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Review

Australia is not rabies-free

Tony Gherardin
Travel Doctor-TMVC Clinic, Lt Bourke Street, Melbourne 3000, Australia

Background: Human rabies is a disease transmitted mainly by bites from infected mammals. Australia has a lyssavirus present among various bat species. The risk to individuals in Australia is low, and bat-handlers within Australia are at greatest risk. For Australians travelling internationally, dogs in the developing world represent a greater risk.
Objective: To highlight the major strategies for prevention of rabies infections, both within Australia and for Australians travelling overseas.
Discussion: Prevention for individuals involves an understanding of risk and avoidance of vectors, the routine use of post-exposure prophylaxis and consideration of pre-exposure prophylactic immunisation. A new rabies vaccine for post-exposure prophylaxis and for pre-exposure immunisation has become available. Australian medical practitioners need to be familiar with these preventive strategies and vaccines. Travellers to Australia must beware of contact with bats.

Keywords: Australia, bats, rabies, rabies vaccines.

Rabies is an acute encephalomyelitis caused by rhabdoviruses of the lyssavirus genus. There are currently seven different genotypes of lyssaviruses recognised, and though all can cause disease in man, the overwhelming majority of cases are classical rabies caused by genotype 1, RABV, transmitted usually by the bite of a dog. Globally, rabies causes over 50,000 deaths each year; mostly in Asia and Africa [1]. Almost half of these are in children. The disease exists among several mammal species, primarily canines. It has widespread global distribution with high risk areas being Africa, Asia, and South America. Humans are accidentally infected through contact of animal saliva through broken skin or onto mucous membranes during a bite. RABV is not present in Australia but the northern coastline remains vulnerable to its accidental importation, being present in parts of neighbouring Indonesia and known to be transported by pet dogs of Indonesian fishermen [2].

In 1996, a novel genotype of lyssavirus was discovered in Australia and called the *Australian Bat Lyssavirus* (ABLV) [3]. It has now been shown to be present amongst all 4 types of flying foxes, *Pteropus* sp. and a subtype has also been found in insectivorous bats. These have a wide distribution over mainland Australia [4]. ABLV is one of several newly recognised lyssaviruses, emerging as technology and a broader understanding of this genus is developing. It is not known when this virus was imported into Australia.

Correspondence to: Dr. Tony Gherardin, Director, Travel Doctor-TMVC Clinic, 393 Lt Bourke Street, Melbourne 3000, Australia; E-mail: tony.gherardin@hfi.com.au

Previous lyssavirus infections in Australia

Only two cases of imported rabies have been recorded. In 1987, a 9 year old boy developed rabies 9 months after returning from India where he had incurred a monkey bite [5]. He died after a 23 day illness. The second case in 1990 had an unusually long incubation period when a 10 year old Vietnamese girl, who had been living continuously in Australia for 5 years after 2 years in a refugee compound in Hong Kong, died from rabies after a 21 day illness [6]. There have now been two deaths from ABLV. In late 1996, a 39 year old woman had been bitten by a yellow-bellied sheath tail bat. One month later she developed symptoms of rabies and died after a 20 day illness [7]. In 1998, a 37 year old woman developed rabies 27 months after having been bitten on the finger by a flying fox and died after a 19 day illness [8].

Risk for lyssavirus infections in Australia

The risk for exposure to rabies viruses is essentially due to exposure to potentially infected animals. Within Australia the handling of bats is the primary risk, and any live bat should be handled with great care and with thick leather gloves. Bat-handlers and veterinarians are at greatest risk but all people who live or work outdoors in areas of high bat populations should be made aware of the potential risk. The prevalence of ABL in flying-foxes is estimated to be 5% [9]. Generally, tourist populations are not at significant risk.

Dog bites in the developing world represent the main risk for Australian travellers. All travellers should be made aware of rabies as a potential risk and counselled to avoid dogs, both stray and pets, in countries where rabies is enzootic. This is particularly true for Asia and Africa. Long-term travellers and expatriates are at higher risk due to length of potential exposure. Children are at greater risk of exposure as they are more likely to be bitten by a dog, and suffer more severe bites. Studies suggest short-term travellers (two weeks) to Thailand have a risk of dog bite of about 1%, while presentations for possible rabies exposures appears more than three times higher for resident expatriates than for tourists [10,11].

Individual prevention

Prevention of rabies infections for an individual involves different strategies. Firstly, creating awareness of risk to facilitate avoidance of the animal vectors. Secondly, the use of post-exposure prophylaxis for all accidental exposures should become routine, and thirdly pre-exposure prophylaxis for those at higher risk is appropriate. This is even more important since rabies immunoglobulins, an essential part of post-exposure treatment, are often not available where the risk is highest. A traveler who has had pre-exposure vaccine, does not require the use of immunoglobulin. Booster shots alone are needed.

Within Australia, awareness of diseases transmitted by bats within at-risk communities requires a coordinated long-term public health strategy, and should include opportunistic messages from general practitioners. Bats carry a variety of other diseases including Hendra and Nipah viruses, also capable of causing fatal encephalitis. All Australian travellers to international areas of rabies transmission should be counselled to avoid dogs and other animals, and to seek early medical attention if an exposure occurs. Travellers should be aware of the principles of post-exposure prophylaxis (PEP), and have considered pre-exposure immunisation (PREP). A discussion of rabies is an important routine part of a travel health consultation (see **Fig. 1**).

Rabies vaccines

Only cell culture and purified embryonated egg vaccines should be used in humans. WHO currently recognizes the following products [1]:

- human diploid cell vaccine, HDCV (France, Germany)
- purified vero cell vaccine, PVRV (France)
- purified chick embryo cell vaccine, PCEC (France, India, Japan)

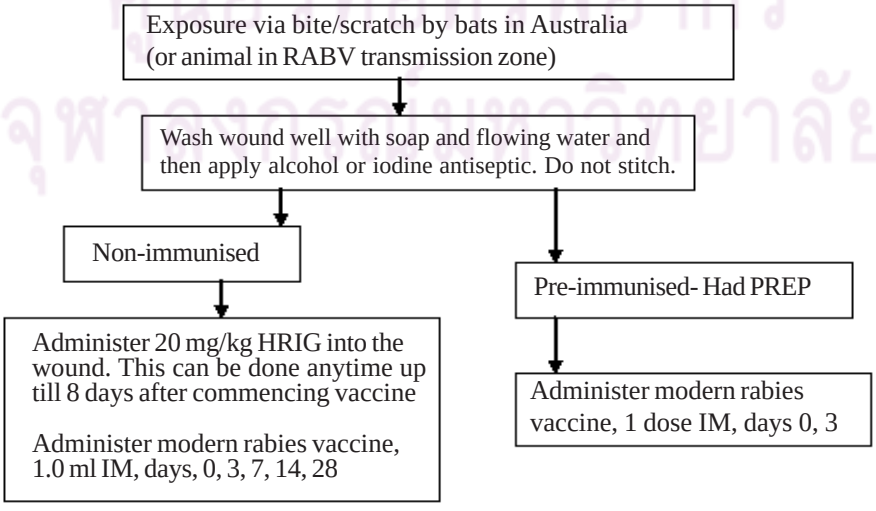

Fig. 1 Explanation chart for post-exposure requirements.

New tissue culture vaccines are now being manufactured in India, China and South America. They are undergoing evaluation for WHO recognition.

Australia had only a single rabies vaccine (HDCV, *Merieux Inactivated Rabies Vaccine*, Sanofi-Pasteur) until December 2005 when a new vaccine was introduced. Purified chick embryo vaccine, PCECV, manufactured by Chiron Vaccines, imported as *Rabipur* by CSL has now been approved in Australia. It can be considered interchangeable with HDCV [12], but it has the advantage of avoiding the 6 % hypersensitivity reactions in previously HDCV immunised individuals [13]. It can be used for PEP for exposures acquired overseas, (potential RABV infections) and ABLV exposures using the IM route.

Use of post-exposure prophylaxis (PEP)

Immediate PEP should be given to people who have sustained a bite, scratch or lick on broken skin, from an Australian bat, or potentially-rabies-transmitting animal in rabies affected areas.WHO has developed proven protocols for the correct management of rabies exposures. They focus on vigorous wound cleansing, administration of rabies immunoglobulin (RIG) into the wounds, and vaccination using modern WHO recommended intramuscular (IM) or intradermal (ID) schedules [1]. The accumulated experience with properly administered PEP in known rabies exposures indicates that this is an extremely effective treatment. In Australia, where there is adequate access to safe vaccines and to human rabies immunoglobulin (HRIG), only IM schedules are recommended. HRIG and vaccine for PEP are made available at no cost to the patient via State Public Health Units.

The IM use of tissue culture rabies vaccines in the management of ABLV is supported by animal studies but there are as yet no Australian data on the ID route for this purpose [9, 14].

Patients occasionally return to Australia with an incomplete PEP, often having had ID doses overseas. The remaining doses should be continued by using the full-dose intramuscular route. Full PEP should also be given to those treated overseas with non-WHO recognized vaccines [1, 9]. Rabies exposed patients, who had a history of prior vaccination with a nerve tissue derived vaccine, are treated as if they had never been vaccinated, including receiving RIG [15,16]. Referral to an Infectious Disease physician or experienced specialised travel medicine clinic is recommended.

While Australia continues to have an adequate supply of human derived rabies immunoglobulin (HRIG), imported as *Imogam*, by Sanofi-Pasteur, many Australians who are exposed are treated while overseas. Globally, rabies immunoglobulin is in short supply and expensive and usually not available at all in the regions that need it most. Some countries that do have RIG, only have access to the more reactogenic equine-derived ERIG. This only reinforces the importance of providing pre-exposure vaccination for tourists and residents travelling to rabies endemic regions where immunoglobulins may not be available.

Pre-exposure (PREP) vaccination

PREP is recommended for those at high risk of explosure, including people with occupational exposures. WHO approves all of the above cell and avian culture vaccines given by IM or ID route for pre-exposure vaccination as three doses at days 0, 3 and 3-4 weeks later. The IM route is recommended if the recipient is taking antimalarials or is immune compromised. In Australia, the IM route is recommended by the NHMRC, although the specialised use of ID PREP by experts is described [14].

There are no cases of rabies recorded in people who have had recommended PEP administered following fully documented boosters without immunoglobulin. It greatly simplifies post-exposure management, avoiding the need for RIG.

Rabies vaccines are considered effective and safe when used for pre-exposure prophylaxis for ABL, although no data exists to recommend the ID route for this purpose. Therefore, only IM route should be used for PREP for ABL. PREP is strongly recommended for people in Australia liable to receive bites or scratches from bats (this includes bat handlers, veterinarians, wildlife officers and others who come into direct contact with bats). In addition, it is strongly recommended for expatriates and travellers who will be spending prolonged periods (ie. more than a month) in rural parts of rabies enzootic areas. PREP is expensive, and so travelers need to be given clear information about risk in order to decide whether to obtain PREP. Long-term travelers, expatriates, children are more likely to obtain PREP.

Booster doses of vaccine

Recent evidence shows that booster injections in a previously vaccinated subject result in strong and long lasting anamnestic antibody response. Thus current recommendations are that routine boosters are not needed unless the subject is in a high risk occupation such as laboratory work with live rabies virus or handling potentially rabid animals [1, 17]. Boosters for those at very high risk, should be guided by neutralising antibody levels. Laboratory workers and selected veterinarians should be tested at 6 monthly intervals, other occupational risk groups at annual intervals. RIG is not indicated in individuals who had prior documented rabies vaccination with an approved tissue culture product.

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