UNIT NO. 2

TRAVEL VACCINES

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ABSTRACT

Immunizations prior to travel contribute to reducing the risk of specific diseases for the traveler as well as the risk of international spread of diseases. Travel vaccines can be grouped as those that are required, routine, and recommended. Environmental and host factors determine the risk of acquiring a disease while traveling. Most important factors are destination, duration of travel, reason for travel and activities during travel. Consequently, an epidemiologic, host-related, and legal requirement-based assessment of the planned trip should be conducted when considering which immunizations are appropriate for a traveler.

RECOMMENDATIONS FOR IMMUNIZATIONS FOR NON-IMMUNE TRAVELERS VISITING A DEVELOPING COUNTRY

Required Vaccines

Vaccination against yellow fever, a disease that occurs only in tropical Africa and northern South America (Figure 1), is the main required vaccine. This requirement is based on the international health regulations (IHR). Although only a few hundred cases of yellow fever are reported to the World Health Organization (WHO) annually, serious underreporting of this disease is occurring. It is estimated that there are actually > 200,000 cases each year. Based on recent epidemiology, it appears that yellow fever may be a reemerging disease with increasing recognition of vectors/animal reservoirs. Although yellow fever has never been reported in Asia, the vectors, *Aedes* and *Haemagogus* mosquitoes, have been observed there. This is why vaccination against yellow fever may not only be required when entering an endemic country, but may also be required when entering Asia after visiting endemic areas elsewhere. In travelers yellow fever is rare, but several cases in unvaccinated travelers have been reported in the past 10 years.

Cholera and plague are the two other diseases addressed in the current IHR that are under revision. Because vaccination against cholera is required only for those traveling to Palau or Sudan after transiting an infected area, the risk of cholera is discussed in the "Recommended Vaccines" section, below. Only two international travelers have been diagnosed with plague since 1966. In most industrialized countries, no plague vaccine is marketed; therefore immunization against this disease is neither required nor recommended by any expert group.

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Although not specifically mentioned in the IHR, immunization against meningococcal disease with quadrivalent vaccine is a requirement for pilgrims and workers in the kingdom of Saudi Arabia.

Figure 1. Areas endemic for yellow fever.

Routine Vaccines

Routine childhood immunizations recommended in national vaccination programs usually include those against diphtheria, tetanus, poliomyelitis, measles, and hepatitis B.

Although no cases of tetanus have been reported recently in travelers, such reports may be hidden in national surveillance data. As was demonstrated by a large epidemic in the former Soviet Union from 1990 to 1997, diphtheria outbreaks may occur under specific circumstances. Several travelers became ill, and some died. Far less serious forms of cutaneous diphtheria are occasionally imported from developing countries; these infections cannot be prevented by immunization.

Poliomyelitis has been eradicated from many parts in the world, but there are still important foci, mainly in South Asia and tropical Africa (Figure 2).

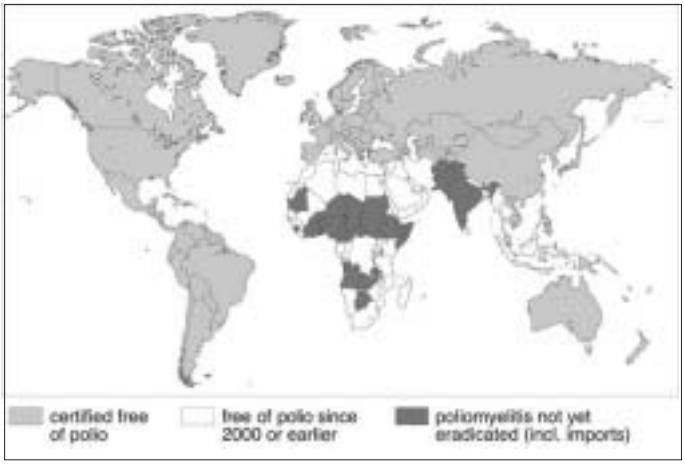

Figure 2. Global poliomyelitis incidence in 2004.

Rabies. The risk of acquiring rabies is particularly high in Asia, where 90% of all human rabies deaths are reported. South Asia has the highest risk. There may also be underreporting in many parts of the world. Hazards to travelers also arise from a low availability of rabies immune globulin and safe vaccine, not necessarily evident from rabies epidemiologic data. Rabies-free areas include Australia, New Zealand, the Pacific Islands, Scandinavia, the United Kingdom, Ireland, Iceland, Italy, France, and Switzerland; in some of these areas, rare cases of rabies transmitted by bats have been reported. In developing countries, of the 0.2 to 0.4% of the traveling population who experience an animal bite each month, many are at risk for rabies. However, no one knows the true rate of exposure to the virus. In the period from 1977 to 2000, 26 cases of imported rabies were diagnosed in Western Europe, mainly in France and in the United Kingdom. Rabies is a particular risk for those who work with animals, explore caves, or travel by bicycle. Rabies is also a particular concern in small children, who often do not tell their guardians that they have been bitten by an animal. In unvaccinated patients developing symptoms, the case-fatality rate is near 100%.

Meningococcal disease. Meningococcal disease has frequently been observed during or after the hajj and to a lesser extent during the umrah pilgrimage by Muslims to Mecca (200 cases per 100,000), but it is rare in travelers staying in countries where the infection is highly endemic (0.04 cases per 100,000). In contrast, in 2004 there were no reported cases of meningococcal disease during or after the hajj. Concern is also justified in those visiting the sub-Saharan "meningitis belt" during months of high transmission with annual regional epidemics. There have been rare reports of *Neisseria meningitidis* being transmitted during air travel of at least 8 hours' duration. The case-fatality rate among travelers is slightly higher than 20%.

Japanese encephalitis. A few dozen cases of Japanese encephalitis have been diagnosed among travelers and expatriates within the past 25 years. The annual rate in travelers was < 1 per 1 million, often these had been at risk by overnighting in farms. Rarely, tourists staying < 4 weeks in Bali may be affected. Most recently the incidence of Japanese encephalitis has decreased in most endemic countries as a result of intermittent irrigation, as opposed to traditional continuous irrigation, of rice fields and other plantations. In addition, in most Southeast Asian countries, pigs, which are the usual host of this disease, are now usually contained to large farms, which are rarely approached by travelers (D.R. Shlim, T. Solomon, A. Oya, personal communication, October 2002).

Cholera. Cholera occurs in approximately 0.2 per 100,000 travelers, with asymptomatic and oligosymptomatic infections being more frequent, as demonstrated in Japanese travelers. The case-fatality rate is < 2% among travelers.

LEARNING POINTS

- **Recommendations for travel vaccines need to be evidenced based, taking into consideration the epidemiology of the vaccine preventable disease, efficacy and safety of the vaccine**
- **Hepatitis A is the most frequently used travel vaccine**
- **Travel vaccines are categorized into routine, required and recommended vaccines**
- **Vaccination against yellow fever, a disease that occurs only in tropical Africa and northern South America, is the main required vaccine.**
- **Although not specifically mentioned in the Internatial Health Regulations, immunization against meningococcal disease with quadrivalent vaccine is a requirement for pilgrims and workers in the kingdom of Saudi Arabia.**
- **Routine childhood immunizations recommended in national vaccination programs usually include those against diphtheria, tetanus, poliomyelitis, measles, and hepatitis B.**
- **For recommended immunizations, it is useful to consider incidence rates and impact, as well as specific risk factors: influenza, hepatitis A, typhoid, rabies, meningococcal disease, Japanese encephalitis, and cholera.**

Table 1. Comparison of Various Expert Recommendations for Immunizations in Nonimmune Travelers Planning to Visit a Developing Country

	Expert Group/Country				
Vaccine	**WHO/World**	**CATMAT/Canada**	**CDC/US**	**CDSC/UK**	**NHMRC/Australia**
Required vaccines					
Yellow fever	**	**	**	**	**
Routine vaccines					
Diphtheria/tetanus	***	***	***	***	***
Polio	**	**	**	**	**
Measles	***	***	***	***	***
Hepatitis B	*	*	*	*	*
Recommended vaccines					
Hepatitis A	***	***	***	***	***/*
Rabies	*	*	*	*	*
Typhoid fever	*	*	*	*	*
Meningococcal	*	*	*	***	*
Japanese encephalitis	*	*	*	*	*
Tuberculosis	*	—/*	—	*	*
Cholera	c	—	—	—	—
Influenza	*	*	*	*	NA

*c = consider in all travelers to endemic countries; CATMAT = Committee to Advise on Tropical Medicine and Travel; CDC = Centers for Disease; Control and Prevention; CDSC = Communicable Disease Surevey Center; NA = not available; NHMRC = National Health and Medical Research; Council; UK = United Kingdom; US = United States; WHO = World Health Organization; *** = all travelers; ** = all travelers when visiting an endemic country; * = risk groups only; — = none;*

Rarely, the virus may be imported by asymptomatic persons, and the obstruction to immunize children in northern Nigeria has in 2004 resulted in a resurgence of the disease in Africa. In travelers residing in industrialized countries, poliomyelitis has not been observed since the early 1990s; but even if travel-related risk has decreased, routine childhood polio immunization still remains a must to ensure immunity. In most industrialized countries oral polio vaccine has been withdrawn from the market because of the risk of vaccine-associated paralytic poliomyelitis, and inactivated polio vaccine is being used.

Hepatitis B is primarily a concern for expatriates living close to the local population and for travelers who fail to take appropriate precautions. The monthly incidence is 25 per 100,000 for symptomatic infections and up to 420 per 100,000 for both symptomatic and asymptomatic infections. Behavioral surveys have demonstrated that 10 to 15% of travelers voluntarily or involuntarily (eg, after an accident requiring an invasive medical procedure or after tattooing) expose themselves to blood and bodily fluids while traveling abroad. Casual sex and nosocomial transmission have been identified as important risk factors. Because routine administration of hepatitis B vaccine to infants and/or adolescents was not initiated until the 1990s in most industrialized countries, many adults remain unvaccinated.

As a result of suboptimal compliance with measles vaccination (< 80% had at least one dose in some regions of European countries), European, African, and Asian travelers often are responsible for outbreaks in the Americas, where the measles vaccine uptake is far better. There are no epidemiologic data known to us on measles among travelers in developing countries, but it is known that at least malnourished children there tend to have a more serious clinical course. To our knowledge, hardly any relevant data exist for travelers on pertussis, *Haemophilus influenzae* type b, mumps, or rubella, diseases for which vaccines are also routinely administered during childhood in industrialized countries. Since patients with acute illness would obviously be contagious and justly would be denied to check-in for a flight, this could have consequences for an entire family.

Recommended Vaccines

For recommended immunizations, it is useful to consider incidence rates and impact (Figure 3) (from Prof Robert Steffen), as well as specific risk factors (summarized in Table 2).

Influenza. Various outbreaks of influenza on cruise ships or after airline flights have been described. The GeoSentinel Surveillance Network collected data on the frequency of respiratory tract infections encountered during travel from September 1997 through August 2001. Respiratory tract infections were the second most common cause of illness among

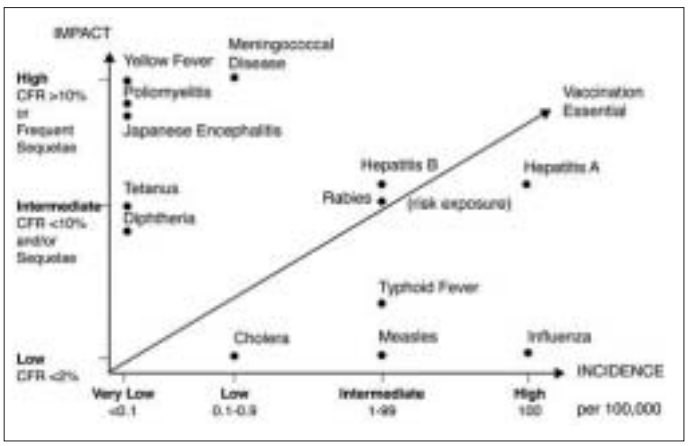

Figure 3. Impact and incidence of vaccine-preventable diseases in travelers to developing countries. CFR = case-fatality rate.

Table 2. Proposed Risk Criteria for Determining the Use of Recommended Travel Vaccines*

Vaccine	Duration of Trip†	Environmental Factor	Host Factor
Influenza	—	Many long flights, cruises	> 50/65 yr, preexisting disease, small children (?)
Typhoid	> few weeks	South Asia, north and west Africa, substandard eating places, or off-tourist itinerary	Gastric anacidity
	> 1 mo	All to developing countries	
Rabies	> 1 mo	High endemicity	High exposure: eg, cyclists, work with animals; children
	> 3 mo	High endemicity	Any exposure
Meningococcal disease	> 1 d > 1 wk	Epidemics, meningitis belt Dry season, meningitis belt	Asplenic
Japanese encephalitis	> 2-4 wk	Rural areas (rice fields), during season	—
Tuberculosis	> 1 mo‡	Close contact with local population	Infants and children
Cholera	—	Work in refugee camp	Gastric anacidity

** This table refers to recommended vaccines. Vaccination against hepatitis A is recommended by most expert groups for all visits to developing countries. †Assuming comparatively good hygienic conditions at destination. ‡Only for infants.*

1,719 persons, and 96 patients (5.6%) were diagnosed with influenza. This condition is likely to be underdiagnosed as not every case would get laboratory confirmation. Influenza was significantly associated with traveling to countries in the northern hemisphere between December and February (odds ratio [OR] 2.34, 95% CI 1.48-3.69), visiting friends and relatives (OR 6.11, 95% CI 1.85-20.11), and traveling for more than 30 days (OR 1.70, 95% CI 1.04-2.78). According to a follow-up survey recently presented, the monthly incidence rate of influenza in travelers exceeds 1%.

Hepatitis A. Hepatitis A, with the exception of influenza, is the most frequent vaccine-preventable infection in nonimmune individuals traveling to developing countries. The average incidence rate has been 3 per 1,000 travelers per month; in high-risk backpackers or foreign-aid volunteers, the rate may be as high as 20 per 1,000 travelers per month. A recent study documented a tenfold lower incidence rate, but a substantial proportion of the population included had a destination in the Caribbean. Even luxury tourists staying at superior tourist accommodations and practicing usual food-consumption behaviors may be at risk for hepatitis A infection. Risk areas for hepatitis A and hepatitis B are shown in Figure 4. Studies in primates have demonstrated that hepatitis A immunization can be protective even when administered postexposure. Based on these results, most travel clinics administer hepatitis A vaccine even when departure is on the same day, and only very few cases of hepatitis A have been documented among travelers who received an adequate dose.

In the past, hepatitis A affected mainly children and took an asymptomatic or oligosymptomatic course in industrialized countries; the infection increasingly occurs in adult and elderly patients and has a case-fatality rate of 1.8% among persons aged 50 years or older. Incapacitation lasts 2 to 3 months even among airline pilots, who are usually highly motivated professionals. Increasingly, even small children with asymptomatic hepatitis A infection (eg, after a stay visiting friends or relatives in the country of the family's origin) create problems because they shed the virus. This results in outbreaks among teachers and staff in schools and nursing homes and among parents of other children who may also become infected.

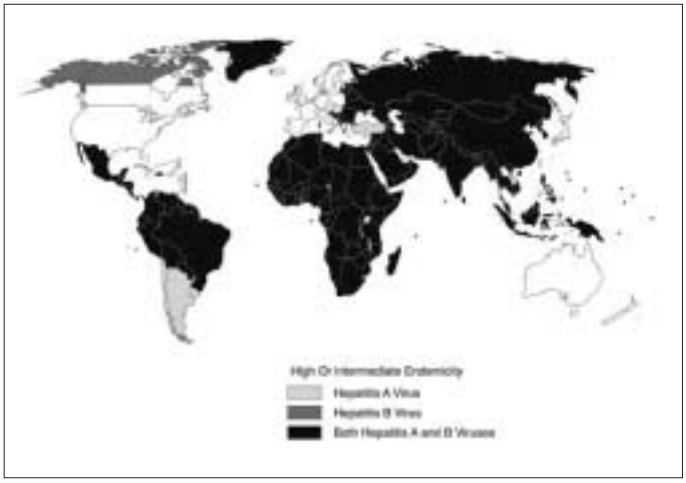

Figure 4. Geographic distribution of moderate to high levels of hepatitis A and/or B virus. Adapted from World Health Organization.[2]

Typhoid fever. Typhoid fever has an incidence rate of 30 per 100,000 travelers per month to South Asia. Elsewhere, the rate of diagnosed typhoid fever is clearly lower; for example, tourists visiting Kenya rarely import typhoid fever. A large proportion of infections are imported by individuals visiting friends and relatives in their country of origin. The case-fatality rate is only 0.3% among travelers.