Rabies

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Information for this chapter was adapted with permission from Alberta Health: Alberta Public Health Disease Management Guidelines: Rabies

1. CASE DEFINITION

Confirmed Case

- Clinical illness* with laboratory confirmation of infection by either:
  - Detection of viral antigen in an appropriate clinical specimen (preferably the brain or the nerves surrounding hair follicles in the nape of the neck) by immunofluorescence ***OR***
  - Findings at autopsy including detection of rabies virus in central nervous system (CNS) tissue by immunofluorescence or RT-PCR and visualization of

Negri bodies by histopathology ***OR***
- Isolation of rabies virus from saliva, cerebrospinal fluid (CSF), or central nervous system tissue using cell culture or laboratory animal ***OR***
- Detection of rabies virus RNA by RT-PCR in an appropriate clinical specimen

Probable Case

- Clinical illness* with laboratory evidence:
  - Detection of rabies-neutralizing antibody in the serum or CSF of an unimmunized person who did not receive rabies immunoglobulin

Suspect Case

- Clinical illness* without laboratory evidence

*Clinical Illness: Rabies is an acute encephalomyelitis dominated by forms of hyperactivity (encephalitic "furious" rabies) or paralytic syndromes (paralytic "dumb" rabies) that almost always progresses to coma and death within 10 days after the first symptom.

2. REPORTING

All HCPs must follow the NWT *Public Health Act*. Measures for contact tracing and legislative requirements are laid out within the *Reportable Disease Control Regulations* and reporting timelines are found in the *Disease Surveillance Regulations*.

Note: the only acceptable methods of reporting to the OCPHO are outlined below. Information provided outside of these methods will not be considered reported unless otherwise stated by a CPHO delegate.

Health Care Professionals

For **Part 1** Call immediately and written report within 24 hours

- A confirmed, probable, or suspect rabies case in a human must be reported **immediately** after diagnosis is made or opinion is formed to the Office of the Chief Public Health Office (OCPHO) by telephone (867) 920- 8646 **AND** complete the Animal Bite/Rabies Investigation Form.
  - Submit to Communicable Disease Control Unit (CDCU) via secure medical fax 867-873-0442 or Secure File Transfer CDCU@gov.nt.ca
- Report all animal bites within 24 hours by completing the Animal Bite/Rabies Investigation Form and submit to:
  - Environmental Health (EH) via Secure File Transfer (SFT): environmental_health@gov.nt.ca
  - An EH Officer follows up on the animal investigation by contacting the person who was exposed and the animals owner if known.
- **Health care providers must call the OCPHO reporting line for post-exposure prophylaxis (PEP) recommendations for any of the following exposures:**
  - The exposure – bite, scratch, etc. is to HEAD or NECK or HANDS of the patient or,

- The animal is a wild mammal or bat,
- The animal lives mainly outside (e.g., sled dog or pet tied outside for most of the time) or,
- The animal cannot be located or is stray/unknown/unidentifiable or,
- The bite/exposure was not provoked or,
- The animal exhibited unusual behavior prior to the incident or,
- The animal for any cause dies within 10 days of the bite/exposure (or 14 days for livestock) or,
- The victim cannot provide a reliable history (young child, under the influence of alcohol or drugs, dementia, etc.)

- Report out of province or out of country rabies exposures or animal bites to CDCU by telephone (867) 920-8646 **immediately**. Information should include name, date of birth, and any positive laboratory reports or relevant information including details on any post exposure prophylaxis provided (name of vaccine, dose, administration route, and dates).
- If there are any updates regarding the case or contacts the appropriate form will need to be resent with additional information.

Laboratories

- Report all positive results to the OCPHO by telephone (867) 920-8646 **AND** by fax (867) 873-0442 **immediately.**

Additional Reporting

- When uncertain about an animals' behaviour or an animal is posing a safety risk it is recommended to report** to the following:
  - For wildlife: Environment and Climate Change (ECC) by calling your local Renewable Resource Officer https://www.gov.nt.ca/ecc/en/report-something#wildlife-emergencies or emailing WildlifeVeterinarian@gov.nt.ca
  - For domestic animals: Local law enforcement (By-law or RCMP)

**Unless there is a bite or exposure to a human do not call public health or the OCPHO.

3. EPIDEMIOLOGY

CAUSATIVE AGENT

- Rabies infection is caused by an RNA virus in the *Rhabdoviridae* family

CLINICAL PRESENTATION - HUMANS:

- Initial symptoms, lasting 4-10 days include headache, fever, malaise, flu-like illness, parenthesis at the site of animal exposure and a sense of apprehension

Two forms of the disease are possible:

- Encephalitic rabies ("furious" rabies) occurs in approximately 80% of human cases
  - Characterized by progressively worsening CNS manifestations such as anxiety, hyperactivity, excited behaviour, dysesthesia (abnormal sense of touch), pruritus

(itching), radicular pain, intense thirst but fear of water (hydrophobia), and dysautonomia (autonomic nervous system does not work properly). They may experience hyper-salivation, resulting in frothing at the mouth.
    - After a few days, death occurs by cardio-respiratory arrest
- Paralytic rabies ("dumb rabies") occurs in approximately 20% of human cases
    - Does not have the same CNS manifestations that furious rabies has
    - Paralysis ascends and the person becomes increasingly confused until coma occurs, then death
    - Paralytic forms are often misdiagnosed
- Rabies is almost invariably fatal

DIAGNOSIS – HUMANS:

- The diagnosis of rabies in humans typically requires more than one test ante-mortem and is made via detection of viral antigen by direct immunofluorescence or rabies virus RNA from appropriate clinical specimens
- Health care providers must consult with the Microbiologist/Virologist on call at ProvLab at University of Alberta Hospital (UAH) if they require stat testing for rabies. The virologist on call is available through UAH Switchboard (780) 407-8822
- The prospect for detecting infectious rabies virus, rabies virus antigen, and/or specific immune response increases as clinical symptoms progress
- Serology cannot distinguish between antibodies resulting from current infection or previous immunization
- Negative serological results do not rule out a rabies infection because antibodies may not develop during infection and seroconversion usually occurs very late or not at all. The majority of patients with rabies infection die without having seroconverted.

TREATMENT

Once symptoms have developed there is no specific treatment. Intensive supportive medical care is usually undertaken, but in most situations rabies is fatal. For patient-specific clinical management, consult your local healthcare professional, pediatrician, infectious disease specialist, and/or the NWT Clinical Practice Guidelines.

RESERVOIR

- Any mammal can develop rabies
- Rabies virus is maintained in nature within various types of wild and domestic carnivores (e.g., foxes, dogs, coyotes, wolves, ferrets, skunks, raccoons, cats) and bats. In developing countries, dogs remain the principal reservoir. Rabbits, hamsters, guinea pigs, gerbils, squirrels, chipmunks, rats, birds and mice are rarely infected. Although rodents and other small mammals are very susceptible to the virus, these small animals rarely survive the encounter with a larger rabid animal. In the NWT, rabies is enzootic

(regularly occurring) in the circumpolar north, particularly above the tree line where the arctic fox is the main reservoir. Rabies has been reported in domestic dogs (usually because of interaction with infected wildlife). In southern NWT, bats also represent a potential exposure risk.

- The Beaufort Delta and Sahtu regions have the highest proportion of animals diagnosed with rabies

TRANSMISSION

- Rabies is transmitted via a bite, scratch or lick that introduces saliva of an infected animal into a fresh break in the skin or contact with intact mucous membranes including the eyes, nose and mouth. Most cases of human rabies involve a bite from an animal with communicable rabies
- Aerosol transmission, although rare, has been reported in caves and laboratory settings
- Although the virus has been isolated from the saliva of infected people, making person-to- person transmission from a human bite is theoretically possible, such transmission has not been confirmed
- Activities that could potentially pose a risk to others include bites, kisses, direct contact between saliva and mucous membranes or broken skin, sexual activity, sharing utensils or cigarettes
- Transmission has been reported following corneal and other organ transplants, where the donors have died of undiagnosed rabies
- Mother-to-child transmission is possible, although rare
- Ingestion of raw meats or other tissues from animals infected with rabies is not likely a source of human infection but is not advised
- There have been documented cases in which people have contracted rabies from cuts or sprays while handling rabid animal carcasses and hides
- The virus is inactivated rapidly in sunlight (1.5h at 30^{o}C) and does not survive for long periods outside of the host (minutes to hours depending on environmental conditions)
- Ultraviolet light, detergent, ethyl alcohol, or a 1:10 dilution of bleach can destroy the virus

INCUBATION PERIOD

- The incubation period varies from a few days to more than 19 years; however, the majority of cases become ill within 90 days of exposure
- The incubation period is dependent on the severity of the wound, site of the wound in relation to the richness of the nerve supply, distance from the brain, the amount and strain of virus introduced, and if protective clothing was worn

PERIOD OF COMMUNICABILITY

- Humans: A person is considered infectious 14 days prior to the onset of symptoms
- Animals: The period of communicability varies depending on the species of the animal
  - On average, dogs and cats could be communicable as long as 10 days prior to clinical illness, but are most infectious 3-4 days before the onset of clinical disease, and throughout the course of disease
  - Period of communicability is not well documented in most animals and may vary across species

INCIDENCE

There have been no human cases of rabies reported in the NWT since rabies has been reportable in Canada. For more information on the epidemiology of Rabies in the Northwest Territories (NWT) see: Epidemiological Summary of Communicable Diseases: Rabies Exposure.

4. PUBLIC HEALTH MANAGEMENT

KEY INVESTIGATION

- Rabies post exposure prophylaxis (PEP) must be considered in every incident in which human exposure to a potentially rabid animal has occurred. Provision of rabies PEP after an exposure is contingent on risk assessment.
- All cases of rabies or rabies exposure (confirmed, probable, or suspect) must be managed as an **urgent time-sensitive issue, requiring immediate public health action**
  - Confirm that the client meets the case definition (confirmed, probable or suspect) OR has been exposed to an animal (wild or domestic) that requires a rabies risk assessment for rabies post-exposure prophylaxis
- Obtain a history of illness or exposure, including the date of onset, signs, and symptoms
- Determine the possible source of infection for all confirmed, probable, and suspect cases, taking into consideration the incubation period, reservoir, and mode of transmission. Assessment may include determining, obtaining, or identifying:
  - Travel/immigration history
  - Animal involved
  - Type of exposure (bite, scratch, other)
  - Details and nature of exposure
  - Geographic location of exposure
  - Immunization status of the animal (if possible, or applicable)
  - Determine the immunization status of the patient; Unless patient has a high-risk occupation or travel history, most of the population is not vaccinated against rabies (see appendix 1)

- Determine contacts, which includes those:
  - potentially exposed to the infected body fluids of the case, and/or
  - exposed to the same source (e.g., animal)

MANAGEMENT OF A BITE/EXPOSURE

- In any exposure situation (see above Reporting section) where the healthcare practitioner is considering administration of rabies immune globulin (RIG) or rabies vaccine**, they must call** the OCPHO Reporting Line at (867) 920-8646 for risk assessment and authorization
  - PEP of previously unimmunized individuals should consist of both rabies immune globulin and rabies vaccine as outlined in appendix 2
  - Determine the client's willingness and commitment to accept and complete rabies PEP. In situations where PEP is indicated, ensuring that risk of rabies and it's severity (fatality rate) and preventability is clearly communicated so the patient can make an informed decision
  - The consent for immunization and the importance of the timing of vaccine administration should be discussed with the client, as well as the required schedule for doses. Plan the immunization schedule with the client and confirm the location where the remaining doses will be given
  - If an individual fails to follow up for PEP, health centres and local public health should make every effort to facilitate further doses and follow up. The most responsible physician should be informed of potential loss to follow up. Clear documentation of efforts to compel the client to finish PEP should be made
  - Persons who present for evaluation and rabies PEP even months after having been exposed should be assessed in the same manner as if the exposure occurred recently. The variation in incubation periods for rabies requires investigation of all self-reported exposure regardless of length of time from incident
  - PEP started in another country requires individual assessment and consultation with the OCPHO
  - Pregnancy and breastfeeding are not contraindications to PEP
- Whenever possible, advise that the animal should be kept alive, contained or quarantined away from others and observable for 10 days following the exposure (or 14 days for livestock)

Animal Exposures Risk Assessment

- The risk of exposure to rabies increases when:
  - The exposure occurred in a geographical area where rabies is present
  - The animal species involved is known to be higher risk
  - The animal was not up to date with their rabies vaccinations
  - The animal looks ill or displays abnormal behaviour
  - The exposure was unprovoked
  - Unprovoked attacks from animals are signs of abnormal behaviour and could indicate an animal has rabies

  - Provoked attacks occur when a human (intentionally or unintentionally) triggers an attack or response, and the response from the animal is a normal response to such an action. Examples include startling, antagonizing, threatening an animal, or entering its territory or space.
- Type of exposure:
  - Bite exposures are the most common form of transmission of rabies virus. Multiple bites with prominent salivary contamination in highly innervated areas and near the brain pose the highest exposure risk
  - Direct contact with a bat can transmit rabies because small sharp teeth may transmit virus without an obvious wound. Direct contact with bats may not be evident and ALL exposures to bats (with or without known contact should be reported).
  - Non-Bite Exposures: can include aerosolization in laboratory settings or in enclosed spaces with bats, scratch from a rabid animal where the animal may have saliva and virus to their limb, or contamination of scratches, abrasions, open wounds, or mucous membranes by infectious material (saliva or brain tissue)

MANAGEMENT OF A CASE

- Because of the near 100% case fatality rate of rabies disease, public health source investigation and identification / prophylactic treatment of all persons exposed to the same source OR that came into contact with infected body fluids of the case should begin immediately if rabies infection is suspected
- Individuals should avoid contact with the saliva and tears of a rabies case
- The number of health care staff involved in care should be limited
- Healthcare providers should consult Infection Prevention and Control professionals and should maintain routine precautions all times during patient care. A point of care risk assessment should be completed at each interaction with the patient to inform the selection of PPE (gloves, gowns, medical masks, and eye protection) to protect nonintact skin and mucosal sites (i.e., eyes, nose, mouth).
- Health care providers should use airborne precautions during aerosol generating procedures such as intubation, suctioning, and autopsy because of potential aerosolization of the virus
- Concurrent disinfection (by detergent and/or 1:10 diluted bleach) of articles soiled with saliva or tears should be done as soon as possible, or be discarded as biohazard waste
- The use of needles or other sharp objects around the case should be limited so as not to risk accidental percutaneous exposure

MANAGEMENT OF CONTACTS

- A contact is a person who:
  - has been bitten by or who has an open wound/mucous membrane exposure to a rabies case or in the case of bats, have simply had direct contact or potential exposure (discovery of a bat in enclosed space such as a bedroom overnight where an exposure may have occurred unknowingly)
  - Was exposed to the same animal source as the rabies case
- Contacts should receive rabies post exposure prophylaxis (PEP) urgently. Post-exposure rabies prophylaxis of previously unimmunized individuals consists of both rabies immunoglobulin and rabies vaccine
- For PEP guidance and standards, NWT adopts the Canadian Immunization section on Rabies PEP, under Part 4—Active Vaccines, Rabies available at: https://www.canada.ca/en/public-health/services/publications/healthy-living/canadian-immunization-guide-part-4-active-vaccines/page-18-rabies-vaccine.html. These are summarized in appendix 2

PREVENTION/PREVENTATIVE MEASURES

- Pre-exposure rabies immunization should be considered for certain risk groups. See Appendix 1 for details
  - If rabies antibody titres fall below 0.5 IU/mL, a booster dose should be administered. Serologic testing is not needed after the booster unless the individual is immunocompromised or taking chloroquine/hydroxychloroquine
- Educate the public and those individuals at risk of animal exposure to avoid close contact with unfamiliar animals, and inform them about the following prevention measures:
  - Have all domestic pets immunized by a licensed veterinarian or a designated, veterinary-trained NWT lay-vaccinator
  - Avoid close contact with unfamiliar animals, wild or domestic, even if they appear friendly
  - Do not keep wild animals as pets. Avoid handling, feeding, or unintentionally attracting wild animals. Cover up potential entrances, such as uncapped chimneys and openings in attics, roofs, and decks to discourage wild animals, such as bats, from taking up residence in or around homes
  - Do not attempt to nurse a wild animal back to health. Seek assistance from a veterinary clinic or city by-law
  - When an exposure occurs, report to the nearest hospital, health centre, or clinic for assessment
  - Report* any animal(s) behaving strangely to the following:
    - For wild life: Environment and Climate Change (ECC) by email WildlifeVeterinarian@gov.nt.ca or calling your local Renewable Resource Officer

https://www.gov.nt.ca/ecc/en/report-something#wildlife-emergencies
    - For domestic animals: Local law enforcement (By-law or RCMP)

  *Unless there is a bite or exposure to a human do not call public health or OCPHO
- Do not handle dead carcasses without the proper PPE including gloves, masks, and eye protection
- When travelling with pets:
    - Ensure rabies immunizations are up to date
    - Keep pets under control to avoid contact with other animals (wild and domestic)

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Appendix 1 – Rabies Pre-Exposure Prophylaxis (PrEP)

Table 1: Rabies PrEP Series by risk group

Note: All rabies PrEP schedules can be administered using the 1-site IM or 2-site ID routes, including any subsequent booster doses if these are needed.

Group	Examples	PrEP Schedule	Serology
Very high risk	People who work with the rabies virus in a research or vaccine laboratory	3 dose primary series on days 0, 7, and 21-28	Every 6 months
High risk	People with regular/frequent bat exposures, people who perform necropsies on mammals due to suspect rabies, rabies diagnostic laboratory workers	3 dose primary series on days 0, 7, and 21-28	Every 2 years For immunocompromised or 65 years of age and older, routine serologic testing can be performed more frequently (every 6 months to 2 years) as per clinical discretion
Moderate risk	Veterinarians and their staff, veterinary students, lay vaccinators for domestic animals, animal control, animal shelter workers, wildlife workers, hunters, trappers, spelunkers (cave explorer), travellers* to areas where rabies vaccine is recommended	**Risk expected to extend 3 or more years, or duration of risk is uncertain:** 2-dose primary series on days 0 and 7-28 A booster dose is also recommended, ideally 12 to 24 months after the second dose. **Risk expected to be less than 3 years:** 2-dose primary series on days 0 and 7-28.	Generally, not recommended
Immuno-compromised	All risk groups identified above	3 dose primary series on days 0, 7, and 21-28	Serology at 2-4 weeks after primary series and after any subsequent/booster doses. If results are needed sooner, testing can be performed at 1 week following the completion of the primary series or booster dose. If very high risk or high risk they should also follow with recommendations for regular periodic serology as outlined above.

*See CATMAT's Statement on pre-exposure vaccination against rabies and animal bite prevention in the traveller: https://www.canada.ca/en/public-health/services/catmat/statement-pre-exposure-vaccination-rabies-animal-bite-prevention-traveller.html

Appendix 2 – Rabies Post Exposure Prophylaxis

Table 2: Post Exposure Prophylaxis procedures are highly dependent on the individual exposure risk assessment. **CPHO or designate must be consulted for all rabies post-exposure prophylaxis.**

Animal Species	Condition of animal at time of exposure	Management of exposed person
Large domesticate mammals (example: Dog, Cat, or Ferret)	Healthy and available for a 10-day observation period	• At first indication of rabies in the animal, consult OCPHO for risk assessment. • Local treatment of wound. See table 3 for more information on wound care. At first indication of rabies in the animal, arrange to have the animal tested for rabies
	Unknown or escaped	• Consult OCPHO for risk assessment • Local treatment of wound
	Rabid or suspected to be rapid	• Consult OCPHO for risk assessment and authorization of PEP • Refer to table 4 for PEP schedule • Local treatment of wound Arrange to have animal tested for rabies if available
Wild or undomesticated mammals (example: Skunk, bat, fox, coyote, racoon and other carnivores)	Regard as rabid unless geographic area is known to be rabies-free	• Consult OCPHO for risk assessment and authorization of PEP • Refer to table 4 for PEP schedule • Local treatment of wound • If the animal is available for rabies testing, in some instances PEP may be delayed no more than 48 hours while awaiting results • Arrange to have animal tested for rabies if available • For bats, consider PEP after direct contact or if contact cannot be ruled out (e.g., sleeping person, child)
Livestock, rodents or lagomorphs (hares and rabbits)		• Consult appropriate public health and environmental health officials. Bites of squirrels, chipmunks, rats, mice, hamsters, gerbils, guinea pigs, other small rodents, rabbits and hares would only warrant post-exposure rabies prophylaxis if the behaviour of the biting animal was highly unusual. Bites from larger rodents (e.g., ground hogs (woodchucks), beavers) require a risk assessment.

Table 3: Wound care based on exposure

Step	PHAC Guidance
Exposure Types	Bite, scratch, or contact with saliva in an open wound or mucosal membranes from a potentially rabid animal.
Immediate wound care	• Wash thoroughly with soap & water ≥ 15 minutes • Then wash the wound with 70% ethanol, an iodine-containing solution or Dakins solution (3 tablespoons of bleach plus ½ teaspoon baking soda in 1 litre of boiled water) • Do not suture the wound (or suture loosely) to allow free bleeding and drainage • Do NOT delay PEP for wound care

Table 4: Rabies PEP vaccine schedule and RabIg

- **Rabies Immunoglobulin (RabIg)**
  - RabIg provides immediate passive protection until the exposed person mounts a long-lasting immune response to the rabies vaccine
  - Recommended dose is 20IU/kg for all age groups. If possible, the full dose of RabIg should be thoroughly infiltrated into the wound and surrounding area. After infiltration, any remaining volume should be injected intramuscularly with a different needle and at a site distant from the site of vaccine administration. Refer to the product monograph for administration guidance: Rabies Immune Globulin product monograph
- **Rabies Vaccine**
  - Rabies Vaccine Preparations used in Canada include IMOVAX® Rabies (HDCV) and RabAvert® (PCECV)

Patient Information[1]	Number of doses	Dose schedule	Rabies Immune Globulin (RabIg)[2]
Immunocompetent Persons			
Previously unimmunized, **OR** Previously immunized with 1 dose, **OR** Previously immunized with 2 doses where the 2nd dose was administered more than 3 years ago	Four doses	Day 0, 3, 7, and 14	Should be given on the first day[3] of initiation of therapy (day 0)
Previously immunized[4] with at least 3 doses, **OR** Previously immunized[4] with 2 doses where the 2nd dose was administered within the last 3 years	Two doses	Day 0 and day 3	RabIg not indicated
Immunocompromised Persons[5]			
previously unimmunized, **OR** moderately to severely immunocompromised at the time of the exposure, regardless of immunization status **OR** Previously immunized with 2 or fewer doses **OR** Previously immunized with 3 doses or more without demonstration of adequate serology after completion of the primary series (no serology test or result less than 0.5 IU/mL)	Five doses	Day 0, 3, 7, 14, 28	One dose of RabIg on day 0[3]; serology should be checked 7 to 14 days after completion of the series to ensure that an acceptable antibody response has developed.
Previously immunized[4] with at least 3 doses with adequate serology after completion of primary series (equal to or greater than 0.5 IU/mL) **AND** mildly immunocompromised or no longer immunocompromised at the time of the exposure	Two doses	Day 0 and day 3	One dose of RabIg on day 0[3]; serology should be checked 7 to 14 days after completion of the series to ensure that an acceptable antibody response has developed.

[1]Pregnancy and breastfeeding are not contraindications to PEP

[2](Refer to the Canadian Immunization guidelines: Rabies vaccines for administration details)

[3]If RabIg is not administered at the initiation of the vaccine series, it should be administered up to and including day 7 after the vaccine series was initiated, but it should not be administered after day 7

[4]Requires documentation of completed course of pre-exposure or post-exposure prophylaxis

[5]**Unimmunized immunocompromised** include people:

- who have immunosuppressive illnesses
- taking chloroquine and other antimalarials
- taking corticosteroids or other immunosuppressive agent