



Our vision:

To excel as a science-based regulator, trusted and respected by Canadians and the international community.

Our mission:

Dedicated to safeguarding food, animals and plants, which enhances the health and well-being of Canada's people, environment and economy.

Key Learning Points

- General information on rabies and distribution in Canada
- Determination of exposure category
- Determination of risk of rabies virus presence in rabies suspect animal

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RABIES TESTING AT THE CFIA: GENERAL INFORMATION AND SUBMISSION GUIDELINES



RABIES

Rabies is a fatal disease of the central nervous system (CNS) resulting from infection by *Lyssavirus*, family *Rhabdoviridae*, the type species which is Rabies Virus (RABV). As RABV can infect all mammals, including humans, rabies is a zoonotic disease. Virus is usually spread through bites from rabid animals, though viral entry via saliva contamination of mucous membranes is also possible. RABV is global in distribution with the exception of Ireland, Japan, New Zealand, a number of Pacific island states and parts of Scandinavia. Australia, the United Kingdom and parts of continental Europe have *Lyssavirus* epizootics in bat species which are occasionally transmitted to other species, including humans. These bat *lyssavirus* are indistinguishable from other *lyssaviruses* in routine diagnostics. In North America, rabies is an endemic disease of wildlife including; skunks, foxes,

raccoons, and coyotes. These species, as well as bats and dogs serve as principal hosts ("reservoirs"). In Canada, the most prevalent variants of the RABV are associated with several bat species, as well as arctic and red foxes, raccoons and skunks, though many of these variants are restricted in their geographic distribution. For example, the Western skunk virus variant is associated with skunk populations in Saskatchewan and Manitoba, the arctic fox virus variant is endemic in arctic and red foxes in northern Canada, whereas the raccoon RABV variant is endemic in the eastern US, and has been the cause of several outbreaks in bordering provinces. RABV variants are adapted to their specific reservoir species. Some secondary hosts may also transmit these virus variants, but this is a rare occurrence. Generally, continuing transmission cycles are not maintained in the secondary

species, sometimes inappropriately referred to as "dead-end" hosts (e.g., cattle, horses and sheep). It is speculated that the behaviors and the dentition of these species account for the rarity of secondary transmission events, rather than the lack of potential, since most shed virus in their saliva. In Canada, all regions have species that may be infected with RABV making transmission of rabies to other mammals, including humans, possible. Information on rabies cases diagnosed at the CFIA laboratories can be found on the CFIA website: www.inspection.gc.ca.



Ottawa Laboratory Fallowfield

CANADIAN FEDERAL LEGISLATION AND CFIA LABORATORIES

Rabies is a federally reportable disease in Canada according to the *Health of Animals Act*, the *Health of Animals Regulations*, and the *Reportable Diseases Regulations*. The CFIA is a federal agency, whose President reports to the Minister of Health. The CFIA will gather diagnostic statistics in order to provide national occurrence reports as well as to meet international

reporting responsibilities. There are currently two CFIA laboratories which conduct rabies testing: the Ottawa Laboratory Fallowfield, (OLF) and the Lethbridge Laboratory (LL). Diagnosis of rabies in suspect animals and humans may be performed by the following tests: fluorescent antibody test (FAT); the formalin fixed assay (FFA); tissue culture inoculation test (RTCIT); virus variant

typing utilizing monoclonal antibody panels or sequencing; and molecular techniques including RT-PCR. All CFIA Laboratories have quality assurance programs and are ISO 17025 accredited. The OLF is a WHO Collaborating Center and an OIE Reference Laboratory for Rabies.

RABIES PATHOGENESIS

Rabies virus is labile outside a living host, and does not remain infective for long periods in the environment. Sunlight (ultraviolet radiation), heat, solvents, detergents, and oxidizing agents have been shown to rapidly inactivate the virus. The time required for complete inactivation is dependent on several factors such as total amount of virus present.

Rabies virus does not penetrate intact skin; it must be inoculated (e.g., by a bite) or deposited into a wound or onto a mucosal surface. Upon

introduction into the body, the virus begins to replicate in cells near the site of entry before infecting the peripheral nerves in this vicinity. The virus then migrates inside the infected peripheral nerve axons to the spinal cord and brain. Viral proliferation within nerve cells leads to neuronal dysfunction, and the infection of neurons in the central nervous system leads to increasingly severe neurological signs.

Once the virus is established in the central nervous system, it again spreads within nerve fibers from the spinal cord and

brain to peripheral organs, most importantly to the salivary glands, where it replicates and is shed in the saliva. The shedding of virus in saliva may occur a few days prior to the appearance of clinical signs. Experimentally, it was found that virus excretion in cats and dogs may occur 8 to 10 days prior to the onset of clinical signs.

There is no evidence to suggest that rabies virus is transmitted in either semen or embryos, or through blood.

**INCUBATION
PERIOD FOR RABIES
IS VARIABLE,
RANGING FROM
WEEKS TO
MONTHS.**

The time between the introduction of the virus into the body and the appearance of the first clinical signs (prodromal period) is known as the incubation period. During this time, the animal is clinically healthy and unable to transmit the disease to others. The incubation period is variable, and may range from weeks to months, though periods of 3-12 weeks are common for domestic animals. This

variability is influenced by the site of site of infection, the viral load, the virus variant, and the animal species that has been infected.

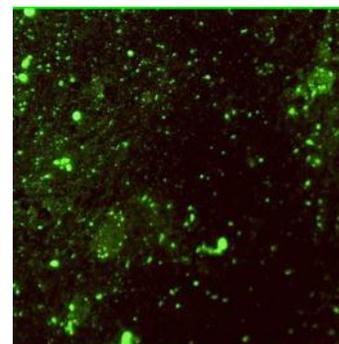
Generally, animals and humans do not mount a measurable immune response during the incubation period. Rabies virus specific antibodies are not always detectable in the serum or cerebrospinal fluid (CSF) even at late stages of infection, during the production of

abundant viral antigens. As such, serological methods that detect rabies antibody can not provide a diagnostic rule-out for rabies, and are not suitable for diagnosis of the disease in animals.

ANIMAL RABIES CASE DEFINITION

Any animal that tests positive for rabies by a test conducted at a CFIA laboratory is a rabies case.

Any animal that tests positive in another laboratory, for example, using the Direct Rapid Immunohistochemistry Test (DRIT) on wildlife surveillance samples, must have the diagnosis confirmed by the CFIA. Such confirmatory testing will be done free of charge.



**Rabies virus infected cells
detected by FAT**



EXPOSURE CATEGORIES TO RABIES SUSPECT ANIMAL (DOMESTIC)

A wild or domestic animal is considered to be rabies “suspect” when: a) there is a case history that includes compatible clinical signs, and b) it is found in a geographic area with either a known epizootic in a rabies reservoir species (i.e., bats, foxes, raccoons or skunks) or a high probability of introduction of rabies based on proximity to known infected areas or importation of the animal from a rabies endemic country.

The CFIA follows the World Health Organization Expert Consultation on Rabies (2nd Report, 2013) definitions of

exposure to determine eligibility for rabies testing. For CFIA purposes, classification of exposure relates both to humans and domestic animals.

Category III exposure is defined as single or multiple transdermal bites or scratches, licks on broken skin, or contamination of mucous membranes with saliva. Animals submitted for testing that have caused a Category III exposure will be tested at no charge.

Category II exposure is defined as nibbling of uncovered skin or minor scratches or abrasions without

bleeding. Animals submitted for testing that have caused a Category II exposure will be tested at no charge.

Category I exposure is defined as touching an animal or licks on intact skin, even if the animal is rabid. For humans, it also includes feeding of animals. There is no possibility of exposure to the rabies virus through these types of contact. Animals submitted for testing that have caused a Category I exposure, or no exposure at all, will be tested subject to cost-recovery.

ANIMAL BEHAVIOR AND CLINICAL SIGNS OF RABIES

Clinical presentation can be quite variable. Prodromal signs are fairly non-specific and can include lethargy, fever, vomiting, and anorexia. These may be followed by some or all of the following: abnormal behaviours, unprovoked aggression, abnormal gait, ataxia, paralysis, seizures, difficulty swallowing, excessive salivation, abnormal vocalizations, and self-mutilation. Infection of the brain with rabies virus leads to behavioural changes in the animal. Examples include nocturnal animals that become

active during the day, wild animals that lose their fear of humans or normally docile pets that show unprovoked aggression. An abnormally acting or biting animal is not necessarily rabid, but if rabies is known to be present in an area it must be given consideration. Many negative interactions with both wild and domestic animals arise from wilful or unintentional provocation. Understanding the “fight or flight” response in animals is important to understanding that an aggressive situation may be due to provocation and not rabies. For example, animals

that feel trapped or are cornered will often become aggressive, injured animals may become aggressive during traumatic situations, and animals that are being hurt may become aggressive, e.g., pulling a cat’s tail. Other reasons might account for the observed behaviour, e.g., a mother animal protecting its young can become aggressive, as can cattle with some metabolic conditions. The complete clinical picture and circumstances surrounding the observed behaviours should be considered during the disease investigation.

CFIA WILL TEST CATEGORY II AND III EXPOSURE SPECIMENS AT NO CHARGE. CATEGORY I EXPOSURE SPECIMENS ARE SUBJECT TO COST-RECOVERY.

RISK OF INFECTION WITH RABIES VIRUS

If the suspect animal displays clinical signs consistent with rabies, then the probability that the animal may have been exposed to rabies virus must be considered. Rabies in bats is endemic in Canada, however, for other species, consideration of the presence of rabies in the local geographic area is warranted. If the rabies suspect animal belongs to a known reservoir

for rabies virus in a geographic location where rabies is common, then there is a risk that the animal may be rabid. If the rabies suspect animal is a domestic animal, or a species not known to be a reservoir species or a reservoir species where terrestrial rabies is not common, then the probability of the animal having rabies is significantly reduced. If it is determined that there is

a risk that the rabies suspect animal may be infected with rabies virus, and a Category II or III exposure has occurred, then testing of the specimen may be indicated. For rabies suspect animals which are domestic species, the vaccination status has no bearing on the determination of the potential presence of rabies virus.



**For further information,
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DECISION TREE FOR RABIES SAMPLE SUBMISSION

The following questions should be answered to determine whether a sample should be considered for submission for rabies testing:

(1) Is the sample a bird, reptile, amphibian, or fish?

- A) **YES**—do not submit.
- B) **NO**—proceed to 2.

(2) Has the rabies suspect animal caused a Category II or III exposure to a human or a domestic animal?

- A) **NO**—do not submit (testing is available under cost-recovery).
- B) **YES**—proceed to 3.

(3) Is the rabies suspect animal a bat?

- A) **YES**—submit for testing.
- B) **NO**—proceed to 4 .

(4) Is there a risk that the rabies suspect animal has been infected with the rabies virus?

A THOROUGH INVESTIGATION AND PROFESSIONAL JUDGMENT ARE REQUIRED TO ANSWER THIS QUESTION. CONSIDER THE FOLLOWING:

Circumstances of the exposure, e.g., the nature of any aggression (unprovoked or intentional/unintentional provocation); the rabies suspect animal's behavior; presence of clinical signs of rabies; the geographic area (e.g., northern and western Canada where rabies is enzootic in terrestrial reservoir species, foxes and skunks, respectively); for domestic animals, is there the potential for contact with a rabid animal, such as a reservoir species or a bat? The vaccination status of the animal should not impact the decision to test.

- A) **YES**—submit for testing.
- B) **NO**—do not submit (testing is available under cost-recovery).

Caveat: For pet species such as dogs and cats with a single act of aggression, but which otherwise appear healthy, an observation period may be warranted.