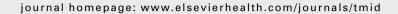
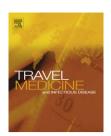


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#### INVITED SUBMISSION

# The present situation of prophylactic vaccination in Japan for travel abroad

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#### **KEYWORDS**

Travel medicine; Vaccination in Japan; Communicable diseases; School-entry **Summary** The current situation of vaccination in Japan is reviewed from a viewpoint of overseas travelers.

Vaccinations before travel to developing countries, where the risk of infection is high, are recommended for two reasons: "individual protection" and "prevention of communicable disease importation". However, there are problems in Japan; some vaccines available commonly in foreign nations are not approved in Japan and the vaccination schedule is not convenient for travelers.

Vaccination is sometimes needed also for travel to Europe and North America. This is because certain vaccinations are required for entering school or studying abroad. In Japan, there is no regulation which recommends vaccination as an entrance requirement. Compared with other nations, Japanese children receive fewer vaccines routinely.

On the other hand, there are different features from other industrialized nations, such as routine childhood BCG vaccination and immunization against Japanese encephalitis in Japan.

Compared with foreign nations, awareness as regards "travel medicine" is lower in Japan. Recognizing this situation will lead to improvement of vaccination of travelers.

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#### Introduction

In many developing countries, the risk for infections is higher than in Japan, and prevention by means of vaccines is important. For long-term residence, of course, but also on short trips, attempts should also be made to preserve the health of the traveler so that the long-awaited pleasant trip does not become a bitter memory. There are also vaccines which need to be given when entering the country, depending on the country or region, such as yellow fever or meningococcal vaccines.

There are also times when prophylactic vaccinations are needed when traveling to North America or Europe. For example, specific vaccines need to have been given when small children or adolescents are transferring to schools in

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the U.S.A. or studying abroad. Vaccination schedules differ from one country to another; even if all the routine vaccinations have been completed in Japan, additional ones may be needed. Compared to Western countries, Japan generally has fewer types of vaccines that are administered routinely, and the numbers of administrations are fewer. Therefore, it frequently happens that vaccinations are needed when traveling abroad.

#### Traveling from Japan to developing countries

#### Recommended vaccines

In industrialized countries, hepatitis A and typhoid fever have been eliminated by improved public health standards, but they are still significant threats in many developing countries. Japanese people, living in an island, do not often have much knowledge or experience with these diseases — either citizens or health care professionals.

Travelers to developing countries should be careful about managing their own health for two reasons. First, for individual hygiene, it is especially important that travelers keep themselves in healthy physical and mental state when living in developing countries with harsh environments. The other reason for caution is to avoid carrying diseases from other countries into Japan. We should avoid becoming ill, returning home, and exposing others to the risk of new imported pathogens.

Many infectious diseases which are easily contracted in developing countries can be prevented by vaccines. Table 1 shows the vaccines which are recommended for Japanese travelers to developing countries.

#### Comparisons with foreign countries

Compared with foreign countries, Japan has little information about "travel medicine" and "health management for travelers." For example, when travelers to areas where hepatitis A is prevalent are surveyed, the proportion of unvaccinated Japanese people is said to be higher than in other industrialized countries. Even when reading the package inserts of the vaccines shown in Table 1, there is no evidence of any statements which take into consideration methods of vaccination specific for travelers or the prevention of infection in foreign countries. Furthermore, besides the vaccines mentioned in Table 1, vaccines for travelers which are used widely in other countries, such as typhoid fever or meningococcal vaccines, have not been approved in Japan. (See below.)

#### Concerning various types of vaccines

#### Hepatitis A

Hepatitis A is fecal—oral infection, acquired by unboiled water and insufficiently cooked foods. Since eating and drinking are daily necessities, there are many opportunities for infection in developing countries. Hepatitis A was once also prevalent in Japan, but the number of cases has fallen rapidly since World War II. Therefore, there is almost no history of natural infection in those younger than 25 years

old, and a small proportion of citizens have antibodies to hepatitis A virus (Fig. 1). Therefore, there is a risk of infection and even short-term travelers should be vaccinated.

There is only one hepatitis A vaccine product on the market in Japan; it contains  $0.5~\mu g$  of inactivated hepatitis A virus antigen per 0.5 ml single vaccination dose. Foreign hepatitis A vaccines have aluminum hydroxide added as an adjuvant, but the Japanese formulation does not contain an adjuvant. In other countries, this vaccine is used in children above the age of 1 and in adults, but in Japan this vaccine has not been approved for children younger than 16 years. Two inoculations with an interval of 2-4 weeks are required in Japan. For longer-term immunization, an additional dose of the vaccine is administered after 24 weeks. In other countries, it has been reported that antibodies develop two weeks after the first vaccination, and the second vaccination is given after 6 months.<sup>1</sup> The international schedule is more convenient for travelers, and the combined vaccine for hepatitis B and typhoid fever is not available in Japan.

#### Hepatitis B

It is important to be immunized completely against this hepatitis B virus, because of the severity of the infection and because it may become a persistent infection, progressing to cirrhosis of the liver and liver cancer. The principal routes of infection are transfusion with blood containing the virus and body fluids and sexual intercourse, reused and imperfectly sterilized syringes and instruments in developing countries.

Table 2 shows a comparison of sex ratios and mean ages for reported cases in which Japanese hepatitis B patients are suspected of having been infected abroad.<sup>2</sup> The incidence of hepatitis B is mainly among men in their prime years, but not all received infected blood transfusions abroad. It is believed that men of this age group had many opportunities of contact with infection sources abroad, such as therapeutic interventions and sexual contact.

#### **Rabies**

In Japan there have been no cases among human beings or animals for several decades, but in 2006 two cases were reported in which travelers were bitten by dogs in the Philippines, became ill after returning to Japan, and died. After this, there was a great demand by Japanese people wishing to be vaccinated against rabies, and widespread shortages of the vaccine occurred. Only one Japanese rabies vaccine product is available on the market at present; it is a tissue-cultured inactivated vaccine using a rabies virus (HEP Flury strain) which was adapted and propagated in chick embryo cells. In Japan, it is often the case that there is only one prophylactic vaccine made by one company for a certain disease, but this situation should be remedied in the future.

The methods of inoculation are "pre-exposure immunization" and "post-exposure immunization"; the schedule used in Japan differs slightly from the method generally used abroad<sup>3</sup> (Table 3). With the pre-exposure immunization schedule used abroad, the three inoculations can be completed within 1 month before travel, which is advantageous. However, the high-potency rabies immunoglobulin

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