27

Rabies

NOTIFIABLE

The disease

Rabies is an acute viral encephalomyelitis caused by members of the lyssavirus genus. The disease may be caused by rabies virus genotype 1 (classical rabies) or less commonly by rabies-related lyssaviruses. The presentations are clinically indistinguishable. Rabies-related lyssaviruses implicated in human disease include European bat lyssaviruses (EBLVs) and Australian bat lyssavirus (ABLV).

Infection is usually via the bite or scratch of a rabid animal, most frequently a dog. In some parts of the world, other animals are important sources of exposure. In parts of Europe (including the UK) EBLV-1 and EBLV-2 are found in insectivorous bats and have occasionally caused human disease.

On rare occasions, transmission of the virus has occurred through body fluids from an infectious animal coming into contact with an individual's mucous membranes. Exposure through mucous membranes has a low probability of infection but must be managed as a significant event. Infection does not occur through intact skin. Virus is present in some tissues and fluids of humans with rabies, but person-to-person spread of the disease has not been documented other than in exceptional circumstances. Cases have occurred rarely outside the UK through corneal grafts and other transplanted tissues taken from individuals with rabies.

The incubation period is generally between three and 12 weeks, but may range from four days to 19 years. In more than 93% of patients, the onset is within one year of exposure. The onset of illness is insidious. Early symptoms may include paraesthesiae around the site of the wound, fever, headache and malaise. The disease may then present with hydrophobia, hallucinations and maniacal behaviour progressing to paralysis and coma, or as an ascending flaccid paralysis and sensory disturbance. Rabies is almost always fatal, death resulting from respiratory paralysis. There is no specific treatment other than supportive care once clinical symptoms develop.

History and epidemiology of the disease

Rabies in animals occurs in all continents except Antarctica, although individual countries and islands are reported to be rabies-free. In the US, classical rabies virus in animals has become more prevalent since the 1950s; skunks, raccoons and bats account for 85% of animal cases. In Asia, Africa, Central and South America, classical rabies virus (genotype 1) is endemic in feral dogs and is also present in domestic dogs. In Mexico and Central and South America, vampire bats carry the classical rabies virus. Most countries that are declared rabies-free probably have rabies-related viruses in their bat populations. In the UK, EBLV 2 has been detected in Daubenton's bats, but not in the most common bat species in the UK, the pipistrelle (HMG, 2017). In other parts of Europe and in Australia, other bat species have been affected.

During the twentieth century, rabies in wildlife spread through parts of Central and Western Europe. Foxes have been the main host, but many other animals have also been infected, particularly dogs. The incidence of endemic, fox-adapted rabies in Western Europe fell dramatically in the last years of the twentieth century. This has been largely due to the immunisation of wild and domestic animals. Rabies continues to be reported in domestic animals imported from rabies endemic countries. Rabies remains prevalent in certain countries in Eastern Europe.

Worldwide an estimated 59,000 people die of rabies each year, with the majority of deaths occurring in Asia (59.6%) and Africa (36.4%) (WHO, 2018a). In the UK, deaths from classical rabies continue to occur in people infected abroad. Such instances are, however, rare, with 25 deaths having been reported since 1946, five of which have occurred since 2000 and the most recent was in 2012. None had received appropriate post-exposure treatment. An estimated 20 million people receive post-exposure treatment across the world each year (WHO, 2018a). Approximately 2000 people each year require post-exposure treatment in England, of which 12% were potentially exposed to bats in the UK and 88% were potentially exposed to an animal overseas (PHE data, 2018).

No case of indigenous human rabies from animals other than bats has been reported in the UK since 1902. In 2002, a man died from rabies caused by EBLV-2 acquired in the UK from a bat (Fooks *et al*., 2003). Only three other human cases of EBLV infection (all fatal) have been reported in the past 30 years in Europe (Nathwani *et al*., 2003).

The rabies immunisation

There are currently two rabies vaccines licensed for intramuscular use in the UK:

- human diploid cell vaccine (HDCV, 2.5 IU/ml) (Rabies Vaccine BP)
- purified chick embryo cell rabies vaccine (PCEC, 2.5 IU/ml) (Rabipur®)

Other WHO approved cell culture-derived vaccines are available in other countries and may contain different concentrations of rabies antigen. The UK licensed products contain 2.5IU rabies antigen in a 1ml dose; other products should be used as recommended by the manufacturer.

The vaccines available in the UK are thiomersal-free. The vaccines are inactivated, do not contain live organisms and cannot cause the disease against which they protect.

HDCV is a freeze-dried suspension of Wistar rabies virus strain PM/WI 38 1503-3M cultured in human diploid cells and inactivated by betapropiolactone. The potency of the reconstituted vaccine is not less than 2.5 IU per 1.0ml dose. It contains traces of neomycin, and human albumin is used as an excipient.

The PCEC rabies vaccine is a freeze-dried suspension of the Flury LEP-25 rabies virus strain cultured in chick embryo cells and inactivated with betapropiolactone. The potency of the reconstituted vaccine is not less than 2.5 IU per 1.0ml dose. It contains traces of amphotericin B, chlortetracycline and neomycin.

The cell-culture derived rabies vaccines may be used interchangeably to provide protection pre- or post- exposure (Cabasso *et al*., 1974; Turner *et al*., 1982; Fekadu *et al*., 1988;

Briggs *et al*., 1992; Strady *et al*., 1998; Strady *et al*., 2000). Intramuscular immunisation with tissue- culture vaccines reliably produces rabies virus neutralising titres in approximately 95% of recipients (Nicholson *et al*., 1987; Fishbein *et al*., 1989; Strady *et al*., 1998). In 95% of individuals, rabies titres are long-lived, particularly if the vaccine has been administered intramuscularly compared with intradermal immunisation (Fishbein *et al*., 1989; Briggs *et al*., 1992; Strady *et al*., 1998; Suwansrinon *et al*., 2006). Immunologically competent persons who have received a primary course of rabies vaccine have a primed immune response, and will respond promptly once they receive a booster dose of vaccine (Rosanoff *et al*., 1979; Turner *et al*., 1982; Fishbein *et al*., 1986; Naraporn *et al*., 1999).

Storage

See chapter 3. https://www.gov.uk/government/publications/storage-distribution-and-disposal-of-vaccines-the-green-book-chapter-3

Presentation

Rabies vaccine BP

The vaccine is supplied as freeze-dried powder and solvent for suspension and for injection. The powder is pinkish beige to orangey yellow. The solvent is a clear, colourless solution. Following reconstitution with the solvent supplied, the suspension will be a pinkish colour and free from particles.

Rabipur

The vaccine is supplied as freeze-dried powder and solvent for suspension and for injection. The powder is white. The solvent is a clear, colourless solution. Following reconstitution with the solvent supplied, the suspension will be a clear-colourless solution and free from particles.

Both vaccines should be used immediately and no later than one hour after reconstitution with the solvent supplied.

Dosage, schedule and administration

For primary pre-exposure immunisation, three doses of rabies vaccine (2.5 IU; one vial) 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.

Alternatively, an accelerated course of primary pre-exposure immunisation may be given if there is insufficient time before travel to complete the 21-28 day course. Three doses of rabies vaccine (2.5IU) 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 (enzootic) areas. Where there is sufficient time to complete the 21-28 day course, this is the preferred schedule for those receiving pre-exposure prophylaxis.

For post-exposure treatment schedules, see Tables 27.3 – 27.5, as the doses required will depend on a risk assessment and the calculation of a Composite Rabies Risk (CRR).

Administration

Vaccines are routinely given intramuscularly into the upper arm or anterolateral thigh (Zuckerman, 2000). However, for individuals with a bleeding disorder, vaccines should be given by deep subcutaneous injection to reduce the risk of bleeding.

The Joint Committee on Vaccination and Immunisation recommends the intramuscular rather than the intradermal route for pre-exposure prophylaxis use of rabies vaccine. The committee also recommends that only the intramuscular route (or deep subcutaneous route for those with bleeding disorders) is used for post-exposure treatment.

Whilst the intramuscular route is preferred, 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 on 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 can be used according to the schedule above. 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 Joint Committee on Vaccination and Immunisation. Intradermal immunisation is reliable only if the whole of the 0.1 ml dose is given properly into the dermis and should only be given by those experienced in the intradermal technique. It should not be used in those taking chloroquine for malaria prophylaxis as this drug suppresses the antibody response if the vaccine is given by the intradermal route (chloroquine does not suppress the antibody response if the vaccine is given by the intramuscular route). Whilst the use of the intradermal route potentially allows the contents of a vial of rabies vaccine to be shared amongst more than one individual, this practice is not recommended and carries the risks of contamination (see chapter 4).

Rabies vaccines can be given at the same time as other vaccines, including other travel vaccines. The vaccines should be given at separate sites, preferably in different limbs. If given in the same limb, they should be given at least 2.5cm apart (American Academy of Pediatrics, 2006). The site at which each vaccine was given should be noted in the individual's records. The vaccinee must keep a record of the vaccine and regimen received as it will influence future post-exposure treatment (see table 27.5).

Disposal

See chapter 3. https://www.gov.uk/government/publications/storage-distribution-and-disposal-of-vaccines-the-green-book-chapter-3

Rabies-specific immunoglobulin

Human rabies immunoglobulin (HRIG) is obtained from the plasma of immunised and screened human donors. Because of a theoretical risk of transmission of vCJD from plasma products, HRIG used in the UK is prepared from plasma sourced from outside the UK. All donors are screened for HIV and hepatitis B and C, and all plasma pools are tested for the presence of nucleic acid from these viruses. A solvent detergent inactivation step for envelope viruses is included in the intramuscular/sub-cutaneous products.

HRIG is used after high risk exposure to rabies to give rapid protection by neutralising the rabies virus at the wound site until rabies vaccine, which should be given at a separate site at the same time, becomes effective.

Storage

Human rabies immunoglobulin (HRIG) should be stored in a refrigerator between +2°C and +8°C. This product is tolerant to ambient temperatures for up to one week, and can be distributed in sturdy packaging outside the cold chain if needed.

Administration

When indicated for post-exposure treatment (see Table 27.5), HRIG at a dose of 20 IU/kg body weight should be infiltrated in and around the cleansed wound. HRIG is of greatest value when infiltrated at the wound site as it neutralises rabies virus at the wound site before the immune system can respond to the vaccine by producing antibodies. Where HRIG is recommended, every effort should be made to administer HRIG at the wound site rather than intramuscularly, as the benefit of intramuscular administration away from the site of the wound is likely to be negligible (WHO, 2018b).

HRIG dosage must be calculated using the weight of the patient and potency of the HRIG batch. The quantity of HRIG on the packaging is the minimum content of the vial, and must NOT be used for calculating the dose.

If infiltration of the whole volume is not possible, any remaining HRIG should be given intramuscularly in the anterolateral thigh, remote from the immunisation site although the additional benefit is likely to be limited. If more than 2 ml is to be given intramuscularly to children, or more than 5 ml to adults, the HRIG should be divided into smaller amounts and given into different sites.

If vaccine is given but HRIG treatment is delayed, HRIG can still be given up to seven days after starting the course of vaccine. HRIG is no longer required once an active antibody response to the rabies vaccine has started to develop. Therefore, HRIG is not indicated more than seven days after the first dose of vaccine, or more than one day after the second dose of vaccine.

Equine immunoglobulin (eRIG) or monoclonal antibody (mAb) products may have been given as part of rabies post-exposure treatment in other countries where access to HRIG is limited. If eRIG or mAb have been administered overseas, HRIG is not required.

Disposal

HRIG is for single use and any unused solution should be disposed - see chapter 3.

Recommendations for the use of the vaccine

Pre-exposure (prophylactic) immunisation and reinforcing immunisations

To determine the need for pre-exposure immunisation, an individual risk assessment of potential exposures should be carried out. Individuals considered to be at risk of exposure to rabies virus are listed in Table 27.1 and Table 27.2 and should be offered pre-exposure rabies immunisation according to the schedule above.

The requirement for booster doses is dependent on an individual's indication for preexposure prophylaxis and the likely frequency of ongoing exposures. In those who may have frequent unrecognised exposures to the virus, e.g. bat handlers, a single reinforcing dose of vaccine should be given one year after the primary course has been completed. Further booster doses should then be given every three to five years or based on serology. Laboratory staff routinely working with the rabies virus should have their vaccine antibody tested at six monthly intervals to determine optimal timing for booster doses. Antibody titres of at least 0.5 IU/ml are considered protective (WHO, 2018b).

Table 27.1 Pre-exposure (prophylactic) immunisation for those within the UK

- laboratory staff routinely working with rabies virus
- workers at Defra-authorised quarantine premises and carriers
- those who regularly handle bats, including on a voluntary basis, in the UK
- veterinary and technical staff who, by reason of their employment, encounter enhanced risk

Table 27.2. Pre-exposure (prophylactic) immunisation for those travelling outside the UK

- animal control and wildlife workers, veterinary staff or zoologists who regularly work in rabies enzootic areas
- travellers to rabies enzootic areas, especially if:
  - post-exposure medical care and rabies biologics at the destination are lacking or in short supply
  - or they are undertaking higher risk activities such as cycling or running
  - or they are living or staying for more than one month

Routine booster doses are not recommended for most travellers. A single booster 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 pre-exposure primary course is considered to be three doses over 21-28 days or an accelerated three dose course (over 7 days) plus an additional dose of vaccine at one year.

Further information on country-specific rabies travel risk is available from the National Travel Health Network and Centre (http://travelhealthpro.org.uk) and, in Scotland, from Health Protection Scotland (www.hps.scot.nhs.uk), Travax (www.travax.nhs.uk – health professionals only, login required) or FitForTravel (www.fitfortravel.nhs.uk). All travellers to enzootic areas should also be informed by their medical advisers of the practical steps to be taken if they are bitten by an animal or have some other types of exposure that puts them at risk of rabies (e.g. when saliva from an infected animal comes into contact with broken skin or mucous membranes such as the eyes, nose, or mouth).

Post-exposure management

Post-exposure management normally consists of wound treatment and risk assessment for appropriate post-exposure treatment. Treatment and immunisation after a possible rabies exposure will depend on the circumstances of the exposure, including the nature of the exposure, the species involved, the country/area and the immune status of the exposed person.

Detailed guidance on risk assessment and management of potential rabies exposure can be found on the Public Health England and Health Protection Scotland websites.

https://www.gov.uk/government/publications/rabies-post-exposure-prophylaxis-management-guidelines

http://www.hps.scot.nhs.uk/giz/resourcedetail.aspx?id=934

Wound treatment

As soon as possible after the incident, the wound should be cleaned by thorough flushing under a running tap for several minutes and washing with soap or detergent and water. A suitable disinfectant should be applied and the wound covered with a simple dressing. Suitable disinfectants include 40 to 70% alcohol, tincture or aqueous solution of povidone-iodine.

Salivary exposures to mucous membranes such as eyes, nose or mouth should be washed thoroughly with clean water as soon as possible.

Primary suture could cause further damage to the wound and may increase the risk of introduction of rabies virus to the nerves. It should be avoided or postponed until post-exposure treatment has commenced. In patients requiring HRIG, sutures (and infiltration of local anaesthetic) should be delayed until HRIG has been infiltrated into the wound.

Risk assessment

Each case requires a full risk assessment based on detailed information about the circumstances of the potential exposure. Health care professionals should try to collect as much of this information as possible to inform the risk assessment. Risk assessment should be carried out rapidly, so that post-exposure treatment, if indicated, can be started promptly. Treatment may need to start before full information is available on the ownership and condition of the biting animal.

Information required to complete the risk assessment and initiate post-exposure treatment:

- patient name, date of birth, age, address, and NHS number if possible
- date of exposure
- species and current health status of animal involved if possible
- country of exposure
- category of exposure
- site (on body) of exposure
- whether the patient is immunosuppressed or has any allergies
- any previous rabies vaccinations or immunoglobulin treatment
- weight of the patient if HRIG is being considered

As the incubation period for rabies can be prolonged, treatment should still be considered even if the interval from exposure is lengthy. Risk assessment should always be done, even if the exposure occurred many months or years previously.

The following features are important considerations in the likelihood of transmission associated with a possible exposure:

Country:

- countries are classified as high, low and no risk for rabies in different animal species.

Animal source:

- rabies can be transmitted by the saliva of any warm blooded animal, including bats, monkeys and rodents as well as cats, dogs and foxes
- animals behaving abnormally represent a higher risk of infection (but normal appearance and behaviour do not exclude rabies)
- unprovoked bites carry greater risk than provoked bites
- a regularly vaccinated animal is unlikely to be rabid but, rarely, vaccinated dogs have transmitted rabies
- domestic dogs or cats behaving normally at 15 days after an exposure would not have been infectious at the time of the exposure. Therefore, where possible, domestic dogs and cats should be observed for 15 days to see if they begin to behave abnormally

Category and site of exposure

- higher risk exposures are those with broken skin, including single or multiple transdermal bites, severe lacerations, or where mucous membranes or an existing skin lesion have been contaminated by the animal's saliva or other body fluid. Intact skin is a barrier against infection
- bites and severe lacerations represent a higher risk than scratches
- bat bites from species in the UK are usually felt and not seen
- proximal bites (e.g. head and neck) represent a shorter incubation period than distal wounds

Immune status of the individual

- Individuals who are primed by pre-exposure rabies immunisation respond more rapidly to post-exposure treatment and in most cases do not require HRIG.
- Post-exposure treatment may often have been started elsewhere and further treatment will depend upon the dates and type of vaccine already received.
- Immunosuppressed individuals (as defined in Chapter 6) should be managed with a greater degree of caution as they may not respond as effectively to rabies immunisation

Post-exposure treatment

Using a combination of the country where the incident occurred and the type of terrestrial mammal or bat involved, and category of exposure (Table 27.3), a Composite Rabies Risk will be calculated (Table 27.4). This is then used, along with the immunisation status and immune competence of the patient to determine the post-exposure treatment required (see Table 27.5).

Table 27.3 Categories of exposure (adapted from WHO)

Category	Terrestrial mammals	Bats
1	No physical contact with saliva For example: • touching, stroking or feeding animals	No physical contact (i.e. no direct contact with the bat's saliva) For example: • touching a bat where the person was protected by a barrier capable of preventing saliva contact, such as a boot, shoe, or appropriate protective clothing
2	Minimal contact with saliva and/or unable to infiltrate wound with HRIG if needed For example: • bruising or abrasions • licks to broken skin (i.e. over insect bites or scratches) • minor scratches (i.e. not down to the muscle) • minor bites (i.e. to covered areas where saliva does not contaminate the wound directly)	Uncertain physical contact (i.e. where there has been no observed direct physical contact (with saliva) but this could have occurred) For example: • handling a bat without appropriate protective clothing(i.e. gloves) • a bat becoming tangled in hair
3	Direct contact with saliva For example: • severe/deep lacerations (i.e. down to the muscle) • major bites (i.e. direct saliva contact with muscle through the wound) • contact of mucous membranes with saliva (e.g. licks)	Direct physical contact with bat's saliva For example: • all bites or scratches • contamination of mucous membrane with saliva or bat droppings/urine • potential unrecognised contact with bat (i.e. any bat found in the room of a sleeping or intoxicated person or young child)

Table 27.4 Composite rabies risk (CRR) table

Combined Country/ Animal risk	Category 1 exposure	Category 2 Exposure	Category 3 exposure
No risk	Green	Green	Green
Low risk	Green	Amber	Amber
High risk	Green	Amber	Red

Following a risk assessment, if post-exposure treatment is indicated, this should be given as in table 27.5. It is particularly important that the first three doses are given as close as possible (within a day or two) of the recommended schedule. Post-exposure rabies vaccine should be given via the intramuscular route (or by deep subcutaneous injection for people with bleeding disorders). Treatment for immunosuppressed individuals should include the

most immunogenic immunisation course available and HRIG, irrespective of previous rabies immunisation status, with antibody testing to ensure response to post-exposure treatment (see Table 27.5).

Table 27.5 Post-exposure treatment based on Composite rabies risk (CRR)

	Post-exposure treatment		
Composite rabies risk	**Non-immunised***	**Fully immunised**	**Immunosuppressed**
Green	None	None	None
Amber	Four doses of vaccine on days 0, 3, 7, and 21	Two doses of vaccine on days 0 and 3-7	HRIG plus five doses of vaccine on days 0, 3, 7, 14 and 30
Red	HRIG** plus four doses of vaccine on days 0, 3, 7, and 21	Two doses of vaccine on days 0 and 3-7	HRIG plus five doses of vaccine on days 0, 3, 7, 14 and 30

* Persons who have incomplete pre- or post-exposure course of rabies vaccine seek advice (as below)

** HRIG is not required more than seven days after the first dose of vaccine, or more than one day after the second dose of vaccine.

If an individual arrives in the UK having started post-exposure treatment via the intradermal route, they should receive the remaining doses via the intramuscular route. Where a regime has been started that is different to that used in the UK, specialist advice should be sought.

Further details can be found in the detailed guidance on risk assessment and management of potential rabies exposures. Specialist advice on the assessment of the risk and appropriate management can be obtained from one of the following:

Country	Contact	Telephone Number
England	Rabies and Immunoglobulin Service (RIgS), National Infection Service, Public Health England, Colindale (PHE Colindale Duty Doctor out of hours)	0208 327 6204 or 0208 200 4400
	or local health protection team (HPT)	See https://www.gov.uk/health-protection-team for contact details
Wales	Duty Virologist, University Hospital of Wales, Cardiff	029 20 742 094 or 029 20 747 747
	or Public Health Wales health protection team (HPT)	0300 003 0032
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	01592 643 355
	Western General Hospital, Edinburgh	0131 537 1000
Northern Ireland	Public Health Agency Duty Room	030 0555 0119

Contraindications

Pre-exposure rabies vaccine should not be given to those who have had:

- a confirmed anaphylactic reaction to a previous dose of rabies vaccine, or
- a confirmed anaphylactic reaction to any component of the vaccine

The PCEC rabies vaccine (Rabipur ®) contains residues of chicken proteins (e.g. ovalbumin) so an alternative rabies vaccine may be considered for pre-exposure immunisation in those with severe egg allergy.

The intradermal 0.1ml pre-exposure vaccine regimens should not be used in those with immunosuppression or those taking chloroquine for malaria prophylaxis, as this can suppresses the antibody response.

There are no contraindications to post-exposure treatment with rabies vaccine (including Rabipur ® for those with severe egg allergies). In the event of a hypersensitivity reaction to a dose of a pre-exposure course, such individuals should still receive post-exposure immunisation if indicated, because the risks of rabies outweigh the risks of hypersensitivity. When there is a history of a hypersensitivity reaction to rabies immunisation, specialist advice should be sought and further doses given under close medical supervision.

Precautions

Minor illnesses without fever or systemic upset are not valid reasons to postpone pre-exposure immunisation.

If an individual is acutely unwell, pre-exposure immunisation should be postponed until they have recovered. This is to avoid confusing the differential diagnosis of any acute illness by wrongly attributing any signs or symptoms to the adverse effects of the vaccine.

Post-exposure treatment should always be started without delay, even in the presence of other illness.

Pregnant women and breast-feeding

Pregnant women and breast-feeding mothers should be given pre-exposure prophylaxis if the risk of exposure to rabies is high following a risk assessment by a health professional and rapid access to post-exposure treatment would be limited.

Post-exposure treatment should be given to pregnant women and breast-feeding mothers when indicated.

Immunosuppression and HIV infection

Individuals with immunosuppression and HIV infection (regardless of CD4 count) may be given pre-exposure rabies vaccines in accordance with the recommendations above. These individuals may not make a full antibody response. Re-immunisation should be considered after treatment is finished and recovery has occurred or, in the case of those with HIV, when there has been immune recovery following commencing antiretroviral treatment (e.g. CD4 count is greater than 200 per mm3).

Individuals who are immunosuppressed (and fulfil criteria in Chapter 6) who have a significant rabies exposure (i.e. red or amber Composite Rabies Risk) should receive five intramuscular doses (2.5IU) of rabies vaccine on days 0, 3, 7, 14 and 30, plus HRIG. Antibody tests are 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.

Adverse reactions

All suspected adverse reactions should be reported to the Medicines and Healthcare products Regulatory Agency (MHRA). Anyone can report a suspected adverse reaction to the MHRA using the Yellow Card reporting scheme (www.yellowcard.gov.uk).

Rabies vaccine may cause local reactions such as redness, swelling or pain at the site of injection within 24 to 48 hours of administration. Systemic reactions such as headache, fever, muscle aches, vomiting and urticarial rashes are rare. Delayed hypersensitivity reactions have been reported from the US. Reactions may become more severe with repeated doses. Neurological conditions, such as Guillain-Barré syndrome, have been reported extremely rarely; a causal association with immunisation is not established.

HRIG may cause local pain and low-grade fever, but no serious adverse reactions have been reported.

Management of cases

Human rabies is a notifiable disease. In the event of a case, or suspected case, of human rabies, the local health protection team should be informed.

Guidance on the management of human rabies is available:

https://www.gov.uk/government/publications/human-rabies-public-health-management-of-a-suspected-case

Supplies

Rabies Vaccine BP is available from Sanofi Pasteur MSD (Tel: 01483 505 515).

Rabipur is available from GlaxoSmithKline (Tel: 0800 221 441) or MASTA (Tel: 0113 238 7550).

Under the Health and Safety at Work Act (HSWA) 1974 and the control of Substances Hazardous to Health (COSHH) Regulations 2002 employers have a responsibility to assess the risks for exposure to hazardous agents, including rabies virus, and to protect employees from those risks as is reasonably practicable (See also Chapter 12). This includes the provision of pre-exposure rabies immunisation if indicated.

In England, rabies vaccine for pre-exposure immunisation will only be provided by Public Health England for bat handlers where no formal employer can be identified. This can be obtained from the PHE Rabies and Immunoglobulin Service (Tel: 020 8327 6204) using the dedicated form (https://www.gov.uk/government/publications/rabies-pre-exposure-request-form). For

other pre-exposure indications, it can be obtained through local pharmacies by private prescription. PHE does not supply pre-exposure rabies immunisation for travellers. Rabies vaccine and HRIG for use in post-exposure treatment are available free of charge to patients and providers from PHE. To facilitate prompt access for patients, NHS services are encouraged to arrange local seven-day access to a small number of doses of rabies vaccine to initiate a course. Any vaccine held locally that is used for post-exposure treatment will be replaced free of charge by PHE. Information may be obtained from the local health protection team (for contact details see https://www.gov.uk/health-protection-team) or PHE Rabies and Immunoglobulin Service (Tel: 020 8327 6204) or out of hours via the PHE Colindale Duty Doctor (Tel: 020 8200 4400)

In Northern Ireland, rabies vaccine for licensed bat handlers where no formal employer can be identified may be obtained on HS21 prescription for administration by the individual's GP; HS21 must not be used for pre-exposure rabies immunisation for travel purposes. Rabies vaccine for post-exposure treatment is available from the Royal Victoria Hospital Pharmacy Department, BHSCT (Tel: 028 9024 0503) and HRIG from the Northern Ireland Blood Transfusion Service (Tel: 077 7461 9337, Duty Biomedical Scientist), advice on risk assessment is available from the PHA Duty Room (Tel: 030 0555 0119), if required.

In Scotland, pre-exposure immunisation is available for bat handlers, where no formal employer can be identified, through normal GP channels. Post–exposure treatment is available through the local on-call infectious diseases consultant.

In Wales, rabies vaccine for pre-exposure immunisation will only be for bat handlers where no formal employer can be identified. This can be obtained from the PHE Rabies and Immunoglobulin Service (see above for contact details and form). Post-exposure treatment is provided through the Duty Virologist, University Hospital of Wales, Cardiff (Tel: 029 2074 7747) or Public Health Wales health protection team (Tel: 030 0003 0032).

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