

## Travel vaccination. Part 2: Area-specific vaccines

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Vaccine requirements and recommendations for specific countries change, so it is important to regularly check reliable information sources.



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In the second of this two-part article on travel vaccination, vaccines recommended for travellers to specific areas are discussed. Preparation for the vaccination encounter and the importance of checking that travellers are up to date with their routine immunisations were reviewed in the first part of this article, published in the December 2008 issue of *Medicine Today*. The recommendations made in this article are based on those made in *The Australian Immunisation Handbook*.<sup>1</sup>

### Hepatitis A

Hepatitis A is the most common vaccine-preventable disease occurring in travellers. The risk of contracting hepatitis A has been estimated as approximately one in 1000 per month of travel in endemic

areas, even for those staying in luxury resorts, and as high as one in 50 per month in those trekking through high-risk rural areas.

Although previously regarded as a benign illness, hepatitis A is associated with an overall death rate of 0.2%, which increases with age. Given the relatively high frequency of this illness in travellers, it remains clear that inadequate numbers of Australians are being vaccinated. O'Brien and colleagues showed that in a study of 232 consecutive travellers with fever presenting to a hospital infectious disease unit, there were eight cases of hepatitis A along with six cases of typhoid and 11 cases of influenza, all 25 cases (10%) being potentially preventable.<sup>2</sup>

VAQTA Hepatitis A Vaccine Inactivated and Havrix hepatitis A vaccines are available in both adult and paediatric formulations. The hepatitis A vaccine Avaxim can be used in individuals aged from 2 years upwards.

Normal human immunoglobulin (NHIG) is not recommended because of international shortage, of concerns regarding unknown biological contaminants and it provides only part protection for up to six months. Active vaccination with almost 100% efficacy against hepatitis A has only been available since 1993, so travellers claiming vaccination prior to this time are likely to have been given NHIG.

The active vaccine can be given even on the day of departure, as immunity is achieved faster than the incubation period should exposure occur.

Hepatitis A vaccine is recommended for virtually all travellers to endemic areas – that is, all developing countries. Screening for anti-HAV IgG may be cost-effective for those born before 1950, those born overseas or those with a past history of unexplained jaundice. Otherwise, two doses of the vaccine, ideally given six to 18 months apart, will confer almost 100% immunity for at least one to two decades. There have been fewer than 10 reports of vaccine failure in the literature worldwide. Significant side effects are extremely rare, and the vaccine is almost always well tolerated.

Hepatitis A vaccines are also available in combination with either the hepatitis B vaccine (Twinrix, Twinrix Junior) or the *Salmonella typhi* (typhoid Vi) polysaccharide vaccine (Vivaxim; for people aged 16 years or over).

### Typhoid

Typhoid can result in severe illness and death. If untreated, mortality rates of 10 to 20% can occur due to bowel perforation, haemorrhage, toxæmia and other effects. In spite of treatment, 2 to 5% of patients may become permanent carriers of *S. typhi*; the likelihood of becoming a carrier increases with age.

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continued

**Table. Examples of area-specific vaccines for travellers**

| Vaccine  | Trade name  |
|--|---|
| <b>Hepatitis A</b>                                   |   |
| Hepatitis A vaccine                                  | Avaxim<br>Havrix 1440, Havrix Junior<br>VAQTA Hepatitis A Vaccine Inactivated |
| Hepatitis A vaccine, hepatitis B vaccine             | Twinrix, Twinrix Junior   |
| Hepatitis A vaccine, <i>Salmonella typhi</i> vaccine | Vivaxim   |
| <b>Typhoid</b>                                       |   |
| <i>Salmonella typhi</i> vaccine                      | Typherix<br>Typhim Vi<br>Vivotif Oral   |
| Hepatitis A vaccine, <i>Salmonella typhi</i> vaccine | Vivaxim   |
| <b>Cholera</b>                                       |   |
| <i>Vibrio cholerae</i> vaccine                       | Dukoral   |
| <b>Japanese encephalitis</b>                         |   |
| Japanese encephalitis virus vaccine                  | Je-Vax  |
| <b>Rabies</b>  |   |
| Rabies vaccine                                       | Merieux Inactivated Rabies Vaccine<br>Rabipur                                 |
| <b>Tuberculosis</b>                                  |   |
| BCG vaccine  | BCG Vaccine   |
| <b>Tick-borne encephalitis</b>                       |   |
| Tick-borne encephalitis vaccine                      | FSME-IMMUN  |
| <b>Yellow fever</b>                                  |   |
| Yellow fever vaccine                                 | Stamaril  |

Typhoid vaccination is recommended for travellers at risk – that is, those travelling to endemic areas where drinking water is unsafe or hygiene is poor. The areas with higher risk are similar to those for hepatitis A, and include especially Asia and Oceania (most notably parts of Indonesia and Papua New Guinea), Africa, Central and South America and eastern Europe. About 50 to 80 cases of typhoid are reported in Australia each year, most of which are in individuals who contracted the disease overseas.

Two vaccines containing purified Vi capsular polysaccharide of *S. typhi* are

currently available and approved for use in individuals aged 2 years and over (Typherix, Typhim Vi). They offer 70 to 90% efficacy (similar to that achieved with influenza immunisation), so travellers may still contract the disease if they ingest food infected with high numbers of *S. typhi*. Boosters are recommended at approximately two- to three-yearly intervals. Side effects are uncommon but may occur.

The oral typhoid vaccine (Vivotif Oral) provides both serological and local gut-mediated immunity, as well as the obvious advantage of an oral delivery to needle-averse individuals. Although only

the three-dose packet is marketed in Australia, the four-dose regimen offered at most travel clinics is likely to be more efficacious and also provides longer cover for five years. The full course needs to be repeated at this time, and the cost is similar to that of the injectable vaccines.

### Cholera

Although cholera vaccination is no longer recommended by the World Health Organization (WHO) as a requirement for any country, longer term travellers (that is, those travelling for greater than one month) to highly endemic areas may be at increased risk, as may those living in local areas where there are current outbreaks.

The currently available cholera vaccine (Dukoral) is an oral, killed recombinant B subunit/whole cell vaccine, effective against both cholera and enterotoxigenic *Escherichia coli* (ETEC). Vaccination is recommended for travellers to high-risk areas, who have lowered gastric immunity (e.g. achlorhydria associated with prolonged use of proton pump inhibitor medication) or who wish to have a higher level of protection against travellers' diarrhoea.

It should be noted that this vaccine is approved for the prevention of travellers' diarrhoea overseas but as it does not have TGA approval in Australia for this indication, doctors are required to prescribe it 'off-label' for this use.

The efficacy for cholera protection is 85% at six months and 60% at two years. The efficacy for protection against ETEC is 60 to 73% at three months. The schedule is two doses in individuals over 6 years of age, and three doses in those aged 2 to 6 years. The interval between doses is one to six weeks.

### Japanese encephalitis

Japanese encephalitis is a severe and often fatal viral disease spread by mosquitoes. It is endemic throughout greater Asia, in both urban and rural areas, with higher

risk in rice paddies and pig farms. Endemic areas in the Torres Strait Islands and East Timor have been the subject of intense publicity over the past few years, and annual outbreaks may occur seasonally, as have occurred, for example, in northern India.

Although the risk to Australian travellers is low, the potential side effects of the vaccination and complications of the disease obligate discussion with all travellers to Asia as to the relevant risk and benefits. Vaccination should be offered to all longer term travellers (that is, those travelling for greater than one month) as well as to all those who wish to be covered. It should be noted that vaccination is part of the routine schedule in many endemic countries. Current NHMRC recommendations are for individuals to be vaccinated if they are travelling in areas of risk for four weeks or more. However, at the time of writing, the one Japanese encephalitis vaccine marketed in Australia (Je-Vax) is unavailable due to supply issues. Two new vaccines are expected to become available in 2009.

### Rabies

Preventive advice about rabies, including pre-exposure vaccination, needs to be considered for visitors to areas of risk. One study of tourists spending an average of 17 days in Thailand reported that 1.3% and 8.9% of them had experienced a dog bite or dog lick, respectively, and 6% of dogs in Thailand are rabid.<sup>3</sup> Rabies carries the highest fatality rate of any vaccine-preventable disease. Its case fatality rate even with treatment is almost 100%.

The WHO recommends pre-exposure vaccination for all persons living in, or visiting for more than 30 days, countries with endemic rabies. The two rabies vaccines available in Australia are the Merieux Inactivated Rabies Vaccine and Rabipur. The risk of hypersensitivity increases with the number of boosters, and a recent paper suggested that an anamnestic response is demonstrable for

up to 14 years after the primary course.<sup>4</sup>

When given according to current WHO recommendations, intradermal administration of the rabies vaccine is an excellent lower cost alternative, but because some individuals are low responders, the NHMRC generally recommends administration by the intramuscular route, unless this is cost prohibitive. In the latter case, the intradermal vaccine is best administered by a vaccinator who has expertise and frequent experience in the technique, where chloroquine or related antimalarials are not being given concomitantly, and with antibody levels checked for response. It is recommended that if the intradermal method is to be used, the vaccine be administered in a travel clinic setting.

### Tuberculosis

Tuberculosis is one of the world's most common and serious diseases, with the WHO estimating eight million new cases and two million deaths due to this disease per year.

Mantoux testing needs to be performed in anyone over the age of 6 months being considered for BCG vaccination. Ideally, this is best performed at an authorised travel or BCG vaccination clinic. The indications for BCG vaccination are decreasing; generally, it is considered only for children aged less than 5 years who will be living for more than three months in a developing country and for those who will spend extended periods of time in high-risk situations. The WHO defines 'high-risk' countries as those with an annual incidence of tuberculosis in excess of 100 per 100,000 population.<sup>5</sup>

### Tick-borne encephalitis

The tick-borne encephalitis vaccine (FSME-IMMUN) offers protection against European tick-borne encephalitis. It is recommended for individuals at high risk of exposure, such as those spending prolonged time in specific rural regions in central and northern Europe.

### Useful websites for travel vaccination information

- Australian Government Department of Health and Ageing's Immunise Australia Program website: <http://immunise.health.gov.au/>
- Travel Clinics Australia's website: <http://www.travelclinic.com.au/>
- US Centers for Disease Control and Prevention's Travelers' Health website: <http://wwwn.cdc.gov/travel/>
- World Health Organization's International Travel and Health website: <http://www.who.int/ith/en/index.html>

The three-dose course is available through the Special Access Scheme and best provided through a travel clinic or medical practitioner well versed in the vaccine's use.

### Yellow fever

Vaccination for yellow fever is a legal requirement for entry into many countries in Africa and tropical South America. The vaccine (Stamaril) is available only from authorised practitioners and travel clinics. It is strongly recommended that travellers seek specific advice from highly experienced travel health clinics with access to frequent updates on outbreaks and the necessity or otherwise for vaccination.

Over the past few years, yellow fever vaccination has been reported in the literature as being associated with a number of deaths, including one case in Australia. The reasons for this remain unclear; however, because most of the cases occurred in the over 50 year old age group, it is suggested that lowered immunity may have contributed. Despite this, the vaccine used in Australia remains one of the safest. Millions of doses of yellow fever vaccine have been given safely worldwide

### Key points

- Hepatitis A vaccine is recommended for virtually all travellers to endemic areas – that is, all developing countries.
- Typhoid vaccination is recommended for travellers to endemic areas where drinking water is unsafe or hygiene is poor.
- Information changes often in the area of travel medicine and so information sources should be checked regularly.
- Ensure appropriate documentation of vaccination is given to the traveller.
- If the practitioner is unfamiliar with the information that should be given or with the relevant vaccines, referral of travellers to a travel health clinic is recommended.

over the past 60 years.

Yellow fever infection has a high case fatality rate and has decimated populations in the past. Travellers to areas at risk clearly require vaccination if they and their contacts are to be protected. However, the vaccine should only be given if it is definitely required for travel to at-risk areas, and then only following a careful appraisal with the patient regarding need and possible contraindications. Visitors to areas at risk should be advised that the 'International Certificate of Vaccination or Prophylaxis' should be carried at all times to avoid possible vaccination at a border crossing and/or quarantine.

### Conclusion

The initial travel health consultation is extremely complex and if followed clearly satisfies Medicare criteria for a level C consultation in terms of both complexity and time. Follow-up consultations to complete a course of vaccines and discuss nonvaccine related travel health issues may be

equally or less complex. Ensure a record of vaccines administered is documented in the medical notes and appropriate certification is given to the patient.<sup>6</sup> Information changes often in the area of travel medicine and so information sources should be checked regularly (see the box on page 53). If the practitioner is unfamiliar with the information that should be given or with the relevant vaccines, referral of the traveller to a specialised travel health clinic is recommended. **MT**

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**COMPETING INTERESTS.** Dr Cohen is the Medical Director of Travel Clinics Australia and author of 'The Traveller's Pocket Medical Guide and International Certificate of Vaccination'.