MedicineToday PEER REVIEWED

Australian immunisation guidelines for international travellers

JONATHAN COHEN MB BS, FACTM, FRACGP, MastFamMed

Vaccine advice for international travel is a fast changing area and it can be challenging to remain up to date with current recommendations. The recently revised *Australian Immunisation Handbook* provides information on the safest and most effective vaccination strategies for travellers based on the latest evidence available.

MedicineToday 2014; 15(2): 57-61

The 10th edition of the *Australian Immunisation Handbook* released in 2013, and updated in January 2014, includes a significant amount of advice on vaccination for international travellers.[1] The guidelines have been developed by the Australian Technical Advisory Group on Immunisation (ATAGI) with approval from the National Health and Medical Research Council (NHMRC). The handbook is distributed to all Australian medical practitioners in hardcopy form and also freely available online (www.immunise.health.gov.au). The guidelines are widely regarded as a gold standard document, with the primary aim of informing clinicians on the safest and most effective vaccination strategies using the highest quality evidence available.

Dr Cohen is Medical Director of Travel Clinics Australia and a Senior Lecturer in the Department of General Practice at Monash University, Melbourne, Vic.

It is important to note that guidelines apply to a general group, whereas each traveller must be considered according to his or her individual needs. The medical practitioner needs to ensure there has been appropriate mutual discussion of the relative risks and benefits of vaccination for each situation and be prepared for some flexibility and variation.

The handbook now comprises five sections:

- Introduction
- Vaccination procedures
- Vaccination for special risk groups
- Vaccine-preventable diseases
- Passive immunisation.

There is also a useful set of appendices and excellent summary tables throughout. The online version includes links to other useful websites for clinicians and the general public.

The key information on each disease and appropriate vaccination is provided in the section on vaccine-preventable diseases. However, as training for vaccination and immunisation is not always optimal, it is recommended that the sections on vaccine injection techniques (section 2.2.5), post-vaccination and adverse events (section 2.3), and vaccination for international travel (section 3.2) and special risk groups (section 3.3), including the pregnant and lactating traveller, are reviewed.

Some of the recommendations made by the ATAGI in the handbook differ from manufacturers' product information for specific vaccinations; in each instance, these discrepancies are noted. Vaccine providers are advised to check for any updates in specific product information, with the latest information available on the TGA website.[2] References for all the recommendations made in the handbook are listed.

This article summarises some of the more important areas for GPs to consider when providing pretravel health advice to patients, focusing on the up-to-date advice given in the handbook.

VACCINES TO CONSIDER FOR TRAVELLERS

Routinely recommended vaccines

Diphtheria
Haemophilus influenzae type b infection
Hepatitis B
Human papillomavirus infection
Influenza
Measles
Mumps
Pertussis
Pneumococcal disease
Poliomyelitis
Rotavirus infection
Rubella
Tetanus
Varicella

Selected vaccines based on risk

Cholera
Hepatitis A
Japanese encephalitis
Meningococcal disease
Rabies
Tick-borne encephalitis
Typhoid fever
Tuberculosis (TB)
Yellow fever

Legally required vaccines for certain destinations

Meningococcal disease
Yellow fever

ROUTINELY RECOMMENDED VACCINATIONS

Although all travellers should be up to date with their routine immunisations as recommended under the National Immunisation Program (NIP) schedule, a small but significant percentage will have missed their routine vaccinations for various reasons. The pretravel consultation is an ideal time to thoroughly review a patient's past vaccination history and to make recommendations to catch up on missed vaccinations.

Tetanus

Tetanus toxoid, combined with diphtheria toxoid, acellular pertussis, hepatitis B, inactivated polio and *Haemophilus influenzae* type b vaccines, is routinely given as DTPa-hepB-IPV-Hib to infants at 2 months of age (but can be given as early as 6 weeks of age) and then at 4 and 6 months of age. A booster dose, usually as DTPa-IPV, is recommended at 4 years of age (but can be given as early as 3.5 years). An adolescent booster with reduced diphtheria and pertussis antigen (dTpa) is then given a part of school-based vaccination programs in year 10, at 15 years of age, although it is now preferentially recommended for 11 to 13 year olds, due to the presumed waning immunity, particularly to pertussis, in this age group. (The small letters in the vaccine acronyms signify a smaller dose of the particular antigen.)

The next booster is not recommended until individuals are aged 50 years or above, unless a person has a tetanus-prone wound and more than five years have elapsed since their last dose. In addition, adults over 65 years of age should be offered dTpa if more than 10 years have elapsed since their last dose.

A tetanus-prone wound is now classified as anything other than a clean minor wound, and so, depending on the risk of the wound, a booster dose is recommended if more than five to 10 years have elapsed since a previous dose.

Travellers to areas with limited access to health services while overseas are advised to have a tetanus vaccine before travelling if they were vaccinated more than five years prior in the case of a high-risk trip, or otherwise if they were vaccinated more than 10 years prior.

Diphtheria

Diphtheria remains a significant risk for travel to many developing areas (including South East Asia and New Guinea) as well as some states of the former Soviet Union and Baltic and eastern European countries, but is also a risk to those with waning immunity to this disease in Australia. Diphtheria toxoid is only available in combination with tetanus toxoid-containing vaccines, as noted above.

Pertussis

Pertussis remains highly prevalent in Australia, with thousands of cases having been reported each year for the past few years. In view of this, it is generally recommended that for those needing a tetanus booster, dTpa be given opportunistically, rather than dT.

Pertussis vaccination is now recommended for higher risk groups, including women planning pregnancy or in the third trimester if more than five years have elapsed since their last dose. The vaccine can also be given to breastfeeding women.

There is now no minimum time interval between being given a single dose of dTpa and after having had a dose of a vaccine containing tetanus and diphtheria toxoids.

Poliomyelitis

A booster of polio vaccine is recommended for travellers to epidemic or endemic areas of polio or countries at risk of imported cases. Notably this currently includes Afghanistan, Pakistan and Nigeria. Outbreaks have occurred in a number of African countries and sporadic cases have been imported elsewhere. A single booster dose is recommended if more than 10 years have elapsed since the previous dose. Inactivated polio vaccine (IPV) can be given either by itself or as dTpa-IPV, again with no minimum time interval necessary after having been given a dT-containing vaccine.

Hepatitis B

Hepatitis B vaccine will have been given to most Australian children and adolescents born since 2000 under the NIP schedule or school-based vaccination programs. Vaccination is recommended for travellers making frequent or long-term visits to intermediate or high endemic areas of hepatitis B (including Central and South America, Africa, Asia and Oceania). Despite the relatively low endemicity of hepatitis B

in Australia, the carrier rate is estimated at approximately 0.5%.[3]

Given that the risk of unplanned and inadvertent exposure to the virus via body fluids is unpredictable and in view of the serious nature of the disease and the wide availability, high efficacy and low cost of this vaccine, universal vaccination is recommended at our travel clinic. A completed course of hepatitis B vaccine is now thought to provide lifelong immunity.

Influenza and pneumococcal disease

Influenza and pneumococcal vaccinations are recommended under the NIP schedule for higher risk age groups, including those aged 65 years or older and those with any relevant underlying medical risk.

Seasonal influenza vaccine should be offered to all travellers to prevent one of the most frequent causes of vaccine-preventable disease in this group. The risk is further increased when travelling during influenza seasons, in larger tourist groups or in confined spaces such as planes, trains and cruise ships.

Measles, mumps, rubella and varicella

Measles, mumps, rubella (MMR) vaccine is recommended before international travel for nonimmune adults born since 1966 who do not have evidence of two doses of the vaccine in the past. (Vaccination is not needed for those born earlier as most are expected to have natural immunity owing to the prevalence of circulating virus and disease at that time.) A clear history of immunity to all three diseases is often difficult to obtain, in which case serological testing can be performed. However, a more practical alternative is to vaccinate all such individuals, as there is no known increase in adverse events in those with pre-existing immunity.

The MMR vaccine can be given as early as 9 months of age in certain circumstances (such as in those travelling to highly endemic areas); however, as the immune response may be suboptimal at that age, the usual 12- and 18-month of age doses of the vaccine should still be administered. The second routine dose of a measles-containing vaccine was rescheduled from July 2013 to be given at the earlier age of 18 months; previously it was given at 4 years of age. This second dose of measles-containing vaccine is recommended to be the MMRV vaccine (see below).

Varicella can have extremely serious sequelae in both children and adults. Varicella vaccination is now routinely recommended at 18 months of age, administered as the MMRV vaccine, and a second dose of varicella vaccine is recommended (but not funded as yet) at least four weeks later. Prior infection with varicella will generally provide lifetime immunity; however, it is not a contraindication to vaccination.

The MMRV vaccine should not be used as the first dose of an MMR-containing vaccine because of the higher risk of adverse events in this case. In general, MMRV vaccine should only be administered between the ages of 18 months and 14 years, and used as a second dose of MMR-containing vaccine at least four weeks after the first dose of the MMR vaccine.

Varicella vaccination in adolescents and adults with two doses of the monovalent varicella vaccine (VV), given at least four weeks apart, is recommended when there is no history of disease, documentation of vaccination, or serology indicating immunity.

Egg sensitivity is no longer considered by the ATAGI as a contraindication to vaccination with the MMR or MMRV vaccines. However, when there is a history of anaphylaxis, immunisation should only proceed under close supervision as discussed in the handbook and according to the Australasian Society of Clinical Immunology and Allergy (ASCIA) guidelines.[1,4]

Live viral vaccines (including the MMR, MMRV and VV vaccines) can be given at the same time as other vaccines, or at least four weeks apart from other live viral vaccines. Before administering live viral vaccines to a traveller who may be immunosuppressed, further advice should be sought from a travel clinic and/or relevant medical practitioner. Measles-containing vaccines may impair tuberculin skin testing for at least four weeks.

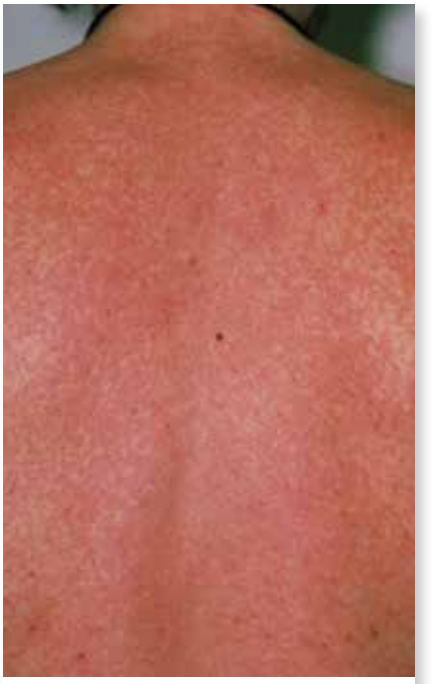

Figure. Severe measles rash.

Given the regular and recent outbreaks of measles and varicella resulting from non-immunised individuals importing these diseases into both Australia and a number of European countries, it is clear that these childhood illnesses remain a significant threat to children and especially to non-immune adult travellers, who are likely to suffer more severe forms of the disease (Figure).

SELECTED VACCINES BASED ON RISK

Hepatitis A

Hepatitis A vaccination is virtually 100% effective and is recommended for all nonimmune individuals from 1 year of age travelling to any developing country or areas of moderate or high endemicity. Serological testing to determine hepatitis A immunity is not routinely recommended but may be necessary to clarify previous vaccination or exposure to the disease.

TRAVEL VACCINATIONS: ONLINE RESOURCES

***The Australian Immunisation Handbook 10th edition 2013* (updated January 2014)**
http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home

National Centre for Immunisation Research & Surveillance (NCIRS)
www.ncirs.edu.au/index.php

Smarttraveller
www.smartraveller.gov.au/tips/health.html

WHO: International travel and health
www.who.int/ith/en/

Centers for Disease Control and Prevention: Travelers' health
http://wwwnc.cdc.gov/travel

Although the disease may be relatively mild in some, there is an overall fatality rate of 0.2%, and this is higher in older age groups. Vaccination is available in monovalent form or in combination with hepatitis B or typhoid vaccine, and a completed course is now thought to provide lifelong immunity to the hepatitis components.

Typhoid

Typhoid vaccination is recommended for individuals from the age of 2 years travelling to endemic areas, including the Indian subcontinent, most of South East Asia and several South Pacific nations.

The parenteral typhoid Vi capsular polysaccharide vaccines provide immunity for up to three years and can be administered concurrently with other vaccines.

The oral live attenuated typhoid vaccine is indicated from the age of 6 years, and provides immunity for one to three years with the three-dose regimen, and three to five years with the four-dose regimen. The oral vaccine should not be taken within eight hours of taking the oral cholera vaccine, or within three days of taking antibiotics.

Both injectable and live oral vaccines offer approximately 70% efficacy, so the traveller should note that food and water precautions are still necessary to reduce the risk of infection.

Rabies and other lyssaviruses

Rabies is virtually 100% fatal and occurs following exposure to body fluids, most often from a dog scratch or bite, but also from any mammal, including bats and monkeys. Because the clinical diseases caused by rabies virus and other lyssaviruses are indistinguishable, the term 'rabies' refers to disease caused by any known lyssavirus species. There have now been three deaths in Australia from exposure to bats carrying the Australian bat lyssavirus (ABL).

Postexposure prophylaxis (PEP) must be implemented following any potential exposure to rabies. This includes thorough washing of the wound, early administration of human rabies immunoglobulin (HRIG) and four doses of rabies vaccine, with a fifth dose given to immunocompromised individuals.

Many Australians are bitten by animals overseas each year and so in addition to discussing avoidance of animals, it is important to discuss and offer the option of pre-exposure prophylaxis (PreP) with three doses of rabies vaccine. PreP removes the need for HRIG, and only two PEP doses are needed should exposure occur. PreP is strongly recommended where HRIG or rabies vaccine may not be readily available, regardless of the length of stay, and particularly for children.

Intradermal vaccination is much cheaper and preferred by travellers; however, it is not routinely recommended in Australia. It is, however, endorsed by the WHO,[5] and often administered at most travel clinics under specified NHMRC criteria (see the handbook for more detail).[1]

Meningococcal C

Meningococcal C vaccination is routinely administered in Australia in infants at 12 months of age. The quadrivalent meningococcal conjugate vaccine (4vMenCV) is indicated for individuals aged 9 months or over who are travelling to endemic areas, in particular the 'meningitis belt' of sub-Saharan Africa, as well as other areas experiencing epidemics. It is recommended for travellers in preference to the polysaccharide vaccine and covers serotypes A, C, W135 and Y.

Evidence of meningococcal vaccination may be required in specific situations – for example, students living in college dormitories in the USA are usually required to be vaccinated against meningococcal disease. In addition, the Saudi Arabian Ministry of Health requires that all pilgrims attending the annual Hajj show evidence of vaccination with the vaccine.

Tick-borne encephalitis

The tick-borne encephalitis vaccine offers protection against European tick-borne encephalitis. It is recommended for travellers with high risk of exposure, such as prolonged rural exposure in specific regions (e.g. hiking or camping in forested areas in endemic regions – central and northern Europe and across northern Asia – during the summer). The three-dose course is available through the Special Access Scheme and best provided through a travel clinic or medical practitioner well versed in its use.

Japanese encephalitis

Japanese encephalitis is an extremely rare but serious mosquito-borne disease endemic throughout greater Asia and is now presumed to be widespread in Papua New Guinea. Vaccination is generally only recommended for those at higher risk of exposure, such as prolonged visits to countries where the disease is endemic, including rural or urban areas, or shorter stays in areas of very high risk, such as rice paddies and pig farms.

Cholera

Cholera vaccination is not routinely recommended for travellers providing the usual precautions are taken to avoid contaminated food and water. However,

the currently available oral vaccine, although not TGA approved for the purpose in Australia, does provide some 'off-label' protection against enterotoxigenic *Escherichia coli* (ETEC) traveller's diarrhoea. It may therefore be recommended for those with increased risk or highly risk averse to ETEC infection.

The efficacy of the vaccine for cholera protection is 85% six months after administration but 60% after two years. The efficacy for protection against ETEC is 60 to 73% three months after administration.

The schedule is two doses of the vaccine in those aged over 6 years, and three doses if aged 2 to 6 years. The interval between doses is one to six weeks. Following primary immunisation, a booster dose is required for those at ongoing risk, six months later for children aged 2 to 6 years and up to two years later for those over 6 years of age. If more than six months have elapsed in children aged 2 to 6 years, or more than two years in adults and children over 6 years, primary immunisation should be repeated.

Yellow fever

Yellow fever vaccination is now recommended for all travellers to areas of either persistent or periodic virus transmission, or if legally required by a country for entry in accordance to WHO international health regulations, which change periodically. Australia currently requires a valid International Certificate of Vaccination or Prophylaxis as certification of entry for travellers arriving from specific countries in tropical South America and sub-Saharan Africa.

There are several contraindications to yellow fever vaccination, including age less than 9 months, pregnancy, breastfeeding, egg allergy, immunosuppression and thymus disorders. Serious adverse events following immunisation are well documented and include vaccine-associated neurotropic and viscerotropic disease. Although very rare, some events have been fatal and appear to be associated with host factors, particularly thymus disorders. Risk increases with advanced age and precaution is therefore urged in adults aged 60 years and over.

Yellow fever vaccine is provided by authorised clinics and should only be administered following appropriate discussion of risks and benefits with the traveller by experienced and knowledgeable practitioners.

Tuberculosis

Tuberculosis (TB) is one the world's most common and serious diseases, with the WHO estimating eight million new cases and two million deaths each 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, and in general vaccination is recommended only for children aged under 5 years who will be living in countries with a high prevalence of TB for extended periods. It should also be considered for those who will spend extended periods of time in at-risk situations.

CONCLUSION

The above general recommendations apply to travellers with normal requirements; however, there are several groups at increased risk, including very young children, pregnant and breastfeeding women, the elderly, the immunocompromised, sports groups, those attending mass gatherings and migrants from high-risk areas returning home to visit friends and relatives. Travellers need to be advised that no vaccine is 100% effective and that preventive risk reduction strategies remain important.

Vaccine advice for international travel is a fast-changing area and it can be challenging to remain up to date with current recommendations. With multiple vaccines currently available and more becoming available each year, and the choice of over 230 countries to visit, we suggest medical practitioners access online resources including those listed in the box. For more complex trips and high-risk groups, or if unsure of requirements, referral to a travel clinic or medical practitioner well versed in travel health is recommended. MT

REFERENCES

1. Australian immunisation handbook 10th edition 2013 (updated January 2014). Canberra: Australian Government Department of Health and Ageing; 2013. Available online at: http://www.immunise.health.gov.au/internet/immunise/publishing.nsf/Content/Handbook10-home (accessed February 2014).
2. Therapeutic Goods Administration. Australian Register of Therapeutic Goods. [Website]. https://www.ebs.tga.gov.au (accessed February 2014).
3. National Hepatitis B Strategy 2010–2013. Canberra: Australian Government Department of Health and Ageing; 2010. Available online at: http://www.health.gov.au/internet/main/publishing.nsf/Content/ohp-national-strategies-2010-hepb/$File/hepb.pdf (accessed February 2014).
4. Australasian Society of Clinical Immunology and Allergy (ASCIA). Acute management of anaphylaxis guidelines (updated September 2013). Available online at: http://www.allergy.org.au/health-professionals/papers/acute-management-of-anaphylaxis-guidelines (accessed February 2014).
5. World Health Organization. WHO guide for rabies pre and post exposure prophylaxis in humans (updated 2013). Geneva: WHO. Available online at: http://www.who.int/rabies/WHO_Guide_Rabies_Pre_Post_Exposure_Prophylaxis_Humans_2013.pdf (accessed February 2014).

COMPETING INTERESTS. Dr Cohen is the Medical Director of Travel Clinics Australia.