CME

Preparing patients to travel abroad safely

Part 2: Updating vaccinations

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abstract

OBJECTIVE To provide, for family physicians without access to a travel clinic, evidence-based recommendations on vaccinating infants and children, adults, pregnant women, and immunocompromised patients traveling to non-Western countries.

QUALITY OF EVIDENCE Searches were undertaken of MEDLINE from 1990 to November 1998 (372 articles); the Cochrane Collaboration Library; publications of the National Action Committee on Immunization and the Committee to Advise on Tropical Medicine and Travel in *Canada Communicable Disease Reports*; the *Canadian Immunization Guide*; and Laboratory Centre for Disease Control, United States Centres for Disease Control, and World Health Organization websites. Evidence-based statements, randomized controlled trials, systematic reviews, and meta-analyses were selected. Vaccination recommendations are based on this evidence.

MAIN MESSAGE Physicians should complete vaccination schedules for children whose primary series is incomplete and vaccinate unvaccinated adults. Hepatitis A is widespread, and travelers to areas where it is endemic should be vaccinated. The elderly should be vaccinated against influenza and pneumococcal disease. Pregnant women should receive vaccines appropriate to their trimester. Immunocompromised patients should be vaccinated, but BCG and live vaccines are contraindicated. Travelers to areas where meningitis, typhoid, cholera, Japanese encephalitis, and rabies are endemic should be vaccinated if they are likely to be exposed. Those traveling to areas where tuberculosis is endemic should take precautions and should have skin tests before traveling and 2 to 4 months after return.

CONCLUSIONS Family physicians can administer all necessary vaccinations. They can advise pregnant women and immunocompromised people about the balance of risk of disease and benefits of vaccination.

résumé

OBJECTIF Procurer aux médecins de famille qui n'ont pas accès à une clinique de santé en voyage les recommandations fondées sur des données probantes concernant la vaccination des nourrissons et des enfants, des adultes, des femmes enceintes et des patients immunodéprimés qui voyagent dans des pays non occidentaux.

QUALITÉ DES DONNÉES Des recensions ont été effectuées dans MEDLINE de 1990 à novembre 1998 (372 articles); la bibliothèque de collaboration Cochrane; les publications du Comité national d'action sur l'immunisation et du Comité consultatif de la médecine tropicale et de la médecine des voyages dans les *Rapports sur les maladies transmissibles au Canada*; le *Guide canadien d'immunisation*; et les sites Web du Laboratoire de lutte contre la maladie, des centres américains de lutte contre la maladie et de l'Organisation mondiale de la santé. Ont aussi été choisis les déclarations fondées sur des données probantes, les essais aléatoires contrôlés, les études systématiques et les méta-analyses. Les recommandations sur la vaccination s'appuient sur ces données probantes.

PRINCIPAL MESSAGE Les médecins devraient veiller à ce que le statut de vaccination des enfants dont la première série n'est pas faite soit complet et vacciner les adultes qui ne le sont pas. L'hépatite A est largement répandue et les voyageurs vers des destinations où elle est endémique devraient être vaccinés. Les personnes âgées devraient recevoir un vaccin antigrippal et antipneumococcique. Les femmes enceintes devraient recevoir le vaccin qui convient à leur trimestre de grossesse. Les patients immunodéprimés devraient être vaccinés, mais le BCG et les vaccins vivants sont contre-indiqués. Les voyageurs à destination de régions où la méningite, la typhoïde, le choléra, l'encéphalite japonaise et la rage sont endémiques devraient être vaccinés s'il est probable qu'ils y soient exposés. Ceux qui se dirigent vers les régions où la tuberculose est endémique devraient prendre des précautions et subir des épreuves cutanées avant le départ et de deux à quatre mois après le retour.

CONCLUSIONS Les médecins de famille peuvent administrer tous les vaccins qui s'imposent. Ils peuvent informer les femmes enceintes et les personnes immunodéprimées des avantages et des inconvénients de la vaccination par rapport aux risques de la maladie.

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Family physicians can advise about risk of disease and benefit of vaccination against childhood illnesses and illnesses at destination for four groups of travelers: adults, children, pregnant women, and immunocompromised patients. Failure to vaccinate has the clearest effects on a societal level: when vaccination rates against pertussis in Japan fell from 70% to only 20% to 40%, cases increased from 393 and no deaths in 1974 to 13 000 and 41 deaths in 1979.[1]

Vaccination is one of the few health interventions that produces more financial benefits than costs.[1] Most vaccines are highly effective: eg, 97% to 99% of children seroconvert after hepatitis A and 95% after hepatitis B vaccination.[1]

Quality of evidence

Searches of MEDLINE from 1990 to November 1998 retrieved 372 articles on travel and immunization; evidence-based statements, randomized controlled trials (RCTs), systematic reviews, and meta-analyses were selected and analyzed for quality using Cochrane Collaboration criteria. The Cochrane Collaboration Library; Laboratory Centre for Disease Control, US Centres for Disease Control (CDC), and World Health Organization websites; the 1998 *Canadian Immunization Guide* (*Guide*); and evidence-based statements from the Committee to Advise on Tropical Medicine and Travel (CATMAT) and the National Advisory Committee on Immunization (NACI) were also searched. These sources provide more evidence-based statements than other works on travel medicine and offer comprehensive advice for patients.

For family physicians, the *Guide*[1] is an authoritative, comprehensive source. The text was prepared by NACI, and a large panel of university, health department, CATMAT, and CDC experts contributed. The statements of CATMAT are accompanied by ratings of the evidence on which they are based (**Table 1**[2]).

Table 1. Strength and quality of evidence as rated in *Canada Communicable Disease Reports*[2]

STRENGTH	
CATEGORY	DEFINITION
A	Good evidence to support recommendation for use
B	Moderate evidence to support recommendation for use
C	Poor evidence to support recommendation for use
D	Moderate evidence to support recommendation against use
E	Strong evidence to support recommendation against use
QUALITY	
GRADE	DEFINITION
I	Evidence from at least one properly randomized controlled trial
II	Evidence from at least one well-designed, nonrandomized clinical trial, from cohort or case-controlled analytic studies (preferably from more than one centre), from multiple time series studies, or from dramatic results in uncontrolled experiments
III	Evidence from opinions of respected authorities on the basis of clinical experience, from descriptive studies, or from reports of expert committees

Updating adults' vaccinations

Adults' vaccinations against childhood illnesses and illnesses at destination should be updated. For each condition, I give the authoritative *Guide*[1] recommendations first and follow them with additional information from other sources.

Tuberculosis. Health care and refugee-camp workers staying for even a month in areas where tuberculosis (TB) is highly endemic could acquire TB. Estimated annual risk of TB in sub-Saharan Africa is 1.5% to 2.5%. There are no estimates of risk for health care and refugee-camp workers in sub-Saharan countries, but the best estimates could come from Western countries in the prechemotherapy era when nurses in TB hospitals had an annual risk of infection that sometimes exceeded 50%.

The *Guide* recommends BCG vaccine for travelers with negative skin tests when they go to areas of high prevalence, particularly areas where serial tuberculin skin testing (TST) and chemoprophylaxis might not be available or where resistance to isoniazid (INH) is high. The *Guide* recommends consultation with travel medicine or infectious disease experts about BCG vaccination.[1]

Health Canada rates the evidence for pretravel TSTs for those traveling to high-prevalence areas

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for 3 months or working in health care as IIIB; for informing travelers with serious immunocompromise of the serious risk associated with TB exposure as IIIA; for avoiding unpasteurized milk as IIIA; and for chemoprophylaxis if a TST becomes positive as IA.[3,4] The BCG vaccine should not be given within a month of administration of a live vaccine because live vaccines suppress the tuberculin reaction.[1]

Cholera. The *Guide* says there is virtually no risk of tourists' acquiring cholera on the usual tourist itineraries in countries with cholera. Risk of death from cholera among international travelers is very low. No country now requires that travelers be vaccinated against cholera. According to the findings of another study,[5] no hard data supports a recommendation to vaccinate all travelers against cholera because rates of infection are similar in countries that routinely vaccinate and countries that do not.

The *Guide* states that health professionals or workers in refugee camps might benefit from vaccination. Health Canada rates the evidence to support vaccinating travelers to areas where cholera is endemic as IIC.[6] Health care or refugee-camp workers, who will have close contact with local populations with a high incidence of the disease, should be vaccinated.

There are two cholera serogroups, 01 and 0139 (Bengal). Serogroup 01 includes the classical biotype (with a ratio of one symptomatic case to every five asymptomatic cases) and the El Tor biotype (with a 1:50 ratio).[1] No vaccine protects against the 0139 serogroup.

Studies of the CVD103-HgR oral vaccine in 4000 subjects showed 90% seroconversion for 6 months.[6] The Cochrane Collaboration considered 32 RCTs and found killed whole cell (KWC) vaccines had 57% efficacy in the first 7 months (95% confidence interval [CI] 50% to 64%); oral KWC vaccines had fewer side effects.[5] Recombinant vaccines are safe, but efficacy data from RCTs are not yet available.[5] A booster shot can be given after 6 months.[1] Administration of the vaccine should be separated by 8 hours from oral typhoid Ty21a vaccine and by 7 days from administration of both antibiotics and antimalarials.[1]

The CATMAT statement does not recommend the parenteral inactivated cholera vaccine for travelers to endemic areas (IID); advises that oral cholera vaccine (CVD 103-HgR) does not protect against ETEC-associated travelers' diarrhea; advises a detailed risk assessment for travelers, such as aid workers, at increased risk (IIC); and advises travelers to follow the CATMAT recommendations for prevention and treatment of diarrhea (IB).[7]

Hepatitis A. Returned travelers account for a large proportion of cases. The risk of developing hepatitis A is about three to five cases per 1000 travelers per month in the developing world. More than 60% of those 60 years and older are immune; fewer younger people are immune because they have not been exposed. Vaccination is recommended for travelers to countries where hepatitis A is endemic, especially if they are traveling in rural or primitive conditions.

The adult vaccine is available in two formulations: Havrix 1440 (with 1440 ELISA U/mL of inactivated hepatitis A antigen) and Vaqta (50 U of hepatitis A antigen/mL). Four weeks after vaccination, 97% to 99% of those vaccinated have protective levels of virus-neutralizing antibody. During outbreaks, no cases have appeared 3 weeks or more after vaccination, suggesting almost complete immunity is provided. A booster at 6 to 12 months probably confers immunity for 20 years.[8,9]

Hepatitis B. Vaccination is recommended for travelers to endemic areas, for health care workers, and for those likely to have sexual contact with residents.[1,10] The Cochrane Collaboration identified only four poor-quality trials of vaccination in health workers, but concluded that vaccination was beneficial.[11]

The vaccine is available under the brand names Recombivax HB and Engerix-B. Three doses are given (at 0, 1, and 6 months), and evidence indicates that vaccinating over a longer period (0, 1, and 12 months) produces a longer-lasting antibody response. Children younger than 2 years have a 95% response rate; those 2 to 19 years, 99%; 20 to 29 years, 95%. Response declines to 71% by age 50 to 59. The response rate is 50% to 70% in immunocompromised people, 60% to 70% in those with renal failure, 70% to 80% in diabetics, and 60% to 70% in those with chronic liver disease.[2] Hepatitis A and B vaccines are available combined under the brand name Twinrix®.

Influenza. The *Guide* recommends vaccinating travelers at high risk of complications of influenza. Health Canada rates evidence for vaccinating travelers who will be exposed during the influenza season at destination or on returning to Canada as IIB.[12] Influenza is common year-round in the developing world, during the southern hemisphere's winter, and on cruise ships. In a Quebec survey, only 40% of those older than 65 were vaccinated against influenza (and 2% against pneumococcal disease).[6] Although 90% of those who die are older than 65, vaccinating travelers younger than 65 is also recommended because it prevents 70% of illness among them.[13]

Japanese encephalitis. Risk to travelers is very low: one case per million travelers. The *Guide* recommends that all those who will spend more than a month in endemic or epidemic areas during transmission season, and those traveling for shorter periods who are going to areas with epidemics or who will have extensive contact with rural people, should be vaccinated.[1] Health Canada rates vaccination for travelers spending more than a month in transmission season in rural areas in listed countries as IIIC.[14]

Studies in the United Kingdom and the United States found that, after two doses, fewer than 80% of patients developed neutralizing antibody titres, and that titres declined substantially after 6 to 12 months to the point where less than 29% had protective titres. After three doses, 90% developed neutralizing antibody titres.[1]

Side effects can include urticaria, angioedema, and itching. Studies of US military personnel found 16 reactions per 10 000 vaccinations. Neurologic side effects are very rare (1 to 2.3 per million vaccinations).

Measles. Although Western visitors to the developing world rarely contract measles, the *Guide* recommends that two doses of measles vaccine be given to all nonimmunized adults born after 1970 who plan to visit areas where measles is endemic.[1] Encephalitis has been noted in 1/1 000 000 vaccinees, a much lower rate than with the natural infection (1/1000).

Meningitis. The *Guide* recommends vaccinating all those traveling to or living in areas with a high incidence of meningococcal disease.[1] Health Canada rates as IIA recommendations to vaccinate health care, research, and refugee-camp workers in epidemic areas; those in traditional endemic areas (sub-Saharan Africa, Kenya, Tanzania, Burundi, and Mongolia); aircrew and military personnel who fly unpredictably; and haj pilgrims to Saudi Arabia (Saudi Arabia requires this vaccination).[15]

Adults' antibody response to group A vaccine could persist as long as 5 years and to group C vaccine for 2 to 4 years, but the duration of response after Y and W-135 vaccine is unknown.[1] Repeat dosing at shorter intervals can be considered for people at risk of fulminant meningococcemia.[1]

Pneumonia. Those older than 2 years with asplenia, splenic dysfunction, or sickle-cell disease, and those older than 65 or with cardiovascular or respiratory problems, should receive pneumococcal vaccination.[1] Currently, a single revaccination is recommended after 3 years for those vaccinated at age 10 or younger, and after 5 years for those vaccinated after age 10.[1]

Polio. The *Guide* states that routine vaccination of adults living in Canada is not necessary, but the following groups should be vaccinated: travelers to countries where polio is endemic or epidemic, laboratory workers handling specimens that could contain poliomyelitis virus, health care workers in close contact with people who could be excreting wild or vaccine strains, and parents of or those caring for children in areas where oral polio vaccine (OPV) is used.[1]

Because of the epidemiologic pattern, only inactivated poliomyelitis vaccine (IPV) is recommended for routine use in Canada. Unvaccinated people should be given primary immunization in three doses of IPV at 0, 1 or 2, and 12 months. Usually, IPV is given subcutaneously, but when given with adsorbed tetanus or diphtheria toxoid, the combined vaccine should be given intramuscularly. Incompletely vaccinated adults should have their course completed with the appropriate number of doses of IPV. Inactivated poliomyelitis vaccine produces immunity to all three types of poliomyelitis virus in more than 90% of people given two doses at least 6 weeks apart, and in 100% after a booster 6 to 12 months later.[1]

The *Guide* advises that booster doses for travelers are not routinely recommended, but a single dose of IPV (or OPV) could be considered for people at greatly increased risk of exposure, such as refugee-camp workers.[1] The CATMAT recommends OPV for foreign travel every 10 years thereafter.[16]

Health Canada rates the recommendation to update polio vaccinations for those planning travel to endemic areas as IIA.[16] The WHO reported the Americas free of polio in October 1994,[16] and CATMAT rates the recommendation not to give boosters to travelers to the Americas as IIA.[16] Rates of polio in Africa, the Middle East, Asia, and the former Soviet Union, however, range from one to 10 per 100 000 travelers. All US travelers vaccinated within the last 5 years had antibodies to serotypes 1, 2, and 3, but only 84% of those vaccinated more than 5 years earlier had these antibodies.[16]

Rabies. The *Guide* recommends preexposure vaccination for people traveling to or living in areas where rabies is enzootic and rabies control programs are inadequate. Preexposure vaccination does not completely protect from rabies after contact and, after exposure to a rabid animal, two booster doses should be given as soon as possible. Health Canada rates evidence that

people should not keep pets and not touch stray animals in developing countries as IIIC.[17]

Travelers receiving a booster dose of human diploid cell rabies vaccine (HDCV) have up to a 6% risk of allergic reactions (urticaria, pruritus); for workers requiring regular boosters, such as veterinarians, RVA vaccine should be used for the next booster.[18]

Rubella. All nonimmune adolescent and adult women of childbearing age should receive one dose of rubella vaccine.[1]

Tetanus and diphtheria. Adults who have not had a primary series should receive tetanus and diphtheria vaccine at 0, 2, and 6 to 12 months, with a booster every 10 years.[1]

Typhoid. Vaccination does not substitute for essential prevention, which is careful selection and handling of food and water. Vaccination will not prevent disease in those who absorb a large number of typhoid organisms.

Health Canada recommends oral typhoid vaccines for "travelers to areas where there is a recognized risk of contracting typhoid fever. This includes all developing countries where the safety of the water supply is not known."[19]

The oral vaccine (Ty21a) is a mutant strain of *Salmonella typhi* and is available in enteric-coated capsules (approved for children 6 years and older and adults) and liquid form (Vivotif Berna L vaccine, approved for children 3 years and older and adults). Capsules should be refrigerated until used and taken with fluid no warmer than 37°C. The liquid form is most effective. It is important that the schedule of taking either three doses of liquid or four capsules on alternate days is followed for optimal protective immune response. People receiving antibiotics should wait 2 days after completing the antibiotic course before commencing the oral vaccine and separate any oral vaccine dose by 8 hours from any dose of mefloquine.[1] There are no data on the efficacy of vaccination for people from non-endemic countries or for children younger than 5 years. Protection persists for at least 5 years, and the *Guide* recommends revaccination after 7 years.

The injectable form of the vaccine contains the virulence antigen Vi of the capsular polysaccharide (ViCPS) of *S typhi* strain Ty2. Indicated for children 2 years and older and adults, it is given as a single injection. In Canada the vaccine is called Typhim Vi® (Pasteur Merieux Connaught). Efficacy of vaccination with ViCPS has not been studied in people from non-endemic areas who travel to endemic areas or in children younger than 1 year. Two RCTs in endemic areas showed a protective immunity of 50% and 74% that was maintained at 17 and 21 months, but declined by 35% after 11 months and by 60% after 27 months. Boosters are recommended after 3 years.[1] A meta-analysis found a 3-year cumulative efficacy of 51% (95% CI 35% to 63%) for three doses of Ty21 and 55% (95% CI 30% to 71%) for one dose of Vi.[20] The oral liquid form of the vaccine thus appears to be preferable, but requires travelers' compliance at home.

Yellow fever. Yellow fever is endemic in the tropical areas of Central and South America and Africa. Protection from disease requires travelers to avoid being bitten by mosquitoes. Vaccination is recommended for travel to those countries, many of which require vaccination, as do some Asian countries that have the transmitting mosquito but not the disease.[1] The vaccine is administered in designated centres. Immunity develops after 10 days and lasts for 10 years; 5% of vaccinees have mild headaches, fevers, or myalgias 5 to 10 days later.

Vaccinating children

Vaccinating children is important: only 87% of Canadian 2-year-olds have received four doses of diphtheria-tetanus-pertussis (DTP) vaccine.[21] The *Guide*[1] is invaluable: it lists the schedule of vaccinations for all age groups and for those not immunized in infancy. Recommendations for DTaP (with acellular pertussis vaccine) and eIPV at 2, 4, and 18 months and at 4 to 6 years and hepatitis B in infancy or adolescence are of particular note. Accelerated vaccination schedules are available for children who have incomplete primary series and must travel.[13,22]

Tuberculosis. The *Guide* recommends BCG vaccine for children with negative TSTs who belong to groups with a high rate of new infections (in excess of 1%/y) or who are at high risk of intimate and prolonged exposure to untreated or ineffectively treated patients with infectious pulmonary TB or patients with TB resistant to INH and rifampin.[1] Health Canada rates evidence for BCG vaccination for children younger than 1 year as IIIB,[3,4] but states, "…the role of BCG vaccination may be particularly important in children especially those <1 year of age."

Cholera. The same indications apply as for adults. The vaccine is approved for children younger than 2 years.[1]

Hepatitis A. Vaccination is recommended for those traveling to endemic areas. About one third of cases in Canada occur in those younger than 15: hepatitis A is often asymptomatic in this age group. Only 3% of Canadian-born preadolescents are immune. Hepatitis A vaccine is available for those 1 to 18 years old as Havrix 720 junior or Vaqta pediatric formulation, each requiring two doses. Those younger than 1 year should receive immune globulin.

Hepatitis B. The NACI recommends universal vaccination before adolescence to control HBV infection. Travel is a good reason to recommend vaccination, particularly if patients are traveling to endemic areas.[1]

Japanese encephalitis. The disease usually affects children; 50 to 300 infections probably occur for each clinical case diagnosed. The same indications apply as for adults. Whenever possible, immunization of infants should be delayed until they are 1 year. Children 1 to 3 years should be given three doses of 0.5 mL (on days 0, 7, and 30) and a booster of 0.5 mL after 2 to 3 years.[1]

Measles. For areas where measles is endemic, monovalent measles vaccine can be given as early as 6 months, but two primary doses must be restarted after the child is 12 months.[1]

Meningococcal disease. For children 3 to 23 months old, two doses of monovalent group A vaccine 2 to 3 months apart provide a high rate of seroconversion and protect 95% of vaccinees during group A outbreaks. Protection lasts 1 year. A single dose of group C vaccine provides an antibody response, but protection against group C meningitis has not been proved.

For children 2 years and older and for adults, group A and C vaccines are more than 90% effective in preventing group A and C meningococcal disease during outbreaks. A single dose gives protection for 2 years. Children 2 years and older and adults produce an antibody response to group Y and W-135 vaccines, but degree of protection has not been determined.

Children 3 to 23 months traveling to areas where they will be at risk of group A disease should receive two doses of quadrivalent vaccine 2 to 3 months apart. Children immunized before they are 1 year old should receive a repeat dose within 2 to 3 months and a booster 6 to 12 months later. Children immunized between 13 and 23 months should receive a repeat dose 1 to 2 years later; children immunized between 2 and 5 years a booster 2 to 3 years later; and children immunized at 6 years or older a booster 5 years later.[1]

Children vaccinated before 2 years old traveling to areas where they will be at risk of group C disease should receive a repeat dose 6 to 12 months later. Children vaccinated after 2 years old should receive a repeat dose 5 years later.

Health Canada rates vaccinating children and adolescents going to epidemic areas[15] as IIA. Health Canada also rates as IIA the statements: children vaccinated at 3 to 5 months old have poor imunogenicity 3 months later, and those vaccinated at 3, 7, and 12 months with A or C have rapidly declining antibodies by 13 to 24 months[15]; after a single dose of vaccine against group A disease at less than 4 years of age, vaccine efficacy is 100% after 1 year, 52% after 2 years, and only 8% after 3 years[15]; and taking a vaccinated child to an endemic area still represents a risk.[15]

Influenza inflames the nasal tissue and permits passage of adherent meningococci: vaccination against influenza could be prudent.[13]

Polio. To avoid vaccine-associated paralytic poliomyelitis (VAPP) the *Guide* recommends exclusive use of IPV in Canada and advises IPV at 2, 4, and 18 months and at 4 to 6 years.[1]

Typhoid. The same indications apply as for adults. The oral vaccine (Ty21a) as an enteric-coated capsule is approved for children 6 years and older, and the liquid form (Vivotif Berna L vaccine) is approved for children 3 years and older. Seroconversion rates of 83% have been reported in Thai schoolchildren. Studies have reported protective efficacy of 17% and 19% among children aged 5 to 9 years, and 54% and 72% among children 10 to 19 years. The injectable form of the vaccine containing the virulence antigen Vi of the capsular polysaccharide (ViCPS) is indicated for children 2 years and younger.[1]

Yellow fever. Yellow fever is endemic in the tropical areas of Central and South America and Africa and occurs in both rural and urban areas. The *Guide* recommends vaccination for all travelers to areas where yellow fever is endemic. Infants younger than 4 months should not be vaccinated because the risk of encephalitis is 1%.[1] Those 4 to 9 months should be vaccinated only if traveling to endemic areas.[2] Those 9 months or older should receive a single dose. Encephalitis rarely occurs in infants older than 3 months.[1]

Vaccinating pregnant women

The authoritative sources agree on these recommendations. The *Guide* states that vaccinating pregnant

women should be undertaken when risk of the disease outweighs risk of the vaccine for both mother and fetus. "Specific fetal damage has not been reported from administration of the currently used live vaccines.... Inactivated vaccines and toxoids are usually considered safe; [there is] no known risk to the fetus from... immune globulin preparations."[1]

The CDC website (http://www.gov.cdc/travel/travel.html) states that women who are pregnant or likely to become pregnant within 3 months should not receive measles-mumps-rubella (MMR) vaccine. Yellow fever or OPV immunization should be given only if there is substantial risk of exposure (waiting until the second or third trimesters reduces theoretical concerns about birth defects).

The CDC states, "No convincing evidence for risk to the unborn baby from inactivated viral or bacterial vaccines or toxoids administered to pregnant women has been documented. These vaccines include: hepatitis A, hepatitis B, rabies, injectable typhoid, meningococcal, pneumococcal, tetanus-diphtheria toxoid (adult formulated), and injectable polio. Immune globulin can be given to pregnant women. Specific information is not available on the safety of cholera vaccine during pregnancy: therefore, it is prudent on theoretical grounds to avoid vaccinating pregnant women."

Tuberculosis. The *Guide* recommends vaccination with BCG vaccine be delayed until after delivery, although no harmful effects on a fetus have been documented.[1]

Cholera. The *Guide* states that, because cholera vaccine is live, it should be used with caution for pregnant women and only when a risk-benefit analysis suggests it is beneficial.[1]

Hepatitis A. The *Guide* advises that the safety of hepatitis A vaccine (HAV) during pregnancy has not been established and that, although risk to a fetus is minimal because the vaccine is prepared from inactivated virus, it should not be given to pregnant women unless there is a definite risk of infection.[1] Health Canada similarly states, "Pregnancy is a relative contraindication because the safety of HAV vaccination has not been studied in pregnancy. However, there is no reason to expect untoward effects on the fetus from an inactivated vaccine should a pregnant woman be considered for vaccination because of increased risk of exposure. Hepatitis A infection may be more serious during pregnancy: immune globulin is an alternative means of protection for short-term exposure."[8]

Hepatitis B. The *Guide* states that pregnancy is not a contraindication to vaccination because the virus is made from non-infectious subunits, and acute hepatitis B infection in pregnant women can result in severe disease for the mother and chronic carrier status for the infant.[1] Health Canada similarly states, "A pregnant woman who has no markers of acute or chronic HBV infection but who is at high risk of acquiring HBV should be offered HBV vaccine.... All pregnant women should be routinely tested for HBsAg at the first prenatal visit.... Repeat testing prior to delivery may be considered in women with continuing high-risk behaviour."[10]

Influenza. The *Guide* recommends vaccination for pregnant women in high-risk groups and states that it is safe at all stages of pregnancy.[1]

Japanese encephalitis. The *Guide* notes that it is not known whether the vaccine can harm a fetus, and the *Guide* and Health Canada both state that pregnant women who must travel to areas where risk of infection is high should be vaccinated when theoretic risks of immunization are outweighed by risk of infection for mother and developing fetus.[18]

Measles. Although there is no known risk, the vaccine should not be given to pregnant women.[1]

Meningitis. Health Canada describes meningococcal polysaccharide vaccines as "safe and immunogenic" and does not exclude pregnant women.[15]

Polio. Polio vaccination is not contraindicated during pregnancy, but IPV should be used and vaccination should be delayed until after the first trimester, if possible.[1]

Pneumonia. Pregnancy is not a contraindication to vaccination with pneumococcal vaccine.[1]

Rabies. Pregnancy is not a contraindication to post-exposure prophylaxis, but preexposure vaccination should be delayed unless there is substantial risk.[1]

Rubella. Vaccination of pregnant women should be avoided, although no fetal damage was observed in more than 700 women vaccinated during pregnancy.[1]

Tetanus. The *Guide* states that there is no evidence that tetanus toxoid is teratogenic, but advises that routine vaccination be delayed until the second

trimester. If a pregnant women suffers a tetanus-prone wound, prophylaxis should be administered.[1]

Typhoid. Oral typhoid vaccine should not be given to pregnant women.[1]

Vaccinating immunocompromised patients

Health Canada states that immunizing agents that contain living microorganisms (measles, rubella, mumps, bacille Calmette-Guérin, yellow fever, and OPV) should not generally be given to immunocompromised patients.[1]

Table 6 of the *Guide* has detailed recommendations: for HIV-positive patients, BCG, yellow fever, oral cholera, oral typhoid (use intramuscular vaccine), and OPV (use eIPV) vaccines are contraindicated.[1]

Influenza. The *Guide* recommends influenza vaccine for people with HIV because their symptoms last longer and their risk of complications from influenza is higher.[1]

Measles. The *Guide* states that measles vaccine is contraindicated for anyone with an impaired immune system, but that it might be appropriate for HIV-infected people with moderate immunodeficiency traveling to areas where measles is endemic.[1]

Polio. Immunosuppressed people can receive IPV without risk.

Rubella. Rubella vaccine should not be given to immunocompromised patients, but HIV-positive children should be vaccinated.[1]

Typhoid. Oral typhoid vaccine should not be given to immunocompromised people.[23] Health Canada recommends injectable Typhim Vi instead.[24]

Yellow fever. Yellow fever vaccine should not be given to immunocompromised people.[1]

Antibody titres will decline faster in HIV patients than in non-HIV patients; revaccination for *Haemophilus influenzae*, pneumococcus, and hepatitis B should be considered.[23] Patients with CD4 cell counts $<300/mm^3$ have decreased antibody response, particularly IgM response to primary vaccination and to polysaccharide-based vaccines.[25] Immunization is advisable early in the disease when CD4 counts are high. Tuberculosis is a substantial risk for travelers with HIV or AIDS. They should be advised about precautions and have TSTs before travel and 2 to 4 months after return.

Key points

- Travelers should complete all primary series of vaccinations for diphtheria, pertussis, tetanus, and polio; measles, mumps, and rubella; and hepatitis A and B, and have recommended boosters as required.
- Those going to areas where these diseases are endemic should be vaccinated against meningitis, typhoid, (possibly) cholera, Japanese B encephalitis, rabies, yellow fever, and (possibly) tuberculosis.
- All elderly travelers should be vaccinated against influenza and pneumococcal disease.
- Most vaccines, including live ones, can be given in the third trimester of pregnancy if risk of exposure warrants such protection.
- Immunocompromised patients should avoid BCG vaccine and live vaccines.

Points de repère

- Les voyageurs devraient recevoir les séries primaires complètes de vaccins contre la diphtérie, la coqueluche, le tétanos et la poliomyélite; et contre la rougeole, les oreillons et la rubéole; et contre l'hépatite A et B; et recevoir les vaccins de rappel au besoin.
- Ceux qui se dirigent vers des destinations où des maladies sont endémiques devraient être vaccinés contre la méningite, la typhoïde, (éventuellement) le choléra, l'encéphalite japonaise de souche B, la rage, la fièvre jaune et (éventuellement) la tuberculose.
- Tous les voyageurs âgés devraient recevoir un vaccin antigrippal et antipneumococcique.
- La majorité des vaccins, y compris ceux de souche vivante, peuvent être administrés durant le troisième trimestre de la grossesse si le risque d'exposition le justifie.
- Les patients immunodéprimés devraient éviter le vaccin BCG et ceux de souche vivante.

Conclusions

Evidence-based recommendations advise that adult and child travelers complete all primary series vaccinations and receive indicated boosters. Nonimmune travelers should be vaccinated aginst hepatitis A (children younger than 2 years receive immunoglobulin); those at risk should be vaccinated against hepatitis B.

Those going to countries where meningitis, typhoid, and cholera are endemic should be vaccinated against

them. Those exposed to endemic TB (eg, health care workers) should use precautions and should receive TSTs before travel and 2 to 4 months after return. Vaccination against rabies and Japanese encephalitis is indicated if an extended stay or a profession, such as biologic field work or veterinary medicine, increases risk. The elderly should be vaccinated against influenza and pneumococcal disease. Vaccines appropriate to their trimester can be given to pregnant women. Immunocompromised patients should be vaccinated, but BCG and live vaccines are contraindicated.

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