

Rabies: Guidance on Prophylaxis and Management in Humans in Scotland

Health Protection Network
Scottish Guidance

December 2010

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Supported by Health Protection Scotland

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Citation for this document

Health Protection Network. Rabies: Guidance on Prophylaxis and Management in Humans in Scotland. Health Protection Network. Scottish Guidance 7. Health Protection Scotland, Glasgow, 2010.

Published by Health Protection Scotland, Clifton House, Clifton Place, Glasgow G3 7LN. Health Protection Scotland is a division of NHS National Services Scotland.

First published December 2010

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Health Protection Network
Health Protection Scotland
Clifton House
Clifton Place
Glasgow G2 7HF

Tel: +44 (0) 141 300 1100

Email: NSS.HPSEnquires@nhs.net

Designed and typeset by:

Graphics Team, Health Protection Scotland

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Foreword

On behalf of the Alliance for Rabies Control, I would like to extend our sincere congratulations to the members of the Rabies Guidance Development Group and Health Protection Scotland for publishing these important and life-saving guidelines to help protect individuals that are at risk of exposure to rabies. As mentioned in this document, rabies is a disease that continues to take the lives of between 50,000 to 70,000 people every year. Clearly, none of these victims should have died because the rabies vaccines that are produced and available today are among the most, if not the most, efficacious vaccines ever developed. In fact, there have been only a very few reported true 'treatment failures', wherein a patient exposed to rabies that subsequently received the correct World Health Organisation (WHO) recommended post-exposure prophylaxis regimen in a timely manner still succumbed to rabies. Thus, one can logically ask the question, 'If the current rabies vaccines and biologicals are so effective, why do people still die of rabies?' One of the main reasons for this tragic circumstance is because there is a lack of educational awareness about how to prevent rabies both in the general public and also amongst health care professionals. Therefore, these guidelines are critically important and timely for health care professionals treating patients that may be at risk of contracting the most deadly disease known to mankind.

While post-exposure prophylaxis is the only means to prevent rabies after an exposure to rabies has occurred, the value of administering pre-exposure rabies vaccination to a person or persons living or working in high risk environments is all too often overlooked. The rabies vaccines currently recommended by WHO for pre-exposure vaccination are safe and have long been used by persons living or working at continuous or frequent risk of exposure, for example rabies researchers and veterinarians working in regions where rabies is endemic. The option of administering pre-exposure vaccination should be carefully considered for persons whose vocation or travel plans will put them at potential risk of exposure. Although the majority of rabies victims died after being exposed to an infected animal in a developing country in Asia or Africa, the risk of contracting rabies in industrialised countries cannot be overlooked, and the role that bats play as vectors of the disease. Due to the extremely high case fatality rate of rabies, every evaluation by a health care professional regarding whether a patient should receive either pre- or post-exposure prophylaxis must be considered to be a life or death decision for the patient in question. These updated guidelines are therefore critically important for all health care professionals living in Scotland. They should be reviewed and become part of the reference material for all health care professionals consulting with patients that may have been exposed or have the potential to be exposed to rabies in the future.

The Alliance for Rabies Control commends the Rabies Guidance Development Group for all of their hard work during the preparation of these guidelines and looks forward to a time when human rabies cases no longer occur anywhere in the world.

A handwritten signature in black ink that reads "Deborah J Briggs". The signature is written in a cursive style with a large initial 'D'.

Dr Deborah J Briggs,

Executive Director,
Alliance for Rabies Control (<http://www.rabiescontrol.net>)
WHO Expert Consultation on Rabies

Acknowledgements

Health Protection Scotland wish to express their appreciation to everyone whose efforts made this guidance possible. In particular to the members of the Guidance Development Group, HPS Graphics, stakeholders, and external reviewers who contributed to and reviewed the content of this guidance.

Abbreviations

BCT	Bat Conservation Trust
BLV	Bat Lyssavirus
CMO	Chief Medical Officer
CPHM	Consultant in Public Health Medicine
EBLV	European Bat Lyssavirus
EH	Environmental Health
EHO	Environmental Health Officer
GP	General Practitioner
HDCV	Human Diploid Cell Vaccine
HPNS	Health Protection Nurse Specialist
HPS	Health Protection Scotland
HRIG	Human Rabies Immune Globulin
HPA	Health Protection Agency
HPN	Health Protection Network
HPU	Health Protection Unit
ID	Infectious disease
i.d.	Intradermal
i.m.	Intramuscular
MHRA	Medicines and Healthcare Regulatory Authority
NHS	National Health Service
PCEC	Purified Chick Embryo Cell (PCEC) rabies vaccine
PrEP	Pre-exposure prophylaxis
PEP	Post-exposure prophylaxis
PRPE	Potentially Rabies Prone Exposure
RVNA	Rabies Virus Neutralising Antibody
SGHD	Scottish Government Health Directorate
SFE	Statement of Financial Entitlements
SNBTS	Scottish National Blood Transfusion Service
SNH	Scottish Natural Heritage
WHO	World Health Organization

1. Introduction

This guidance has been produced by the Rabies Guidance Development Group at the request of the Scottish Health Protection Network (HPN) Steering Group. It replaces the current guidance in Scotland, Health Protection Scotland's '*Health Protection Management of Rabies*' which was last updated in May 2007.

This guidance provides advice on pre-exposure prophylaxis and post-exposure prophylaxis against rabies in humans.

The guidance is aimed at:

- General Practitioners (GPs)
- Front-line Hospital staff
- Infectious Disease (ID) Physicians and Microbiologists
- Travel Health Medicine Practitioners
- Consultants in Public Health Medicine (CPHM)
- Health Protection Scotland Consultants
- Health Protection Nurses
- Occupational Health Practitioners
- Animal Health and other Government bodies.

It may also be of interest to those with repeated potential exposure to potentially rabid animals through paid or voluntary work, and to their employers or charitable bodies.

1.1 Aim and scope

This guidance aims to provide easily accessible advice based on evidence, or expert consensus, on immunisation against rabies both before and after a potentially rabies prone exposure, including:

- who should receive pre-exposure prophylaxis (PrEP)
- what PrEP should consist of, including primary course and boosters
- who should receive post-exposure prophylaxis (PEP)
- what PEP should consist of, including active and passive immunisation
- the administrative and financial arrangements.

The guidance does not provide advice on the clinical management of cases, or of the handling of animals, except where the latter affects the management of potential human exposure.

2. Background and Risks

Rabies is an acute viral infection that is almost universally fatal in people without PrEP or PEP. Transmission is usually through contact with saliva via the bite of an infected animal, or through broken skin, or mucous membrane.

Dogs are the main transmitter of rabies virus to humans worldwide. Less commonly rabies can be caused by other *Lyssaviruses* including European bat *Lyssaviruses* (EBLV). In Scotland most requests for advice follow potential exposure to bats.

The World Health Organization (WHO) has estimated the annual reported number of human rabies deaths globally to be between 50,000 and 70,000. Most deaths occur in developing countries, particularly in Africa and South East Asia.¹ Visitors, workers in, and travellers to, these areas are at particular risk.

Indigenously acquired rabies is exceptionally rare in the UK. The first, and to date only, death in 100 years from UK acquired rabies occurred in a bat-worker in Scotland in 2002.²

European bat Lyssavirus type 2 (EBLV-2) is now known to be enzootic in Daubenton's bats (*Myotis daubentonii*) in the UK, albeit at low but fluctuating levels and the occasional presence of the virus in other species cannot be ruled out. In 2008, 3% of Daubenton's bats tested in Scotland were positive for antibodies to EBLV-23. In Scotland two Daubenton's bats have been identified as positive: one in 2008 where viral genetic material was amplified from a saliva swab from a live bat as part of the Scottish Natural Heritage (SNH) active surveillance,³ and one in 2009 where virus was isolated from a bat carcass as a result of passive surveillance undertaken by the Veterinary Laboratories Agency.⁴

The number of people experiencing 'potentially rabies prone exposures' (PRPE) and requiring PEP includes not only those exposed to potentially rabid animals abroad, or in the UK as a result of their occupation, but members of the public, volunteers, and professionals with potentially rabies prone exposures to indigenous bats. As well as receiving PrEP, it is vital that people who frequently handle bats wear appropriate personal protection.

The incubation period for rabies depends upon the size of the inoculum and the distance of the inoculum from the victim's central nervous system. The incubation period has been reported to be as short as a few days, and as long as a few years.⁵

3. Pre-exposure Prophylaxis

3.1 Primary Course

3.1.1 Indications

PrEP is indicated for people with:

- continuous exposure:
 - laboratory workers who routinely handle rabies virus material.
- frequent exposure:
 - those who, in the course of their work, regularly handle imported animals and bats e.g.:
 - at animal quarantine centres
 - at zoos
 - at animal research and acclimatisation centres
 - at ports
 - carrying agents authorised to carry imported animals
 - veterinary and technical staff of Animal Health
 - certain inspectors appointed by Local Authorities (LA) under the Animal Health Act.1981 (but not dog wardens for whom the risk of exposure is low and for whom prompt PEPI is likely to be more appropriate)
 - those who frequently handle bats in the UK
 - those who live in or visit enzootic areas who by the nature of their activity are at special risk of contact with rabid animals (e.g. animal sanctuary volunteers, trappers, veterinary staff or zoologists)
 - health workers who are likely to come into close contact with a patient with rabies in the UK.

PrEP should also be considered for people with:

- infrequent exposure:
 - travellers and workers who plan to visit an enzootic area especially
 - those without access to prompt medical advice, rabies vaccine and immunoglobulin. (Advice is available for health professionals from TRAVAX (<http://www.travax.nhs.uk>) and the general public from Fitfortravel (<http://www.fitfortravel.nhs.uk>)
 - those who may be exposed to rabies because of their travel activities (e.g. cycling, running)
 - children, who may be at particularly high-risk because they lack awareness of the need to avoid animals or to report an animal bite.

PrEP is not indicated for members of the general UK population not described above, for example people with occasional potential exposure to indigenous bats.

3.1.2 Dosage and Schedule

A primary course of vaccination consists of:

- Three doses of 1.0ml rabies vaccine given intramuscularly (i.m.) into the deltoid muscle (or anterolateral thigh in infants) on days 0, 7 and 28, in all age groups
- Alternatively the third dose can be given from day 21 if time is short.

Rabies vaccines currently licensed in the UK:

- Human Diploid Cell Vaccine (HDCV). (Rabies Vaccine BP[®] - Sanofi Pasteur MSD)
- Purified Chick Embryo Cell (PCEC) Rabies Vaccine. (Rabipur[®] - Chiron/Novartis)

These vaccines may be used interchangeably for primary courses, boosters, and PEP.

3.2 Boosters: indications, dosage, and schedule

Boosters should be considered for people with:

- continuous exposure, who should have their antibody titre checked every six months and receive a booster if their antibody titre falls below an acceptable level. Laboratories have their own standards for what constitutes an acceptable level for protection against continuous exposure
- frequent exposure, who should receive a single booster 12 months after their primary course. In line with current evidence, they should ideally have their antibody titre checked every 3 years and receive a booster if antibody titre is below the acceptable level of 0.5 IU/ml.^{6,7} In the absence of testing boosters should be administered every 3-5 years.

Boosters are not routinely required for people with:

- infrequent exposure, who do not require routine boosting or serologic testing after their primary course

Most people who receive a three dose i.m. course of cell-cultured rabies vaccine will still have detectable neutralising antibody many years later, without any boosting.^{8,9}

Measuring Rabies Virus Neutralising Antibody (RVNA) titres when indicated will allow an accurate determination that there has been an adequate immune response, and prevent unnecessary boosting which can in some incidents lead to clinical problems.^{10,11}

If the primary course was administered to any other schedule or using a product of doubtful potency, advice on boosters should be sought from Health Protection Scotland (HPS).

3.3 Administrative arrangements

3.3.1 Entitlement to PrEP

The Chief Medical Officer's (CMO) letter of November 2002 (SEHD/CMO(2002)11) stated:

'Pre-exposure immunisation with human diploid rabies vaccine should be offered and is available free from the NHS, to a number of groups of people listed in the Health Departments' 1996 Immunisation Against Infectious Disease, section 27.3 and 27.4, including licensed bat handlers. In addition Health Departments now recommend that those regularly handling bats, not just licensed bat handlers, should be immunised against rabies'.ⁱ

3.3.2 Charging for PrEP

The National Immunisation Policy – Immunisation against infectious disease 2006 - The Green Book⁷ (updated 13 October 2010) – notes that bat workers should not be charged for vaccinations. The Scottish Government policy is clear that bat workers should not be charged for vaccination. For these individuals, and where there is an identified employer, the employer should cover the cost of vaccination. Where there is no identified employer, the individual may approach their GP practice for vaccination, who should provide it free of charge.

The Statement of Financial Entitlements (SFE)¹² in its present form clearly says that vaccinations against rabies (for certain groups, but not including travellers) are included in 'Additional Services'. Remuneration is paid to the GP by the Health Board through the global sum and so there should be no charge to the patient.

Annex J of the SFE states the eligibility for vaccination of the following groups at special risk (Names of the organisations and posts asterisked * have been updated for the purpose of this guidance):

1. at kennels and catteries approved by DEFRA* for the quarantine of imported dogs, cats, etc
2. at quarantine premises in zoological establishments
3. by carrying agents authorised to carry imported dogs, cats, etc

i [http://www.sehd.scot.nhs.uk/cmo/CMO\(2002\)11.pdf](http://www.sehd.scot.nhs.uk/cmo/CMO(2002)11.pdf)

4. at approved research and acclimatisation centres where primates and other imported mammals are housed
5. in laboratories handling rabies virus
6. at seaports and airports where they are likely to come into contact with imported animals or animals on ships or aircraft, eg HM Revenue and Customs* and police officers
7. as veterinary and technical staff of DEFRA staff employed by the Animal Health agency*
8. as inspectors appointed by Local Authorities under the Diseases of Animals Act or employed otherwise who, by reason of their employment, encounter enhanced risk
9. those who regularly handle bats, including on a voluntary basis and where an area is declared to be rabies-infected by the Scottish Government
10. Persons directly involved in control measures carried out under the direction of the Consultant in Public Health Medicine* (Communicable Disease and Environmental Health) together with veterinary surgeons engaged in private practice within the infected area and their ancillary staff.

Any person, of whatever age, who is in one of the categories specified in Annex J is entitled to receive rabies vaccination free of charge either from their employer or from their GP practice.

The SFE does not stop employers with occupational health services vaccinating their staff for any condition, including seasonal flu and rabies. If these individuals are vaccinated by an occupational health service or privately the immunisation including vaccine costs will rest with the employer or the individual.

If vaccinated by the GP practice the patient may have to pay a prescription charge if they are required to do so normally.

GPs are free to charge travellers and those patients not on their list, for private prescriptions and private vaccinations.

3.3.3 Procurement of vaccine

The CMO letter of November 2002 (SEHD/CMO(2002)11) stated:

'GPs should order vaccine through stock order scheme or write prescriptions for individuals in the usual way.'

GPs should prescribe the vaccine, according to its license, on the GP 10 for patients who are entitled to free PrEP. This would incur prescription charges where appropriate. In these circumstances the cost of the vaccine will come from the prescribing budget. For those not eligible for free vaccination, GPs should use a private prescription. Stock order scheme can be used to order rabies vaccine for active PEP.

3.3.4 Charging for titres

People in the continuous or frequent exposure group, and who fall under one of the categories specified in Annex J are entitled to have their RVNA titres checked free of charge. They should request this service from their employer, or in cases where there is no clear employer, through their GP practice.

For titres accessed through an occupational health service or privately, the cost will rest with the employer or the individual. Laboratories in the UK who undertake private testing are:

Biobest Laboratories Ltd

Charles Darwin House,
The Edinburgh Technopole,
Milton Bridge,
Nr Penicuik,
EH26 0PY

Tel: 0131 440 2628

Website: <http://www.biobest.co.uk/>

VLA Weybridge

The Sample Reception Area,
Veterinary Laboratories Agency,
New Haw,
Addlestone,
Surrey,
KT15 3NB

Tel: 01932 357345/335

Website: <http://www.defra.gov.uk/vla/>

The HPN recommends using VLA Weybridge for testing Scottish samples from individuals who are eligible under Annex J of the SFE states to have their titres checked free of charge. VLA Weybridge is an international reference laboratory for rabies testing and investigation; they perform many tests per month and would be involved in investigation of any possible exposure incidents in the UK. VLA Weybridge will keep a registry of all Scottish samples sent to them, including titres results. Biobest laboratories are fully accredited and test to internationally agreed standards, and this recommendation should in no way be seen as critical of their service. Those arranging private testing can choose to send to either laboratory.

In General Practice, the cost of testing is provided under general NHS reference laboratory services and samples should be sent to the local NHS lab for onward transmission.

4 Post-exposure Risk Assessment and Management

4.1 Risk Assessment

4.1.1 Principles

Anyone who presents to any non-medical person or organisation (for example the Bat Conservation Trust (BCT)) worried that they might have had a 'potentially rabies prone exposure' (PRPE) should be very strongly advised to seek medical advice to allow a prompt risk assessment to be carried out.

People with a PRPE usually present to primary care (GP or practice nurse) or A&E (front-line hospital staff). Unless the health professional is confident about being able to perform a full, expert risk assessment, the person should be referred to their local Infectious Disease (ID) department for management. A list of the regional Infectious Disease Units in Scotland is included in Appendix 5.

The risk assessment is based upon:

- the likelihood of the animal carrying rabies, which depends upon its:
 - species
 - behaviour
 - origin
 - state of health or laboratory results
 - vaccination status.
- the likelihood of the exposure allowing transmission of rabies virus, which depends upon the likelihood of saliva or neural tissue coming in contact with:
 - a breach in the patient's skin, or
 - the patient's mucous membranes.

- the person's vaccination status:
 - fully vaccinated, if they have:
 - had a well documented appropriate course of PrEP or PEP
 - had a previously documented rabies antibody titre of at least 0.5IU/ml.
 - not fully vaccinated, if they have:
 - never received PrEP or PEP
 - had incomplete/inadequate PrEP.

If in doubt, patients should be managed as not fully vaccinated. Individuals who are immunosuppressed or have HIV, may require different PEP management and specialist advice should be sought in that event.

This guidance addresses the risk assessment of PRPE to bats in the UK or abroad, and to terrestrial mammals abroad separately.

4.1.2 Bats

The species of bat does not affect the decision on whether to administer PEP. Although only Daubenton's bats have been identified with EBLV in the UK, it is possible that any species of bat may be infected. While smaller bats with smaller teeth are less likely to inflict wounds, any bat may do so.

Even though infected bats are more likely to behave abnormally, the bat's state of health does not affect the decision on whether to administer PEP. *Lyssavirus* infected bats can be apparently healthy. Any bat that is active by day, or is found in a place where bats are not usually seen – for example in an inhabited room or on an open lawn, or is unable to fly, is more likely to be rabid than an apparently healthy bat. Such bats are more easily approached. It is unusual for a member of the public to have a PRPE to a healthy bat. If the bat has died, laboratory investigation may confirm rabies infection. Bats are a protected species and cannot be destroyed to determine rabies status.

Bats may carry *Lyssavirus* anywhere in the world (with the exception of New Zealand). The part of the world where the PRPE occurred does not therefore affect the decision on whether to give PEP. Contact with bats, their saliva or neural tissue constitutes a PRPE even in countries which are free of classical rabies. In the UK, bats are the only wild animal reservoir of *Lyssavirus*.

The nature of the exposure is critical to the risk assessment and the outcome of PEP. Was there a possibility of contact between the bat's saliva or neural tissue and the patient's skin or mucous membrane? What was the exact nature of the contact?

4.1.2.1 Categories of PRPE with bats (Figure 1)

There are three categories of PRPE with bats:

- I **No significant risk:** This would occur if it is certain that there has been no direct physical contact with the bat's saliva or neural tissue, or if the person was protected by a barrier capable of preventing such contact, such as a boot, shoe, or appropriate protective clothing. Contact with bat droppings, blood and urine do not constitute a risk^{13, 14} although the use of appropriate personal preventive measures should be emphasised in such settings.
- II **Low-risk:** Where there has been no observed direct physical contact, but it is likely to have occurred, for example a bat found in room of sleeping person.
- III **High-risk:** Single or multiple trans-dermal bites or scratches & bruising. Minor bites without breaking of the skin (covered areas of arms, trunk, and legs). Major bites (multiple or on face, head, finger or neck). Contamination of mucous membrane with saliva or neural tissue.

4.1.3 Terrestrial animals in enzootic countries or regions

a) What is the likelihood of the animal carrying rabies?

- What animal was it, and how was it behaving?

The main risk comes from wild carnivores, and stray companion dogs and cats. All carnivores shedding rabies virus through their saliva are most likely to be in the terminal phase of illness, and therefore are likely to be behaving abnormally, although apparently normal behaviour is not a guarantee of insignificant risk.

Although the risks from herbivores such as cattle, horses, deer, rodents and primates are much lower than wild animals, cats and dogs, they can transmit the virus, and exposures to them may constitute a risk.

- Is the animal's state of health known? If so, what is it? If not, can it be ascertained?

PEP should be commenced as soon as possible if indicated after PRPE but if 15 days have elapsed since the PRPE to a cat or dog which remains well and is behaving normally (i.e. does not have clinical rabies), PEP can be abandoned. The animal's vaccination status may suggest rabies infection is unlikely but cannot be completely relied on.

- Was the animal indigenous to the country, or imported?

This information is important in interpreting whether it was from a country or region that is free of terrestrial rabies or where rabies is enzootic (see below).

- Was the country or region at high-risk, low-risk, or no risk of classical rabies?

A country may be considered at negligible risk of classical rabies when all the following apply:

- rabies in animals is notifiable
- an effective system of disease surveillance in animals is in operation
- all regulatory measures for the prevention and control of rabies in animals have been implemented including effective importation procedures
- no case of indigenously acquired classical rabies infection has been confirmed in man or any animal species during the previous two years according to the Office International des Epizooties definition of a rabies free country. (This status would not be affected by the isolation of a BLV such as EBLV-1 or EBLV-2.)
- no imported case in carnivores has been confirmed outside a quarantine station for the previous six months.

The management algorithm (figure 1 on page 19) uses the geographical classifications of 'no risk,' 'low-risk,' and 'high-risk' to inform decisions on the need for Human Rabies Immune Globulin (HRIG) and/or vaccine. The latest country classification is listed on the HPS website <http://www.hps.scot.nhs.uk/giz/publicationsdetail.aspx?id=46633> and on Travax (<http://www.travax.nhs.uk>). Travax also gives additional regional detail, case numbers and outbreak information.

b) How likely is the exposure to be rabies prone?

- Was there contact between the animal's saliva and the patient's broken skin or mucous membrane? What was the exact nature of the contact?

4.1.3.1 Categories of PRPE with terrestrial animals (Figure 2)

There are three categories of PRPE with terrestrial animals:

- I **No significant risk:** Touching or stroking an animal with no realistic possibility of transdermal transfer of the animal's saliva.
- II **Low-risk:** Licks of the skin or other contact with saliva (e.g. feeding animals), minor scratches, bruising or abrasions without bleeding, minor bites without breaking of the skin (covered areas of arms, trunk, and legs). All bites, licks and scratches from herbivores, rodents, and primates.
- III **High-risk:** Single or multiple transdermal bites or scratches, licks on broken skin, major bites (multiple or on face, head, finger or neck).

Contamination of mucous membrane with saliva (i.e. licks).

4.2 Management

4.2.1 Principles

Post-exposure management usually consists of immediate wound care (if there is a wound) and risk assessment for appropriate PEP. PEP comprises active immunisation with rabies vaccine, with or without passive immunisation with Human Rabies Immune Globulin (HRIG).

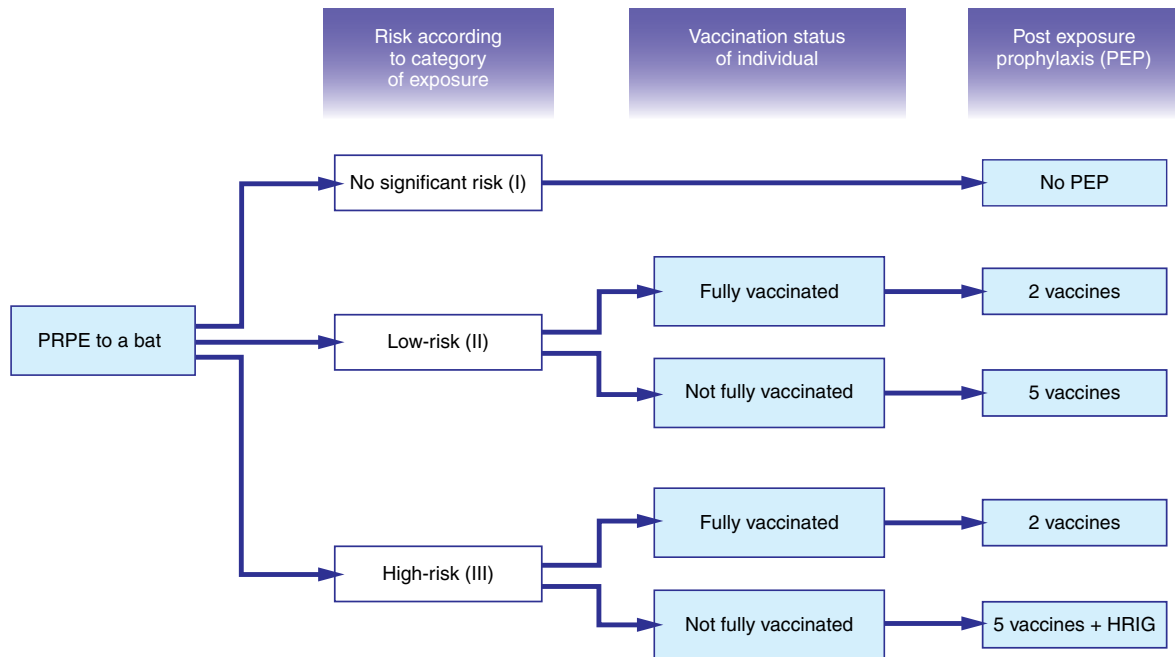
The more severe the wound, the closer the wound to the brain and the longer the time period between exposure and presentation, the more urgent the need for prompt management, as, once a person shows symptoms of infection the outcome is almost invariably fatal.

The mainstay of PEP is rabies vaccine. HRIG may provide short term immunity in the first seven days after the commencement of active immunisation. After seven days the antibody level induced by active immunisation (vaccine) is many orders of magnitude greater that can be provided by passive immunisation (HRIG).

HRIG is indicated for individuals who have had a high-risk exposure and are not previously fully vaccinated. HRIG is not indicated if more than seven days have elapsed since commencement of active immunisation.

4.2.2 Summary of management

Figure 1: Management of 'potentially rabies prone exposure' (PRPE) to a bat



Notes

Risk according to category of PRPE to a bat

- I. **No significant risk:** This would occur if it is certain that there has been no direct physical contact with the bat's saliva or neural tissue, or if the person was protected by a barrier capable of preventing such contact, such as a boot, shoe, or appropriate protective clothing. Contact with bat droppings, blood and urine do not constitute a risk. Transmission by aerosol in bat caves is almost unheard of.
- II. **Low-risk:** Where there has been no observed direct physical contact, but it is likely to have occurred, for example a bat found in room of sleeping person.
- III. **High-risk:** Single or multiple trans-dermal bites or scratches & bruising. Minor bites without breaking of the skin (covered areas of arms, trunk, and legs). Major bites (multiple or on face, head, finger or neck). Contamination of mucous membrane with saliva or neural tissue.

Vaccination status of individual

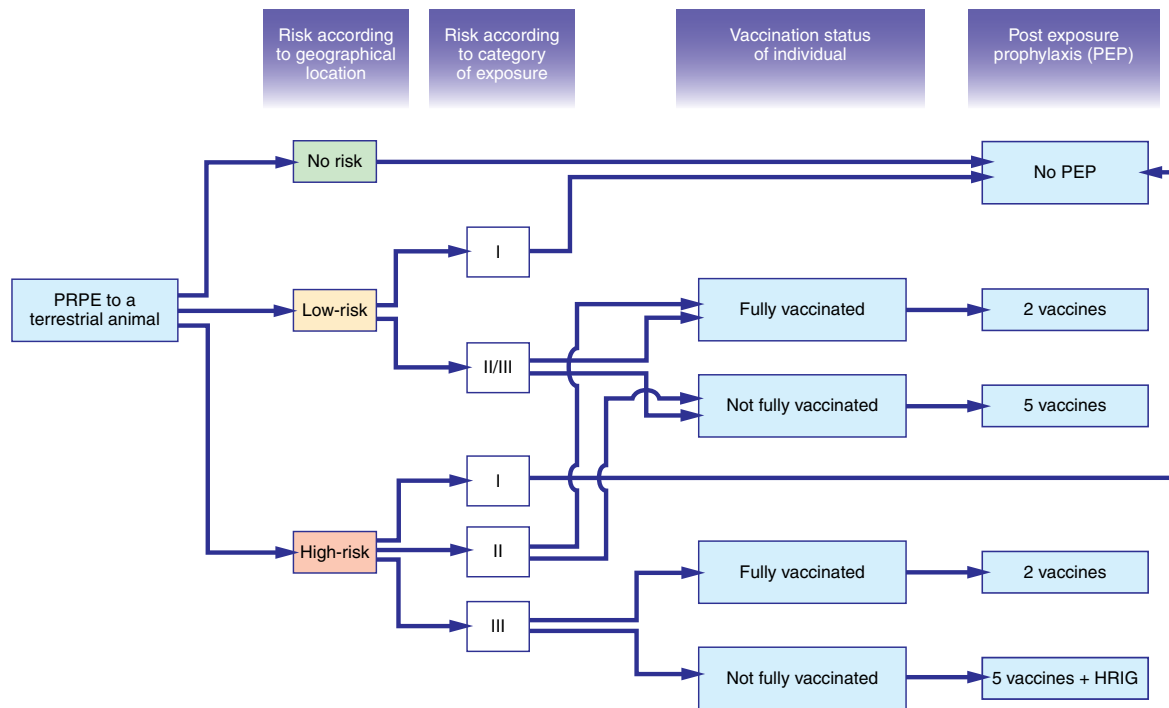
- **Fully vaccinated:** if they have had a well documented appropriate course of pre-exposure immunisation (PrEP) or post-exposure prophylaxis (PEP), or a previously documented rabies antibody titre of at least 0.5IU/ml
- **Not fully vaccinated:** if they have never received PrEP or PEP, or had incomplete/inadequate PrEP.

Post-Exposure Prophylaxis (PEP)

PEP should be administered as soon as practical after a PRPE, even if there has been a delay between the PRPE and presentation for evaluation.

- **2 vaccines:** A full dose of rabies vaccine given i.m. on days 0 and 3
- **5 vaccines:** A full dose of rabies vaccine given i.m. on days 0, 3, 7, 14 and 28
- **HRIG:** 20 IU/kg body weight for adults and children. Infiltrate as much as possible around the wound site even if the wound has healed. For multiple bites over a large area then dilute HRIG with saline to increase volume available.

Figure 2: Management of 'potentially rabies-prone exposure' (PRPE) to a terrestrial animal



Notes

Risk according to geographical location classified as 'No risk', 'Low-risk' or 'High-risk'

The latest country classification list can be found on the HPS website (<http://www.hps.scot.nhs.uk/giz/publicationsdetail.aspx?id=46633>). Travax (<http://www.travax.nhs.uk>) gives additional regional detail and information on outbreaks and cases.

Risk according to category of PRPE to a terrestrial animal

- I. **No significant risk:** Touching or stroking an animal with no realistic possibility of transdermal transfer of the animal's saliva.
- II. **Low-risk:** Licks of the skin or other contact with saliva (e.g. feeding animals), minor scratches, bruising or abrasions without bleeding, minor bites without breaking of the skin (covered areas of arms, trunk, and legs). All bites, licks and scratches from herbivores, rodents, and primates.
- III. **High-risk:** Single or multiple transdermal bites or scratches, licks on broken skin, major bites (multiple or on face, head, finger or neck). Contamination of mucous membrane with saliva (i.e. licks).

Vaccination status of individual

- **Fully vaccinated:** if they have had a well documented appropriate course of pre-exposure immunisation (PrEP) or post-exposure prophylaxis (PEP), or a previously documented rabies antibody titre of at least 0.5IU/ml.
- **Not fully vaccinated:** if they have never received PrEP or PEP, or had incomplete/inadequate PrEP.

Post Exposure Prophylaxis (PEP)

PEP should be administered as soon as practical after a PRPE, even if there has been a delay between the PRPE and presentation for evaluation.

- **2 vaccines:** A full dose of rabies vaccine given i.m. on days 0 and 3
- **5 vaccines:** A full dose of rabies vaccine given IM on days 0, 3, 7, 14 and 28
- **HRIG:** 20 IU/kg body weight for adults and children. Infiltrate as much as possible around the wound site even if the wound has healed. For multiple bites over a large area then dilute HRIG with saline to increase volume available.

4.2.3 Wound care

Prompt wound care can substantially reduce the risk of rabies. As soon as possible after the incident the wound or site of exposure (e.g. mucous membrane) should be cleaned by thorough flushing under a running tap for several minutes and washing with soap or detergent and water. A virucidal agent such as povidone-iodine solution or 40-70% alcohol should be applied and the wound covered with a simple dressing.

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.

4.2.4 Dosage, schedule and administration of active PEP

A course of active PEP consists of a full dose of 1.0 ml rabies vaccine given i.m. into the deltoid (or anterolateral thigh in infants) at either:

- 0 and 3 days, or
- 0, 3, 7, 14 and 28 days.

Day 0 is the date of the first administration which should be as soon as practicable after the risk assessment has indicated its necessity.

4.2.5 Dosage, schedule and administration of passive PEP

A passive course of PEP consists of 20 IU/kg of HRIG for adults and children, ideally as much as possible, given around the wound site, even if the wound has healed. If this is anatomically difficult, it can be given in the anterolateral thigh. If more than 5ml is administered (2ml in children under 20kg) HRIG should be administered in divided doses. If there are multiple bites over a large area then HRIG can be diluted with saline to increase the volume of solution for infiltration. HRIG should never be given at the same anatomical site as rabies vaccine.

HRIG should be given as soon as possible after it has been indicated by the risk assessment, preferably within 24 hours.

As the preparations of HRIG vary in potency and volume, it is critical to know:

- The potency of the batch to be used. Different manufacturers describe potency in different ways, and HRIG batches from the same manufacturer vary in potency
- Weight of patient
- Volume in vials (vials contain between 1-2mls, depending on batch and manufacturer of HRIG). The correct volume for each patient should be calculated and indicated on the supplied proforma, which is issued to the health care provider with the HRIG.

The following are examples of how to calculate dosage, and how many vials are needed:¹⁵

Child weight, 19kg; HRIG potency is 500 IU/1.1mls; vials contain 2.2mls

- Required units total = $19 \times 20 = 380$ IU
- Administer $(380 \times 1.1)/500 = 0.8$ mls
- Supply 1 vial

Adult weight, 85kg; HRIG potency is 500 IU/1.1mls; vials contain 2.2mls

- Required units total = $85 \times 20 = 1700$ IU
- Administer $(1700 \times 1.1)/500 = 3.7$ mls
- Supply 2 vials

Adult weight, 70 kg; HRIG potency is 150 IU/ml; vials contain 2 ml

- Required units total = $70 \times 20 = 1400$
- Administer $1400/150 = 9.3$ mls
- Supply 5 vials

4.3 Administrative Arrangements

Rabies vaccine used as part of PEP is provided free to the patient. GP's can obtain vaccine through stock order but it is recognised that not all community pharmacies will hold rabies vaccine and there maybe a delay in obtaining it via this route. Since PEP should be instituted as soon as possible after a PRPE, if delay is likely then patients should be referred to the local ID physician for immediate management.

HRIG currently available in Scotland is an unlicensed product, held by Scottish National Blood Transfusion Service (SNBTS). It is recommended that all requests for HRIG are channelled through the local ID physician to ensure appropriate risk assessment, product dosing and administration. In addition there is accompanying unlicensed plasma product documentation which needs filled in for each treatment. The requesting clinician should contact their nearest SNBTS Service Centre to arrange for supply and delivery of HRIG.

West (*Gartnavel General, Glasgow*) **Tel:** 0141 357 7802/3/4

South East (*Royal Infirmary, Edinburgh*) **Tel:** 0131 536 5392

North East (*Forresterhill, Aberdeen*) **Tel:** 01224 552 322

5. Roles and Responsibilities

5.1 General Practitioners, Practice Nurses, Occupational Health and front-line Hospital Staff

GPs, practice nurses and occupational health practitioners should be able to advise on the necessity for PrEP and administer primary and booster courses as appropriate. They should be aware which laboratories will perform serologic testing (see section 3.3.4), and advise on this or offer this service as appropriate.

GPs, practice nurses, front-line hospital staff, or occupational health are likely to be the first point of medical contact for people who have had a PRPE. The health professional should seek the advice of an ID physician if there is any doubt as to whether the incident carries a risk of exposure to rabies. Unless the health professional is entirely clear on the protocol for risk assessment and administration of PEP the patient should be referred to the appropriate ID department for management and for all instances where HRIG is indicated.

5.2 Infectious Disease Physician/Consultant

The ID physician should, when consulted by a health professional, assist in the risk assessment of any PRPE. The ID physician will take on the management of patients requiring PEP as appropriate and after discussion with the referring health professional. Patients requiring HRIG should be managed by the ID physician. The ID physician should inform their NHS Board HPU of any information suggesting that the wider population might be at risk.

5.3 Consultant in Public Health Medicine

The CPHM has no responsibility in the management of individual occurrences of PRPE. If a member of the public asks for the advice of the CPHM regarding a PRPE, the CPHM should advise them to contact their GP immediately and ascertain if there is any wider risk to the general public. If a GP, or front-line member of hospital staff contacts the CPHM they should be directed to this guidance and, if necessary advised to seek the opinion of an ID physician. If the CPHM identifies any risk to the wider public they should decide on and ensure the implementation of appropriate measures to safeguard the public's health. The CPHM should consider the need to communicate advice to professional colleagues and members of the public, and, in consultation with their communications teams, the formulation of a reactive or proactive media strategy.

5.4 Health Protection Scotland

HPS's 'Fitfortravel' website provides the general public with advice on PrEP for travellers. Travax provides specialist advice to health care professionals and clinicians throughout the UK (registration required). HPS also advises health protection professionals and clinicians throughout Scotland on the indications for PrEP in non-travellers.

HPS has no responsibility in the management of individual occurrences of PRPE. If a member of the public asks advice from HPS regarding a PRPE, HPS should advise them to contact their GP immediately and ascertain if there is any wider risk to the general public. If HPS identifies any risk to the wider public they should inform the appropriate CPHM. If a GP, or front-line member of hospital staff contacts HPS they should be advised to access this guidance and if appropriate seek the opinion of an ID physician.

HPS does not currently have a surveillance system for incidents of PRPE and does not need to be informed of such incidents.

5.5 Other agencies

5.5.1 Bat Conservation Trust

The BCT is a charity whose aims include promoting awareness of bats. It works with other organisations to promote best practise when handling bats or dealing with bat issues.

BCT run a telephone helpline throughout the year with an additional out of office hours service from May – September. Helpline staff are often the first point of advice when someone comes into contact with a bat. Helpline staff do not give medical advice. They do advise callers on wound care and stress that that the caller MUST seek medical advice from their GP.

The BCT will also ascertain where the bat is and if still present what condition it is in (alive/dead). When a bat is still present staff will give advice on retaining the bat safely and or avoiding further risk to humans. They can then contact a local bat expert to:

- remove the bat,
- identify the species,
- observe the bat's behaviour and
- give any other information that might be helpful e.g. in assessing the risk, preventing further encounters.

5.5.2 Scottish Natural Heritage

Scottish Natural Heritage (SNH) is a non-departmental public body, funded by Scottish Government and responsible through Ministers to the Scottish Parliament. Its purposes are to promote the care and improvement, responsible enjoyment, greater understanding and appreciation, and sustainable use of the natural heritage, now and for future generations. Its mission is to promote 'All of nature for all of Scotland'.

SNH provides advice to members of the public and other interest groups on the management of bats and their roosts. Many of these enquiries come from home owners/occupiers with bats in their property. SNH employs licensed bat workers to visit (principally) domestic premises to collect the necessary information and provide advice to the occupants as required. Bat workers sometimes need to handle bats in the course of their work and are therefore required to have up-to-date rabies vaccinations and to wear the appropriate protective clothing as a condition of their employment.

Since 2003, SNH has taken the lead on a programme of active EBLV seroprevalence monitoring in Scotland, focussing primarily on Daubenton's bats. This study has provided annual national estimates of EBLV-2 seroprevalence in this species from a selection of sample sites and has detected a single bat with evidence of the virus. The information from this study is used to inform policy on the management of bat roosts and our advice to others.

5.5.4 Scottish Government

Scottish Government works to ensure that National Policies across the areas of animal and human health respond to the challenge of rabies and change in epidemiology and treatment. Implementation is across the Animal Health Agency, Local Authorities, NHS Boards, and other organisations.

In the case of a significant rabies incident the NHS Board must notify the Chief Medical Officer's team of the Scottish Government using the out of hours contact number if necessary.¹⁶

5.5.5 Pharmacy

Hospital pharmacies may have some involvement in arranging supply and delivery of HRIG but initial requests for HRIG should be channelled through one of the three main SNBTS Service Centres (see section 4.3). It is expected that responsibility for supply of HRIG will revert to hospital pharmacies once the transition of plasma products from SNBTS to pharmacies is completed during 2011.

6. References

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- 7 Department of Health (2006) Immunisation against infectious disease 2006 - The Green Book (updated 13 October 2010). http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/@dh/@en/documents/digitalasset/dh_063658.pdf. [Accessed 24, November 2010].
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- 11 Naraporn, N, Khowplod, P, Limsuwan, K, Thipkong, P, Herzog, C, Glueck, R, Tantawichien, T, and Wilde, H. Immune response to rabies booster vaccination in subjects who had postexposure treatment more than 5 years previously. *J Travel Med*, 1999; 6:134-6.
- 12 The Statement of Financial Entitlements (SFE). http://www.isdscotland.org/isd/servlet/FileBuffer?namedFile=GMS_statement_of_financial_entitlements_200910.pdf&pContentDispositionType=inline [Accessed 24, November 2010].
- 13 CDC. Human Rabies Prevention—United States, 2008: Recommendations of the Advisory Committee on Immunization Practices. *MMWR Recomm Rep*. 2008;57(RR-03):1–28.
- 14 Transmission by aerosol in bat caves is almost unheard of. See Irons JV, Eads RB, Grimes JE, Conklin A. The Public Health Importance of Bats. *Texas Rep Biol Med*. 1957;15:292-298.
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Appendix 1: Development of the guideline

This guideline represents the view of a multidisciplinary group convened in Scotland for this purpose in 2009, and working together for the course of a year. Under the auspices of the Health Protection Network (HPN), the guideline development group (GDG) followed a systematic development framework proposed by the HPN (see <http://www.hps.scot.nhs.uk/pubs/redirect.aspx?id=38927>), in line with the principles of SIGN methodology.

Recommendations given in this guideline resulted after careful review and consideration of the evidence available and principles of best practice. The evidence base for this guideline was synthesised from that collated using an explicit search strategy devised by the GDG to identify relevant guidelines from English speaking countries, only supplemented by supporting literature to cover identified evidence gaps. The search covered MEDLINE, EMBASE, CINAHL and various public health databases, meta-search engines, and internet, from 1990 to August 2010. The evidence base was updated during the course of development of the guideline, and the search was supplemented by reviewing references and key guidelines identified from WHO, CDC, the European Union, and from personal databases of the guideline development group members. Further details on the search strategy can be requested from HPS – contact found through the HPN website <http://www.hps.scot.nhs.uk/about/contactus.aspx>.

The GDG appraised selected guidance documents with the AGREE instrument and supporting literature using basic appraisal principles. The GDG found that the conventional grading systems available do not correspond to the range of literature and evidence supporting this document. As a result of this, it was unanimously decided not to grade the recommendations given in the guideline. Reference to supportive evidence has been given, though, where relevant literature was found.

Professionals involved in the investigation and management of immunisation against rabies in Scotland, are expected to take this guideline fully into account when exercising their professional judgment. The guidance does not, however, override the individual responsibility of professionals to make decisions appropriate to the circumstances of the individual cases, in consultation with partner agencies and stakeholders.

Implementation of this guidance is the responsibility of health professionals across Scotland. Professionals are reminded that it is their responsibility to implement the guidance, in their local context, in light of their duties to avoid unlawful discrimination and to have regard to promoting equality of opportunity.

Nothing in this guidance should be interpreted in a way which would be inconsistent with compliance with those duties.

Rabies Guidance Development Group

John Cowden, Health Protection Scotland (HPS)

Consultant Epidemiologist (Chair)

Sam Allan, Ayrshire & Arran NHS Board

ID Consultant,

Lynda Browning, Health Protection Scotland (HPS)

Epidemiologist

Julie Gallagher, Lothian NHS Board

General Practitioner

Fiona Genasi, Health Protection Scotland (HPS)

Nurse Consultant

Rachel Green, Scottish Blood Transfusion Service (SNBTS)

Clinical Director

Hilary Kirkbride, Health Protection Agency (HPA)

Consultant Epidemiologist

Malcolm McWhirter, Scottish Government Health Directorate

Senior Medical Officer

Chris McGuigan, Tayside NHS Board

Consultant in Public Health Medicine (CPHM)

Cameron Stewart, Animal Health & Chair of Scottish Zoonoses Group

Veterinary Officer,

Anne Youngman, Bat Conservation Trust (BCT)

Scottish Bat Officer,

Alex Sánchez-Vivar, Health Protection Scotland

National Coordinator of the Health Protection Network (HPN)

Appendix 2: Contact Details

Telephone numbers

Health Protection Scotland	0141 300 1100
Bat Conservation Trust helpline:	0845 1300 228

Scottish National Blood Transfusion Service Centres:

West (<i>Gartnavel General, Glasgow</i>)	0141 357 7802/3/4
South East (<i>Royal Infirmary, Edinburgh</i>)	0131 536 5392
North East (<i>Forresterhill, Aberdeen</i>)	01224 552 322

Scottish Infectious Disease Units

Aberdeen Royal Infirmary	0845 456 6000
Crosshouse Hospital	01563 521 133
Gartnavel General Hospital	0141 211 3000
Monklands Hospital	01236 748 748
Ninewells Hospital	01382 680 111
Victoria Hospital	01592 643 355
Western General Hospital	0131 537 1000

Websites

HPS	http://www.hps.scot.nhs.uk
HPS Rabies Geographical Country list	http://www.hps.scot.nhs.uk/giz/publicationsdetail.aspx?id=46633
TRAVAX	http://www.travax.nhs.uk
Fitfortravel	http://www.fitfortravel.nhs.uk

Notes

