

Vaccination during pregnancy

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Abstract

Question One of my patients is studying to become a dental hygienist. Owing to the program requirements, she received several vaccinations last week, including measles-mumps-rubella, varicella, and hepatitis B (HB) vaccines, as well as a tetanus booster. However, today a blood test confirmed that she is currently 6 weeks pregnant. What is known about the safety of these vaccines during pregnancy, and are there any general recommendations for vaccines for women who are planning to become pregnant or who are currently pregnant?

Answer The combination measles-mumps-rubella vaccine and the varicella vaccine are live attenuated vaccines, and are contraindicated during pregnancy owing to theoretical concerns. However, there is no evidence that there are increased risks of malformations, congenital rubella syndrome, or varicella syndrome attributable to these vaccines. The HB and tetanus vaccines are composed of noninfectious particles or toxoids, and theoretically should cause no increased risk to the developing fetus. In addition, limited observational data also support no increased risk of any adverse pregnancy outcomes; consequently, administration of the HB and tetanus vaccines might be, if indicated, considered during pregnancy.

Résumé

Question Une de mes patientes étudie pour devenir hygiéniste dentaire. Pour répondre aux exigences du programme, elle a reçu divers vaccins la semaine dernière, notamment contre la rubéole, la rougeole et les oreillons, la varicelle, l'hépatite B (HB), ainsi qu'un vaccin de rappel contre le tétanos. Par ailleurs, aujourd'hui, une analyse sanguine a confirmé qu'elle était actuellement enceinte de 6 semaines. Que sait-on de l'innocuité de ces vaccins durant la grossesse et y a-t-il des recommandations concernant les vaccins pour les femmes qui planifient une grossesse ou sont actuellement enceintes?

Réponse Le vaccin combiné contre la rubéole, la rougeole et les oreillons et celui contre la varicelle sont des vaccins vivants atténués et ils sont contre-indiqués durant la grossesse en raison de préoccupations théoriques. Par ailleurs, il n'y a pas de données probantes à l'effet qu'il y ait des risques accrus de malformations, de syndrome congénital de la rubéole ou de syndrome de la varicelle attribuables à ces vaccins. Les vaccins contre l'HB et le tétanos se composent de particules non infectieuses ou toxicoïdes et, théoriquement, ils ne devraient pas accroître les risques pour le fœtus en développement. De plus, des données d'observation limitées corroborent aussi qu'il n'y a pas de risques accrus d'effets indésirables sur l'issue de la grossesse; par conséquent, l'administration des vaccins contre l'HB et le tétanos, si elle est indiquée, pourrait être envisagée durant la grossesse.

Women are sometimes exposed to live or inactive vaccines during pregnancy or shortly before conception. Although live vaccines are contraindicated in pregnancy, that recommendation is based on theoretical risk rather than evidence. Inactive vaccines pose no theoretical risk, and recommendations reflect this.

Live vaccines during pregnancy

Theoretically the live attenuated virus in a vaccine could cross the placenta and result in viral infection of the fetus. Owing to this concern, most live attenuated vaccines, including the measles-mumps-rubella (MMR) and varicella vaccines, are contraindicated during pregnancy.¹

Measles-mumps-rubella vaccine. Wild-type rubella infection might result in spontaneous abortion, stillbirth,

and, of most concern, congenital rubella syndrome (CRS), with its hallmark characteristics of sensorineural deafness, congenital heart defects, microcephaly, learning difficulties, and eye and bone defects. Measles infection in pregnancy might result in substantial maternal morbidity, an increased abortion rate, prematurity, stillbirth, and possibly congenital malformations. The data for mumps infection are not consistent, with some studies showing a possible increased rate of spontaneous abortion.²

There have been no reports of congenital malformations attributable to the MMR vaccine virus. The Centers for Disease Control and Prevention (CDC) estimated the theoretical risk to the fetus of CRS following vaccination with the rubella vaccine to be 0% to 1.6%.² In 1971, the CDC established the Vaccine in Pregnancy registry of women who had received rubella vaccines

within 3 months before or after conception. By 1989 there were data on 1221 inadvertently vaccinated pregnant women. There was no evidence of an increase in fetal abnormalities or cases of CRS in the enrolled women or the 321 rubella-susceptible women; therefore, enrolment in the registry ended.^{2,3}

Motherisk conducted a prospective controlled study that included 94 women exposed to the rubella vaccine in the 3 months before conception or during the first trimester of pregnancy. The Motherisk team reported no difference in pregnancy outcomes or malformation rates between the exposed and the nonexposed groups, and no adverse effects consistent with CRS.⁴ These data have been confirmed in other immunization campaigns and studies.⁵⁻⁸

Varicella vaccine. Varicella virus infection during pregnancy is associated with a risk of congenital varicella syndrome, characterized by low birth weight, skin scarring, ophthalmologic defects, limb hypoplasia of bone and muscle, neuropathic bladder, and gastrointestinal and neurologic abnormalities.⁹

There are no reports of congenital varicella syndrome after exposure to varicella vaccine during pregnancy. A registry was established by the manufacturer in collaboration with the CDC to monitor maternal and fetal outcomes of women who were inadvertently immunized with varicella vaccine in the 3 months before conception or at any time during pregnancy. Among the 737 women with pregnancy outcomes available, there were no patterns of defects and no infants were born with features consistent with congenital varicella syndrome among any of the women enrolled or among the seronegative women.¹⁰

Inactive vaccines during pregnancy

Immunization during pregnancy with vaccines containing inactive viruses or toxoids is not expected to be associated with any increased risks to the fetus.

Hepatitis B (HB) vaccine. Hepatitis B infection in a pregnant woman might result in severe disease for the mother and possibly an increase in preterm birth; however, it is not associated with increased abortion rates, stillbirth, or congenital malformation. Therefore, the biggest concern of maternal infection is vertical transmission of the virus to the offspring, as 70% to 90% of babies will remain chronically infected into adult life and be prone to cirrhosis and hepatocellular carcinoma.¹¹ The HB vaccine is an inactivated (recombinant) virus vaccine; and because the vaccine is composed of noninfectious HB surface antigen particles, it should theoretically cause no increased risk.¹² There were no adverse pregnancy outcomes reported in several small studies following women vaccinated with HB vaccine during pregnancy.¹³⁻¹⁶

Although there is limited evidence, there appears to be no increased risk of adverse fetal outcomes when the HB

vaccine is administered during pregnancy. Pregnancy is therefore not considered a contraindication to vaccination, and the Advisory Committee on Immunization Practices (ACIP)¹² and the Public Health Agency of Canada¹⁷ recommend that the vaccine should be offered to pregnant women at high risk of acquiring HB infection.

Tetanus. Tetanus can cause severe morbidity in the mother and mortality in the neonate.¹⁸ The tetanus vaccine contains noninfectious toxoids. The American Congress of Obstetricians and Gynecologists recommends use of tetanus immune globulin, as there is no evidence of any adverse effects to the fetus from the vaccine.¹⁹ In addition, Dastur and colleagues evaluated the efficacy and safety of a single-dose tetanus toxoid on 200 unimmunized primigravidae women in the last trimester of pregnancy. No adverse effects were encountered in the mothers and there was no increase in stillbirths.²⁰ These results were confirmed in 2 case-control studies.^{18,21}

The ACIP recommends that pregnant women receive the combined tetanus and diphtheria vaccine if indicated. Previously vaccinated pregnant women who lack the primary series of immunizations or who have not received booster shots in the past 10 years should complete the primary series or receive booster doses. Even though there is no evidence that tetanus and diphtheria toxoids are teratogenic, vaccination during the second or third trimester is preferred.²² Also, immunization will protect the mother for several years and passively protect the infant for several months after delivery.²³

Conclusion

Exposure to either live or inactive vaccines during pregnancy has not been associated with an increased risk of adverse pregnancy outcomes, and no child to date has been born with CRS or varicella syndrome following rubella or varicella vaccination of the mother anytime during pregnancy. However, despite this evidence-based information, these vaccines remain contraindicated during pregnancy, and the Public Health Agency of Canada and the ACIP continue to recommend that women avoid becoming pregnant for approximately 1 month following vaccination. They do state that if pregnant women are exposed to these vaccines or if pregnancy occurs soon after vaccination, the women should be counseled regarding the theoretical risks to the fetus and vaccination should not be a reason to consider termination of pregnancy.^{1,17}

Competing interests

None declared

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MOTHERISK Motherisk questions are prepared by the Motherisk Team at the Hospital for Sick Children in Toronto, Ont. Ms Narducci is a doctoral candidate in the Faculty of Pharmacy at the University of Toronto. Ms Bozzo is Assistant Director of the Motherisk Program, and Ms Einarson continues to be a member of the Motherisk team as a consultant.

Do you have questions about the effects of drugs, chemicals, radiation, or infections in women who are pregnant or breastfeeding? We invite you to submit them to the Motherisk Program by fax at 416 813-7562; they will be addressed in future Motherisk Updates.

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