

## Rabies

**Rabies occurs in warm-blooded mammals and is transmitted to humans, most often by a bite or scratch from an infected animal, usually a dog**

### Key Messages

**Rabies is a viral disease transmitted to humans usually by a bite or scratch from an infected animal (usually a dog).**

**The disease is preventable if the correct post-exposure treatment (PET) is provided quickly.**

**Accessing correct PET can be challenging in some countries.**

**Rabies cases are rare in travellers but animal bites and scratches are not, travellers should be aware of the risk and know what to do if they are bitten or scratched.**

**Rabies is almost always fatal once symptoms appear.**

**Pre-exposure rabies vaccines are recommended for some travellers.**

## Overview

Rabies is a viral zoonotic encephalitis caused by a lyssavirus infection. Rabies viruses belong to the *Mononegavirales* order of the *Rhabdoviridae* family and genus *Lyssavirus*. After exposure, the virus replicates in muscle tissue and spreads via the peripheral nervous system to the spinal cord and the brain. In the brain, the virus replicates and disseminates rapidly, via the nervous system, to many different tissues, including the salivary glands. Death occurs due to neuronal dysfunction at the molecular level [1].

Rabies is present on all continents, except Antarctica, with over 95 percent of human deaths occurring in the Asia and Africa regions [2]. Rabies occurs in warm-blooded mammals (both domestic and wild mammals including bats) and is transmitted to man, most often by a bite or scratch from an infected animal, usually a dog. Rabies can also be transmitted when body fluids from an infectious animal (usually saliva) come in to contact with mucous membranes (e.g. on the eyes, nose or mouth) or broken skin [2].

Survival is extremely rare, rabies is almost invariably fatal, but it has been documented in 15 cases, albeit with severe sequelae in most of those cases [1, 3]. In all but one case, the survivors received one or more doses of rabies vaccine before the onset of clinical rabies [3].

Rabies is preventable if the correct post-exposure treatment (PET) is provided quickly. Tragically, many people fail to access this treatment. Human rabies cases are often unreported, so it is difficult

to provide reliable figures on global incidence [3]. However, dog-mediated rabies is estimated to cause 59,000 human deaths annually [1, 3, 4]. Children are at particular risk; approximately 40 percent of all people bitten by suspected rabid animals are children under 15 year old [1, 2]. Owing to their size and stature, children are often bitten around the face or head [5]. Bites in this area are expected to have a shorter incubation period (the time between infected animal bite/scratch and rabies symptoms appearing) [6].

Rabies is not common in western travellers. The World Health Organization (WHO) describes it as a neglected tropical disease predominantly affecting poor and vulnerable populations in remote rural locations [2]. However, it has been estimated that 0.4 percent of travellers have experienced an at-risk bite per month of stay in a rabies-endemic country [7]. It is important that travellers visiting rabies endemic areas are aware of the risk and know what to do if they are bitten or scratched. PET can be expensive and difficult to obtain in some areas [8].

## **Risk areas**

Rabies exists on all continents except Antarctica [2]. Information and vaccine recommendations for individual countries can be found on our [Country Information pages](#).

The risk of human cases is highest in countries where the virus circulates in dogs [1] and in up to 99 percent of cases, dogs are responsible for transmission to humans [1, 2].

According to the World Health Organization (WHO) more than 95 percent of human cases occur in Africa and Asia [2] mainly in rural communities where measures to prevent dog to human transmission have not been implemented [3]. Cost and limited availability of PET in some countries contributes to high mortality rates [2, 3].

In Africa, WHO estimates that 21,476 human deaths occur annually due to dog-mediated rabies. In Asia, 35,172 human deaths occur every year as a result of dog-mediated rabies, with India accounting for the most deaths both in Asia, and worldwide [3].

In Latin America and the Caribbean, efforts to eliminate rabies in dogs have resulted in a significant decrease in human cases [3]. In western Europe, Canada, USA, Japan and some Latin American countries dog rabies has been eliminated. Australia and many Pacific island nations have always been free from dog-mediated rabies. Such countries may still report imported cases [3]. However, the virus still exists in terrestrial wild animals (those living predominantly on land) and rabies related lyssaviruses may occur in bats [1, 3].

Although bat rabies accounts for a relatively small proportion of human cases worldwide, it now accounts for the majority of human rabies cases in the Americas [2, 3]. Bat rabies is also an emerging public health threat in Australia and Western Europe [2]. In North America and Europe, the disease is mainly confined to wild animals (particularly bats and foxes in Europe, and in North America coyotes, skunks and racoons). Human cases in North America have usually followed exposure to an infected bat [3].

Regions such as Australia, the United Kingdom (UK) and parts of Western Europe are considered free of rabies in terrestrial animals. However, in these areas, bats may carry lyssavirus (bat rabies). Although rare, this can be transmitted to humans or other animals following contact with saliva of an infected bat, most often by a bite. The most recent case of bat lyssavirus detected in a UK bat was in October 2018 [9]. Bat lyssaviruses can cause disease in humans that is indistinguishable from rabies [10].

Most of Western Europe is rabies-free in terrestrial animals due to the success of co-ordinated wildlife oral vaccination programmes, together with the availability of effective commercial vaccination for domestic animals [11]. However, sporadic animal cases outbreaks are reported.

Rabies re-emerged in wild foxes in north-east Italy in 2008; this outbreak spread to the regions of Veneto, Trento and Bolzano resulting in over 200 cases in wild and domestic animals. Following fox vaccination campaigns the last case occurred in February 2011 and the outbreak was resolved in March 2011 [12].

In northern Greece, between October 2012 and March 2014, a total of 45 rabid animals (37 foxes, five dogs, two cattle and one cat) were reported. These were the first animal rabies cases reported in Greece since 1987. Following extensive vaccination and surveillance campaigns, no animal rabies has been detected since May 2014. Intensive surveillance and monitoring continue [13].

Incidents involving imported animals also occur. In France, a rabid dog was imported from North Africa in 2011 [14]. In May 2015, a dog was diagnosed with rabies. Investigations showed the dog had been taken to Algeria and developed rabies on return to France. Following a surveillance period during which no secondary rabies cases were detected [15]. A rabid puppy was also imported into the Netherlands from Morocco via Spain in 2012 [16].

Outside Western Europe, occasional outbreaks are reported in regions where rabies disease burden is not usually high. Countries in the Middle East are facing increasing problems due to wildlife rabies [17]. In 2018, an animal rabies outbreak involving wild and domestic animals was reported in northern Israel, with the first cases detected in October 2017 [18].

## **Risk for travellers**

Cases of rabies in travellers are rare. However, bites and scratches from potentially rabid animals occur more frequently and it is often difficult to determine whether an animal is infected [8].

In 2011, a single case of human rabies was reported in Europe. In 2012, two human cases were reported among European citizens. Between 2013-17 six further cases were reported in travellers who visited endemic countries outside Europe:

- a case reported from the Netherlands in a man following exposure to an unknown source in Haiti.
- a Spanish resident bitten by a dog in Morocco

- a French resident infected by a canine strain in Mali
- a Dutch resident bitten by a dog in India
- a case reported by France in a traveller with exposure in Pakistan
- a French child bitten by a dog in Sri Lanka [19].

A survey of 2,697 travellers receiving PET in GeoSentinel clinics following possible exposure to rabies between 1997 and 2012 found that 70 percent had been exposed while in Asia, mostly in Southeast Asia [8]. Dogs accounted for most exposures among travellers, but non-human primates (such as monkeys) were responsible for one quarter of the possible exposures. The proportion of non-human primate exposures was even higher among tourists, female travellers and travellers to Southeast Asia. Cats and bats were the next most common animal exposures reported [8].

## Rabies in UK Travellers

In Great Britain, the last case of indigenous rabies in a terrestrial animal occurred in 1922. The last recorded cases of animal rabies outside quarantine occurred in 1969 and 1970 when two imported dogs died soon after completing six months quarantine. Since then, nearly all cases of rabies in the UK have occurred in quarantined animals or in people who were infected abroad.

In the UK, no human cases of locally acquired (indigenous) rabies from animals, apart from bats, have been reported since 1902 [6]. In the UK, a human case of rabies was confirmed in a bat handler who died from indigenously acquired European Bat Lyssavirus 2 (EBLV2) in Scotland in 2002 [6, 20]. There are two types of bat lyssavirus found in the UK (EBLV-1 and EBLV-2); with EBLV-1 detected for the first time in the UK in 2018 [9].

There were 25 human deaths in the UK from imported rabies between 1902 and 2005 [21-24]. Where information was recorded, all but one of these resulted from a dog bite. Sixteen of the 25 deaths were following a bite that occurred on the Indian Sub-Continent [21].

Two further imported cases from rabies were reported in 2009 and 2012; neither were known to have received pre or post-exposure rabies treatment:

- an individual who had worked in an animal sanctuary in South Africa and died of rabies in Northern Ireland in January 2009 [25]
- an individual bitten by a dog whilst visiting South Asia in 2012 [26]

A further case was imported into the UK during 2018. This individual died of rabies following a cat bite in Morocco [27]

Each year approximately 2,000 people require post-exposure treatment through Public Health England: 12 percent of these individuals are potentially exposed to bats in the UK and 88 percent were potentially exposed to an animal overseas [6].

## Transmission

Rabies virus is found in the saliva of an infected animal. The virus is transmitted to humans by a bite or scratch, or when saliva from an infected animal comes into contact with broken skin or mucous membranes (eyes, nose, or mouth). Very rarely, rabies has been contracted following laboratory exposure to the virus [28] or after transplantation of organs from an infected individual [2, 29]. Except for transmission following organ transplant, person to person transmission has never been proven [30].

Following exposure, the virus travels to the central nervous system via the peripheral nerves. The virus replicates in the brain and disseminates to many different tissues.

## Signs and symptoms

The incubation period of rabies is usually between three and 12 weeks; in rare cases it can be as short as four days or up to 19 years [30, 31]. In more than 90 percent of patients, the onset is within one year of exposure. According to the WHO, the incubation period depends upon factors such as the amount of virus inoculated, the amount of tissue at the site of the bite or scratch, and the proximity of the bite to the central nervous system [3]. Bites to highly innervated regions such as the head, neck and hands are expected to have shorter incubation periods [6].

The early symptoms are often non-specific with fever, headache, myalgia (muscle pain), and fatigue. Paraesthesia (abnormal sensation such as burning, tingling or pricking) can occur at the site of the bite. The disease progresses either to the more common furious rabies, or the less common paralytic or 'dumb' rabies [2].

Furious rabies is characterised by laryngeal spasms, which occur in response to attempts to drink water; these can be accompanied by a feeling of terror. Deterioration, coma and death ensue over the following days.

The paralytic form of rabies is often misdiagnosed. Paraesthesia and weakness often first occur around the bite site and begin to ascend the bitten limb. The paralysis results in respiratory failure and inability to swallow. Death usually occurs within one to three weeks.

## Diagnosis and treatment

All travellers who have a possible exposure to the rabies virus, whether by bites, scratches, or other means, should seek medical advice without delay. Seeking medical care also applies to travellers in areas considered low risk for rabies as other infections may be transmitted by the bite, or the animal may have been imported or crossed the border from an endemic country. Medical advice should be sought without delay even if pre-exposure vaccine was received.

There are no tests to diagnose rabies infection in humans before the onset of symptoms [2]. However, the correct use of modern rabies vaccines, wound management and administration of

rabies immunoglobulin (RIG) soon after exposure, is effective in preventing symptoms of rabies appearing, even following high-risk exposures in nearly all cases [1].

Unfortunately, once the symptoms of rabies have appeared, the disease is almost always fatal [2]. There are no known survivors of dog rabies virus infection [31]. A few patients who have developed rabies following bat bites in the Americas have survived rabies [30, 32].

## Preventing rabies

### Avoiding animal bites

Contact with wild or domestic animals (including bats) during travel should be avoided. Travellers should be advised:

- not to approach animals
- not to attempt to pick up an unusually tame animal or one that appears to be unwell
- not to attract stray animals by offering food or by being careless with litter
- to be aware that certain activities may attract dogs (e.g. running, cycling)

### Pre-exposure vaccines

Pre-exposure vaccines are recommended for individuals considered to be at risk of exposure to rabies virus [6] (see below). A record of vaccination should be carried and shown to those administering emergency treatments in a post-exposure situation. Pre-exposure rabies vaccine reduces both the number rabies vaccine treatment doses needed after a bite, and the need for rabies immunoglobulin in most circumstances [32], which is in short supply in many countries [33].

### Action following a possible rabies exposure

All travellers should be advised to perform first aid treatment and to seek medical advice as soon as possible. Although modern rabies vaccines and rabies immunoglobulin may be available in major cities of most developing countries, availability is variable depending on geographic region [33].

The following advice can be given regarding first aid following a possible rabies exposure:

- Urgent action is required; treatment should be commenced as soon as possible after the exposure.
- Immediately flush the wound thoroughly under running water for several minutes and wash with detergent or soap.
- Apply a suitable disinfectant to the wound such as 40-70 percent alcohol or tincture/aqueous solution of povidone-iodine
- Apply a simple dressing to the wound.

- Seek immediate medical advice about the need for PET and possible antibiotics to prevent a wound infection.
- Suturing of the wound should be postponed until PET has started.
- Saliva exposure to the eyes, mouth and nose should be washed thoroughly with water [6].

Tetanus vaccine may be necessary if the traveller is not up-to-date as animal bites may be considered tetanus-prone wounds.

See also post exposure management and guidance below.

## Vaccine information

### Availability of vaccine

There are two rabies vaccines licensed for use in the UK, both of which are inactivated. Unlicensed products are occasionally available when licensed products are in short supply (please refer to manufacturer/distributor for these products).

Accessing safe and effective rabies vaccine products when traveling overseas may be difficult, and vaccine derived from animal brain tissue maybe the only type available. In some areas, modern rabies vaccines may only be obtained privately or in rabies treatment centres. Rabies immunoglobulin is frequently difficult to locate [33].

### Rabies pre-exposure vaccine

Individuals considered at risk of exposure to rabies viruses within the UK include:

- laboratory workers routinely handling rabies virus
- workers at Defra-authorized quarantine premises and carriers
- bat handlers who regularly handle bats, including on a voluntary basis, in the UK
- veterinary and technical staff who due to their employment maybe at increased rabies risk

Individuals considered at risk of exposure to rabies travelling outside the UK include:

- animal workers who regularly travel to rabies enzootic areas
- travellers to rabies enzootic areas especially if:
  - those visiting areas where access to post-exposure treatment and medical care is limited
  - those planning higher risk activities such as cycling and running
  - long-stay travellers (more than one month)
  - health workers in rabies enzootic areas who may have direct contact with rabies infected patients

See our [Country Information pages](#) to see individual recommendations for each destination.

For primary pre-exposure immunisation, which primes the immune system, three doses of rabies vaccine (2.5 IU) should be given intramuscularly on days 0, 7 and 28. The third dose can be given from day 21 if there is insufficient time before travel [6].

Alternatively, an accelerated schedule of primary pre-exposure vaccine may be given if there is insufficient time before travel to complete the 28 day course. Three doses of rabies vaccine (2.5 IU) should be given intramuscularly on days 0, 3 and 7, with an additional dose at one year if they will continue to travel to high risk areas [6].

Where there is enough time to complete the 28-day course, this is the preferred schedule for pre-exposure prophylaxis [6].

Following a full course of pre-exposure rabies vaccine, the immune system is primed and an efficient antibody response is expected following administration of post exposure treatment doses of vaccine [6, 34] (see also ‘immunosuppression’ section).

Details of licensed vaccines are found in Table 1 below:

**Table 1: Vaccine schedules**

Vaccine	Route of administration	Schedule	Pre-exposure recommendations*[6]	Age range
<a href="#">Rabies Vaccine BP</a> (Human diploid cell vaccine) (HDVC)	Intra-muscular	3 doses Day 0, 7 and 21 or 28*  <b>Rapid Regimen:</b> 3 doses Day 0, 3, 7 and a further dose at 1 year	Primary course (3 doses of vaccine) Booster dose**	***No minimum age stated in the Summary of Product Characteristics (SPC)
<a href="#">Rabipur</a> (Purified chick embryo cell vaccine) (PCECV)	Intra-muscular	3 doses Day 0, 7 and 21 or 28*  <b>Rapid Regimen:</b> 3 doses Day 0, 3, 7 and	Primary course (3 doses of vaccine) Booster dose**	***Can be given from any age



		a further dose at 1 year	
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The SPC should be consulted prior to the administration of any vaccine.

The vaccines shown in the table can be used interchangeably [6].

**\*see Rabies. Chapter 27. Immunisation against infectious disease. Tables 27.1 and 27.2**

**\*\*Booster dose depends on an individual's indication for pre-exposure prophylaxis and frequency of ongoing exposures. Those with frequent contact who may have unrecognised exposures to the virus e.g. bat handlers, a single reinforcing dose of vaccine should be given one year after the first three doses has been completed and a further booster dose given at three to five years or based on serology.**

**Laboratory staff routinely working with rabies vaccine antibody levels should be tested at six monthly intervals to determine optimal timing for booster doses. Antibody titres of at least 0.5 IU/ml are considered protective [6].**

**Multiple routine booster doses are not recommended for most travellers. However boosting with a single dose of vaccine can be considered following a risk assessment in those who have completed a primary course over one year ago and are travelling again to a high risk (enzootic) area. A complete primary course is considered to be a three dose pre-exposure immunisation course over 21-28 days or an accelerated three dose course over 7 days plus an additional dose at one year or at the first opportunity after one year.**

**\*\*\* Although the vaccine can be given at any age, the risk of animal bites may be higher once the child is independently mobile. Children are often bitten around the face or head, a type of bite considered to be a higher risk due to the expected shorter incubation period.**

In some vaccine shortage situations, the [Medicines and Healthcare products Regulatory Agency \(MHRA\)](#) and the [Department of Health and Social Care \(DHSC\)](#) allow vaccine companies to import alternative vaccine products for use. See information on [vaccine supply shortages and use of](#)

[unlicensed medicines](#). Please contact the vaccine suppliers for information.

## Intradermal route of administration

The intramuscular route is the preferred route to administer rabies vaccines. Pre-exposure rabies vaccination using the intradermal (ID) route is approved by the WHO [1]. However, this route is not licensed in the UK for rabies vaccine and it requires expert practised technique. ID immunisation is reliable only if the whole 0.1 ml dose is given properly into the dermis and should only be given by those experienced in ID technique. It is advised that suitably qualified and experienced healthcare professionals may use the off-label ID route for rabies vaccine administration, but it is the prescriber's responsibility, as it is not covered by the Product Licence [6]. It should not be used for travellers taking chloroquine for malaria prophylaxis as this drug suppresses the antibody response if the vaccine is given by the intradermal route [6].

The use of one vial to vaccinate more than one individual carries a risk of contamination and is not recommended [6].

## Interrupted or accelerated courses

Ideally, those at risk should receive pre-exposure vaccination with three doses of rabies vaccine before travel. Both the 0, 3, 7, 365 (i.e. a fourth dose at 1 year) schedule and the 0, 7 and 21 day schedule can be given using either product, where there is less than four weeks before departure [6].

A record of vaccination should be carried, as this will be useful during post-bite evaluation.

If only part of a pre-exposure vaccination course has been administered, a risk assessment should be undertaken to determine the post-exposure treatment required [34].

Due to immunologic memory, intervals longer than those routinely recommended between vaccine doses do not generally impair the immunologic response [35]. Therefore, individuals who have previously received an interrupted or incomplete course of rabies vaccine, can resume and complete, rather than restart a vaccine course [1]. Travellers should carry their vaccine records to show the health care professional managing post-exposure care.

## Contraindications

### Pre-exposure vaccines

- Confirmed anaphylactic reaction to a previous dose of rabies vaccine or any component of the vaccine [6]
- The PCEC rabies vaccine (Rabipur ®) [36] contains residues of chicken proteins (e.g. ovalbumin); alternative rabies vaccine may be considered for pre-exposure immunisation in those with severe egg allergy [1, 6].

## Post-exposure vaccines

In view of the almost invariably fatal outcome of rabies, there are no contraindications to vaccination when post-exposure treatment is indicated [1, 6, 37]. However, subjects considered to be at risk of a severe hypersensitivity reaction should receive an alternative rabies vaccine if a suitable product is available [1, 6, 37].

## Post-vaccination serology (blood test)

In England, post-vaccination serology, to determine the level of rabies neutralising antibody is not routinely recommended except for those who work with animals or in laboratories with the rabies virus, where serology can inform optimal timing for booster doses, and following exposures in immunosuppressed individuals. Most travellers are at infrequent risk of rabies exposure and do not require serological testing [6].

## Adverse events

Adverse events to rabies vaccine tend to be mild and transient and include itching, pain, and erythema (redness) at the injection site. Less commonly fever, malaise, headaches, dizziness, and urticarial (raised itchy rash) occur. Delayed hypersensitivity (allergic) reactions and neurological problems such as Guillain-Barre have been reported [36, 37].

## Post-exposure management

This includes treatment of the wound and detailed risk assessment to determine necessary post-exposure treatment with rabies vaccine and in some circumstances human rabies immunoglobulin. Necessary details of the exposure incident to be considered are:

- site and severity of the wound
- circumstances of the bite
- species, behaviour and appearance of the animal involved
- health of the animal following the bite
- vaccination status of the animal
- country the exposure occurred and origin of the animal
- vaccination status of the individual at risk

## Immunosuppression

Immunosuppressed individuals may not make a full antibody response. Re-immunisation may need to be considered following completion of immunosuppressive treatment and recovery of the immune system [6]. All immunosuppressed individuals require post-exposure treatment with five

doses of vaccine and HRIG for a significant rabies exposure (i.e. red or amber Composite Rabies Risk) [6, 34], with follow up blood tests at the time of the fourth dose of vaccine and following completion of the course if needed [34].

## Post exposure guidance

[Rabies post exposure management guidelines](#) and [information for individuals who have been bitten by a bat](#), are available from PHE. Specialist advice must be sought for all individuals requiring post-exposure rabies management, including possible bat exposures in the UK.

### Urgent specialist advice for health professionals regarding PET is available from:

**England** - PHE Rabies and Immunisation Service, National Infection Service, Public Health England, Colindale on 020 8327 6204 or 020 8200 4400. (PHE Colindale Duty Doctor out of hours: 0208 200 4400)

**Wales** - Duty Virologist, University Hospital of Wales, Cardiff: 029 20 742 094 or 029 20 747 747

**Northern Ireland** - Public Health Agency Duty Room: 0300 5550119

**Scotland** - Local on-call infectious diseases consultant:

Aberdeen Royal Infirmary - 0345 456 6000

Crosshouse Hospital, Ayrshire - 01563 521 133

Queen Elizabeth Hospital, Glasgow - 0141 201 1100

Monklands Hospital, Lanarkshire - 01236 748 748

Ninewells Hospital, Dundee - 01382 680 111

Victoria Hospital, Fife - 01582 643 355

Western General Hospital, Edinburgh - 0131 537 1000

## Resources

- [Public Health England: Rabies risk assessment, post exposure treatment and management](#)
- [Public Health England: Administration of rabies vaccine and immunoglobulin](#)
- [Novartis. Rabipur. Summary of Product Characteristics](#)
- [Sanofi Pasteur. Rabies BP. Summary of Product Characteristics](#)
- [Vaccine Update: #BeRabiesAware. August 2018](#)
- [World Health Organization: Rabies](#)

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Published Date: 25 Mar 2019

Updated Date: 25 Mar 2019