

Approach to management of suspected rabies exposures

What primary care physicians need to know

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Case descriptions

Case 1. A 35-year-old man is jogging in his neighbourhood and runs past a house where the family dog is leashed to a fence. He gets too close and the dog bites him on the leg. He seeks care from his family physician who wonders about the need for rabies postexposure prophylaxis (PEP).

Case 2. A 15-year-old girl is sitting on a park bench with her mother on a warm summer day. All of a sudden, she feels pain in her lower leg and notices that a raccoon has bitten her. Startled, she yells out and the raccoon runs away. She is taken to the emergency department for treatment and the physician on duty wonders about the need for rabies PEP.

Case 3. A 60-year-old woman wakes up at her cottage one morning and finds a bat flying around her bedroom. She chases it out of the cottage and mentions the story to her neighbour. Her neighbour recalls reading something about “bats and rabies” and suggests that the woman discuss the issue with her family physician.

Case 4. During a routine annual physical examination, the family physician of a 22-year-old university student notices a scar on the student's right leg. When asked about the cause, the patient sheepishly admits that a dog bit him 3 months ago during his summer vacation in India. Despite feeling and appearing clinically well, the physician contemplates calling the local public health department for advice regarding the need for rabies PEP.

Rabies is a preventable viral disease primarily infecting domestic and wild animals.

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Abstract

OBJECTIVE To review the role of primary care physicians, in conjunction with local public health units, in the management of suspected rabies exposures and to outline the current guidelines for the administration of rabies postexposure prophylaxis.

SOURCES OF INFORMATION Published guidelines on the topic of rabies were reviewed and additional articles were identified from key references. Various public health websites were also explored. Most evidence was level II or III.

MAIN MESSAGE Primary care physicians must always consider the risk of rabies when treating patients who have had animal-to-human exposures (eg, bite, scratch), and if indicated, postexposure prophylaxis must be administered as soon as possible because the infection is fatal once clinical symptoms develop.

CONCLUSION Human cases of rabies are almost entirely preventable if suspected exposures are identified and managed promptly and properly. Primary care physicians must continue to work together with local public health officials in order to minimize the threat of this deadly virus.

Résumé

OBJECTIF Revoir le rôle du médecin de première ligne, en collaboration avec le département local de santé publique, devant une possibilité d'exposition au virus de la rage et rappeler les directives concernant l'administration de la prophylaxie post-exposition à ce virus.

SOURCES DE L'INFORMATION On a relevé les directives de la littérature concernant la rage et repéré d'autres articles à partir des références bibliographiques. On a aussi consulté divers sites Web sur la santé publique. La plupart des preuves étaient de niveaux II ou III.

PRINCIPAL MESSAGE Le médecin de famille doit toujours penser au risque de rage en présence de patients qui ont été en contact avec un animal (p. ex., morsure ou égratignure) et s'il y a indication, s'assurer que la prophylaxie post-exposition soit administrée dès que possible puisque cette infection est fatale lorsque les symptômes cliniques apparaissent.

CONCLUSION Les cas de rage chez l'humain sont presque entièrement évitables si l'exposition est identifiée et traitée promptement et adéquatement. Le médecin de première ligne doit travailler de concert avec les agents locaux de santé publique afin de minimiser la menace que présente ce virus mortel.

The virus can be transmitted to humans through close contact with a rabid animal. Exposures consist of bites and nonbites (eg, scratches, cuts, exposure of mucous membranes) and have also occurred via organ transplantation from infected individuals.^{1,2} In Ontario, according to the Health Protection and Promotion Act, physicians are obligated to report any suspected human rabies exposure to their local public health departments for risk stratification.³ This is logical given that many patients who have had exposures present initially to primary care physicians (eg, family physician, emergency department physician) for medical treatment. The importance of recognizing and reporting suspected exposures to public health authorities stems from the nature of the rabies virus itself. The rabies virus is inevitably fatal in humans once it reaches the central nervous system. Patients develop inflammation of the brain (encephalitis) and usually die within a few days.^{2,4,5} If, however, a patient receives treatment in the form of PEP before the onset of symptoms, then clinical disease will be prevented.^{1,2,4,6} After exposure, the incubation period before clinical symptoms develop has been reported to be about 20 to 60 days, with some sources reporting symptoms as early as 5 days, depending on the severity of the encounter (eg, multiple bites to the head and neck region).¹ The patient, therefore, must be treated quickly with PEP to prevent the development of a fatal infection. Cases of human rabies have occurred even months or years after exposure. The latest rabies-related death in Canada involved a patient from Alberta who presented with clinical symptoms of rabies 6 months after suffering a bat bite.⁵ It is therefore important to consult public health authorities for all patients who present with suspected rabies exposures irrespective of the incubation period that has elapsed.^{1,3}

In Canada, PEP consists of a combination of wound treatment along with the administration of rabies vaccine (active immunization) and human rabies immune globulin RabiG (passive immunization) to a patient after an exposure to a potentially rabid animal.^{1,7} In the province of Ontario, PEP is a public health responsibility, and the decision to start treatment is made in consultation with the local Medical Officer of Health.³ If indicated, the vaccine and RabiG are delivered to the patient's primary care physician for administration. The Medical Officer of Health not only serves as an authority to provide advice to physicians on the management of suspected rabies exposures, but also helps ensure that the supply of vaccine does not become depleted. There is currently a limited supply of rabies vaccine available in North America.⁸

Sources of information

Most of the articles reviewed were recently published guidelines or systematic reviews and contained level II and III evidence. Additional articles were identified from key references within articles. Information on this topic was also obtained from various public health websites,

including the Public Health Agency of Canada, the US Centers for Disease Control and Prevention, and the Ontario Ministry of Natural Resources.⁸⁻¹⁰

Epidemiology

In Canada, the prevalence of human infection with the rabies virus is low.¹ Since 2000, there have only been 3 clinical cases, with the most recent occurring in Alberta in 2006.⁵ All 3 cases involved unrecognized bat exposures and resulted in fatalities, as PEP was not administered.^{1,5} The reason for the low number of cases has to do with Canada's strong public health infrastructure.¹⁰ In Ontario, mandatory vaccination of domestic animals, along with an oral bait vaccination program that delivers rabies vaccine to wildlife has helped reduce the incidence of animal rabies and minimize the risk of human exposure.⁹ Rabies, however, is still a serious public health threat in developing countries. In Asia and Africa there are approximately 50 000 human deaths each year resulting from rabies infection.^{6,10} Given the increasing amount of international travel, the risk of rabies exposure remains an important public health issue worldwide. In 2007, more than 70 countries around the world participated in the first annual World Rabies Day to raise awareness in support of human rabies prevention and animal rabies control.¹¹ Citizens traveling to rabies-endemic countries are of particular concern in Canada. Canadian family physicians must feel comfortable counseling their patients on the risks of rabies exposure while traveling as well as assessing the need for PEP should a suspected exposure occur.

Practical approach

When physicians encounter a patient presenting with an animal-to-human exposure, a proper history should be taken in order to generate a preliminary risk assessment. Some suggested questions to ask include the following:

- **WHERE did the exposure occur?** This is important, as the rabies virus is more prevalent in some countries than in others (eg, developing countries).
- **WHAT type of animal was involved?** Typically in Canada, wild animals (eg, raccoons, skunks, foxes, bats) are more likely to be infected with the rabies virus than are domestic animals (eg, dogs, cats, ferrets). Small rodents (eg, rats, mice, squirrels) and lagomorphs (eg, rabbits, hares) usually do not carry the rabies virus¹ (**Table 1**).³

Levels of evidence

Level I: At least one properly conducted randomized controlled trial, systematic review, or meta-analysis

Level II: Other comparison trials, non-randomized, cohort, case-control, or epidemiologic studies, and preferably more than one study

Level III: Expert opinion or consensus statements

Table 1. Rabies postexposure prophylaxis (PEP) guide

ANIMAL TYPE	CONDITION OF ANIMAL AT TIME OF EXPOSURE	PEP RECOMMENDATIONS
Dogs, cats, and ferrets	Healthy and available for 10-d observation	PEP should not be initiated unless animal develops clinical signs of rabies*
	Rabid or suspected to be rabid Unknown or escaped	Start PEP immediately
Skunks, raccoons, foxes, bats, [†] and other carnivores	Consider rabid unless proven negative by laboratory tests [‡]	Start PEP immediately
Livestock, rodents, lagomorphs (rabbits and hares), and other mammals	Consider individually	Bites of squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, other small rodents, rabbits, and hares almost never require PEP unless behaviour of animal was highly unusual

*During the 10-d observation period, consult a veterinarian and the public health department if any sign of illness develops in the animal that might be consistent with rabies. If it is determined that the animal is exhibiting clinical signs of rabies, the exposed victim should be started on PEP and the animal should be immediately euthanized and sent for testing to confirm the diagnosis. Consider starting PEP immediately if the bite wound is to the head and neck region.

[†]If a bat is found in a room where someone was sleeping unattended or where the person sleeping was an infant, a child, impaired, or mentally challenged, risk of exposure should be assumed to be high, and the local public health unit should be contacted.

[‡]If available, the animal should be euthanized and tested as soon as possible. Holding for observation is not recommended. Discontinue PEP if laboratory test results of the animal are negative for rabies.

Adapted from the *Canadian Immunization Guide*, 7th edition, and the *Guidelines for Management of Suspected Rabies Exposures*.^{1,3}

- **WHY did the exposure occur?** An unprovoked exposure is usually more typical of a rabid animal's behaviour than a provoked exposure.^{1,4}
- **WHO is the animal's owner?** It is important if the animal involved is a domestic dog, cat, or ferret, as public health inspectors can track down the location of the animal for observation purposes. If the animal is healthy, it might be possible to avoid administering PEP to the exposed patient^{1,4,6} (Table 1^{1,3}).

The next step in evaluating the patient involves examining the wound. Immediately wash and flush the wound thoroughly with soap and water or a povidone-iodine solution, if available. This is very effective in reducing rabies transmission.¹ Next, examine the patient for any signs of infection that might warrant antibiotic therapy. If the patient is due for a tetanus vaccination, provide it at this time.¹⁻³

Finally, a decision regarding the need for vaccination and RabIg must be made. This is usually done in consultation with public health authorities.¹⁻³ In Ontario, the appropriate dose of RabIg along with 5 doses of rabies vaccine will be sent to the reporting physician's office or emergency department for administration.³ The 2 vaccines licensed for rabies PEP in Canada are IMOVAX Rabies (human diploid cell vaccine)^{1,7} and RabAvert (purified chick embryo cell culture vaccine),^{1,7} and the 2 RabIg products available are Imogam and HYPERRAB S/D. Both the RabIg and vaccine must be kept under cold-chain conditions in a refrigerator between 2°C and 8°C before administration.¹

Postexposure prophylaxis

Human rabies immune globulin. Human rabies immune globulin is administered as 1 dose on the first day of PEP treatment only (day 0). The dose is 20 IU/kg, and RabIg is supplied in 2-mL vials containing 150 IU/mL. The public

health department usually provides a chart to help calculate the amount of RabIg required for administration. Use the following formulae to calculate the dose required and Table 2³ to determine how many vials to administer:

$$20 \text{ IU/kg} \times (\text{patient weight in kg}) \div 150 \text{ IU/mL} = \text{dose in mL}$$

OR

$$9.09 \text{ IU/lb} \times (\text{patient weight in lb}) \div 150 \text{ IU/mL} = \text{dose in mL}$$

Table 2. Human rabies immune globulin (RabIg) dose-weight table: RabIg is supplied in 2-mL vials containing 150 IU/mL.

PATIENT'S TOTAL WEIGHT		NO. OF VIALS
LB	KG	
≤33	≤15	1
34-66	16-30	2
67-99	31-45	3
100-132	46-60	4
133-165	61-75	5
166-198	76-90	6
199-231	91-105	7
232-264	106-120	8
265-297	121-135	9
298-330	136-150	10

Adapted from *Guidelines for Management of Suspected Rabies Exposures*.³

If anatomically feasible, the full dose of RabIg should be thoroughly infiltrated in the area around and into the exposed wounds. Any remaining volume should be injected intramuscularly (IM) at a site distant from vaccine administration (eg, opposite deltoid [or thigh muscle in infants] to where the vaccine was injected).²

If there is no exposed wound, the entire dose of RabIg should be given IM with no more than 4 mL per injection site. For example, a 60-kg patient would require 8 mL of RabIg (20 IU/kg x 60 kg = 1200 IU; 1200 IU ÷ 150 IU/mL = 8 mL) to be administered into the exposed wounds. If no exposed wounds are present, all of the RabIg should be injected IM at 2 muscle sites (4 mL per site).³

Postexposure prophylaxis failures have occurred in cases in which RabIg was not administered appropriately (eg, wounds were not infiltrated or the dose was not calculated properly).^{1,2} The purpose of administering RabIg is to provide patients with immediate, but temporary, antibodies that begin to neutralize the virus during the time when their immune system is generating an active antibody response to the multiple doses of rabies vaccine.² If RabIg is not administered on day 0 of the PEP regimen, it can be given up to 7 days after the first dose of rabies vaccine has been received. After the seventh day, RabIg is no longer indicated, as an active antibody response to vaccine is presumed to have occurred.²

Vaccine. The rabies vaccine is administered in 5 doses over a total of 28 days. Each dose (1 mL) should be given IM in the deltoid (or anterolateral upper thigh in infants) on day 0, 3, 7, 14, and 28. The dose of vaccine should *never* be given in the gluteal muscle, as administration in this area might result in lower neutralizing antibody titres.² The vaccine should also *never* be given at the same site that RabIg was administered. Although most of the above instructions will be explained when consulting with public health officials, it is important for health practitioners to review the pharmaceutical monograph before administering the vaccine.^{1,3}

Postexposure prophylaxis against the rabies virus (combining wound treatment, local infiltration of RabIg, and vaccine administration) is uniformly effective when given appropriately and when there is not a substantial delay in treatment after exposure.² The above rabies PEP regimen applies to all suspected human exposures except for exposures in those who have received PEP previously (eg, those who have had previous animal-to-human exposures and received treatment). In these circumstances, no RabIg is required after a subsequent exposure and only 2 doses of vaccine are administered (1 dose on day 0 and 1 dose on day 3).^{1,3} It is important to emphasize to patients that receiving rabies PEP only protects them against the most recent exposure and does not provide lifelong immunity. All subsequent exposures require additional assessment to determine the need for PEP; if necessary, a less intensive course is provided as described above. The latter statement also applies to individuals who have received rabies preexposure prophylaxis (eg, veterinarians, animal workers, and travelers to rabies-endemic areas).^{1,6,10}

EDITOR'S KEY POINTS

- While rabies infection among humans is relatively rare in Canada, the potential for exposure to the virus still exists through domestic and wild animals, especially bats, and through international travel.
- Although the incubation period of the rabies virus is 20 to 60 days in most cases, there have been cases involving longer incubation periods ranging from several months to years. The rabies virus is inevitably fatal in humans once it reaches the central nervous system; however, if patients receive postexposure prophylaxis before the onset of symptoms, then clinical disease will be prevented.
- Postexposure prophylaxis consists of a combination of wound treatment and active (rabies vaccine) and passive (human rabies immune globulin) immunization.

POINTS DE REPÈRE DU RÉDACTEUR

- Même si l'humain contracte rarement la rage au Canada, cette infection demeure possible via divers animaux domestiques ou sauvages, notamment les chauves-souris et aussi lors de voyages à l'étranger.
- La période d'incubation de la rage est le plus souvent de 20 à 60 jours, mais on a observé des cas où elle atteignait plusieurs mois ou années. Chez l'humain, la rage est inexorablement fatale une fois que le virus a atteint le système nerveux central; la phase clinique sera toutefois évitée si le patient reçoit la prophylaxie post-exposition avant l'apparition des symptômes.
- La prophylaxie post-exposition comprend le traitement de la blessure et une immunisation active (vaccin anti-rabique) et passive (immunoglobuline humaine).

Case resolutions


Case 1. The jogger has likely provoked the dog by getting too close, causing the dog to bite him. In this case, the dog, a domestic pet that is likely vaccinated, can be isolated and observed for a 10-day period. If the animal does not show any clinical signs of rabies during the observation period, then the jogger does not need PEP. Studies have shown that dogs, cats, or ferrets that are infected and contagious for rabies will show clinical signs within 10 days. If these signs occur, the jogger should be given PEP immediately, and the dog should be euthanized and sent for confirmatory testing. If the rabies test on the animal is negative, PEP can be stopped.

Case 2. The girl was a subject of an unprovoked attack by a wild animal. These 2 features create a high-risk scenario for a suspected rabies exposure, and unless the wild animal is caught, tested, and found not to have the rabies virus, the girl should be given PEP.

Case 3. Bites and scratches from bats can be very minor and often go undetected if a person is attacked while sleeping. It is therefore recommended that any person who finds a bat in his or her bedroom after a period of unattended sleep be given PEP. If the bat can be isolated and tested for rabies, then PEP can be stopped in the event of a negative test result.

Case 4. This case emphasizes the importance of reporting all suspected rabies exposures to the local health department, irrespective of the time that has elapsed. In most cases the incubation period of the rabies virus is 20 to 60 days, but there have been cases involving longer incubation periods ranging from several months to years. The most recent rabies fatality in Alberta illustrates this point (eg, 6-month incubation period). The student's potential exposure should be reported to the local public health department and PEP should be started.

Conclusion

While cases of rabies infection among humans are relatively rare in Canada, the potential for exposure to the virus still exists via domestic and wild animals, especially bats.¹ Rabies also continues to be a substantial public health problem in developing countries, heightening the potential exposure for Canadians who travel internationally.⁶ Advise patients that preventive measures such as vaccinating domestic animals against rabies and avoiding contact with wild or stray animals are effective strategies to prevent viral spread.^{6,9} Front-line medical practitioners should be encouraged to report all animal-to-human exposures to local public health authorities so that a proper risk assessment for rabies can be made. By working together to identify suspected rabies exposures early, most human infections can be prevented. 

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Competing interests
None declared

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Protecting your family and pets against rabies

Steps to protect your family and pets against rabies

- Have your domestic pets vaccinated by a licensed veterinarian.
- Warn your family, especially young children, to stay away from wild or stray animals.
- Take measures to discourage wild animals from taking up residence in your home or on your property. For example, cover up potential entrances, such as uncapped chimneys and openings in attics, roofs, and decks. You might want to contact a professional for advice.
- Do not keep wildlife as pets.
- Report any animals behaving strangely to your local public health department or animal control office.
- Do not attempt to nurse a sick animal back to health. Contact your local public health department or animal control office for assistance.
- Report all dead animals found on your property to your local public health department. If you need to remove the carcass, wear protective gloves and use a shovel or other device to avoid direct contact.
- If you think you or any member of your family has been in contact with a suspected rabid animal, immediately contact your local public health department or family physician, or go to your local emergency department for advice regarding the need for postexposure prophylaxis.
- If a suspected wild rabid animal that has come in contact with a family member or domestic pet is available for capture, call your local public health department to arrange for definitive testing.

Adapted from the Ontario Ministry of Natural Resources.⁹

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