Vaccinations in Pregnancy

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Adult immunization rates have fallen short of national goals partly because of misconceptions about the safety and benefits of current vaccines. The danger of these misconceptions is magnified during pregnancy, when concerned physicians are hesitant to administer vaccines and patients are reluctant to accept them. Routine vaccines that generally are safe to administer during pregnancy include diphtheria, tetanus, influenza, and hepatitis B. Other vaccines, such as meningococcal and rabies, may be considered. Vaccines that are contraindicated, because of the theoretic risk of fetal transmission, include measles, mumps, and rubella; varicella; and bacille Calmette-Guérin. A number of other vaccines have not yet been adequately studied; therefore, theoretic risks of vaccination must be weighed against the risks of the disease to mother and fetus. Inadvertent administration of any of these vaccinations, however, is not considered an indication for termination of the pregnancy. (Am Fam Physician 2003;68:E299-309. Copyright© 2003 American Academy of Family Physicians.)

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The administration of vaccines during pregnancy poses a number of concerns to physicians and patients about the risk of transmitting a virus to a developing fetus. This risk is primarily theoretic. Live-virus vaccines are therefore generally contraindicated in pregnant women. According to the Centers for Disease Control and Prevention (CDC),[1] if a live-virus vaccine is inadvertently given to a pregnant woman, or if a woman becomes pregnant within four weeks after vaccination, she should be counseled about potential effects on the fetus. Inadvertent administration of these vaccines, however, is not considered an indication for termination of the pregnancy.

No evidence shows an increased risk from vaccinating pregnant women with inactivated virus or bacterial vaccines or toxoids.[1] Therefore, if a patient is at high risk of being exposed to a particular disease, if infection would pose a risk to the mother or fetus, and if the vaccine is unlikely to cause harm, the benefits of vaccinating a pregnant woman usually outweigh the potential risks.

Physicians should consider vaccinating pregnant women on the basis of the risks of vaccination versus the benefits of protection in each particular situation, regardless of whether live or inactivated vaccines are used.

Vaccines commonly administered by family physicians, and their indication for use during pregnancy, are summarized in *Table 1*.[1]

Women of childbearing age often are concerned about whether breastfeeding is safe during immunization. Physicians should reassure their patients that no vaccines are contraindicated during breastfeeding.[1]

Tetanus and Diphtheria

The tetanus and diphtheria toxoids vaccine (Td) is effective in preventing tetanus and diphtheria, two potentially life-threatening conditions. Diphtheria is an infection of the nasal, pharyngeal, laryngeal, or other mucous membranes that can cause neuritis, myocarditis, thrombocytopenia, and ascending paralysis.[2] Tetanus infection can cause production of a neurotoxin, leading to tetanic muscle contractions.

Td toxoid is routinely recommended for susceptible pregnant women. While no evidence exists to prove that tetanus and diphtheria toxoids are teratogenic,[1] waiting until the second trimester of pregnancy to administer Td is a reasonable precaution, minimizing any concern about the theoretic possibility of such reactions.[1] Previously vaccinated pregnant women who have not received a Td vaccination within the past 10 years should receive a booster dose. Pregnant women who

Routine vaccinations that generally are safe during pregnancy include diphtheria, tetanus, influenza, and hepatitis B.

are not immunized or only partially immunized should complete the primary series.[1]

Influenza

Fever, malaise, myalgia, and upper respiratory tract symptoms or infections characterize influenza infection. Most severe complications are the result of pneumonia secondary to influenza infection. There are three strains of influenza (A, B, and C), with types A and B responsible for epidemics in the United States.

The influenza vaccine is a killed virus preparation with an annually adjusted antigenic makeup. It should be administered annually between October and December to high-risk patients. The vaccine should be administered to all pregnant women who will be in the second or third trimester of pregnancy during the influenza season (which peaks from December to March in temperate climates but may extend into May in 20 percent of influenza seasons).[3] This recommendation is based on data from pandemics of 1918 and 1957, as well as limited studies done since then demonstrating that women in their second or third trimesters have higher morbidity, similar to other high-risk patients, from influenza infection.[4]

Immunization should be avoided in most patients during the first trimester to avoid a coincidental association with spontaneous abortion, which is common in the first trimester. However, pregnant women with medical conditions that increase their risk for complications from influenza (e.g., asthma, cardiovascular disease, diabetes, suppressed immune system) should be vaccinated before the influenza season regardless of the pregnancy trimester. Studies of influenza immunization with more than 2,000 pregnant women have demonstrated no adverse fetal effects.[1]

Hepatitis A

Hepatitis A infects approximately 100,000 persons annually in the United States, of which 100 die.[5] It is acquired via the fecal-oral route by person-to-person contact or ingestion of contaminated food or water.

TABLE 1
Immunizations During Pregnancy

Considered safe if otherwise indicated	Contraindicated during pregnancy or safety not established	Special recommendations pertain
Tetanus and diphtheria toxoids (Td)	BCG*	Anthrax
Hepatitis B	Measles*	Hepatitis A
Influenza	Mumps*	Japanese encephalitis
Meningococcal	Rubella*	Pneumococcal
Rabies	Varicella*	Polio (IPV)
		Typhoid (parenteral and Ty21a*)
		Vaccinia*
		Yellow fever*

**—Live, attenuated vaccine.*

BCG = bacille Calmette-Guérin; IPV = inactivated polio virus.

Adapted from Guidelines for vaccinating pregnant women. Recommendations of the Advisory Committee on Immunization Practices (ACIP). Atlanta, Ga.: Centers for Disease Control and Prevention, 2002.

Hepatitis A vaccines are derived from viruses grown in diploid cell cultures and are formalin inactivated.[5] Safety of hepatitis A vaccination during pregnancy has not been determined. Because hepatitis A vaccine is produced from inactivated virus, the risk to the developing fetus is expected to be low. Therefore, theoretic risks of vaccination should be weighed against the risk for hepatitis A infection in pregnant women who may be at risk for exposure. Examples calling for immunization include travel to endemic areas or intravenous drug use during pregnancy.[6]

Finally, if a pregnant woman is exposed to hepatitis A, administration of immune globulin is strongly recommended; this agent is considered safe during pregnancy and is more than 85 percent effective in preventing acute hepatitis infection.[3]

Hepatitis B

Hepatitis B infection is caused by a DNA-containing virus and is transmitted through contact with infected blood, sexual activity, and sharing of intravenous needles. Hepatitis B infection may be asymptomatic, or it may result in fulminant hepatitis.

The risk of developing chronic illness associated with complications of cirrhosis, hepatocellular carcinoma, and a chronic carrier state has been a key factor in the recommendation for universal vaccination of all children. Vaccination should also be offered to any interested adult and strongly recommended to those at risk.[2] Risk factors for a pregnant woman include having had sex with a man who has sex with men, having multiple sexual partners, using or abusing intravenous drugs, having occupational exposure, and being a household contact of acutely infected persons or persons with a chronic carrier state.

The hepatitis B vaccine contains viral surface antigen produced by recombinant DNA technology. It is administered in three doses, at birth and at one and six months of age, and has minimal to no side effects. Because it contains noninfectious hepatitis B surface antigen particles and should cause no risk to the fetus, neither pregnancy nor lactation is a contraindication to vaccination.[1]

Pneumococcal

Streptococcus pneumoniae is a gram-positive diplococcal bacterium that is a major cause of pneumonia, meningitis, and bacteremia. Risk factors for pneumococcal infection in pregnant women include diabetes, cardiovascular disease, asplenia, immunodeficiency, asthma, and other respiratory diseases.

The current vaccine includes purified capsular polysaccharide from the 23 most common types of *S. pneumoniae.* It is recommended by the CDC for use in adults with any of the aforementioned risk factors.[3]

The Advisory Committee on Immunization Practices (ACIP) currently recommends that women at high risk be given this vaccination before, but not during, pregnancy. The safety of the pneumococcal vaccine during pregnancy has not been evaluated, although no adverse consequences have been reported among newborns whose mothers were inadvertently vaccinated.[1]

Polio

Poliovirus is an enterovirus with three different strains that cause disease. Exposure may result in asymptomatic infection as well as nonparalytic and paralytic disease. Asymptomatic patients can transmit the disease to susceptible persons. The disease continues to be a problem worldwide, but all recent domestic polio cases have been caused by the strains of virus found in the oral polio vaccine (OPV). This situation has resulted in a change in the ACIP's recommendation for use of inactivated polio vaccine (IPV), instead of OPV or a combination of OPV-IPV for all routine vaccinations.[1] IPV is inactivated by formaldehyde, and its use has eliminated vaccine-associated polio infection.[7]

Although no adverse effects have been documented with OPV or IPV in pregnant

Varicella vaccination is contraindicated during pregnancy because of potential adverse effects on the fetus.

women or their fetuses, both vaccines should be avoided during pregnancy on a theoretic basis. However, the CDC states that IPV may be administered in accordance with the recommended schedules for adults if a pregnant woman is at increased risk for infection and requires immediate protection against polio.[1] Situations that might warrant immediate protection in pregnancy include possible occupational exposure or travel to areas of endemic polio. The 2003 recommended immunization schedule for adults is available online at www.aafp.org/x14956.xml.

Varicella

The varicella-zoster virus causes chickenpox and may rarely cause serious complications, such as encephalitis and pneumonia. The risk of these complications increases with age. Furthermore, up to 15 percent of infected persons have herpes zoster later in life.[8]

The varicella vaccine contains live attenuated varicella-zoster virus. Immunization during pregnancy is contraindicated because the effects on the fetus are unknown. Women who are vaccinated should avoid becoming pregnant for one month following each injection. The presence of pregnant household members does not constitute a contraindication to vaccination of others within the house.[9] If a susceptible pregnant woman is exposed to varicella, however, administration of varicella-zoster immune globulin should be strongly considered.[1]

If a pregnant woman is inadvertently vaccinated with the varicella vaccine or becomes pregnant within four weeks of being vaccinated, she should be counseled regarding potential effects on the fetus. Theoretic risks to the fetus are very small, and exposure to the varicella vaccine is not an indication for termination of pregnancy.[1]

The CDC and the vaccine manufacturer have created a registry for inadvertent vaccination during pregnancy *(Table 2)*. Data from more than 300 deliveries indicate no birth defects compatible with congenital varicella syndrome.[10]

Meningococcal

In the United States, meningococcal disease is the leading cause of bacterial meningitis in children ages two through 18 years. Approximately 3,000 cases of meningococcal disease occur annually, and 10 to 13 percent of cases are fatal, despite administration of antibiotics early in the illness.[11]

Meningococcal vaccine contains the purified polysaccharide of four serogroups of *Neisseria meningitidis.* Routine vaccination is recommended for high-risk groups, including military recruits, patients with terminal complement component deficiencies, and persons with anatomic or functional asplenia. College freshmen, particularly those living in dormitories, are at modestly increased risk. The ACIP recommends that college freshmen who want to reduce their risk for meningococcal

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disease be vaccinated. The American Academy of Family Physicians states that physicians need not initiate discussion of this vaccine as part of routine medical care, given the large number of issues that are of greater importance in the care of young adults (such as alcohol use, accident prevention, and prevention of sexually transmitted diseases). However, colleges may provide education on meningococcal infection and vaccination to those who are interested.[12,13]

Vaccination also may benefit travelers to areas in which *N. meningitidis* is endemic or epidemic, such as sub-Saharan Africa.[11,14]

Studies have shown that the meningococcal vaccine is safe and efficacious when given to pregnant women.[1]

Measles, Mumps, and Rubella

Measles, which is caused by the measles virus, typically presents with fever, coryza, a generally ill appearance, and a confluent, erythematous, maculopapular rash. Mortality occurs in one to two per 1,000 cases, often secondary to pneumonia or encephalitis.[3]

Mumps results from infection with the mumps virus and can lead to parotitis, meningoencephalitis, and orchitis. Neurologic complications, such as deafness, can also occur as a result of mumps infection.

TABLE 2
Registries for Inadvertent Immunizations During Pregnancy

Smallpox	
Centers for Disease Control and Prevention Inadvertent Smallpox Immunization Registry	404-639-8253
Varicella	
VARIVAX Pregnancy Registry	800-986-8999
All (general)	
VAERS: Vaccine Adverse Event Reporting System	800-822-7967; www.vaers.org

Measles, mumps, and rubella vaccine should not be given to pregnant women, because of potential adverse effects on the fetus.

Rubella, or German measles, is caused by the rubella virus. Although usually a benign infection in adults, congenital rubella can result in birth defects that include cardiac, ophthalmologic, auditory, and neurologic disorders.[8]

The measles, mumps, and rubella vaccine (MMR) contains live attenuated measles, mumps, and rubella viruses. MMR and its component vaccines should not be administered to pregnant women. Women should be counseled to avoid becoming pregnant within four weeks of vaccination.[1]

Pregnancy has been considered a contraindication to vaccination with the rubella vaccine because of potential adverse effects on the fetus. Following introduction of the RA 27/3 rubella vaccine, the CDC established a registry for women who received rubella vaccine within three months of conception.[15] Pregnancy outcomes in 683 vaccine recipients showed no evidence that the rubella vaccine caused any fetal abnormalities or congenital rubella syndrome.[15] However, rubella-specific IgM has been detected in cord blood, suggesting possible subclinical infection.[16] Because of the theoretic risk, guidelines state that precautions should be used to prevent rubella vaccine administration during pregnancy,[15] but pregnancy testing before vaccination is not considered to be necessary.[17]

A woman who conceives within one month before or after MMR vaccination should be counseled about theoretic concerns for the fetus. However, inadvertent vaccination of a pregnant woman is not considered to be a reason to terminate the pregnancy.[15]

Other Vaccinations

Vaccinations typically not administered on a routine basis by family physicians and other

vaccines of interest include anthrax, smallpox, rabies, Japanese encephalitis, yellow fever, BCG, typhoid, cholera, and plague.

ANTHRAX

Anthrax is caused by the spore-forming bacterium *Bacillus anthracis,* occurring in humans in three forms: cutaneous, inhalational, and gastrointestinal. While human anthrax infections had been reported in South and Central America, Southern and Eastern Europe, Asia, Africa, and the Middle East, no cases had been reported in the United States from 1992 until the autumn of 2001. The potential use of anthrax in acts of bioterrorism has long been a concern because of its stability, high mortality, and high potential for respiratory transmission. Many details of the recent U.S. cases are available on the CDC Web site (www.cdc.gov), and more are expected as the investigation of these cases continues. The American Academy of Family Physicians has established a Web site (www.aafp.org/btresponse) on bioterrorism and the role of family physicians in emergency situations.

The anthrax vaccine adsorbed, which was developed in 1965, is prepared from a bacteria-free culture containing the three major toxin components produced by the bacteria: the protective antigen, the lethal factor, and the edema factor. The recommended immunization schedule consists of three injections given at two-week intervals, followed by another three doses at six-month intervals.[18]

Initial studies and animal trials indicate response rates of 83 to 95 percent (as measured by IgG titers) after one to three vaccinations.[18] Local reactions of varying severity occur in up to 25 percent of recipients, but systemic reactions are rare. Anthrax is infrequently encountered in the natural environment, and immunization is generally indicated only for laboratory personnel working with production of *B. anthracis* cultures, and those with occupational exposure to anthrax spores despite restrictions on imported animal hides.[18]

Benefits of pre-exposure vaccination for bioterrorism preparedness cannot be effectively calculated for the population at large, but in select groups (i.e., military troops, emergency response personnel), these risks may warrant vaccination. Vaccination also may be used in conjunction with antibiotics as part of postexposure prophylaxis.[18]

No studies to date have addressed the safety of the anthrax vaccine during pregnancy. As with other non–live-virus vaccines, anthrax vaccine adsorbed does not carry theoretic risks of fetal infection. As such, vaccination should be considered on a case-by-case basis and administered only when the potential benefits outweigh the potential risks to the mother and fetus.[18]

SMALLPOX

Smallpox is an orthopoxvirus, was certified as eradicated in 1980, and no longer occurs naturally. Prodromal symptoms include a high fever and oral lesions that ulcerate, followed by a macular rash. The rash becomes raised, then umbilicated and pustular, particularly when on the face and extremities. Smallpox is usually spread by fomite and large-droplet nuclei to household and close contacts from the prodromal period until seven to 10 days after rash onset.[19]

Recent world events have brought to light the threat of terrorists who may deliberately release smallpox, and have prompted an evaluation of vaccination policies and emergency preparedness.

The U.S. Department of Homeland Security, in cooperation with the CDC, has implemented a "pre-event" vaccination program for persons at the highest risk of exposure and lowest risk of complications from vaccination. Detailed information about the smallpox vaccination program is available online at www.smallpox.gov and www.cdc.gov.

Vaccinia vaccine should not be administered to pregnant women for routine nonemergency indications.[19] Pregnant women who have had a definite exposure to smallpox

virus (i.e., face-to-face, household, or close-proximity contact with a smallpox patient) and are, therefore, at high risk for contracting the disease should be vaccinated.[1]

Smallpox infection among pregnant women has been reported to result in a more severe infection than among nonpregnant women. Therefore, the risks to the mother and fetus from experiencing clinical smallpox substantially outweigh any potential risks regarding vaccination. While the vaccinia vaccine has not been shown to be teratogenic or to cause congenital malformations, the virus has been reported to cause fetal infection on rare occasion, with subsequent risk of skin lesions, preterm delivery, stillbirth, or infant death. Women should therefore actively avoid becoming pregnant for at least four weeks after vaccination and until the scab has completely healed and fallen off. Vaccination should also be avoided for household or close contacts of women who are pregnant. A pregnancy test may be considered for women who might be pregnant with the caveat that very early pregnancies will not be detected.[19] Inadvertent vaccination during pregnancy, however, should not be considered a reason to terminate the pregnancy.

The safety of breast milk after maternal vaccination has not been studied, so women who are pumping or breastfeeding should not receive the vaccine. Household contacts of breastfeeding infants theoretically can be immunized; however, it is reasonable to defer pre-event vaccination of household contacts of infants younger than one year since data suggest higher risks of adverse effects in this age group.[20] Pre-event vaccination is contraindicated in infants younger than one year.[1]

As with any vaccination, these risks need to be weighed against the potential benefits, given the individual circumstance of each patient.

Patients with close-proximity contact with a smallpox patient should be vaccinated regardless of their pregnancy status or that of their household contacts. Because infection during pregnancy has been reported to cause a more aggressive course of disease than in the nonpregnant state, the risks of vaccination would be outweighed by the risks of disease in these situations. Vaccinia Immune Globulin (VIG) is also available from the CDC by Investigational New Drug Protocol for the treatment of adverse reactions to the vaccine, such as progressive vaccinia, eczema vaccinatum, and severe generalized vaccinia.[20]

RABIES

Rabies is a viral infection transmitted most commonly by the saliva of infected animals. Nonspecific prodromal symptoms progress to encephalitis marked by confusion, hallucinations, and bizarre thoughts that are interspersed by shortening periods of lucid thought. Dysregulation of the autonomic nervous system and involvement of the brainstem and cranial nerves lead to the classic "foaming at the mouth" appearance.

Three forms of inactivated rabies vaccines are available in the United States, all considered equally safe and efficacious. Passive immunization is achieved through administration of human rabies immune globulin (HRIG). Indications for pre-exposure rabies immunization depend on the likelihood of exposure. For the U.S. population as a whole, no such immunization is recommended, but it may be considered in animal workers and travelers to enzootic areas who anticipate animal exposure.[21]

With any animal bites occurring out of this country, as well as with bites from a domestic bat, woodchuck, skunk, raccoon, or fox, and with abnormally acting pets or wild animals, the animal should be euthanized, and the brain tested for infection. Bites from normally acting dogs, cats, and ferrets in the United States warrant a 10-day observation period, with prophylaxis and euthanization of the animal deferred. Postexposure rabies vaccination may be started pending the results of these tests, depending on local rabies incidence rates. In patients who have not been immunized previously, 20 IU per kg of HRIG is given at the wound site for high-risk bites or if testing is

positive. Patients with previous vaccinations do not need HRIG but do require revaccination on a modified schedule.[2,21,22]

There have been no identified associations between rabies vaccination and fetal abnormalities. Considering the potential maternal and fetal consequences of untreated rabies exposure, similar guidelines should be used for postexposure prophylaxis in pregnant and nonpregnant patients. If a substantial risk of exposure to rabies remains after risk-factor modification, pre-exposure prophylaxis may be indicated during pregnancy.[2,21]

JAPANESE ENCEPHALITIS

Japanese encephalitis (JE) is the leading cause of viral encephalitis in Asian countries, with one quarter of cases having a fatal outcome, and residual neuropsychiatric sequelae occurring in up to one half of survivors.[22,23] Most human infections occur in rural areas, where flooded rice fields support large populations of the Culex mosquitoes that transmit the virus. Transmission peaks in late summer but varies regionally and may be year-round in tropical areas. Travelers to rural parts of Asia have a highly variable risk of acquiring JE infection, estimated at approximately one in 5,000 per month. In the case of short-term travel to urban areas, however, risks of acquiring JE infection are less than one per million.[23]

JE vaccination is recommended only for travelers with a significant risk of exposure. In general, those spending at least a month in endemic areas during the transmission season and those planning to participate in outdoor activities exposing them to unavoidable mosquito bites should be vaccinated. The most widely used JE vaccine (the Biken vaccine) is an inactivated virus vaccine that produces a 99-percent rate of seroconversion after three doses.

No specific data are available regarding JE vaccine safety in pregnancy. Since JE infection during the first and second trimesters has been associated with intrauterine infection and miscarriage, the vaccine is not recommended during this time.[23] Infections during the third trimester have not been associated with adverse outcomes in newborns, but few data are available. In deciding whether to vaccinate a pregnant woman, the theoretic risks of vaccination must be weighed against the maternal and fetal risks associated with JE infection, given the likelihood of exposure. Vaccination should be considered before conception in a woman who will be traveling to high-risk areas while pregnant, in conjunction with optimized mosquito-bite precautions.[2,23]

YELLOW FEVER

Yellow fever is a viral hemorrhagic fever syndrome spread by mosquitoes in parts of South America and Africa; it has urban and rural forms. The yellow fever vaccine is a live, attenuated virus grown in chick embryos. It is indicated for use in laboratory workers involved with the virus and in persons planning to travel to endemic areas. It is contraindicated in persons with anaphylactic reactions to eggs and immunocompromised persons, as well as infants under nine months of age, because of an age-related risk of encephalitis.[1,2,24] A validated International Certificate of Vaccination is required by some countries. Current information for these requirements may be obtained from the CDC Information Services (www.cdc.gov).

No specific evidence is available to demonstrate the safety of yellow fever immunization during pregnancy. Since theoretic concerns of fetal infection exist, however, vaccination is generally not recommended during pregnancy. A physician's waiver will often suffice for international travel requirements. Mosquito exposure must be minimized as much as possible. When travel cannot be postponed and mosquito exposure is likely, however, yellow fever vaccination may be considered.[2,24]

BCG VACCINE

Mycobacterium tuberculosis causes more than 8 million new cases of tuberculosis (TB) annually, the majority of them in developing countries. The number of cases reported in the

United States has increased since the mid-1980s, as has the incidence of multi–drug-resistant TB. Despite this trend, the incidence of disease in the United States is low enough that routine immunization is not recommended.

BCG (bacille Calmette-Guérin) vaccine is a live vaccine derived from a strain of *Mycobacterium bovis.* Although many different BCG vaccines are available worldwide, only the Tice strain is available in the United States. The efficacy of the vaccine in protecting children from active disease has been shown to be about 80 percent, but the efficacy in adolescents and adults is significantly less and highly variable across studies.[25] The use of BCG vaccination as a TB prevention strategy in the United States is reserved for certain children with unavoidable ongoing exposure to untreated or multi–drug-resistant TB. Physicians who are considering the use of BCG vaccine in their patients are encouraged to consult the TB control programs in their area.

It is likely that the BCG vaccine has been given to thousands of pregnant women in other countries. While no harmful fetal side effects have been identified to date, data from BCG immunization research have not been studied extensively in pregnant women. Use of the BCG vaccine is not recommended during pregnancy.[25]

TYPHOID

Most cases of typhoid fever in developed countries occur in travelers who recently have returned from high-risk areas, such as South America, India, and western Africa, or intermediate-risk areas, such as Mexico, Haiti, north Africa, and Iran. Transmission of *Salmonella typhi* is significantly increased with travel during local epidemics and ingestion of food from street vendors. Primary prevention consists of hand washing, drinking only safe water, peeling all fruits and vegetables, and eating well-cooked foods.

The two types of typhoid vaccination in use today are a live attenuated oral vaccine and a parenteral polysaccharide vaccine. Both forms require that immunization be completed at least two weeks before exposure. The oral vaccine is given on alternate days in four doses, with reported efficacy rates varying greatly (50 to 95 percent). Its use is contraindicated in infants, immunocompromised persons, and those with abnormal gastrointestinal function, as well as pregnant women. The purified capsular polysaccharide (Vi) vaccine is given as a single injection. It has similar efficacy rates, but its use is not contraindicated in the immunocompromised population.[26]

Neither form of typhoid vaccine is officially recommended during pregnancy. The oral form is contraindicated in pregnancy because it is a live virus, presenting theoretic risks of transmission to the fetus. This contraindication does not exist with the parenteral form; however, studies demonstrating the latter's efficacy and safety during pregnancy have not been performed. Potential benefits and risks of immunization should be considered on an individual basis.[2,26]

CHOLERA

Cholera is an acute diarrheal disease endemic to Africa, Asia, and Latin America. It is caused by a toxin from *Vibrio cholera* bacteria, which live in, and are transmitted by, the fecal-oral route from contaminated water sources. No cholera vaccines are currently licensed for use in the United States. However, two improved oral vaccines are available in other countries: a killed, whole cell recombinant vaccine (WC/rBS), and a live, attenuated strain (CVD103-HgR). Both are more effective, better tolerated, and longer lasting than the parenteral vaccine. These may be considered for use in populations at immediate risk of a cholera epidemic or for travelers to areas of high endemicity.[27]

Parenteral cholera vaccination is no longer recommended by the World Health Organization. Officially, cholera vaccination requirements no longer exist for any country. Should proof of vaccination be requested, a physician's statement of medical contraindication

usually suffices.[27] Current information for these requirements may be obtained from the CDC Information Services (www.cdc.gov).

No specific information exists on the safety of parenteral cholera vaccination during pregnancy. Preliminary data indicate safety of the killed vaccine in pregnancy and breastfeeding, but the live vaccine should be avoided due to theoretical safety concerns.[27] Because cholera during pregnancy is a serious illness, exposure should be minimized during pregnancy whenever possible.

PLAGUE

Plague, a disease caused by *Yersinia pestis,* is naturally hosted by rodents and their fleas. Although rare in the United States, it occurs more commonly in semi-rural areas of Africa, Asia, and South America. The plague vaccine is no longer commercially available in the United States. It was previously recommended only for use in travelers to endemic areas who had a high risk of exposure to wild rodents and fleas. Its efficacy was not well studied. All persons with definite exposure should receive a seven-day course of appropriate antibiotics (often tetracyclines, doxycycline, or trimethoprim-sulfamethoxazole [Bactrim, Septra]).[28]

The effects of plague vaccine on the developing fetus are not known. Pregnant women should avoid high-risk situations and use insecticides and other protective measures. Prophylactic antibiotics that are safe during pregnancy may be considered in women with a substantial risk of infection.

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