

## #Be Rabies Aware

Rabies is an acute viral infection that is almost always fatal once symptoms develop. It is the leading cause of death out of all diseases spread from animals to humans (zoonoses) and more than 59,000 people die each year from rabies worldwide, with 95% of these deaths occurring in Africa and Asia.

All warm blooded animals, such as dogs, cats, monkeys, bats and other wildlife, can develop rabies. It is spread through the saliva of an infected animal, with dog bites being the cause of more than 99% of human rabies deaths globally.

It is important that travellers are aware of the potential rabies risks from animals to ensure they don't put themselves at risk while abroad. By avoiding touching or feeding animals; this may reduce the risk that they are bitten, scratched or licked by an animal that is carrying rabies.



Rabid animals may not always show signs of disease. If someone has been bitten, scratched or licked by an animal overseas, they should seek local medical attention whilst abroad and then contact their doctor on returning home to ensure they complete any necessary post-exposure treatment.

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In the UK, European Bat Lyssavirus 2 (EBLV-2), a virus related to the 'classical' rabies virus, has been detected in one species of bats and infection with EBLV-2 can lead to clinical rabies infection in humans. Anyone who is bitten or scratched by a bat in the UK should receive a risk assessment to inform a decision on the need for post-exposure treatment.

Approximately 2000 people each year require post-exposure treatment in England, of which 12% were potentially exposed to bats in the UK and 88% exposed to an animal overseas. Following a review by the Joint Committee on Vaccination and Immunisation (JCVI) in February 2018, the guidance for rabies post-exposure treatment (PET) and pre-exposure prophylaxis in the UK has been updated. This special edition of Vaccine Update will describe how to manage animal bites abroad or bat bites in the UK, as well as important information about immunosuppressed patients and pre-exposure prophylaxis.



## Changes to rabies pre-exposure prophylaxis

Rabies pre-exposure prophylaxis with rabies vaccine continues to be a course of three doses of rabies vaccine (2.5 IU; one vial) given intramuscularly on days 0, 7 and 21-28. Following review by JCVI, an accelerated schedule is an alternative option if there is insufficient time before travel to complete the 21-28 day course.

Pre-exposure prophylaxis reduces the need for rabies immunoglobulin and the number of rabies vaccines given if bitten by a potentially rabid animal. People who have received a primary pre-exposure course (including at least three documented doses) and then had an animal bite (or other animal exposure) would be managed as fully immune for the purposes of post-exposure treatment.

### Who should get rabies pre-exposure prophylaxis?

Certain jobs or leisure activities may increase people's risk of exposure to rabies virus. In these cases, a health professional should carry out an individual risk assessment to decide if the person should be offered pre-exposure rabies immunisation. The groups that should be considered for rabies pre-exposure prophylaxis can be found in the Green Book ([weblink 1](#)).

**Table 1. Current pre-exposure prophylaxis recommendations in England**

Risk group	Primary course	Boosters	Additional comments
Laboratory workers, working with rabies virus	Days 0, 7, 21-28 (intramuscular)	At one year after primary course, then subsequently based on antibody results	Vaccine and antibody test via occupational health or private provider
Bat handlers*	Days 0, 7, 21-28 (intramuscular)	At one year after primary course and then EITHER: every 3-5 years OR based on antibody results	Antibody tests are all non-NHS services and must be done by a private provider
Animal handler	Days 0, 7, 21-28 (intramuscular)	At one year after primary course and then EITHER: every 3-5 years OR based on antibody results	Vaccine and antibody test via occupational health or private provider
Travellers	Days 0, 7, 21-28 ** (intramuscular) OR Days 0, 3, 7, 365 (intramuscular) OR Days 0, 7, 21-28 (intradermal; off-label)	Single booster opportunistically at any time from one year after post primary course if needed***	Private provider

\* PHE provides vaccine for those who regularly handle bats in the UK only when no formal employer can be identified. Where the bat-handling is performed as part of employment duties it is the employer's responsibility to provide vaccine.

\*\* This is the preferred schedule for travellers receiving pre-exposure prophylaxis, where there is sufficient time to complete the 21-28 day course.

\*\*\* The need for boosters will depend on the activities being undertaken by the traveller, the rabies risk in the country being visited and the ability to access post-exposure medical care and rabies biologics. A booster may also be considered for those travellers with primary vaccination more than five years previously.

## Who is responsible for providing rabies pre-exposure prophylaxis?

Public Health England (PHE) does not supply pre-exposure rabies immunisation for travellers. This should be sourced through travel clinics or private prescription.

Legally, employers have a responsibility to assess the risks for exposure to hazardous agents, including rabies virus, and to protect employees from those risks as far as is reasonably practicable. This includes the provision of pre-exposure rabies immunisation if indicated. In England, rabies vaccine for pre-exposure immunisation will only be provided by PHE for bat handlers where no formal employer can be identified. Where the bat-handling is performed as part of employment duties, it is the employer's responsibility to provide rabies vaccine for that individual.



## Can pre-exposure vaccine be given via the intradermal route?

The Green Book states that suitably qualified and experienced healthcare professionals may give the vaccine via the intradermal route for pre-exposure prophylaxis. This 'off label' use of the intradermal route is at the prescriber's own responsibility as this is not covered by the manufacturer's Product Licence. For pre-exposure intradermal immunisation, 0.1 ml (0.25 IU) of the vaccine may be used according to the routine schedule (days 0, 7, 21-28).

Although approved by the World Health Organization, a two-site two-dose intradermal vaccine course has not been recommended for use in the UK by the JCVI. PHE does not advise switching between IM and ID course for pre-exposure prophylaxis.

## What is the difference between the routine primary pre-exposure course and the accelerated course?

Where there is sufficient time to complete the 21-28 day course, this is the preferred schedule for those receiving pre-exposure prophylaxis.

The accelerated primary pre-exposure course is an alternative schedule that can be considered in certain circumstances where there may not be sufficient time before travel to complete the 21-28 days course. It involves a total of four doses of rabies vaccine (2.5IU; one vial) given intramuscularly. The first three doses are given over a one week period and the final dose is given one year later (days 0, 3, 7 and 365).

## Why is an additional dose required at one year to complete the primary accelerated course?

The fourth dose at one year (day 365) is not a booster dose, but is considered part of the accelerated schedule to complete the primary course. The rationale behind this fourth dose at one year is to ensure the person is fully primed for a longer period of time, and can therefore make a prompt antibody response if needed. With the accelerated course antibody responses may wane more rapidly than someone given the standard 21-28 day pre-exposure schedule.



If the individual only receives the first three out of the four doses in the accelerated schedule, they would be considered 'fully immune' for the purposes of post-exposure treatment. However without the final (day 365) dose the individual may not be completely primed and the post-exposure treatment would need to be given promptly. If the patient misses the fourth dose (day 365) in the accelerated schedule, this should be given at the next opportunity. A booster can then be given any time from one year after the day 365 dose.

## What are the new recommendations for booster doses in travellers?

A primary course of rabies pre-exposure prophylaxis in immunocompetent individuals (given according to an approved schedule) has been shown to be effective in providing long term priming and immunity for rabies (when combined with a post-exposure treatment course following an exposure). Many travellers may not require a booster dose of vaccine following their primary course. The need for boosters will depend on the activities being undertaken by the traveller, the rabies risk in the country being visited and the ability to access post-exposure medical care and rabies biologics. An individual risk assessment should be undertaken to understand these factors and decide on the need for a booster dose.

The purpose of the booster is to ensure the individual is fully primed for a longer period of time to allow sufficient time to access post-exposure medical care in remote areas. Although booster doses can be given at any time from one year after the primary pre-exposure course and can be offered on an opportunistic basis rather than at a defined time point, the booster may be most effective if offered five years or more after the primary pre-exposure course. If a booster dose is given to travellers, only one booster is needed in the patient's lifetime.



Further information for travellers on preventing rabies is available from the National Travel Health Network and Centre (NaTHNaC) at [weblink 5](#).



## Rabies risk from animal bites abroad

Rabies is spread from any warm-blooded infected animals or bats to people through bites, scratches or exposure to infected saliva through broken skin or mucous membranes. Although there is no cure for rabies once symptoms develop, post-exposure treatment (i.e. rabies vaccine with or without rabies immunoglobulin) is highly effective in preventing disease if given correctly and promptly after exposure.

If a patient presents with a bite, scratch or lick from an animal or bat abroad, a risk assessment is important to decide what PET should be offered to the patient. Public Health England's Rabies and Immunoglobulin Service (RIgS) can carry out this risk assessment with the health professional managing the patient. To simplify and speed up this process, health professionals are asked to gather as much of the following information as possible before contacting RIgS:

- patient name, date of birth, age, address, and NHS number
- date of exposure
- species of the animal involved and, if feasible, it's current health status
- country the exposure occurred in
- specific details of the bite or other exposure
- site (on body) of the exposure
- whether the patient is immunosuppressed
- whether the patient has any allergies
- any rabies vaccinations or rabies immunoglobulin treatment given following the bite or in the past
- weight of the patient (in case rabies immunoglobulin is being considered)

The risk assessment will take into account the rabies risks associated with the country and type of animal involved, along with a categorisation of the exposure to calculate a Composite Rabies Risk (red/amber/green). The PET that patient needs will be based on this Composite Rabies Risk and whether the patient has had rabies vaccine in the past. Further information on the revised rabies risk assessment process can be found in the Rabies Green Book chapter at [weblink 1](#) and in PHE's rabies post-exposure treatment management guidelines at [weblink 2](#).

In the past, unimmunised patients who were bitten by an animal in a high risk country would usually receive a course of five rabies vaccines with or without rabies immunoglobulin. The new evidence-based recommendations are that these patients require four doses of rabies vaccine given on days 0, 3, 7 and 21. The need for immunoglobulin will depend on the specific details of the patient's risk assessment. This change is based on strong international evidence showing that four doses of vaccine are sufficient for immunocompetent patients to make a protective antibody response to rabies virus.

To facilitate prompt PET for patients, local NHS services are encouraged to provide access to a small number of doses of rabies vaccine to initiate a course. Any vaccine held locally that is used for PET will be replaced free of charge if the RIgS team are contacted on the next working day.

## Administration of rabies immunoglobulin

Rabies vaccine is the mainstay of rabies post-exposure treatment, but human rabies immunoglobulin (HRIG) may be advised as part of the post-exposure treatment (PET) for higher risk wounds. HRIG contains rabies antibodies that have been obtained from the plasma of immunised and screened human donors from outside the UK. It is used to provide short term passive immunity by neutralising the rabies virus at the wound site until the rabies vaccine becomes effective.

The rabies antibody level produced by vaccination is much greater than that provided by HRIG, so while there is benefit in HRIG administration as part of the initial management of certain exposures, it is not indicated more than seven days after the first dose of rabies vaccine or if the patient has already received two doses of vaccine.

To be effective, HRIG must be infiltrated into and around the wound rather than being given as an intramuscular injection. The benefit of intramuscular administration away from the site of the bite or laceration is likely to be negligible. Rabies vaccine and HRIG should not be given at the same anatomical site.

The maximum recommended dose of HRIG is 20 IU/kg (all ages), so knowing the patient's weight is important. Giving too much HRIG may interfere with the ability to mount an antibody response to the vaccine.

HRIG is different from other immunoglobulins that you might have administered before, as a specific volume should be administered and not necessarily the full contents of all vials provided. When HRIG is issued from PHE for your patient, the volume that should be administered will be calculated for you and included in the risk assessment paperwork. The quantity of HRIG noted on the packaging is the minimum content of the vial, and shouldn't be used for calculating the dose required for your patient. Any residual HRIG should be discarded.

Further information on the administration of rabies vaccine and HRIG at [weblink 4](#).



**Dog bite on hand and legs**

## How to manage a patient with a bat bite

During the summer months, bat activity increases, and particularly in hot dry weather, the bats may get exhausted or dehydrated, be found on the ground and then picked up by people. Although the UK has been free of rabies in terrestrial animals since 1922, European Bat Lyssavirus-2 (EBLV-2) has been found in bats across the UK. EBLV-2 is a virus related to the 'classical' rabies virus and infection with EBLV-2 can lead to clinical rabies infection in humans.

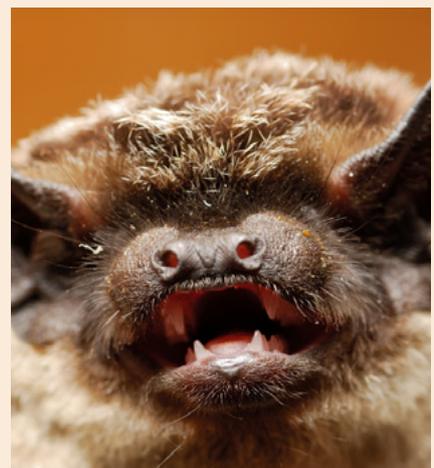
Bat bites can occur if someone picks up a bat without wearing appropriate protective gloves, so never pick up a bat with bare hands. Bat bites in the UK are felt rather than seen and rarely if ever draw blood.

In the rare event that a patient presents following contact with a bat, it's important to carry out a prompt risk assessment and initiate rabies post-exposure treatment, typically a course of rabies vaccine over 21 days.

RIgS are available to provide specialist advice and support for the management of bat bites, and can be contacted on 0208 327 6204. Before contacting RIgS, find out details of the exposure, whether the patient is immunosuppressed or has any allergies, and if they have had any previous rabies vaccination. Any vaccine administered by a GP surgery or hospital as part of a post-exposure treatment course will be replaced free of charge by RIgS if they are contacted on the next working day.

People who regularly handle bats in their job or voluntary work should have received pre-exposure vaccination against rabies, but they also require prompt post-exposure treatment following an exposure and therefore should be managed in the same way.

**Guidance on completing a risk assessment and post-exposure treatment can be found at the PHE rabies webpage ([weblink 2](#)).**



## Immunosuppressed patients and rabies prevention

Patients who are severely immunosuppressed may not always respond effectively to rabies vaccination and therefore face an increased risk of developing clinical rabies following an exposure to a rabid animal. PHE's new guidance now outlines the new way in which this small number of patients will be managed to increase the chance that they can mount a good immune response to rabies post-exposure treatment.

Severely immunosuppressed patients are considered to be those fulfilling the criteria in chapter 6 of the Green Book as the conditions where the individual should not receive live vaccines. A full list of the severely immunosuppressed groups is included in Annex 1 of PHE Guidelines on managing rabies post-exposure. This classification does not include patients who are diabetic, those who take inhaled steroids for asthma, or HIV positive patients with an undetectable viral load and CD4 count more than 200.

Severely immunosuppressed patients who have a significant exposure (i.e. amber or red Composite Rabies Risk) will be offered a longer course of post-exposure rabies immunisation and rabies immunoglobulin (HRIG) following a significant exposure, regardless of any previous rabies vaccinations. The post-exposure treatment course consists of five doses of rabies vaccine given at day 0, 3, 7, 14 and 28. This is similar to the old post-exposure schedule used in the UK. Even if the immunosuppressed patient has received a full course of rabies pre-exposure prophylaxis, they will still be given five doses of vaccine and HRIG following an exposure.

Antibody tests are also recommended to confirm response to the post-exposure treatment, for example at the same time as the fourth dose (i.e. day 14) and following completion of the course if needed. RIgS will be able to provide further details on the antibody tests required if the risk assessment indicates your patient falls into this category.

Where severely immunosuppressed individuals are involved in, or planning to start, activities that may increase their risk of exposure to the rabies virus, they should be counselled about the risks and that there is a chance that they may not respond effectively to rabies post-exposure immunisation. This is particularly important for bat handlers in the UK, but may be relevant for anyone whose jobs or leisure activities may bring them into regular contact with animals at risk of rabies infection.

## Rabies and Immunoglobulin Service (RIgS)

The RIgS team is based in PHE's National Infection Service at Colindale and are available to assist health professionals with enquiries and rabies post-exposure risk assessments.

See [weblink 3](#) for contact details of your local health protection team who may also be able to help with rabies post-exposure risk assessments.

Contact details for the provision of specialist advice on the assessment of the risk and appropriate management of potential rabies exposures in Northern Ireland, Scotland and Wales can be found in the Green Book ([weblink 1](#)).

## RlgS contact details (for healthcare professionals only):

**Hours:** Monday-Friday 09:00-17:00

**Telephone:** 020 8327 6204

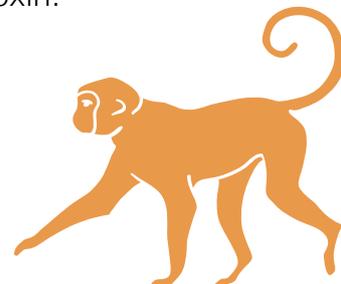
**Email:** [rigs@phe.gov.uk](mailto:rigs@phe.gov.uk) (for NON-urgent enquiries only)

### Out of hours (OOH) Mon-Friday outside of the core hours:

- rabies post-exposure treatment (PET) is considered urgent but not a medical emergency. PET will not usually be issued in the evenings or at night
- exceptions are severe bites or lacerations to the head and neck in an untreated patient
- a PHE on-call consultant is available for emergencies and assistance with the risk assessment during the OOH period
- most risk assessments and dispatch of post-exposure treatment can be performed the next working day
- at weekends and bank holidays, vaccine and immunoglobulin will be issued for pick up at a single timed slot only

### Other services within the RlgS team

In addition to providing risk assessments for post exposure to rabies, the RlgS, does the same for vulnerable patients exposed to chickenpox, shingles, measles, hepatitis A and hepatitis B and provide immunoglobulin if indicated. We also issue botulinum and diphtheria antitoxin.



### Web links

weblink 1	<a href="https://www.gov.uk/government/publications/rabies-the-green-book-chapter-27">https://www.gov.uk/government/publications/rabies-the-green-book-chapter-27</a>
weblink 2	<a href="https://www.gov.uk/government/publications/rabies-post-exposure-prophylaxis-management-guidelines">https://www.gov.uk/government/publications/rabies-post-exposure-prophylaxis-management-guidelines</a>
weblink 3	<a href="https://www.gov.uk/health-protection-team">https://www.gov.uk/health-protection-team</a>
weblink 4	<a href="https://www.gov.uk/government/publications/rabies-administration-of-vaccine-and-immunoglobulin">https://www.gov.uk/government/publications/rabies-administration-of-vaccine-and-immunoglobulin</a>
weblink 5	<a href="https://travelhealthpro.org.uk/">https://travelhealthpro.org.uk/</a>