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Rabies – offering travellers pre-exposure vaccination

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Difficulty in accessing rabies postexposure prophylaxis in developing countries is one of the main reasons to offer travellers pre-exposure vaccination.

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Rabies is an acute infectious zoonotic disease in mammals, characterised by central nervous system symptoms and signs, paralysis and death. The cause is a neurotropic virus found in the saliva of rabid animals, most commonly domestic dogs, although monkeys, bats or, indeed, any mammal may be infected. The virus may be transmitted by biting or skin abrasion, and also rarely by aerosol or direct fluid contact across mucous membranes or transplantation of infected organs.[1]

The incubation period can vary from one week to many years; however, it is generally one to three months.[1] Symptoms can include fever, pain, tingling and paraesthesias, progressing to symptoms of encephalitis and death. The two forms of presentation are 'furious' rabies with hyperactivity, excitable behaviour, hydrophobia and, occasionally, aerophobia, followed by cardiorespiratory arrest. The 'paralytic' form consists of gradual paralysis, coma and death.

Australian medical practitioners are aware of the risks associated with the related lyssavirus in people exposed to bats. Both the rabies virus and the Australian bat lyssavirus (ABL) belong to the family Rhabdoviridae, genus *Lyssavirus*.

PREVALENCE

Rabies is not rare. According to the WHO, more than 55,000 people die of rabies annually, 40% of whom are children, with dogs as the main source.[1] Rabies occurs in over 150 countries, mainly developing nations, especially in Asia and Africa, but it is also present in North America, parts of Europe and the Mediterranean region.

In India alone, there are an estimated 25,000 deaths per year from the disease, and worldwide 15 million people require postexposure vaccination annually.[2] In Thailand, up to 400,000 individuals receive a course of three postexposure rabies

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A CASE STUDY HIGHLIGHTING PROBLEMS IN ACCESSING RABIES POSTEXPOSURE PROPHYLAXIS

A 21-year-old Australian law student on exchange in Kuala Lumpur, Malaysia, travelled with friends to Cherating, a small town on the north-east coast of peninsular Malaysia, for a weekend surfing trip. While there, a stray dog approached him trying to play with his rubber sandals. The student immediately avoided contact by moving away; however, the dog jumped up and bit the student on his knee, breaking the skin but without drawing blood.

Four days later, the student attended a local hospital requesting postexposure rabies vaccination; however, he was told it was 'too late' for vaccination. Approximately seven days after this, he developed a skin rash, and attended a second hospital in the area requesting testing for rabies and vaccination, but he was told that the hospital 'did not stock rabies vaccine'. He then travelled to a major hospital in Kuala Lumpa, where he was told a vaccine would be 'ineffective'.

Sixteen days after the bite, the student developed mild tingling in his right leg close to the wound site, with associated leg pain, night sweats and lethargy. Worrying that this was symptomatic rabies, he returned again to the general hospital, his fourth visit to a hospital, where he was finally able to receive a vaccine, but in order to avoid a long wait to have it administered, he had to attend a separate, fifth, hospital.

Subsequently the student returned to Australia where he was given rabies immunoglobulin and the remaining postexposure doses of rabies vaccine in accordance with Australian and international guidelines. He remains quite healthy.

vaccinations each year. That country has a total of approximately one million dogs, of whom up to 100,000 are rabid.[3,4] A 1994 study of tourists spending an average of 17 days in Thailand reported that 1.3% and 8.9% of travellers were bitten or licked, respectively, by a dog and over half the travellers in the study favoured the introduction of pre-exposure rabies vaccination for travellers to areas at risk.[5]

Closer to home, Bali, a long-favourite holiday destination for Australians and their families, and free of reported cases of rabies for over a decade, has reported a significant number of deaths among the local population from rabies following dog bites. The Victorian Department of Human Services started issuing alerts in 2008 recommending rabies vaccination 'be considered' in those planning travel to Bali.[6]

Victorian data show that the number of postexposure rabies cases has increased each year, from 113 in 2008, to 175 in 2009, and to 217 in 2010, with South-East Asia being the most common area in which travellers are bitten (Victorian Department of Health data 2008–2010, personal communication, April 2011). Extrapolating these figures nationally, hundreds of Australian travellers are being bitten each year by dogs or monkeys and require postexposure prophylaxis. This number is far greater than the number of people acquiring tetanus in Australia, yet virtually every Australian is vaccinated against that disease. In fact, the number of Australians bitten by a potentially rabid animal overseas appears to be the same order of magnitude as the number of cases of hepatitis A reported in Australia. This implies the need to at least discuss with, and preferably offer, all Australian travellers to rabies endemic areas the option of pre-exposure vaccination.

PRE-EXPOSURE VACCINATION

The dose of rabies vaccine for pre-exposure prophylaxis is 1.0 mL given by intramuscular injection on days 0, 7 and 28 (human diploid cell rabies vaccine [HDCV] can be given intramuscularly or subcutaneously). For further details on available vaccines and administration recommendations, see the current edition of *The Australian Immunisation Handbook*[7] and the current WHO guidelines.[8]

Offering travellers pre-exposure vaccination has the following advantages if they are subsequently exposed to a rabid animal:

- there is no subsequent need for rabies immunoglobulin, which can be difficult to obtain in some countries
- there is a longer time window between exposure and the need to start postexposure vaccination
- it is convenient (by saving cost and time lost in looking for postexposure treatment in the holiday destination)
- only a further two doses of vaccine are required post exposure
- distress and anxiety are reduced at the time of exposure because the person will already have antibodies against the rabies virus – this last point is vital for children, who may not always tell an adult that they have been exposed, with potentially dire consequences.

Current NHMRC guidelines recommend pre-exposure vaccination for all persons living in or visiting (for more than 30 days) countries with endemic dog rabies.[7] In particular, high-risk groups who should be offered pre-exposure vaccination include:

- travellers spending prolonged periods in, or those frequently visiting, rabies endemic areas
- cavers
- cyclists
- expatriate workers
- veterinarian or animal handlers
- wildlife officers
- park rangers
- animal food handlers.

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TABLE. WHO CATEGORIES OF RABIES EXPOSURE AND RECOMMENDED ACTION[8]

Category of exposure to suspected rabid animal	Post-exposure measure
Category I – touching or feeding animals, licks on intact skin (i.e. no exposure)	None
Category II – nibbling of uncovered skin, minor scratches or abrasions without bleeding	Immediate vaccination and local treatment of the wound
Category III – single or multiple transdermal bites or scratches, licks on broken skin, contamination of mucous membrane with saliva from licks, exposure to bats	Immediate vaccination and administration of rabies immunoglobulin; local treatment of the wound

Other factors that should be taken into consideration when deciding whether to initiate postexposure prophylaxis include:

- the likelihood of the implicated animal being rabid
- the clinical features of the animal and its availability for observation and laboratory testing.

In developing countries, the vaccination status of the suspected animal alone should not be considered when deciding whether or not to initiate prophylaxis.

Australia recommends travellers be routinely offered the option of pre-exposure vaccination before travelling to rabies endemic areas regardless of the duration of the visit.

POSTEXPOSURE PROPHYLAXIS

In 2010, the US Centers for Disease Control (CDC) recommended the five-dose postexposure prophylaxis schedule be reduced to four doses for immunocompetent individuals potentially exposed to rabies.[9,10] This recommendation has now also been advised by the Australian Technical Advisory Group on Immunisation (ATAGI).[11]

If a person is bitten or licked by an animal in a country where known cases of rabies have been reported, he or she should be advised to:

- wash the skin area thoroughly with hot soapy water for five minutes and flush with povidone–iodine because this significantly reduces the risk of infection
- seek urgent medical treatment.

Travellers should be aware of the treatment they should be given if they think they have been exposed to rabies. It should preferably comprise human rabies immunoglobulin (HRIG; at a dose of 20 IU/kg body mass) plus four 1.0 mL doses of HDCV (given intramuscularly or subcutaneously) or purified chick embryo cell rabies vaccine (PCECV; given intramuscularly).

The immunoglobulin should ideally be given with the first dose of vaccine, but it can be given up to day 7 after the first vaccination. It should not be given any later in the vaccination course. It should be infiltrated locally as much as possible to neutralise any virus. If there is not enough tissue in the area (such as around a finger), the remainder should be given by deep gluteal intramuscular injection.

Rabies vaccine is generally given on days 0, 3, 7 and 14 (and 28 for ABL or if the person is immunocompromised). Alternative regimens exist as noted in the WHO guide.[8]

Tetanus cover should also be validated or administered, and prophylactic antibiotics given.

Giving this advice to intending travellers may be inadequate, however, because, as highlighted by the case on page 74, a number of potentially serious problems may occur. These include the following:

- the vaccine or immunoglobulin may not be available
- the immunoglobulin offered may cause serum sickness or come from dubious sources
- vaccines with increased risk of side effects or types that are less effective may be used
- advice given to the traveller by locals may not be accurate, resulting in inadequate treatment
- the cost of obtaining vaccines in some areas may be prohibitive to many travellers.

The Table summarises the WHO categories of exposure to a suspected rabid animal and the recommended course of action.[8]

POSTEXPOSURE PROPHYLAXIS IN PEOPLE PREVIOUSLY VACCINATED

If pre-exposure vaccination has been given within the previous two years only two rabies vaccine doses of 1.0 mL are needed, given on days 0 and 3. The wound also needs to be managed locally. HRIG is not needed in those who have been vaccinated in the past.

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KEY POINTS

- Rabies is a serious disease with virtually 100% mortality.
- The disease is preventable provided that the correct and timely postexposure prophylaxis is given.
- Risk of potential exposure to rabies from a dog or monkey bite is not rare.
- A bite from a dog, monkey, bat or any other mammal mandates postexposure prophylaxis when in a country where rabies is endemic.
- Rabies vaccine, and especially rabies immunoglobulin, may be unavailable in developing countries. This is the main reason to offer travellers pre-exposure rabies vaccination.
- Pre-exposure vaccination needs to be discussed routinely with all travellers visiting rabies endemic areas.
- Pre-exposure vaccination needs to be offered more frequently than is currently done.
- In Australia pre- and postexposure vaccination is available at most dedicated travel clinics and public hospital emergency departments.

VACCINE AVAILABILITY IN AUSTRALIA

Pre- and postexposure vaccination is available at travel medicine clinics and hospital emergency departments throughout Australia. Postexposure vaccinations and immunoglobulin for patients at risk are supplied in Australia at no cost by the State and Territory health authorities. MT

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

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