 weeks by administration of the live attenuated measles vaccine.

Active immunization via derivatives of live attenuated viruses from the Edmonston B strain are typically used. This vaccine produces a mild, noncommunicable infection which can prevent disease in 90% of recipients. After vaccination, 5% of recipients will experience a fever, and 10-20% will have a mild rash. The standard recommendation for women is to postpone conception for 3 months after vaccination due to a theoretical risk of fetal infection following maternal vaccination. There are no reports to substantiate this potential risk. Two reports exist, the first studied 7 women who received the vaccine between the 2nd and the 8th month of pregnancy. None of the infants of these women had any

adverse effects. In addition, the second study followed 37 women with first trimester vaccination and once again no adverse effects were seen in their offspring. Actual infection with measles is at most associated with an increased risk of prematurity or spontaneous abortion, but not birth defects; therefore, it is likely that vaccination is also not associated with birth defects. It should, however, be noted that if hyperthermia (fever above 102 for several days) results due to the vaccination, then there may be an increased risk for certain birth defects, most notably neural tube defects. In this case, MSAFP and Level II ultrasound should be offered to the pregnant woman.

VARICELLA-ZOSTER

(chicken pox and shingles):

Varicella-zoster virus is the virus responsible for chicken pox and shingles. The primary infection with varicella-zoster virus results in chicken pox, with secondary infections resulting in shingles. Varicella-zoster is a member of the herpesvirus family. Like other herpesviruses, varicella-zoster can persist in a latent form.

Chicken pox (varicella) is an acute contagious disease that usually occurs in childhood. It is highly contagious, although less infectious than smallpox or measles. Chicken pox is believed to be spread through respiratory droplets, although the infection mechanism is not fully understood. Symptoms of chicken pox include exanthem-type rash and fever. The rash generally begins on the face or scalp, spreading rapidly to the trunk. The rash usually spares the extremities. The incubation period for chicken pox is approximately 13 to 17 days, with fever and a few "spots" being the first sign of infection. The incidence of infection in the United States is roughly 2-3 million cases annually, appearing to be seasonally affected (i.e., in the winter when children are back at school and more prone to exposure).

Shingles (zoster) results when the latent form of the chicken pox virus is activated. Those who have had chicken pox are at risk for developing shingles later in life. It is commonly a disease of adulthood, although cases of childhood shingles have been reported. Symptoms of shingles include painful lesions on the skin. The incidence of zoster is estimated at 3.4 per thousand cases per year. Zoster is reported year round, supporting the hypothesis that zoster can manifest itself subsequent to, or not subsequent, to re-exposure.

Immunization to chicken pox and zoster is not readily available, although some experimental immunizations are being tested. Immunity to chicken pox through previous infection or exposure without developing acute infection can be determined by serum antibody tests. Antibodies to chicken pox and zoster are of the IgG, IgA and IgM classes.

The incidence of chicken pox in pregnancy is approximately 240-1500 cases per year, or about 5 in 10,000 gestations. Maternal viremia is thought to spread the infection to the placenta and fetus but the attack rate is very low, with the incidence of intrauterine varicella after maternal infection being 25%. Maternal infection during 8 to 20 weeks poses the greatest risk to the developing fetus.

The findings associated with varicella infection during pregnancy include skin scarring, limb hypoplasia, cortical atrophy and eye defects. Infants with the most severe manifestations appear to be infants who were prenatally exposed during the first trimester. The risks for fetal anomalies is estimated to be between 2.3-4% above the background risk for first trimester exposures and 0.6% above the background risk for second and third trimester exposures.

The incidence of shingles (zoster) during pregnancy has not as yet been estimated. Risks of congenital malformations in pregnancies complicated by zoster infections are thought to be minimal. Zoster is not a viremic infection and therefore is unlikely to affect the developing fetus.

When a pregnant woman has been exposed to chicken pox during pregnancy, passive immunization

with Varicella-Zoster immunoglobulin (VZIG) is offered within 96 hours of exposure. A dosage of 5 ml is usually recommended for adults. The rationale for passive immunization is to prevent the mother from developing severe chicken pox. Chicken pox infection in adulthood is generally more clinically severe, and more so during pregnancy.

When a pregnant patient has been exposed to chicken pox and is concerned about possible teratogenic effects, a few options are available. Counseling regarding information on the risks of maternal infection and possible teratogenic effects is indicated. In addition, Level II ultrasound for any detectable fetal anomalies can be offered.

MUMPS

Mumps is an acute, generalized, communicable disease caused by a paramyxovirus. The usual incubation period is 14 to 18 days, with wide variability. Transmission of the mumps virus occurs via droplet spread or direct contact with infected saliva.

Mumps generally affects children between the ages of 5 to 15 years. Approximately one third of mumps infections are subclinical. In those cases with clinical manifestations, the symptoms are swelling of one or both parotid glands, salivary glands, meninges and testes of postpubertal males. Other symptoms of infection include fever, excessive tiredness, and lack of appetite. Gestational mumps is rare and is usually benign, with severity of the symptoms similar to those of the non-pregnant patient.

Risks of fetal malformations subsequent to mumps exposure appear to be unlikely. However, there appears to be a significant risk of spontaneous abortion following maternal infection. This risk appears to be greatest in the first trimester, although this risk is possible throughout pregnancy. Fetal loss also tends to occur within two weeks of maternal infection.

Animal studies on mumps exposure during pregnancy have suggested a possible association with birth defects, although data is very minimal. A possible association with endocardial fibroelastosis and gestational mumps infection has been described, but is not defined by any controlled study. No other human studies on mumps exposure during pregnancy have suggested an increased risk for birth defects.

Passive immunity to mumps through mumps Ig has proven ineffective and is no longer commercially available.

Active immunization is currently available and recommended for non-pregnant susceptible patients and others who are not immune. More than 90% of individuals who are not immune will develop immunity after vaccination. Vaccination results in a subclinical, noncommunicable infection, rarely associated with side effects.

Vaccination during pregnancy has been associated with placental infection, although follow up studies on tissue obtained after elective termination following vaccination showed no signs of placental infection. Recommendations that women wait three months before conceiving following vaccination is based on a theoretical risk of placental infection, not actual reports of placental infection. Mumps vaccination is not likely to be associated with an increased risk for birth defects since mumps infection itself is not likely to increase the risk for fetal malformations. The most serious risk associated with mumps infection is the risk of spontaneous abortion following mumps infection.

RUBELLA

Rubella has been classified as a member of the togavirus family. Rubella is known to be extremely contagious, with an attack rate close to 100%. It is a mild illness with few clinical manifestations, making it easy to escape clinical detection.

Rubella is transmitted both directly and by droplet. Individuals are highly contagious from a few days prior to the onset of the rash until a few days after it appears. Incubation is generally 2 1/2 weeks with a range of 2 to 3 weeks. Symptoms in children include rashes, fever and generalized weakness. In adults these symptoms include low grade fever, malaise, cough, conjunctivitis and diffuse lymphadenopathy around the neck. Joint pain can persist for up to 10 days after the rash fades.

Transmission during a primary maternal infection can occur, while transmission during a maternal reinfection is rare. This indicates that maternal immunity serves to protect the fetus as well.

It has been well documented that the gestational age at the time of infection is the most important determinant of fetal effects. For accurate risk assessment in pregnancies that develop maternal infection, the timing in pregnancy, along with the route of infection must be assessed. The overall risk for birth defects following first trimester exposure is thought to be about 69%. When infection occurs prior to the 11th week of pregnancy the risk is thought to be approximately 90%. Fetal infection rates decline significantly between 12 and 28 weeks of gestation. These findings suggest that the placenta may partially prevent transfer of the virus to the fetus, but that this barrier is least effective during the first and last trimesters of pregnancy.

Fetuses exposed in utero can have a wide range of complications. Clinical features of congenital rubella infection can be divided into three categories: 1) transient manifestations, 2) permanent manifestations and 3) late-onset manifestations. It is also known that the rate of spontaneous abortion following primary maternal infection is high. The higher rate of chromosome abnormalities also suggests that the infection may have an effect on the rate of chromosome aberrations.

Transient manifestations occurring in the neonate include hepatosplenomegaly, thrombocytopenia, hepatitis, corneal clouding and bone lucencies. Approximately 50% of infants with these types of malformations also have intrauterine growth retardation (IUGR).

The most common permanent manifestations include defects of the heart and blood vessels, the eye and the central nervous system. 80% or more of rubella infants have deafness. Heart defects are more common in infants exposed during the first trimester. More than half of the infants infected with rubella during the first 2 months of gestation have congenital heart disease (CHD), usually vascular stenosis or patent ductus arteriosus. CHD is rarely seen with maternal infection beyond 11 weeks gestation. Up to 50% of individuals with congenital rubella have resulting CNS abnormalities, including microcephaly, as well as behavioral and psychiatric disorders.

Late-onset manifestations include deafness, endocrinopathies, ocular abnormalities, vascular defects and ongoing CNS disease. Hearing loss can worsen over time, as well as appear suddenly after years of normal hearing. Mental retardation and behavioral abnormalities have been reported to either worsen or first appear later in life, suggesting that the rubella virus can persist in the brain and become reactivated after years of latency. Insulin-dependent diabetes mellitus occurs in as many as 20% of adults with congenital rubella infection, while thyroid abnormalities occur in 5%.

Vaccinations with live attenuated rubella virus are currently available and are recommended for those who are thought not to have established immunity against rubella previously. These vaccinations are especially recommended for women of childbearing age who do not demonstrate immunity against rubella.

Concerns have been raised about the possibility of an infant developing congenital rubella syndrome subsequent to maternal vaccination. Data to date suggests that the risk of having an infant with birth defects following immunization during pregnancy or three months prior to conception is minimal. The theoretical risk is thought to be about 1.7%, although no cases of congenital rubella syndrome following immunization three months pre or post conception have been observed. For this reason,

immunization during pregnancy or within three months prior to conception is contraindicated. However, if immunization should occur, the risk of birth defects is thought not to warrant interruption of pregnancy.

SUMMARY

Although measles has been associated with an increased risk of prematurity and spontaneous abortion, the majority of cases of prenatal measles infection or vaccination will probably put a woman's pregnancy at little or no greater risk for adverse outcome above the background risk.

Prenatal exposure to chicken pox (varicella zoster) has been associated with an increased risk for birth defects. The risk for fetal anomalies following first trimester exposure is estimated to be between 2.3-4% above the background risk and 0.6% above the background risk for second and third trimester exposures.

Mumps during pregnancy has been associated with an increased risk of spontaneous abortion. This risk appears to be greatest in the first trimester, although this risk is possible throughout pregnancy. Vaccination for mumps during pregnancy has not been associated with an increased risk of birth defects.

Fetal infection following primary maternal rubella infection is highest when infection occurs before 12 weeks and after 28 weeks gestation. The risk for birth defects after first trimester exposure or when the mother develops symptoms of exposure or "infection" is approximately 69%, with congenital heart disease seen only in those infants with maternal infection prior to 11 weeks. Hearing loss is the most common birth defect, occurring in up to 80% of the infected infants. Although there is a theoretical risk of rubella infection after immunization, no cases have been reported.

For more on the web: [about Chicken Pox](#)