



COMMUNICABLE DISEASE SECTION

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Rabies: What You & Your Healthcare Provider Should Know

Rabies in California and the County of San Bernardino

- The primary reservoirs for rabies in California are bats and skunks; 75% of rabid animals reported in California between 2001-2008 were bats.
- During the same time frame, six human rabies cases were reported in California. Two of those six cases were exposed in California and resulted from exposure to rabid bats. Additionally, one human rabies case was reported in California in May 2011, and exposure is thought to have resulted from rabid feral cats.¹
- From 2001 to 2011, the County of San Bernardino reported 77 rabid bats and 1 rabid fox.
- However, the DPH Laboratory routinely tests a variety of wild and domestic animals, including skunks, raccoons, cats, and dogs. The most recent report of a rabid dog in the County of San Bernardino was in 1948, a rabid cat was last reported in 1993, and a rabid fox was last reported in 2001.

Transmission

- A bite or scratch from a rabid animal can transmit rabies virus through infectious saliva. Nonbite exposures (contamination of open wounds, abrasions, mucous membranes, or scratches) to brain/nervous system tissue can also transmit rabies virus.
- Person-to-person transmission of rabies virus is rare and not well-documented.
- Rabies virus becomes noninfectious when it dries out and when it is exposed to sunlight. Different environmental conditions affect the rate at which the virus becomes inactive, but in general, if the material containing the virus is dry, the virus can be considered noninfectious.

Symptoms

- Symptoms of rabies infection usually appear 3 to 8 weeks after exposure, but can appear within days or up to many years later.
- The rabies virus infects the central nervous system, ultimately causing disease in the brain and death. The early symptoms of rabies in people include fever, headache, and general weakness or discomfort. As the disease progresses, more specific symptoms appear and may include insomnia, anxiety, confusion, slight or partial paralysis, excitation, hallucinations, agitation, hypersalivation (increase in saliva), difficulty swallowing, and hydrophobia (fear of water). Death usually occurs within days of the onset of these symptoms.

¹ <http://www.cdph.ca.gov/data/statistics/Documents/rabies-episummary.pdf>. Accessed July 14, 2011.

- Once symptoms have developed, no drug or vaccine will improve the chance for survival. Only a few patients with human rabies have survived with intensive medical care; all other patients have died despite treatment.

Evaluation of Exposures

Evaluation of an exposure to rabies virus is complex and involves several factors. The decision to recommend rabies post-exposure prophylaxis (PEP) should consider the circumstances of the exposure; species, health, and vaccination status of the animal to which the person was exposed; and availability of the animal for rabies testing or observation under quarantine.

Prevention: Pre- and Post-exposure Prophylaxis

For information about rabies vaccines and immunoglobulin available in the United States, please see Appendices A and B.

Rabies pre-exposure prophylaxis^{2 3}

In California, pre-exposure vaccination should be offered to persons at increased risk of rabies exposure. This "frequent risk" category includes veterinarians, animal handlers, animal control officers, laboratory workers potentially exposed to rabies virus, and persons traveling to and spending time (e.g., >1 month) in foreign countries where canine rabies is endemic. (See Appendix C)

1. Primary vaccination

- Three 1.0-mL injections of HDCV or PCEC vaccine should be administered intramuscularly (deltoid area) -- one injection per day on days 0, 7, and 21 or 28. Vaccine preparations for intradermal administration are no longer available in the United States.

2. Booster doses

Continuous risk

- People who work with rabies virus in research laboratories or vaccine production facilities are at the highest risk for unapparent exposures. Such persons should have a serum sample tested for rabies antibody every six months. Intramuscular booster doses of vaccine should be administered to maintain a serum titer corresponding to at least complete neutralization at a 1:5 serum dilution by the RFFIT.

Frequent risk

- This group includes other laboratory workers such as those performing rabies diagnostic testing, spelunkers, veterinarians and staff, and animal-control and wildlife officers in areas where animal rabies is enzootic. The frequent-risk category also includes persons who frequently handle bats, regardless of location in the United States. Persons in the frequent risk group should have a serum sample tested for rabies antibody every 2 years; if the titer is less than complete neutralization at a 1:5 serum dilution by the RFFIT, the person also should receive a single booster dose of vaccine.

Infrequent risk

- Veterinarians, veterinary students, and terrestrial animal-control and wildlife officers working in areas where rabies is uncommon to rare (infrequent exposure group) and at-risk international

² CA Compendium of Rabies Control and Prevention, 2004

³ http://www.cdc.gov/rabies/specific_groups/travelers/pre-exposure_vaccinations.html Accessed January 26, 2012.

travelers fall into this category and do not routine pre-exposure booster doses of vaccine after completion of primary pre-exposure vaccination.

Rabies post-exposure prophylaxis (PEP)⁴

Rabies post-exposure vaccinations are highly effective at preventing rabies if given as soon as possible following an exposure. (See Appendix D)

1. **Local wound cleaning:** The first step in preventing infection with rabies is prompt, thorough local cleaning of the wound/scratch with soap and water. Simple local wound cleaning has been shown to markedly reduce the likelihood of rabies in animal experiments.⁵
2. **Patients not previously vaccinated for rabies:** These patients should receive both active and passive immunization. Human rabies immune globulin (HRIG) and the first dose of rabies vaccine should be given on the same day as soon as possible after exposure. (HRIG should be given within 7 days of the first vaccination.)

Active Immunization:

- On March 19, 2010, the Advisory Committee on Immunization Practices (ACIP) released recommendations for a reduced (4-dose) vaccine schedule for PEP to prevent human rabies (previously ACIP recommended a 5-dose rabies vaccination regimen). The reduction in doses recommended for PEP was based in part on evidence from rabies virus pathogenesis data, experimental animal work, clinical studies, and epidemiologic surveillance. These studies indicated that 4 vaccine doses in combination with HRIG elicited adequate immune response and that a fifth dose of vaccine did not contribute to more favorable outcomes.⁶
- These new ACIP recommendations differ from current rabies vaccine label instructions, which still list the 5-dose series for PEP. Alterations of current product labels for human diploid cell vaccine (HDCV) and purified chick embryo cell vaccine (PCECV) are not anticipated by the producers of human rabies vaccines licensed for use in the United States. (See Appendix A)
- Four 1mL doses of rabies vaccine (HDCV, PCECV, or rabies vaccine adsorbed (RVA) should be administered as soon as possible after exposure on Day 0 and then again on Days 3, 7, and 14. The vaccine is given by the IM route in the deltoid area (lateral aspect of the upper arm). For pediatric patients, intramuscular administration in the anterolateral aspect of the thigh is recommended. Rabies vaccine should never be given in the gluteal region.
- **NOTE:** The number of doses recommended for persons with altered immunocompetence has not changed; for such persons, PEP should continue to comprise a 5-dose vaccination regimen (on days 0, 3, 7, 14, and 28) with 1 dose of HRIG.

Passive Immunization:

- HRIG is administered only once (i.e., at the beginning of rabies PEP) to previously unvaccinated persons to provide immediate antibodies until the patient responds to rabies vaccination by

⁴ http://www.cdc.gov/rabies/medical_care/index.html Accessed January 25, 2012.

⁵ CA Compendium of Rabies Control and Prevention, 2004.

⁶ http://www.cdc.gov/rabies/resources/acip_recommendations.html Accessed January 26, 2012.

actively producing antibodies. HRIG should be administered at a dose of 20 IU/kg body weight for all age groups.

- If anatomically feasible, the full dose of HRIG should be infiltrated into the subcutaneous tissue and/or muscle around the wound site(s), and any remaining volume administered intramuscularly at an anatomical site distant from vaccine administration (e.g. opposite deltoid).
 - HRIG should never be administered in the same syringe or at the same anatomical site as vaccine and should never be administered in the gluteal area unless that is the site of exposure.
 - If HRIG is not given with the first dose of vaccine, it can be given through the seventh day following administration of the first vaccine dose. Beyond the seventh day, HRIG is not indicated since an antibody response to cell culture vaccine is presumed to have occurred.
3. **Patients previously vaccinated for rabies:** These patients should receive active immunization only. If a person has previously received post-exposure vaccinations or received pre-exposure vaccinations, only two doses of vaccine (on Day 0 and Day 3) are needed. Human rabies immune globulin is not required. (See Appendix E)
4. Tetanus and antibiotic prophylaxis should be given as indicated.

SAMPLE RECORD:

Recommended Schedule for: _____ DOB _____

| Scheduled Dose | | Date Due |
|----------------|----------------|----------------------------------|
| Day 0 | HRIG | |
| | Rabies vaccine | |
| Day 3 | Rabies vaccine | |
| Day 7 | Rabies vaccine | |
| Day 14 | Rabies vaccine | |
| Day 28 | Rabies vaccine | *immunosuppressed patients only* |

Appendix A: Rabies Vaccines and Immunoglobulin in the United States

| Rabies Vaccines and Immunoglobulin Available in the United States | | | |
|--|-------------------|---|-----------------------------|
| Type | Name | Route | Indications |
| Human Diploid Cell Vaccine (HDCV) | Imovax® Rabies | Intramuscular | Preexposure or Postexposure |
| Purified Chick Embryo Cell Vaccine (PCEC) | RabAvert® | Intramuscular | Preexposure or Postexposure |
| Human Rabies Immune Globulin | Imogam® Rabies-HT | Local infusion at wound site, with additional amount intramuscular at site distant from vaccine | Postexposure |
| Human Rabies Immune Globulin | HyperRab TM S/D | Local infusion at wound site, with additional amount intramuscular at site distant from vaccine | Postexposure |

Appendix B: Resources for Rabies Vaccine & Immunoglobulin

Patient Assistance Programs

Sanofi Pasteur's Patient Assistance Program (providing Imogam[®] Rabies-HT and Imovax[®] Rabies as well as other vaccines) is now administered through the Franklin Group. A healthcare professional or patient can either contact the Franklin Group directly, or call the customer service team (1-800-VACCINE) who will transfer them to the Franklin Group. The Franklin Group will review the application against the eligibility criteria. For more information about the program or to request an application, please contact the Sanofi Pasteur, Inc. Patient Assistance Program (Franklin Group) at 1 (866) 801-5655.

Novartis' Patient Assistance Program for RabAvert[®] is managed through RX for Hope and can be accessed at 800-244-7668. Instructions and request forms are also available at the Rx for Hope website [RabAvert Patient Assistance Program](#).

Appendix C: Rabies Pre-exposure Prophylaxis

| Rabies Preexposure Prophylaxis Guide | | | |
|---|---|---|--|
| Risk Category | Nature of Risk | Typical Population | Preexposure Recommendations |
| Continuous | Virus present continuously, often in high concentrations. Specific exposures likely to go unrecognized. Bite, nonbite, or aerosol exposure. | Rabies research laboratory workers; rabies biologics production workers. | Primary course. Serologic testing every 6 months; booster vaccination if antibody titer is below acceptable level. |
| Frequent | Exposure usually episodic, with source recognized, but exposure also might be unrecognized. Bite, nonbite, or aerosol exposure. | Rabies diagnostic lab workers, spelunkers, veterinarians and staff, and animal-control and wildlife workers in rabies-enzootic areas. All persons who frequently handle bats. | Primary course. Serologic testing every 2 years; booster vaccination if antibody titer is below acceptable level. |
| Infrequent | Exposure nearly always episodic with source recognized. Bite or nonbite exposure. | Veterinarians and terrestrial animal-control workers in areas where rabies is uncommon to rare. Veterinary students. Travelers visiting areas where rabies is enzootic and immediate access to appropriate medical care including biologics is limited. | Primary course. No serologic testing or booster vaccination. |
| Rare (population at large) | Exposure always episodic with source recognized. Bite or nonbite exposure. | U.S. population at large, including persons in rabies-epizootic areas. | No vaccination necessary |

Appendix D: Rabies Post-exposure Prophylaxis for Non-immunized Individuals

| Postexposure Prophylaxis for Non-immunized Individuals | |
|---|--|
| Treatment | Regimen |
| Wound cleansing | All postexposure prophylaxis should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidine-iodine solution should be used to irrigate the wounds. |
| RIG | If possible, the full dose should be infiltrated around any wound(s) and any remaining volume should be administered IM at an anatomical site distant from vaccine administration. Also, RIG should not be administered in the same syringe as vaccine. Because RIG might partially suppress active production of antibody, no more than the recommended dose should be given. |
| Vaccine | HDCV or PCECV 1.0 mL, IM (deltoid area), one each on days 0 , 3, 7, and 14. |

Appendix E: Postexposure Prophylaxis for Previously Immunized Individuals

| Postexposure Prophylaxis for Previously Immunized Individuals | |
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| Treatment | Regimen |
| Wound cleansing | All postexposure prophylaxis should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidine-iodine solution should be used to irrigate the wounds. |
| RIG | RIG should not be administered. |
| Vaccine | HDCV or PCECV 1.0 mL, IM (deltoid area), one each on days 0 and 3. |