Chapter 11
Vaccinations in Pregnancy

I. Dale Carroll and Jenny Visser

Key Points

- Pregnant women are relatively immune-suppressed, so:
  - Live vaccines are generally contraindicated.
  - Vaccines may have suboptimal effects.
- Inactivated viruses and bacterial vaccines and toxoid vaccines are considered safe.
- Pregnant women should receive influenza- and pertussis-containing vaccines.
- Delay vaccinations until the second or third trimester when possible.
- Make an individualised risk assessment based on safety and efficacy of vaccine and the actual risk of exposure.

General Considerations

One of the goals of maternal vaccination is the protection of the infant against infectious diseases. Many times, the most effective way of protecting the unborn and newly born infant is to immunise the mother. Many antibodies can be passed transplacentally to the infant and thus provide a level of protection prior to and

I.D. Carroll (✉)
The Pregnant Traveler, Spring Lake, MI, USA
e-mail: travdoc@travdoc.com

J. Visser
Department of General Practice, University of Otago, Wellington, New Zealand
e-mail: jenny.visser@otago.ac.nz

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Table 11.1 Immunisations in pregnancy

Vaccine	Type of vaccine	Maternal risk from disease	Fetal risk from disease	Maternal risk of vaccine	Fetal risk of vaccine	Comment
Anthrax	Bacterial particles	May be more severe in pregnancy	Increased risk of miscarriage or preterm birth	None known	None known	
BCG	Live bacterial	Course of disease not affected by pregnancy	Congenital tuberculosis occurs	None known	Possible disseminated infection (theoretical)	Not effective enough to be felt useful
Brucellosis	Live bacterial	Not affected by pregnancy	Miscarriage and preterm birth	No data	No data	Prophylactic antibiotics are preferred to vaccination
Cholera/diarrhoea Oral	Live bacterial	Diarrhoea more severe, dehydration, acidosis	Increased risk of abortion or premature birth	No data available	No data available	Oral antibiotic prophylaxis for cholera felt to be preferred due to poor efficacy of vaccine
Hepatitis A	Inactivated virus	Possibly increased severity in third trimester	Increased risk of miscarriage or preterm birth	None known	None known	
Hepatitis B	Purified surface antigen	Possibly increased severity in third trimester	Miscarriage or preterm birth. Transmission to newborn	None known	None known	Use in pregnancy recommended in nonimmune women
Herpes zoster	Live virus	Not affected by pregnancy	Possible congenital varicella syndrome	No data available	No data available	Dose of live virus is greater than in varicella vaccine
Human papilloma virus (HPV)	Inactivated virus	Rapid growth of condylomata in pregnant	Viral transmission to fetus	None known	None known	Use of other methods of STD prevention is preferred

Immune globulins	Immune globulin			None known	Single report of congenital anomaly	Use usually limited to postexposure prophylaxis
Influenza	Inactivated virus	Increased morbidity and mortality	Increased risk of miscarriage	None known	None known	Use in all trimesters is advised
						Use of live virus not recommended
Japanese encephalitis	Inactivated virus	Animal data suggests adverse pregnancy outcome	Embryo-fetal death common in animals. No human data	None reported	None known	Preferred over the use of live vaccine in pregnancy
Measles	Live virus	Not affected by pregnancy	Increased miscarriage. Possible congenital anomalies	None known	None confirmed	Use only if exposure is likely and unavoidable
Meningitis	Conjugate/ polysaccharide	Not affected by pregnancy	Depending on severity of maternal illness	None known	None known	Registry exists for reporting conjugate use in pregnancy
Mumps	Live virus	Not affected by pregnancy	Possible increased rate of miscarriage	None known	None confirmed	Use only if exposure is likely and unavoidable
Pneumococcal	Polysaccharide	Disease may be more severe in pregnancy	Premature delivery, fetal death	None known	None known	Consider in splenectomised, immunosuppressed or those with sickle cell anaemia
Polio (eIPV)	Inactivated virus	Possibly increased disease severity in pregnancy	High mortality rate in neonatal disease	None known	None known	Use of live oral vaccine not recommended
Rabies	Killed virus	100 % fatality	Fatal to fetus if mother dies	None known	None known	Pre- and postexposure schedule same as in non-pregnant

(continued)

Table 11.1 (continued)

Vaccine	Type of vaccine	Maternal risk from disease	Fetal risk from disease	Maternal risk of vaccine	Fetal risk of vaccine	Comment
Rabies immune globulin	Immune globulin	100 % fatality	Potentially fatal to fetus	None known	None known	Dosage schedule same as in non-pregnant
Smallpox	Live virus	Not affected by pregnancy	Not affected by pregnancy	None known	Vaccinia virus may be transmitted to fetus	Use limited to instances of high risk of exposure
Rubella	Live virus	Not affected by pregnancy	High rate of miscarriage and multiple congenital anomalies	None known	None confirmed	Use only if exposure is likely and unavoidable. Registry exists for reporting use in pregnancy
Tetanus, diphtheria, pertussis (Tdap)	Toxoid	Not affected by pregnancy	Neonatal pertussis	None known	None known	Update during each pregnancy. Delay administration until third trimester if convenient
						(Malaria prophylaxis may interfere with immune response)
Tick-borne encephalitis	Inactivated virus	Not affected by pregnancy	Viral transmission to fetus	None known	None known	
Tuberculin skin test	Toxoid	Course of tuberculosis not affected by pregnancy	Congenital tuberculosis	None known	None known	Reaction to test appears unaltered by pregnancy
Typhoid Vi	Polysaccharide	Increased risk of diarrhoea, GI bleeding, perforation	Increased risk of abortion, fetal death	None known	None known	

Typhoid oral	Live bacterial	Increased risk of diarrhoea, GI bleeding, perforation	Increased risk of abortion, fetal death	Nausea, vomiting, diarrhoea	None known	Theoretical risk of mutation into pathogenic form. Inconvenient side effects of nausea and vomiting
Varicella	Live virus	Increase in severe pneumonia	Congenital varicella in second and third trimesters	None known	None confirmed	Use only if exposure is likely and unavoidable. Registry exists for reporting use in pregnancy
Yellow fever	Live virus	Not affected by pregnancy	Depending on severity of maternal illness	Possibly diminished immune response in pregnancy	Vaccine virus may be transmitted to newborn	Use only if exposure is likely and unavoidable. Immune response may be diminished. Postvaccination titres encouraged

immediately after birth. The primary goal of vaccination during pregnancy is, of course, to protect the mother (Table 11.1).

Because controlled studies are not carried out on pregnant women, data is not available regarding individual vaccines in pregnancy. However, there are no known significant risks involved in vaccinating pregnant women with inactivated virus or bacterial vaccines or toxoids. Live vaccines may pose a theoretical risk to the fetus. The benefits of vaccinating pregnant women usually outweigh potential risks when the likelihood of disease exposure is high and unavoidable and when infection would pose a risk to the mother or fetus. When feasible, the itinerary may need to be modified to avoid the risk of exposure to the disease.

Immunologic changes that occur during pregnancy, however, may in some cases dampen the immune response that one wishes to obtain by these vaccines. This has been seen to some extent with yellow fever vaccination and perhaps also with hepatitis B vaccination.

If possible, vaccination should be delayed until the second or third trimester, to avoid possible teratogenic febrile effects during the first trimester.

Toxoids

Tetanus, Diphtheria and Pertussis Vaccines (Tdap) Tetanus, diphtheria and pertussis vaccines are ones that are recommended for all pregnant women if they are not already immune. It is generally recommended that the combined vaccine be given during the third trimester of pregnancy to provide maximum benefit to both the mother and infant. There has been some concern that malnutrition, vitamin A deficiency or malaria chemoprophylaxis might interfere with an adequate immune response; therefore, the vaccine should be given whenever possible before the initiation of malaria chemoprophylaxis.

Tuberculin Skin Testing Mantoux testing, if indicated, is safe in pregnancy and interpreted according to the same criteria as in the non-pregnant.

Polysaccharide, Killed Bacterial and Conjugate Vaccines

Pneumococcal Morbidity from pneumonia is increased in pregnancy, largely due to respiratory and cardiovascular changes. Premature labour and fetal death may result from this. Thus, any recommendation for the use of pneumococcal vaccine is not altered by pregnancy. Patients and travellers, who might be considered for this vaccine, would include those who are immunosuppressed, have had a splenectomy or have sickle cell disease. Maternal vaccination has been shown to increase milk concentrations of IgA antibodies, so there is benefit to the newborn as well.

Meningococcal Studies of polysaccharide vaccine (MPSV4: quadrivalent meningococcal polysaccharide vaccine) use during pregnancy have not demonstrated adverse effects among either pregnant women or newborns. The available data regarding the use of the conjugate (MCV4: quadrivalent meningococcal) vaccine during pregnancy have shown no vaccine-related ill effects.

Typhoid Typhoid may be a more serious disease in pregnancy, with a higher incidence of complications such as bleeding intestinal ulcers. There is also an increased risk of abortion and fetal death. Transplacental infection of the fetus may also occur. Typhoid vaccination is recommended whenever it might otherwise be indicated. Both the injectable and the oral forms of vaccine are considered acceptable during pregnancy, but due to the slowing of gastrointestinal function and resulting side effects, the injectable form might be preferred. With either vaccine, no more than 70 % efficacy can be expected; thus, food and water precautions remain important.

Inactivated Virus Vaccines

Hepatitis A Hepatitis A infection during pregnancy may result in serious maternal consequences with fetal loss or vertical transmission to the fetus; therefore, vaccination during pregnancy is recommended.

Hepatitis B In the case of hepatitis B, the danger of the disease lies in the risk of transmission to the infant. While there is some evidence of a lower antibody response in pregnancy, vaccination of pregnant women with this vaccine has been shown to be safe and effective and is recommended in nonimmune women.

Influenza Influenza results in increased morbidity and mortality during pregnancy. Vaccination with the inactivated influenza vaccine is now recommended for all pregnant women at any stage of pregnancy.

Polio This disease, should it occur during pregnancy, may result in as high as a 40 % neonatal mortality, and there is an increased risk of maternal paralytic disease in pregnancy. The enhanced inactivated polio vaccine (eIPV) is preferred for its safety both in the pregnant patient and in the community. The live oral polio vaccine (OPV) is no longer available in most countries and is considered contraindicated in pregnancy, but there are reports of pregnant women having received it with no evidence of fetal or maternal harm.

Japanese Encephalitis The Japanese encephalitis virus causes embryo-fetal death in experimental animals and has been known to be passed transplacentally. The cell-derived, inactivated Jespect®/Ixiaro® vaccine would theoretically be safe in pregnancy. The live vaccine is contraindicated. Despite the lack of available data, due to severe consequences of the disease, it would seem prudent to vaccinate pregnant

women for whom exposure is likely. Mosquito avoidance should, however, remain the mainstay of prevention.

Rabies Because rabies is almost universally fatal, the consensus has long been that postexposure rabies vaccination should be used during pregnancy when indicated. There is presumptive evidence of transplacental passage of antibodies. This supports the use of pre-exposure vaccination when there is a substantial risk of maternal exposure to the disease.

Human Papilloma Virus (HPV) Recent data hint that there may be an association between high-risk HPV and pre-eclampsia. This plus the fact that many travellers become exposed to sexually transmitted diseases makes us consider this vaccine in counselling pregnant travellers. The HPV vaccine contains inactivated virus and thus is considered safe in pregnancy. Another consideration recommending the use of this vaccine during pregnancy is the vertical transmission of the virus to the fetus at the time of birth.

Tick-Borne Encephalitis The virus may be transmitted transplacentally, but there is little data on the consequences of this. There have been reports of high fever after the administration of the vaccine to young children, but this does not seem to be as common in adults. The manufacturers recommend its use in pregnancy only after careful, individual consideration.

Live Virus Vaccines

It is primarily the viral illnesses such as rubella and varicella that have shown the propensity to cause recognisable patterns of fetal damage if they occur during pregnancy. Thus, there is added reason to protect against these viruses during pregnancy. But the vaccines available for such protection are live viruses, altered from their original teratogenic form but with the theoretical potential nonetheless of causing the very pattern of birth defects that they are designed to prevent. Several decades of available data on inadvertently administered vaccine are somewhat reassuring, but these vaccines should be avoided during pregnancy wherever possible.

Mumps Some spontaneous abortions and other fetal anomalies have been reported when this disease occurs in the first trimester. In the rare event that exposure to this disease is likely to occur in a nonimmune pregnant woman, administration of the vaccine would be considered preferable to contracting the disease.

Measles Available data would seem to indicate an increased rate of abortion as well as a perinatal mortality rate of 10 % and possibly fetal anomalies if the disease is contracted during pregnancy. There is also the risk of serious maternal complications, particularly pneumonia and fetal loss, if this disease occurs during pregnancy. As with the mumps vaccine, no adverse maternal or fetal events have been reported following the inadvertent administration of this vaccine during pregnancy.

Rubella This is probably the most feared viral infection during pregnancy. Pre-vaccine statistics showed an almost 100 % incidence of congenital rubella syndrome (CRS) if the disease is contracted in the first trimester and up to 60 % in the second trimester.

Despite careful observation, no such syndrome has been seen to occur with vaccination, even though there is evidence of passage of the vaccine virus to the fetus. If there is risk of rubella infection in a nonimmune pregnant woman, use of the vaccine is felt to be preferable to contracting rubella during the pregnancy. It should be noted that about 2 % of women do not respond with sufficient antibody production to develop immunity. Rubella immune globulin may be considered as an alternative postexposure prophylaxis, but there is very little data to support its efficacy.

Varicella As with rubella, there is a risk of a syndrome of congenital defects associated with maternal varicella infection, and this disease can have serious maternal and fetal consequences if contracted late in pregnancy. For susceptible pregnant individuals with unavoidable likely exposure to this virus, the vaccine would be considered preferable to the disease. As with rubella, one may consider the use of postexposure varicella immune globulin, but its efficacy remains unproven.

Herpes Zoster Herpes zoster (shingles) is not known to be more common or more severe during pregnancy, but it may have serious fetal effects. Because the zoster vaccine contains a significantly larger dose of virus than the routine varicella vaccine, however, its use in pregnancy is not advised.

Yellow Fever Yellow fever is a very serious disease with up to 50 % mortality rate in native populations and thus needs to be avoided during pregnancy. There is reassuring data from several sources regarding the safety of this vaccine during pregnancy.

Meanwhile, the efficacy data is conflicting, with some data showing a lower antibody titre when this vaccine is given during pregnancy. The relative immune suppression that occurs with pregnancy or a difference in nutritional status might explain this difference. Even the lower titres, however, were not correlated with any diminished protectiveness of the vaccine. The consensus remains that if yellow fever exposure is likely and unavoidable during the travel, the vaccine should be given. Under these circumstances, however, it might be wise to obtain a titre to test for immunity. If travel requirements and no disease exposure are the only reason to vaccinate, then it would be preferable to provide the pregnant traveller with an appropriate waiver.

Live Oral and Bacterial Vaccines

BCG Tuberculosis is a serious disease even in pregnancy. The BCG vaccine, however, is of limited value in adulthood. Although no harmful effects to the fetus have been associated with BCG vaccine, disseminated infections with other mycobacteria have been reported in the infants of infected mothers, and so its use, being a live bacterium, is not recommended during pregnancy.

Typhoid When speaking of typhoid vaccine, some recommend the preferential use of live, oral vaccine. There is at least a theoretical risk, however, that the vaccine strains might replicate and cross the placental barrier, causing fetal harm similar to that seen with *Salmonella typhi.* In addition, decreased gastrointestinal motility along with increased exposure to gastric acid might either decrease the vaccine's effectiveness or enhance the risk of gastroenteritis. Also, one of the more common side effects of this vaccine is nausea and vomiting, a problem already frequent in pregnancy. These considerations might make the use of the Typhim Vi® vaccine preferable during pregnancy.

Cholera and Traveller's Diarrhoea Recent studies point out the severe risk that cholera presents during pregnancy. Traveller's diarrhoea is also likely to be more frequent and more severe in pregnancy. To date, the benefit from the available vaccines has been found to be short-lived and incomplete, and they are not usually recommended except when the traveller will be working in high-risk areas such as refugee camps. Dukoral® as an inactivated vaccine is probably safe to use in pregnancy, but as with the oral typhoid vaccine, the side effects of nausea and vomiting may reduce its benefit in an already nauseated pregnant patient.

Immune Globulin

Generally, the immune globulins are felt to be safe in pregnancy, but because the immune globulins are a human blood product, the possibility of inadvertent disease transmission remains. There remain conditions, however, such as varicella and rabies where postexposure use of these products is highly recommended, even in pregnancy.

Unusual Vaccines

These are vaccines of various types which are not in common use but the need for which might arise under special circumstances.

Anthrax At least one review estimates that this disease predisposes to miscarriage and preterm delivery. Most experts primarily recommend various medications for postexposure prophylaxis. In a study of women who became pregnant shortly after receiving the vaccine, there was no increased incidence of adverse pregnancy outcomes.

Smallpox The vaccine is prepared from vaccinia virus, a virus that occurs only in the laboratory. Infection with this virus has been reported in the fetus after maternal immunisation. Thus, the administration of smallpox vaccine is not recommended during pregnancy.

Brucellosis Brucellosis is known to cause abortion and preterm delivery in domestic animals and to a lesser degree in humans. Vaccination against this disease is usually limited to persons in high-risk occupations. Prophylactic or treatment doses of co-trimoxazole or rifampin are recommended instead of the vaccine.

Further Reading

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