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Contributors:

Dr. Earle Goodman, Editor
Dr. Leroy Dorminy, Co-Editor

Animal Rabies Prevention & Control

Adapted and edited by Peter Quesenberry (DVM, MPVM) from an article by _____ at the Centers for Disease Control and Prevention.

Rabies is a fatal viral zoonosis and a serious public health problem. The recommendations in this article serve as a basis for animal rabies prevention and control programs.

Part I

A. Principles of Rabies Prevention and Control.

1. **Rabies Exposure.** Rabies is transmitted only when the virus is introduced into bite wounds, open cuts in skin, or onto mucous membranes from saliva or other potentially infectious material such as neural tissue.
2. **Human Rabies Prevention.** Rabies in humans can be prevented either by eliminating exposures to rabid animals or by providing exposed persons with prompt local treatment of wounds combined with post exposure vaccination. In addition, pre-exposure vaccination is effective and helpful.
3. **Domestic Animals.** Local governments should initiate and maintain effective programs to ensure vaccination of all dogs, cats, and ferrets and to remove strays and unwanted animals.
4. **Rabies in Vaccinated Animals.** Rabies is rare in vaccinated animals. If such an event is suspected, it should be reported to public health officials.
5. **Rabies in Wildlife.** The control of rabies among wildlife reservoirs is difficult.

Note from the Editor

This is our Silver Anniversary (25th) Issue. Over the years, we have been blessed by the contributions of very knowledgeable authors. We also owe a debt of gratitude to our readers, who have made suggestions for future articles and have provided practical tips that help us balance technical and practical information.

The first issue of this publication focused on rabies. The response was so great that we decided to continue for several years with the theme of "zoonotic conditions" (diseases and parasites of animals which can cause health problems in humans). Since the original articles were published, there have been many advances in the knowledge of these conditions. Therefore, from time to time we will revisit these topics, beginning with this issue's update on rabies.

While this information was developed for the U.S, it applies to a great extent to most areas of the world. However, one of the main areas of variation is the problem of wildlife and how it impacts directly and indirectly on human rabies. For that reason, only general information is given in this article.



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Christian Veterinary Mission • 19303 Fremont Ave. N., Seattle, WA 98133

Phone: (206) 546-7569 • Fax: (206) 546-7548 • Email: missionvet@aol.com Website: www.cvmusa.org

Therefore laws prohibiting the importation, distribution, and relocation of wild animals are very important.

6. **Rabies Surveillance.** Laboratory-based rabies surveillance is an essential component of rabies prevention and control programs.
7. **Rabies Diagnosis.** Rabies testing should be performed by a qualified laboratory. Cares should be taken to ensure that the brain and its parts are recognizable by the laboratory. Only send in the head or brainstem, except in the case of very small animals, such as bats. It is better to refrigerate the specimen than to freeze it. In addition try not to use chemicals to preserve the tissue. Questions about testing of fixed tissues should be directed to the local rabies laboratory.
8. **Rabies Serology.** Some "rabies-free" areas may require evidence of vaccination and a blood test for importation purposes. Note - even if an animal has titers of rabies antibodies in its blood, a current vaccination or a booster vaccination are also important.

B. Prevention and Control Methods in Domestic and Confined Animals.

1. Preexposure Vaccination and Management.

- **Primary Vaccination.** Within 28 days after primary vaccination, a peak rabies antibody titer is reached and the animal can be considered immunized. An animal is currently vaccinated and is considered immunized if the primary vaccination was administered at least 28 days previously and vaccinations have been administered correctly.
- **Booster Vaccination.** Regardless of the age of the animal at initial vaccination, a booster vaccination should be administered 1 year later. An animal is considered currently vaccinated immediately after a booster vaccination.
- **Overdue booster vaccination.** If a previously vaccinated animal is overdue for a booster, it should be revaccinated.

Immediately following the booster, the animal is considered currently vaccinated and should be placed on an annual or triennial schedule depending on the type of vaccine used.

- **Livestock.** Consideration should be given to vaccinating livestock that are particularly valuable or that might have frequent contact with humans.
- **Confined Wild Animals.** No parenteral rabies vaccines are licensed for use in wild animals or hybrids (the offspring of wild animals crossbred to domestic animals). Wild animals or hybrids should not be kept as pets.
- **Maintained in Exhibits and in Zoological Parks.** Captive mammals that are not completely separate from all contact with possible rabies carriers can become infected. Moreover, wild animals might be incubating rabies when initially captured. Therefore, wild-caught animals susceptible to rabies should be quarantined for a minimum of 6 months before being exhibited. Employees who work with animals at such facilities should receive pre-exposure rabies vaccination. The use of pre- or post-exposure rabies vaccinations for employees who work with animals at such facilities might reduce the need for euthanasia of captive animals. Carnivores and bats should be housed in a manner that precludes direct contact with the public.

2. Stray Animals. Stray dogs, cats, and ferrets should be removed from the community.

3. Importation and Movement of Animals.

a. Local Laws. Always check the local regulations on the importation and movement of animals. The movement of dogs from areas with dog-to-dog rabies transmission for the purpose of adoption or sale should be prohibited. This practice poses the risk of introducing canine-transmitted rabies to areas where it does not currently exist.

4. Additional Helpful Procedures. Methods or procedures which enhance rabies control include the



following: identification, licensing, house-to-house visitation of animal-owners, issuing of citations to owners for failing to vaccinate or license their animals, and hiring of staff to implement animal control laws.

5. Post-exposure Management. Any animal potentially exposed to rabies virus by a wild, carnivorous mammal or a bat that is not available for testing should be regarded as having been exposed to rabies.

a. Dogs, Cats, and Ferrets. Unvaccinated dogs, cats, and ferrets exposed to a rabid animal should be euthanized immediately. If the owner is unwilling to have this done, the animal should be placed in strict isolation for 6 months. Rabies vaccine should be administered upon entry into isolation or 1 month prior to release to comply with preexposure vaccination recommendations. Animals with expired vaccinations need to be evaluated on a case-by-case basis. Dogs, cats, and ferrets that are currently vaccinated should be revaccinated immediately, kept under the owner's control, and observed for 45 days. Any illness in an isolated or confined animal should be reported immediately to the local health department.

b. Livestock. All species of livestock are susceptible to rabies; cattle and horses are among the most frequently infected. Livestock exposed to a rabid animal and currently vaccinated should be revaccinated immediately and observed for 45 days. Unvaccinated livestock should be slaughtered immediately. If the owner is unwilling to have this done, the animal should be kept under close observation for 6 months. Any illness in an animal under observation should be reported immediately to the local health department.

The following are recommendations for owners of livestock exposed to rabid animals:

1) If the animal is slaughtered within 7 days of being bitten, its tissues may be eaten without risk of infection, provided that liberal portions of the exposed area are discarded.

2) Neither tissues nor milk from a rabid animal should be used for human or animal consumption. Pasteurization temperatures will inactivate rabies virus; therefore, drinking pasteurized milk or eating cooked meat does not constitute a rabies exposure.

3) Having more than one rabid animal in a herd or having herbivore-to-herbivore transmission is uncommon; therefore, restricting the rest of the herd if a single animal has been exposed to or infected by rabies might not be necessary.

c. Other Animals. Other mammals bitten by a rabid animal should be euthanized immediately.

6. Management of Animals that Bite Humans.

a. Dogs, Cats, and Ferrets. Rabies virus may be excreted in the saliva of infected dogs, cats, and ferrets during illness and/or for only a few days prior to illness or death. A healthy dog, cat, or ferret that bites a person should be confined and observed daily for 10 days; administration of rabies vaccine to the animal is not recommended during the observation period to avoid confusing signs of rabies with possible side effects of vaccine administration. Such animals should be evaluated by a veterinarian at the first sign of illness during confinement. Any illness in the animal should be reported immediately to the local health department. If signs suggestive of rabies develop, the animal should be euthanized. Any stray or unwanted dog, cat, or ferret that bites a person may be euthanized immediately and the brain tested. If in doubts, the exposed person should receive post-exposure treatment.

b. Other Biting Animals. Other biting animals which might have exposed a person to rabies should be reported immediately to the local health department. If the biting animal cannot be caught, then the exposed animals or humans should be considered as exposed to rabies and receive post exposure treatment. If the biting animal is captured, then it should be quarantined and observed, or euthanized and the brain tested for rabies.



7. Outbreak Prevention and Control. If a rabies outbreak with numerous animals is expected, it should immediately be reported to local authorities.

C. Prevention and Control Methods Related to Wildlife. The public should be warned not to handle or feed wild mammals. Wild mammals and hybrids that bite or otherwise expose persons, pets, or livestock should be considered for euthanasia and rabies examination. A person bitten by any wild mammal in an area where rabies is endemic should be considered as exposed to rabies and receive post-exposure treatment.

Carnivores. The use of licensed oral vaccines for the mass vaccination of free-ranging wildlife should be considered in selected situations. The distribution of oral rabies vaccine should be based on scientific assessments of the target species and followed by timely and appropriate analysis of surveillance data.

Bats. Bats should be excluded from houses, public buildings, and adjacent structures to prevent direct association with humans. Such structures should then be made bat-proof by sealing entrances used by bats.

Part II: Recommendations for Parenteral Rabies Vaccination Procedures

A. Vaccine Administration. Animal rabies vaccines should be restricted to use by, or under the direct supervision of a veterinarian. All vaccines must be administered in accordance with the specifications of the product label or package insert.

B. Vaccine Selection. Part III lists all vaccines licensed by USDA and marketed in the United States at the time of publication. New vaccine approvals or changes in label specifications made subsequent to publication should be considered as part of this list. Any of the listed vaccines can be used for revaccination, even if the product is not the same brand previously administered. Vaccines used in local rabies-control programs should have a 3-year duration of immunity. This constitutes the most effective method of increasing the proportion of immunized dogs and cats in any population. No

laboratory or epidemiologic data exist to support the annual or biennial administration of 3-year vaccines following the initial series.

C. Adverse Events. Currently, no epidemiologic association exists between a particular licensed vaccine product and adverse events, including vaccine failure.

D. Wildlife and Hybrid Animal Vaccination. The safety and efficacy of parenteral rabies vaccination of wildlife and hybrids have not been established, and no rabies vaccines are licensed for these animals. Parenteral vaccination (trap-vaccinate-release) of wildlife rabies reservoirs may be integrated into coordinated oral rabies vaccination programs to enhance their effectiveness. Zoos or research institutions may establish vaccination programs, which attempt to protect valuable animals, but these should not replace appropriate public health activities that protect humans.

E. Accidental Human Exposure to Vaccine. Human exposure to parenteral animal rabies vaccines listed in Part III does not constitute a risk for rabies infection. However, human exposure to vaccinia-vectored oral rabies vaccines should be reported to state health officials.

F. Rabies Certificate. All agencies and veterinarians should use a Rabies Vaccination Certificate, or an equivalent which can be obtained from vaccine manufacturers.

Twelve Questions About Human Rabies and Its Prevention

This article is abstracted from an article published in the Journal of Infectious Diseases in Clinical Practice (2000) 9: 202-207

Rabies, described as early as the 23rd century B.C., may be one of the oldest recorded infectious diseases of mankind. It is a fatal infection caused by a highly neurotropic, bullet-shaped, single-stranded RNA virus.



Rabies causes more than 40,000-60,000 deaths worldwide each year, primarily in countries where canine rabies is endemic and the delivery of health care is poor. The epidemiology of human rabies is ultimately linked to cycles of rabies virus transmission in animals.

This article will address some representative scenarios and common questions about rabies and its prevention.

1. A graduate student, before departing for rural Latin America to study, questions whether she should receive primary rabies vaccination. Who should receive the primary or preexposure vaccination?

Preexposure prophylaxis, given by the intradermal (ID) or intramuscular (IM) route, is indicated for certain high-risk groups.

The decision to give preexposure prophylaxis is complicated by several factors: a very low incidence of rabies reported in travelers, the relatively high cost of preexposure rabies prophylaxis (in excess of \$300), and the need to begin the vaccination series at least 3 weeks before departure.

Nevertheless, preexposure prophylaxis should be considered for international travelers likely to come in contact with animals in areas where canine rabies is present and where immediate access to appropriate medical care, including safe and effective biologics, may be difficult. Sources of information on rabies in various geographic regions include the Centers for Disease Control and Prevention Travel Website.

Preexposure prophylaxis simplifies postexposure prophylaxis by eliminating the need for rabies immune globulin (RIG) and may provide a measure of protection in the event that a true exposure is not recognized. It does not eliminate the need for appropriate wound treatment and additional vaccinations in the case of a known exposure. Routine serologic testing to confirm seroconversion is not necessary except in the case of immunocompromised individuals. Chloroquine has been noted to reduce the response to the vaccine.

Therefore, if preexposure prophylaxis is given ID, it must be completed prior to initiation of anti-malarial treatment. If a patient is already taking anti-malaria medications, the vaccine should be given IM.

2. A missionary traveling to Southeast Asia to do health care work wonders if the rabies vaccine is available should he need it. What types of rabies biologics are available abroad?

Cell culture vaccines are clearly the standard. They are effective and well tolerated. In the United States, human diploid cell vaccine (HDCV), rabies vaccine adsorbed (RVA) derived from fetal rhesus lung diploid cell, and purified chick embryo cell vaccine (PCEC) are available. Other cell culture vaccines used outside the United States include purified vero cell rabies vaccine (PVRV) and purified duck embryo vaccine (PDEV). In addition, many countries still use vaccines produced from animal nerve tissue that have a high rate of adverse reactions (neuromuscular reactions in 1 per 200 to 1 per 2000 persons vaccinated). Purified equine RIG has been used effectively in countries where human RIG is not available. Travelers should be aware that in some areas unpurified antirabies serum of equine origin immune globulin may be offered and is associated with a high rate of serious adverse reactions, including anaphylaxis.

3. A pet owner asks if she should obtain rabies vaccination because she thinks she got saliva on her hands while playing with her dog that had killed a rabid raccoon earlier that day. What constitutes a rabies exposure?

Rabies is transmitted when the virus is introduced into bite wounds, breaks in the skin, or onto mucous membranes. Three questions to ask are: 1) Was the person bitten? 2) Did saliva or central nervous system material from a rabid animal contaminate an open wound or mucous membrane? and 3) Was the animal in question a bat? (see question 4). If all can be answered no, then no exposure occurred and postexposure prophylaxis is not required. Petting a rabid animal, and contact with blood, urine, or feces of a rabid animal does not constitute an exposure and is not an indication



for prophylaxis. If the answer to at least one of these questions is yes, then exposure to rabies is a possibility and the likelihood that the animal has rabies must be considered.

Questions often arise regarding contact with saliva. In general, if the material containing the virus is dry it can be considered noninfectious because the rabies virus is inactivated by desiccation and ultraviolet radiation. Rabies cannot be transmitted from an animal that does not have active infection. Infectious material (saliva or neural tissue) would have to get in the mouth or on the claw of that animal (the dog in the above scenario) and then promptly introduced through the skin or onto mucous membranes. This would be only remotely feasible in an immediate sequential exposure, and such a case has never been described. Local health departments can assist in deciding the likelihood that an animal has rabies and whether post-exposure prophylaxis is indicated. Animals exposed to rabid animals need to be evaluated by a veterinarian and reported to the local health department immediately.

4. Parents, waking their 16-month-old son in the morning, find a bat in the corner of the room and they question if the child needs to see a doctor. Why is there a concern about bats?

Excluding dog bites that occurred outside of the country, 22 of the 31 (71%) human cases of rabies in the United States since 1980 have been associated with bat rabies virus variants. Although the histories sometimes conflict, of the 22 rabies patients, only 2 reported a bat bite, 10-12 had apparent contact with bats (many where saliva, teeth, or other contact likely occurred), and in 8-10 no exposure to bats or other source of infection was reported. In these latter cases, an unreported or undetected bat bite remains the most plausible hypothesis. Therefore, post-exposure prophylaxis should be considered when direct contact between a person and a bat might have occurred, unless the person can be certain a bite, scratch, or mucous membrane exposure did not occur; for example, consider the potential for direct contact in situations in which a sleeping person wakes to find a bat in the room or an adult witnesses a bat in the room with a previously unattended child, mentally disabled

person, or intoxicated person. Examination for a bite wound alone is inadequate. If, as in the example above, the bat in question is available for testing, and a clear exposure has not occurred, initiation of post-exposure prophylaxis may be delayed 24-48 hours for testing of the bat. If a bite or other clear exposure occurs, post-exposure prophylaxis should begin immediately and may be stopped if laboratory testing shows that the bat is not rabid.

5. Campers notice several bats fluttering in the trees above them. They wonder if they should get treatment. Can rabies be caused by aerosol transmission?

Although nonbite routes of infection are possible, they are exceedingly rare and not applicable to usual public exposures. There have been two reports of rabies transmission to laboratory workers. Both workers were exposed to concentrated aerosols of rabies virus. In the 1950s, two cases of purported aerosol transmission to humans were associated with Frio Cave, Texas, which was inhabited by millions of bats. While the patients did not recall a bite before they died, complete exclusion of a bite is not possible. The conditions under which aerosol transmission might occur are rare and unique, and it would be extremely unusual for them to be applicable to public exposures. Merely seeing a bat or being in the vicinity of bats does not constitute an exposure.

6. A nurse calls asking if she should give postexposure prophylaxis intradermally to a patient bitten by a rat. How is the secondary or postexposure prophylaxis administered?

Rabies prophylaxis in the setting of exposures to small mammals, including rodents, lagomorphs (rabbits and hares), and insectivores (e.g., shrews), is almost never required. These animals are not reservoirs and there have been no documented cases of rabies transmission to humans by these animals. If there is a question, a call to the local health department may be helpful.

When postexposure prophylaxis is required, all doses of vaccine are given IM in the deltoid area



(anterolateral thigh is acceptable for small children). The gluteal area should not be used. For those who have had prior vaccination (with HDCV, RVA, or PCEC; or documented history of antibody response to other vaccines), only two doses are required and RIG should not be used. For those with no prior vaccination, RIG should be thoroughly infiltrated around the wound area. Any remaining should be injected IM at a site distant from the vaccine administration. If RIG was not given when vaccination was begun, it can be administered through the seventh day after vaccination was started. Beyond the seventh day it is not indicated. Though no controlled trials have been performed, extensive experience from many parts of the world indicates that postexposure prophylaxis, consisting of local wound treatment, passive immunization (RIG), and vaccination, is effective if given in an appropriate and timely manner.

7. A student is bitten by a neighbor's dog on the way to school and presents to the emergency room for wound treatment. The emergency room providers wonder if rabies vaccination is needed at this time. When can rabies prophylaxis be delayed while animals are held for quarantine and observation?

A healthy dog, cat, or ferret that bites a person should be confined and observed for 10 days. Any illness in the animal should be reported immediately to the local health department and evaluated by a veterinarian. If the animal remains healthy, patients do not need to begin rabies prophylaxis. If the biting dog, cat, or ferret is a stray animal, it should either be observed for 10 days or be euthanized immediately and submitted for rabies examination. Management of animals other than dogs, cats, and ferrets depends on the species, the circumstances of the bite, the epidemiology of rabies in the area, the biting animal's history and current health status, and potential for exposure to rabies. Public health and animal control officials can assist in these actions and decisions.

8. A physician calls the health department inquiring if she should request rabies diagnostic tests on a comatose patient. When should a

diagnosis of rabies be considered and what specimens should be sent?

Rabies should be considered in the differential diagnosis of any patient who presents with acute progressing encephalopathy of unknown cause. The lack of an exposure history should not deter pursuing the diagnosis, since most patients in the United States have no definitive exposure history. Once symptoms of rabies begin, the natural history is rapid clinical deterioration and death. Patients with encephalopathy who are clinically improving generally do not need rabies testing.

If rabies is suspected, samples that should be sent for study include nuchal skin biopsy, saliva, serum, and cerebral spinal fluid. The postmortem diagnosis of rabies is made by examination of brain tissue. Because of the rarity of the disease and lack of effective treatment, antemortem brain biopsy is not indicated. However, biopsies done for other diseases (e.g., herpesvirus encephalitis), if negative, can be tested for evidence of rabies virus infection.

9. An emergency room doctor sees a patient with an infected raccoon bite 6 weeks after it occurred and questions if it is still useful to give rabies prophylaxis. How long after an exposure would prophylaxis still be considered?

Clearly, treatment with RIG and the vaccine should be given immediately if the exposure was high risk. The usual incubation period for rabies in humans is 3-8 weeks. However, incubation periods of 6 years or longer have been documented. Thus, if a true exposure has occurred, prophylaxis (including RIG) should still be given, regardless of the length of time between exposure and clinical presentation for evaluation, although no studies on the efficacy of such tactics are available.

10. A mother whose daughter has been scratched by a stray cat wonders what the risk of the RIG and vaccine is for her child. What are the adverse reactions of the RIG and vaccine?

With HDCV, local reactions (pain, erythema, swelling, itching) have been commonly reported (30-74%). Systemic reactions (headache, dizziness,



abdominal pain, nausea, muscle aches) have been reported in 5-40% of recipients. Three cases of neurologic illness resembling Guillain-Barré syndrome that resolved without sequelae in 12 weeks have been reported. Rare reports of other nervous system disorders have been temporally associated with HDCV vaccine, but a causal relationship has not been established. There is no evidence that any viruses have ever been transmitted by commercially available RIG in the United States.

Of note, rabies is almost always caused by a bite. Non-bite exposures rarely cause rabies. Local or state public health officials should be contacted about the prevalence of rabies in any given area and the need to give prophylaxis for scratches or other low-risk encounters.

11. A patient with HIV infection wonders if his response to postexposure vaccination will be appropriate. Do immunosuppressed patients require special consideration?

Patients who are immunosuppressed should postpone preexposure vaccinations and avoid situations for which rabies preexposure prophylaxis is indicated. If this is not possible, they should be vaccinated by IM injection and have their antibody titer checked 2-4 weeks after the series. When postexposure prophylaxis is needed, it is also important that a serum sample be tested for rabies antibody to ensure that an acceptable response has developed. The minimum acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by the rapid fluorescent focus inhibition test (RFFIT). No rabies postexposure failures have been attributed to HIV infection.

12. A camper has had the first two vaccine doses of the postexposure series when the state laboratory reports that the skunk that bit him tested negative. What is the value of a negative direct fluorescent antibody (DFA) test?

The direct fluorescent-antibody (DFA) test for detection of rabies virus antigen in brain tissue is used as the primary diagnostic test in every public health laboratory in the United States, and has a

sensitivity approaching 100% [2]. Rabies diagnosis and prophylaxis of potential human exposures are based on the observation that the rabies virus reaches the salivary glands and is excreted in saliva only after replication in the central nervous system. Absence of rabies virus antigen in the brain of an animal by DFA examination (i.e., a negative diagnostic test result) essentially precludes the presence of virus in saliva, the risk of rabies transmission, and the need for postexposure prophylaxis. Since initiation of current testing procedures in 1958, there is no evidence that a false-negative laboratory test has ever led to rabies in a person subsequently left untreated.

Summary

Current public health practice has made human rabies rare in the United States. Preexposure prophylaxis is available for select high-risk groups. Potential exposures to rabies will continue to occur, and patients will often present to their physicians for guidance. A careful history of exposure and, if needed, consultation with state health departments can guide the use of postexposure prophylaxis. Appropriate wound treatment and administration of rabies vaccines and RIG prevent rabies infection in exposed individuals. Further information, including the recommendations of the Advisory Committee on Immunization Practices (ACIP), can be found at the following CDC website, www.cdc.gov/ncidod/dvrd/rabies.



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Contributors:

Dr. Earle Goodman, Editor. Dr. Leroy Dorminy,
Co-Editor

The Editor

Dr. D. E. Goodman
P.O. Box 166
Turbeville, SC 29162, USA
Cvmvdtdrdeg@ftc-i.net

Co-Editor

Dr. Leroy Dorminy
P.O. Box 526
Ocilla, GA 31774, USA
P/F: (229) 468-7711
missionvet@aol.com

Production & Distribution

Christian Veterinary Mission
19303 Fremont Ave., N.
Seattle, WA 98133, USA
gcollard@cvmusa.org

