27 Rabies

27.1 Introduction

27.1.1 Rabies is an acute viral infection resulting in encephalomyelitis. The incubation period is generally between two and eight weeks, but may range from nine days to two years or more. 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 spasms, or 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 treatment.

27.1.2 Infection is usually via the bite of a rabid animal. Rarely, transmission of the virus has occurred through mucous membranes. It does not occur through intact skin. Virus is present in some tissues and fluids of patients with rabies, but person-to-person spread of the disease has not been documented with the exception of six cases acquired through corneal grafts. No case of indigenous human rabies has been reported in the United Kingdom since 1902 although cases occur from time to time in persons infected abroad.

27.1.3 Rabies in animals occurs in all continents except Australasia and Antarctica. Canine rabies is endemic throughout most of Asia, Africa and Latin America. In Europe foxes are the predominant host but many other animals become infected including dogs and cats, cattle, horses, badgers, martens and deer; mass oral immunisation campaigns have reduced the numbers of reported cases of animal rabies in recent years. In the United States, rabies in animals has become more prevalent since the 1950s; skunks, raccoons and bats account for 85% of animal cases. The UK has been free of indigenous animal rabies since 1922 apart from the identification of a single rabid bat on the Sussex coast in 1996.

27.2 Vaccine

27.2.1 Rabies human diploid cell vaccine (HDCV) is a freeze dried suspension of Wistar rabies virus strain PM/WI 38 1503-3M cultured in human diploid cells and inactivated by beta-propiolactone. The potency of the reconstituted vaccine is not less than 2.5 International Units per 1ml dose. It contains traces of neomycin.

■ 27.2.2 The freeze dried vaccine should be stored at 2-8°C and not frozen. It should be used immediately after reconstitution with the diluent supplied and any unused vaccine discarded after one hour. It may be given by deep subcutaneous, intramuscular or intradermal injection (see 27.4.3 and 27.4.5) usually into the deltoid region.

■ 27.2.3 Rabies-specific immunoglobulin

Human rabies immunoglobulin (HRIG) is obtained from the plasma of immunised human donors. It is used after exposure to rabies to give rapid protection until rabies vaccine, which should be given at the same time, becomes effective.

■ 27.3 Recommendations

■ 27.3.1 Pre-exposure (prophylactic) immunisation

Pre-exposure immunisation with human diploid cell rabies vaccine should be offered, and is available free from the NHS, to:

a. Laboratory workers handling the virus.

b. Those who, in the course of their work, regularly handle imported animals e.g.

- at animal quarantine centres
- at zoos
- at research and acclimatisation centres where primates and other imported animals are housed
- at ports e.g. certain Customs and Excise officers
- carrying agents authorised to carry imported animals
- veterinary and technical staff at the Ministry of Agriculture, Fisheries and Food (MAFF), the Scottish Office, Agriculture, Environment and Fisheries Department, (SOAEFD) and the Department of Agriculture for Northern Ireland (DANI).
- inspectors appointed by local authorities under the Diseases of Animals Act. (This does not include all local authority dog wardens for whom the risk of exposure is low and for whom post exposure prophylaxis in the event of an incident is likely to be more appropriate.)

c. Licensed bat handlers

d. Workers in enzootic areas abroad who by the nature of their work are at special risk of contact with rabid animals (e.g. veterinary staff or zoologists).

e. Health workers who are likely to come into close contact with a patient with rabies.

■ 27.3.2 Pre-exposure immunisation is also recommended for those living or travelling in enzootic areas who may be exposed to unusual risk of being infected or are undertaking especially long journeys in remote parts where medical treatment may not be immediately available. (More detailed country by country advice is contained in the UK Health Departments' book 'Health Information for Overseas Travel'). For these individuals, the vaccine is not supplied free from the NHS.

■ 27.4 Route of administration and dosage

■ 27.4.1 For primary pre-exposure protection, three doses of 1.0ml of HDCV should be given, on days 0, 7 and 28, by deep subcutaneous or intramuscular injection in the deltoid region. (The antibody response may be reduced if the gluteal region is used.)

■ 27.4.2 For travellers who are not animal handlers, two doses of 1.0ml by deep subcutaneous or intramuscular injection four weeks apart can be expected to give immunity in 98% of recipients and may be acceptable if post exposure treatment is likely to be readily available. For those at continued exposure a further dose should be given 6-12 months later.

■ 27.4.3 **Use of the intradermal route:** When more than one person is to be immunised, the vaccine may be administered in smaller doses (0.1ml) by the intradermal route in either of the above schedules. The intradermal route may also be used for rapid immunisation of, for example, staff caring for a patient with rabies, giving 0.1ml of vaccine intradermally into each limb (0.4ml in all) on the first day of exposure to the patient. **Intradermal immunisation is reliable only if the whole of the 0.1ml dose is properly given 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 suppresses the antibody response. The use of the intradermal route is on the doctor's own responsibility as this is not covered by the manufacturer's Product Licence.**

■ 27.4.4 **Reinforcing doses:** Where post-exposure treatment is readily available, as in the UK, reinforcing doses are not normally required for individuals who have received three doses of vaccine unless exposure occurs (when post exposure treatment should be given) or unless exposure is regular and continuous (e.g. laboratory workers handling the virus, licensed bat handlers).

■ 27.4.5 For those at regular and continuous risk in the UK, and where post-exposure treatment is not readily available and there is continued risk, single reinforcing doses of vaccine should be given at two to three year intervals, the interval to be reviewed after 2-3 reinforcing doses (but see 27.4.6 and 27.5.1).

■ 27.4.6 The three dose primary pre-exposure course produces protective antibody in virtually 100% of recipients and makes routine post-immunisation serological testing unnecessary. Serological testing is advised for those who work with live virus. They should have their antibodies tested every six months, and be given reinforcing doses of vaccine as necessary to maintain protective levels. Serological testing is otherwise only advised for those who have had a severe reaction to a previous dose of vaccine to confirm the need for a reinforcing dose.

■ 27.4.7 All travellers to enzootic areas should also be informed by their medical advisers of the practical steps to be taken if an animal bite is sustained (see 27.4.8).

■ 27.4.8 **Post exposure treatment**

In the event of possible exposure, firstly, as soon as possible after the incident, the wound should be thoroughly cleansed by scrubbing with soap and water under a running tap for five minutes. Secondly, the name and address of the owner of the animal should be obtained and the animal observed for ten days to see if it begins to behave abnormally. If necessary, the assistance of local officials should be sought. Thirdly, advice should be taken from a local doctor. If the animal is wild or a stray and observation is impossible, the doctor will know if rabies occurs in the locality and if immunisation is advised.

■ 27.4.9 For travellers returning to this country who report an exposure (break in skin or contamination of mucosal surface) to an animal abroad, treatment, including cleaning the wound as above, should be started as soon as possible while enquiries are made about the prevalence of rabies in the country concerned and, where possible, the ownership and condition of the biting animal. Information should be sought from the PHLS Virus Reference Division, London (0181-200 4400); in Scotland, the Scottish Centre for Infection and Environmental Health (0141-946 7120); in Northern Ireland, the Public Health Laboratory, Belfast City Hospital (01232 329241).

■ 27.4.10 Subsequent treatment will depend on the risk of rabies in the country concerned and the immune status of the individual, and **each incident has to be judged on its merits. Points to consider include if the animal is indigenous (native) or not, its behaviour, the site and severity of bite and whether the bite was provoked.**

■ 27.4.11 Summary of post-exposure prophylaxis:

Rabies risk in country of incident	Unimmunised/incompletely immunised individual*	Fully immunised individual
No Risk (27.4.13)	None	None
Low Risk (27.4.15)	5 doses HDCV	2 doses HDCV
High Risk (27.4.17)	5 doses HDCV plus human rabies specific immunoglobulin	2 doses HDCV

*persons who have been immunised by the intradermal route, or who have received fewer than 3 doses of vaccine, or whose last dose of vaccine was given more than 2 years previously.

■ 27.4.12 **NO RISK:** generally no rabies post exposure prophylaxis needed, however each incident needs to be judged separately (see 27.4.10).

■ 27.4.13 The following countries are considered 'no risk':

Europe:	*Cyprus, Faroe Is, Finland, Gibraltar, Greece, Iceland, Ireland, Malta, Norway (mainland), Mainland Spain exc N.African coast, Sweden, United Kingdom, Portugal, Italy (except the Northern & Eastern borders).*
Americas:	*Bermuda, St Pierre & Miquelon, Anguilla, Antigua & Barbuda, Bahamas, Barbados, Cayman Is, Dominica, Guadaloupe, Jamaica, Martinique, Montserrat, Netherlands Antilles, St Christopher & Nevis, St Lucia, St Martins, St Vincent & the Grenadines, Turks & Caicos Is, Virgin Is.*
Asia:	*Japan, Singapore, Taiwan.*
Oceania:	*American Samoa, Australia, Belau, Cook Is, Federated States of Micronesia, Fiji, French Polynesia, Guam, Kiribati, New Caledonia, New Zealand, Niue, Northern Mariana Is, Papua New Guinea, Samoa, Solomon Is, Tonga, Vanuatu, Western Samoa.*

■ 27.4.14 **LOW RISK**: vaccine only required:

a Previously unimmunised individuals should be given five doses of 1.0ml HDCV, one each on days 0, 3, 7, 14 and 30.

b Previously fully immunised individuals should be given two doses of 1.0ml HDCV, one on day 0 and one between days 3-7.

Vaccine must be given by deep subcutaneous or intramuscular injection into the deltoid region (not gluteal) or, in a child, the anterolateral aspect of the thigh.

■ 27.4.15 The following countries are considered low risk:

France, Belgium, Germany, Luxembourg, Netherlands, Switzerland, Denmark, USA and Canada.

If the animal can be reliably observed and remains well for 10 days, immunisation may not be required.

■ 27.4.16 HIGH RISK

a. Previously unimmunised individuals should be given immunoglobulin as well as vaccine as follows:

i. Immunoglobulin: human rabies specific immunoglobulin 20iu/kg body weight, up to half the dose infiltrated in and around the wound after cleansing and the rest given by intramuscular injection;

ii. Vaccine: five doses of 1.0ml HDCV by deep subcutaneous or intramuscular injection into the deltoid muscle (not the buttocks) or, in children, anterolateral thigh, one each on days 0, 3, 7, 14 and 30.

b Previously fully immunised individuals: two doses of 1.0ml HDCV given as above, the first on day 0 and the second between days 3-7. Immunoglobulin treatment is not needed.

■ 27.4.17 Countries considered high risk are:

Parts of Mexico, El Salvador, Guatemala, Peru, Colombia, Ecuador, India, Nepal, Pakistan, Philippines, Sri Lanka, Thailand, Vietnam. Also most other countries in Asia, Africa and South America.

■ 27.4.18 Up to date advice should be obtained from the Virus Reference Division, Central Public Health Laboratory, Colindale, London (0181-200 4400) or in Scotland from the Scottish Centre for Infection and Environmental Health (0141 946 7120) as the country-by-country risk groups may change.

■ 27.4.19 Human rabies is a notifiable disease. In the event of a case of human rabies, the Consultant in Communicable Disease Control (in Scotland, the Chief Administrative Medical Officer) should be informed.

■ 27.5 Adverse reactions

■ 27.5.1 HDCV may cause local reactions such as redness, swelling or pain at the site of injection within 24-48 hours of administration. Systemic reactions such as headache, fever, muscle aches, vomiting, and urticarial rashes have been reported. Anaphylactic shock has been reported from the USA and Guillain-Barré syndrome from Norway. Reactions may become more severe with repeated doses.

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

■ 27.5.3 Suspected adverse reactions should be reported to the Committee on Safety of Medicines using the yellow card system.

■ 27.6 Contraindications

■ 27.6.1 There are no absolute contraindications to HDCV, although if there is evidence of hypersensitivity, subsequent doses should not be given except for post-exposure treatment.

■ 27.6.2 Pre-exposure vaccine should only be given to pregnant women if the risk of exposure to rabies is high.

■ 27.7 Supplies

■ 27.7.1 Human diploid cell vaccine (HDCV) is available from Pasteur Merieux MSD Ltd (Tel. 01628 773200).

HDCV for pre-exposure immunisation of those at occupational risk is available from the PHLS Virus Reference Division, Tel. 0181-200 4400. For others, it can be obtained through local pharmacies by private prescription.

For post-exposure use, vaccine is supplied by centres listed in the PHLS Directory. Information may be obtained from the PHLS Virus Reference Division, the Scottish Centre for Infection and Environmental Health or Northern Ireland Public Health Laboratory, Belfast City Hospital, Lisburn Road, Belfast BT9 7AB.

■ 27.7.2 Human rabies immunoglobulin (HRIG) is manufactured by Bio Products Laboratory (BPL) and supplied through some Public Health Laboratories (see above), also BPL and the Scottish National Blood Transfusion Service. Supply centres in Scotland for HDCV and HRIG are listed in the Scottish Office Home and Health Department, Memorandum on Rabies. In Northern Ireland, HDCV and HRIG are available from The Public Health Laboratory, Belfast City Hospital (Tel. 01232 329241).

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