**Rabies: an update for nurses in general practice**

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Published Online:4 Dec 2019 <https://doi.org/10.12968/pnur.2019.30.12.589>

Practice nurses have an important role to play in raising the profile of rabies as a travel-related hazard. **Hilary Simons, Rachael Fletcher** and **Katherine Russell** give an update for nurses working in this area of practice

Abstract

Many thousands of human deaths are attributed to rabies infection globally each year; once the symptoms of rabies occur, death is almost always inevitable. Rabies is a zoonosis—a disease of animals that can be transmitted to humans—and can occur in all warm-blooded animals. Rabies remains a neglected disease that impacts most on impoverished and disadvantaged populations living in rabies endemic regions, who may have limited or no access to good healthcare facilities and safe rabies vaccine products. Practice nurses are well placed to raise travellers' awareness of the risk of rabies at a destination, and provide guidance on pre-travel vaccination and post-exposure treatment.

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Rabies is a zoonosis—that is a disease of animals that can be transmitted to humans—and can occur in all warm-blooded animals. Transmission of rabies to humans from dogs accounts for more than 99% of human rabies deaths annually (World Health Organization, 2018a).

Rabies remains a neglected disease that impacts most on impoverished and disadvantaged populations living in rabies endemic regions, who may have limited or no access to good healthcare facilities and safe rabies vaccine products.

Effective pre-exposure rabies vaccine and post-exposure rabies treatment products are available in most high-income countries, including the UK. However, deaths from rabies in un-vaccinated travellers still occasionally occur.

Provision of travel health services can be complex and health professionals should ensure that they are working within their level of competence (Royal College of Nursing, 2018). Practice nurses are well placed to raise travellers' awareness of the risk of rabies at a destination and within a specific travel itinerary. It is important to offer clear advice about avoiding contact with animals, management of bites, scratches and mucous membrane exposures from animals, as well as guidance on pre-travel rabies vaccination and post-travel treatment in the event of a rabies-prone exposure.

Rabies

*Rabies lyssavirus* (genus *Lyssavirus*) is shed in the saliva of an infected animal. The virus is transmitted from animal to animal, or from animal to human via a wound such as a bite or scratch, or through the direct contact of mucous membranes or broken skin with infectious material (ie saliva, brain or other infected tissue). Transmission of the virus from human to human has been recorded following transplantation of tissues, corneas and organs (Srinivasan et al, 2005; Chen, 2017). The virus is neurotropic; entering a nerve and/or muscle cell at the wound site, the virus multiplies and eventually ascends to the brain resulting in encephalitis, which is almost always fatal.

Rabies occurs in over 150 countries worldwide. All mammals, including bats and wild and domesticated animals, are susceptible to and can transmit rabies infection (World Health Organization, 2018a).

Approximately 59 000 human deaths occur globally each year, with 99% of these being due to dog bites. Most human cases are reported in Asia and Africa and many of these reports are in children under 15 years (World Health Organization, 2018a). Control of dog populations, strict animal quarantine requirements, together with dog and wild animal vaccination in endemic areas, have been very successful strategies in reducing or eliminating dog-mediated rabies in many parts of the world, and thus human rabies infection. Dog vaccination programmes are key to the success of the World Health Organization target to reach zero human deaths from rabies by 2030 (World Health Organization, 2018a; 2018b).

While dog bites present the greatest risk worldwide, in some areas such as the Americas, bat rabies also accounts for a significant number of human deaths. There may also be spill over into other animal species, so any animal exposure in a rabies-endemic area should be considered a potential risk.

Countries where rabies has been eliminated in terrestrial animals (ie those that live predominantly or entirely on land), such as the UK, may still have rabies-related lyssaviruses present in their bat populations. *European Bat Lyssavirus 1* and *2* have been detected in bats in the UK and therefore all bites from bats in the UK or abroad should be risk assessed and post-exposure treatment commenced where necessary (Public Health England, 2019).

Clinical presentation and management of human rabies infection

Although human rabies may often be considered as part of the differential diagnosis in countries where canine rabies is known to exist, diagnosis may be challenging, especially where the disease is not frequently encountered (Chacko et al, 2016). Rabies has a diverse range of early symptoms and patients may present in any clinical setting; diagnosis is dependent on recognition of the clinical signs of the disease and identifying a history of contact with a possibly infected animal in a rabies endemic area (Warrell and Warrell, 2015).

After an incubation period that may be as short as 5 days or as long as several years, the first signs of rabies virus infection may be non-specific, such as malaise, sore throat, general weakness and headache. An early specific clinical sign is tingling, pricking and/or pain at or close to the site of the bite. Psychological symptoms, including anxiety or depression and insomnia, may be observed. After around 2–10 days, neurological symptoms follow (see below) with a rapidly progressing encephalitis. Rabies infection may present as one of two forms; ‘furious’ rabies, where symptoms include aggressive behaviour, twitching muscles, hallucinations and seizures. Neurological damage to areas of the brain that control swallowing may result in hypersalivation and swallowing difficulties; such is the fear of swallowing, hydrophobia may be evident if water is offered. Even the smallest stimuli, such as a draft of cool air can trigger aerophobia (fear of drafts or fresh air). The second form, ‘paralytic’ rabies, presents less frequently, with an ascending muscle weakness, loss of sensation and eventually paralysis, coma and cardiac or respiratory arrest (Rupprecht et al, 2018).

A very distressing aspect of rabies infection is that without sedation, the patient can be often lucid and aware between episodes of hyperactivity. There is currently no effective cure for rabies, therefore treatment, which includes pain relief and sedation, focuses on symptom management and palliation. Death usually occurs within 2 weeks.

Although rabies is almost always fatal, the World Health Organization acknowledges a handful of survivors (World Health Organization, 2018a). However most of these reported survivors did not achieve complete neurological recovery (de Souza and Madhusudana, 2014).

Rabies in travellers

Rabies is rare in international travellers. Carrara et al (2013) describe 60 cases reported in global travellers between 1990–2012; reasons for travel included visiting friends and relatives (23%) and tourism (13%). A significant number of cases (43%) were in migrants returning to their country of origin for the first time for a variety of reasons, including to visit friends and relatives. The majority (85%) were bitten by a dog and many (40%) were exposed to rabies during travel to Asia.

To date, 28 cases of rabies in humans have been imported in to the UK since 1902. The most recent, in 2018, was in an individual who died of rabies following a cat bite in Morocco (Public Health England, 2018a).

In England, approximately 3000 people each year need post-exposure rabies treatment following exposure to an animal (Public Health England, 2019). The majority of these exposures occurred while overseas (88%), but others were related to exposures to bats in the UK (12%) (Public Health England, 2018b).

Key contacts for the UK travel health practitioner

### Specialist advice

Urgent specialist advice for health professionals regarding post-exposure treatment:

* England—PHE Rabies and Immunisation Service, National Infection Service, Public Health England, Colindale. Tel: 0330 128 1020 (PHE Colindale duty doctor out of hours: 0208 200 4400)
* Rabies Immunoglobulin Service. Requests for stock and advice about issuing should be directed to this service (Tel: 0330 128 1020)
* Wales—Duty Virologist, University Hospital of Wales, Cardiff. Tel: 029 20 742 094 or 029 20 747 747
* Northern Ireland—Public Health Agency. Tel: 0300 5550119
* Scotland—Local on-call infectious diseases consultant

National Travel Health Network and Centre Advice Line—contact details at: <https://travelhealthpro.org.uk/contact>

Travax Helpline—for Travax subscribers. Details at: <https://www.travax.nhs.uk/about-travax>

### Vaccine companies

GSK. Rabipur. Summary of Product Characteristics.

<https://www.medicines.org.uk/EMC/medicine/14933/SPC/Rabipur/>

Sanofi Pasteur. Rabies BP. Summary of Product Characteristics.

<https://www.medicines.org.uk/emc/product/1527/smpc>

For information about Verorab, contact Sanofi Pasteur

Human rabies exposure: prevention strategies

[*Table 1*](https://www.magonlinelibrary.com/doi/full/10.12968/pnur.2019.30.12.589#T1) shows what the traveller needs to know about rabies prevention. Most human rabies deaths occur in people who have not received any pre-exposure rabies vaccination, or where post-exposure treatment has not been started promptly, especially where the rabies-prone injury is severe. With correct pre-exposure vaccination, proper wound washing and appropriate timely post-exposure treatment (with rabies vaccine and/or rabies immunoglobulin when indicated), prevention of rabies infection is usually successful. Vaccination and treatment failures are rare (Rupprecht et al, 2018; World Health Organization, 2018a), but when they occur they can usually be attributed to inadequate or delayed post-exposure treatment.

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| **Table 1. What the traveller needs to know about rabies prevention** |
| * Always carry your rabies vaccination record card
 |
| * Do not touch or feed any animals abroad
 |
| * Infected animals may act normally or be subdued or aggressive. Be cautious of all animals (including pets, domesticated animals or those in zoos or temples)
 |
| * Be vigilant if undertaking higher risk activities, eg running or cycling
 |
| * Report any bites, scratches, licks or mucous membrane exposures from an animal—wash the wound with soap and water for at least 15 minutes and seek reputable medical care
 |
| * Remind children of the dangers from animals and get them to tell you if they've been bitten, scratched or licked. Supervise young children or babies closely around animals
 |
| * Ideally get a record of vaccines given and route of administration if treated abroad
 |
| * Always contact your GP on return to the UK if you had an animal bite, scratch, lick or mucous membrane exposure whether it was treated at the time, or not. You may need further advice and a course of vaccine
 |

Rabies vaccine and human rabies immunoglobulin (HRIG) may be in short supply, or even unavailable, in some parts of the world (Jentes et al, 2013). Country specific information is not given here, but practitioners may find the resource provided by the International Society of Travel Medicine useful (see *Further reading and useful resources*).

### Pre-exposure vaccination

It may be appropriate to offer pre-exposure rabies vaccination before travel to a rabies enzootic area. The need for vaccination should be based on an individual risk assessment. Travellers considered to be at increased risk of exposure to the rabies virus include (Public Health England, 2018b):

* Those likely to be at occupational risk, for example working with animals
* Travelling to areas where post-exposure care/treatment may be limited
* Individuals likely to undertake higher risk activities, including cycling or running
* Travelling to live or stay in a rabies enzootic area for more than 1 month.

Pre-exposure vaccinations may also be appropriate within the UK for the small number of individuals who are at increased occupational risk of rabies virus exposure. Employers are responsible for assessing the risks to employees and protecting them where appropriate (Public Health England, 2018b). Vaccine recommendations for occupational risk differ from the recommendations given to travellers (Public Health England, 2018b). Patients with queries around occupational exposure should be directed to occupational health services.

Pre-exposure rabies vaccination results in ‘active’ immunity; this type of immunity usually confers protection which is long-lasting. Where a WHO-approved vaccination product and schedule are used in a healthy person, rabies vaccination is very effective and results in rabies viral-neutralizing antibody (VNA) being produced (Rupprecht et al, 2018). This antibody persists (immune memory) in the vaccine recipient and although levels may wane over time, they are rapidly and efficiently restored following booster doses of vaccine.

In the UK, the two products with marketing authorization (license) are:

* Human diploid cell vaccine (HDCV, 2.5 IU/ml) (Rabies Vaccine BP)
* Purified chick embryo cell rabies vaccine (PCEC, 2.5 IU/ml) (Rabipur).

These vaccines require cold chain storage and must be used within an hour of reconstitution.

Vaccine shortages do occur on occasion and products without UK marketing authorisation may be the only available option. Verorab, licensed for use in many countries (Toovey, 2007), is an example of a WHO-approved rabies vaccine without UK marketing authorisation that has been available in the UK at times of vaccine shortages (National Travel Health Network and Centre, 2019). Please see the *Further reading and useful resources* section of this article for more information.

Pre-exposure rabies vaccination consists of a 3-dose schedule of inactivated rabies vaccine, given intra-muscularly (IM) on days 0, 7 and 21–28. The rabies vaccine products used in the UK may be used interchangeably (Public Health England, 2018b). Intradermal (ID) administration of the rabies vaccine has been approved by the WHO (2018b) for pre-exposure vaccination. While IM injection is the preferred route of administration in the UK, the prescriber can take responsibility for giving the vaccine ‘off-label’ ID, remembering that this route is only reliable if the whole 0.1 ml is delivered properly into the dermis. ID administration of the rabies vaccine is not covered by the manufacturers' product license (Public Health England, 2018b).

In June 2018, new recommendations for an accelerated pre-exposure rabies vaccine schedule were published, providing another option for travellers who have insufficient time to complete the regular 21–28-day course. This is a 4-dose schedule, with vaccine given IM on days 0, 3 and 7 with the fourth dose at 1 year, completing the primary course (Public Health England, 2018b).

### Booster doses

After a primary course of rabies vaccine, booster doses may not be necessary for many travellers (World Health Organization, 2018a), but new guidance from Public Health England (2018b; 2018c) advises that one booster dose can be considered at any time from 1 year after a primary course, based on individual risk assessment. A booster dose pre-exposure will quickly raise antibody levels in somebody who is adequately ‘primed’. This can be beneficial for the traveller with an itinerary that takes them to remote areas, and/or where access to good medical care (including rabies vaccine) may be limited.

This booster is a one-off dose, which does not need to be repeated; having a booster dose does not change the important need for post-exposure treatment following a bite, scratch, lick or mucous membrane exposure (see post-exposure treatment). All persons who receive a pre-exposure booster dose must still carry out immediate first aid to their wound and seek reputable medical care where post-exposure treatment options should be considered.

### Post-exposure treatment

Guidelines for managing rabies post-exposure have been produced by Public Health England (2019).

Post-exposure treatment consists of thorough wound washing (with soap and water and ideally for at least 15 minutes) and administration of rabies vaccine with or without human rabies immunoglobulin (HRIG). If carried out correctly and quickly after exposure, this regimen is very effective at preventing human rabies. Other issues, such as tetanus vaccination and the need for antibiotic treatment following animal bites, should also be considered at this point.

Clinicians should determine the treatment required after considering the risk of rabies in the animal and geographical locations, along with the person's immune status and history of rabies vaccination status.

### In an adequately primed person

In an adequately primed person, ie who has received three doses of an approved rabies vaccine pre-exposure (and thus is presumed to have antibody already), and where the record of previous rabies vaccine can be seen and is authentic, post-exposure treatment usually consists of only two further doses of rabies vaccine (Public Health England, 2019). Post-exposure regimens and routes of administration may differ from country to country.

In a healthy person, post-exposure rabies vaccine is expected to very quickly raise the level of rabies antibody, reinforcing protection. Individuals who are immunocompromised may not always respond effectively to the rabies vaccination and as such post-exposure treatment recommendations differ. HRIG plus a further five doses of rabies vaccine may be advised, even if a pre-exposure rabies course has been given. Public Health England (2019) provides more specific information about managing this group of patients.

### A non-vaccinated or partially vaccinated person

A non-vaccinated or partially vaccinated person will typically need four doses of rabies vaccine and may require HRIG depending on the assessment of the exposure. HRIG contains rabies antibodies that, when infiltrated into the wound, are thought to neutralize any rabies virus present and provide ‘passive’ immunity giving time for the body to develop ‘active’ immunity as a response to the rabies antigen in the rabies vaccine doses.

It is beyond the scope of this article to provide specific information on post-exposure; UK practitioners should refer to national guidelines (Public Health England, 2019).

Conclusion

Rabies continues to cause many thousands of deaths each year in people who live in rabies-endemic regions. Although very rare, cases of rabies are occasionally reported in returning international travellers. The travel health consultation should include reference to rabies as a travel-related hazard for travellers to rabies-endemic regions. Practice nurses have an important role to play in raising awareness of rabies, advising on the option of pre-exposure vaccination and on what to do in case of a bite whether or not pre-exposure vaccination was given.

Key points

* Rabies is a viral infection that can occur in warm-blooded animals. Rabies virus is usually spread to humans through the bite or scratch from an infected animal
* Rabies is preventable if appropriate post-exposure treatment is administered in good time; this may be difficult to access at some destinations
* Rabies is almost always fatal once symptoms appear
* Travellers should be counselled, before travelling, on actions to take in the event of a possible rabies exposure
* Travellers should carry documentation of any rabies vaccines given prior to travel
* Potential rabies exposures reported on return to the UK should be assessed promptly and urgent specialist advice sought

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