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Rabies

Introduction

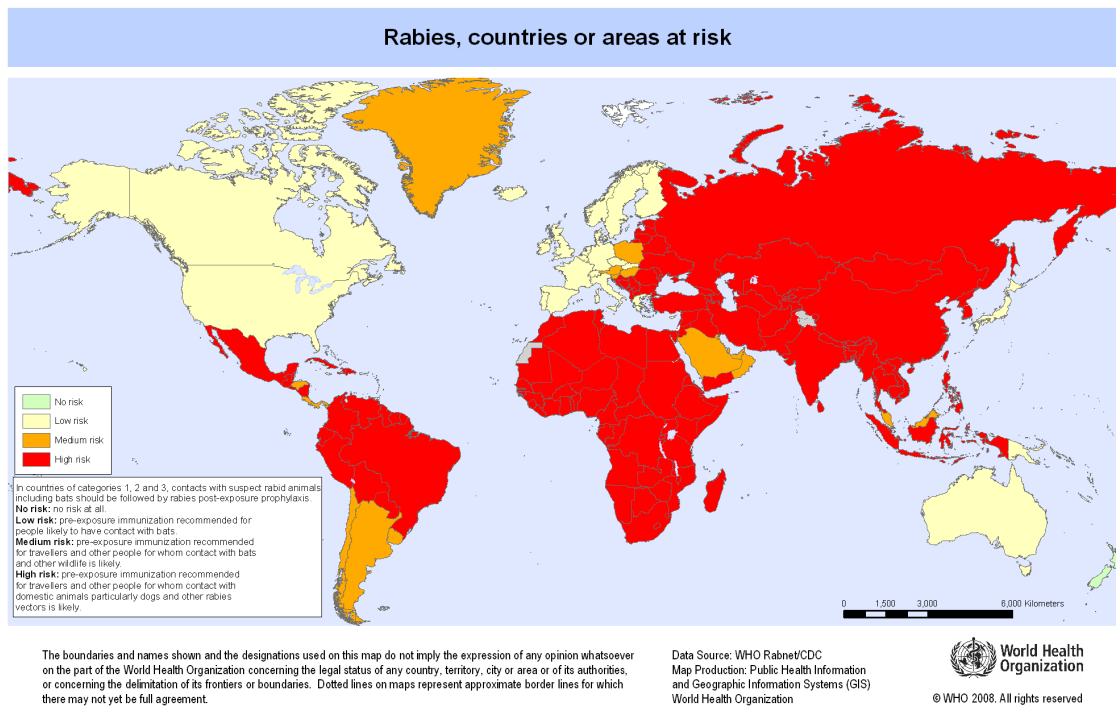
Rabies virus is a member of the genus *Lyssavirus*, of the family *Rhabdoviridae*, or bullet-shaped viruses. The virus attacks the central nervous system, causing progressive paralysis, encephalitis and coma. Once symptoms are present, rabies is a fatal infection.

Rabies occurs in warm-blooded mammals (both domestic and wild) and is transmitted to man, usually by a bite from an infected animal.

Epidemiology

Global epidemiology

Rabies: Countries at risk 2008



Map courtesy World Health Organization (International Travel and Health, 2009).

According to WHO data, more than 3 billion people are at risk of acquiring rabies in at least 85 countries worldwide [1]. Most parts of the African and Asian continents and many parts of Latin America are endemic for rabies. An estimated 10 million people worldwide receive post-exposure treatments each year after being bitten by a suspected rabid animal, usually a dog [1].

The annual number of deaths worldwide caused by rabies is estimated to be between 50,000 and 60,000; accurate data on the worldwide incidence is scarce. More than half of the deaths occur in South Asia, but the true disease burden of rabies is thought to be largely underestimated especially in Africa. The vast majority (>95%) of the deaths occur in regions where stray dog populations are ineffectively controlled. This, combined with limited availability of human post-exposure prophylaxis, contributes to the high mortality rates [1].

The UK is considered free of rabies in terrestrial animals; cases of rabies in bats are occasionally reported.

Most of Western Europe is rabies-free due to the success of co-ordinated wildlife oral vaccination programmes, together with the availability of effective commercial vaccination for domestic animals [2]. However, since October 2008, an outbreak of rabies in wild animals has occurred in the Friuli-Venezia Giulia region of north-east Italy [3], the first outbreak of rabies in Italy since 1995. Incidents involving imported animals also occur, such as the rabid dog imported into south western France from North Africa in 2004 [4]. Rabies is endemic in wild animals of North America and in the forests of Eastern Europe.

Rabies in UK travellers

The last case of indigenous terrestrial animal rabies occurred in Great Britain in 1922. The last recorded cases of animal rabies outside quarantine occurred in 1969 and 1970 when two imported dogs died soon after completing six months quarantine. Since then, nearly all cases of rabies in the UK have occurred in quarantined animals or in people who were infected abroad. The exception was human rabies in a bat handler infected with European Bat Lyssavirus 2 (EBL2) in Scotland in 2002 [5]. It is now recognised that UK bats can carry EBL2; a rabid bat was found in Surrey in 2004, another in Oxfordshire in 2006 and one in Shropshire in 2008 [6,7,8].

There have been 24 human deaths in the UK from imported rabies since 1902. All but two of these resulted from a dog bite (one was from a cat and the other exposure was unknown) and 63% of deaths were after a bite that occurred on the Indian Sub-Continent. The four cases that have been imported since 2001 are:

- an overseas visitor from Nigeria who sustained a dog bite on the lower leg five months prior to clinical symptoms [9].
- a UK resident who was bitten by a dog whilst in the Philippines [10]
- a British woman who sustained a dog bite during a two week holiday to Goa, India and died of rabies in the UK in 2005 [11]
- a British woman who had worked in an animal sanctuary in South Africa and died of rabies in Northern Ireland in January 2009 [12].

None of these cases were known to have received pre-or post-exposure rabies prophylaxis.

Risk for travellers

It is estimated that rabies kills more than 50,000 people each year worldwide [13]. Most of these deaths occur in Asia, Africa and Latin America, and follow a bite from an infected dog. Each of these regions have large stray dog populations that pose a risk to humans if they are bitten or have other trans-cutaneous or mucosal exposure to infected saliva. Other mammalian hosts of rabies in these regions include bats, monkeys, mongoose and jackal.

In North America and Europe the disease is mainly confined to wild animals (particularly bats, racoons, foxes, coyote, and skunks); in North America human cases have usually followed exposure to an infected bat.

Transmission

Rabies virus is found in the saliva of an infected animal. The virus is transmitted to humans by a bite, or when saliva from an infected animal comes into contact with broken skin or mucous membranes (eyes, nose, or mouth). Rarely, rabies has been contracted following laboratory exposure or after transplantation of organs from an infected individual [14,15].

Signs and symptoms

The incubation period of rabies is between 20 and 90 days; in rare cases it can be as short as a few days or as long as several years. The prodrome is often non-specific with symptoms of fever, headache, myalgia, and fatigue. Paresthesiae can occur at the site of the bite. The disease progresses to the more common furious rabies, or the less common paralytic or 'dumb' rabies.

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

The paralytic form of rabies is often misdiagnosed. Paresthesiae and weakness often first occur around the bite site and begin to ascend the bitten limb. The paralysis results in respiratory failure and inability to swallow. Death usually occurs within 1-3 weeks.

Treatment

All travellers who have a possible exposure to the rabies virus, whether by bites, scratches, or other means, should seek medical advice without delay. Seeking medical care also applies to travellers in areas considered low risk for rabies as other infections may be transmitted by the bite, or the animal may have been imported or crossed the border from an endemic country [4]. Medical advice should be sought without delay even if pre-exposure vaccine was received.

Although a few patients have survived rabies [16], the disease is considered fatal once symptoms manifest themselves.

Prevention

Contact with wild or domestic animals during travel should be avoided. Travellers should be advised:

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

Pre-exposure vaccine should be given to [travellers at risk](#). A record of vaccination should be carried and shown to those administering emergency treatment in a post-exposure situation

Receiving rabies vaccine prior to travel does not eliminate the need for post-exposure medical evaluation and additional doses of rabies vaccine.

Advice should be given to all travellers regarding first aid in the case of a possible rabies exposure [17].

- This is an emergency. Treatment should be commenced as soon as possible after the exposure.
- Immediately wash the wound with soap and running water for 5 minutes.
- If possible apply an iodine solution (tincture or aqueous solution of povidone-iodine), ammonium compounds e.g. cetrimide solution 0.15%, or 40-70% alcohol.
- Seek immediate medical advice about the need for rabies vaccination and possible antibiotics to prevent a bite wound infection. Tetanus vaccine may be necessary if the traveller is not up-to-date.

Rabies Pre-Exposure Vaccine

Indications for use of vaccine

Assessment of the need for pre-exposure rabies vaccine includes [18]:

- The incidence of rabies in the destination countries.
- The availability and quality of rabies vaccine and rabies immune globulin (RIG).
- The planned activities of the traveller.
- The duration of stay.
- The possibility of unrecognised or unreported exposure (e.g. young children).

Rabies pre-exposure vaccine should generally be given to adults and children who are at risk of rabies including

- Those travelling to remote areas where medical care is not readily available
- Those undertaking higher risk activities (e.g. cycling, running)
- Those who are travelling for long periods through rabies endemic countries
- Those at occupational risk e.g. vets, animal handlers, and laboratory workers who handle the virus.

Other specific indications for vaccination can be found in *Immunisation against Infectious Disease* [17].

The rationale for receiving pre-exposure vaccine is that it gives the individual time to reach medical treatment in the event of an animal bite or scratch; it may also protect an individual who has an unapparent exposure. Those who have received a pre-exposure course of rabies vaccine will require two further doses of vaccine post-exposure (according to UK schedules), rather the full course of five vaccines. In addition, rabies immune globulin (RIG) will not be necessary.

Accessing safe and effective rabies vaccine products in low income countries may be difficult, and vaccine derived from animal brain tissue may be the only type available. In some areas modern tissue culture rabies vaccines may only be obtained privately or in rabies treatment centres. RIG is frequently difficult to locate and only available in major cities [18].

Travellers should be advised to perform first aid treatment on a wound and to seek medical advice as soon as possible

Availability of vaccine (in the UK)



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

Details of licensed vaccines are found in the Table:



Table. Vaccine schedules

Vaccine	Manufacturer/distributor	Route of administration	Schedule	Length of Protection	Age Range
Rabies Vaccine BP (Human diploid cell vaccine) (HDCV)	Sanofi Pasteur MSD	Intramuscular	3 doses. Day 0, 7 and 28*	For those at regular and continuous risk, a single reinforcing dose should be given 1 year after the primary course and thereafter at 3-5 year intervals. For those at intermittent risk travelling to rabies endemic areas a booster dose should be given from 2 years after the primary course.	No minimum age stated in SPC, however, vaccine should be considered for children from the age of approximately 1 year. Bites in children may be higher risk as they often occur around the face or head.

The SPC should be consulted prior to the administration of any vaccine.

*see interrupted/accelerated courses

Vaccine	Manufacturer/distributor	Route of administration	Schedule	Length of Protection	Age Range
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<p>Rabipur® (Purified chick embryo cell vaccine) PCECV)</p>	<p>Distributed by MASTA</p>	<p>Intramuscular</p>	<p>3 doses. Day 0, 7 and 21 or 28*</p>	<p>For those at regular and continuous risk, a single reinforcing dose should be given 1 year after the primary course and thereafter at 3-5 year intervals.</p> <p>For those at intermittent risk travelling to rabies endemic areas a booster dose should be given from 2 years after the primary course.</p>	<p>Can be given from any age. Vaccine should be considered for children as bites may be higher risk as they often occur around the face or head</p>
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The SPC should be consulted prior to the administration of any vaccine.

*see interrupted/accelerated courses

It is good practice to continue a course of rabies with the same brand of vaccine. However, should this not be possible, the vaccines can be used interchangeably.

Intradermal route of administration

The intradermal (ID) route is not licensed in the UK for any rabies vaccine and is not recommended by the UK Department of Health [16]. ID vaccination requires specialist training and expert technique. Pre-exposure vaccination using the ID route is approved by the WHO [1]. Clinicians who chose to administer rabies vaccine intradermally must assume responsibility for using this method [17].

Interrupted or accelerated courses

Ideally, those at risk should receive pre-exposure vaccination with three doses of inactivated rabies vaccine before travel. A 0, 7 and 21 day schedule can be given using either product, where there is less than four weeks before departure [17].

If there are time constraints to the full pre-exposure course, a single dose is likely to prime the immune system; travellers should complete the pre-exposure course of vaccine during their travels. A record of vaccination should be carried as this will be useful during post-bite evaluation.

Travellers need to understand that if less than the recommended three doses of vaccine have been administered pre-exposure, in the event of a possible exposure, a full post-exposure course of vaccine will be required. However, RIG will not usually be necessary.

Expert advice may be needed for individuals who have previously received an interrupted or incomplete course of vaccine and who are travelling to an area where they may be at risk.

Contraindications

- Acute febrile or other infectious illness.
- Allergy to any constituent of the vaccine.
- Individuals who develop symptoms suggestive of hypersensitivity after vaccination should not receive further doses of the same vaccine.
- Rabipur vaccine is propagated on chick embryo cell, and is therefore contraindicated for those with have a known anaphylaxis to egg.

Post vaccination serology

Post vaccination serology, to determine the level of rabies neutralizing antibody, may be useful in some circumstances, but should not be undertaken routinely for travellers. Further advice is available by calling the [NaTHNaC advice line for health professionals](#).

Advice regarding vaccination and post vaccination serology for those at occupational risk and bat handlers is available from the [Health Protection Agency](#).

Adverse events

Adverse events to rabies vaccine tend to be mild and transient and include itching, pain, and erythema at the injection site. Less commonly fever, malaise, headaches, dizziness, and urticaria occur. An immune-complex reaction (serum sickness) of urticaria, pruritis and malaise occurs in about 6% of persons receiving booster doses of HDCV [19].

Post exposure prophylaxis

Advice regarding post-exposure prophylaxis should be sought from the Health Protection Agency (HPA) Virus Reference Division, Colindale on 020 8200 4400.

If they are not available, the duty doctor at the HPA Centre for Infections should be consulted (020 8200 6868).

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Further reading

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Health Protection Agency Centre for Infections. Rabies. Available at:
http://www.hpa.org.uk/infections/topics_az/rabies/guidelines.htm

World Health Organization. RABNET. Available at <http://www.who.int/rabies/rabnet/en/>

Links

Rabies Bulletin Europe: <http://www.who-rabies-bulletin.org/>

Pan American Health Organization, Rabies page:
<http://www.paho.org/Project.asp?SEL=TP&LNG=ENG&ID=64>

[World Health Organization. Rabies Fact Sheet](#)

World Health Organization, Rabnet: <http://www.who.int/globalatlas/default.asp>