

INFORMATION PAPER

DHA-IHB
31 August 2017

SUBJECT: Rabies Disease and Rabies Vaccine.

1. Purpose. To describe Rabies disease and vaccine to prevent it.
2. Facts.
 - a. Microbiology. Rabies is a zoonotic disease (a disease that is transmitted from animals to humans), caused by the rabies virus, of the Lyssavirus genus, within the family Rhabdoviridae.
 - b. Disease. Rabies is transmitted through the bite of a rabid animal. The virus is transmitted in the saliva of rabid animals and generally enters the body via infiltration of virus-laden saliva from a rabid animal into a wound (e.g. scratches), or by direct exposure of mucosal surfaces to saliva from an infected animal (e.g. bites). The rabies virus infects the central nervous system, causing disease in the brain and death. The early symptoms of rabies in people are similar to that of many other illnesses, including 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 (CDC Yellow book 2016).
 - c. Epidemiology. Rabies is found on all continents, except Antarctica. Regionally, different viral variants are adapted to various mammalian hosts and perpetuate in dogs and wildlife, such as bats and some carnivores, including foxes, jackals, mongooses, raccoons, and skunks. In certain areas of the world, canine rabies remains enzootic, including parts of Africa, Asia, and Central and South America. Bats are an important source of human rabies transmission in North America (CDC Yellow Book 2016).
 - d. Vaccines.
 - (1) Imovax® (Rabies) manufactured by Sanofi Pasteur and RabAvert® (Rabies) manufactured by Novartis are currently two inactivated rabies vaccines available for use in the United States.

- (2) Imovax® is a human diploid cell vaccine (HDCV) harvested from a human cell line, that may contain human albumin, neomycin, phenol, and trace amounts of beta- propriolactone.
 - (3) RabAvert® is a purified chick embryo cell (PCEC) vaccine harvested from chickfibroblasts, that may contain bovine gelatin, human albumen, potassium glutamate, sodium EDTA, chicken protein, and traces of neomycin and amphotericin B.
- e. Vaccine Precautions.
- (1) In view of the almost invariably fatal outcome of rabies, there is no contraindication to post-exposure prophylaxis (PEP). When a person with a history of hypersensitivity must receive rabies vaccine for PEP, antihistamines may be given; epinephrine and advanced medical care should be readily available and performed under the observation of an allergist.
 - (2) Pre-exposure vaccination is contraindicated in people with a history of anaphylaxis to the vaccine or any vaccine component.
 - (3) Although limited data are available for rabies vaccination of pregnant women, children, and infants, post-exposure or pre-exposure rabies vaccine may be administered to these groups when clearly clinically indicated, using the same doses and timing as vaccination of other at-risk groups.
 - (4) Radiation therapy, antimalarials, corticosteroids, other immunosuppressive agents and immunosuppressive illnesses may diminish the protective efficacy of the vaccine. Pre-exposure vaccination should be administered to such persons with the awareness that the immune response may be inadequate. Immunosuppressive agents should not be administered during post-exposure therapy unless essential for the treatment of other conditions. When rabies post-exposure prophylaxis is administered to persons who are immunosuppressed, a serum sample on day 14 (the day of the fourth vaccination) should be tested for rabies antibody to ensure that an acceptable antibody response.
 1. For persons with immunosuppression, rabies PEP should be administered using a 5-dose vaccine regimen (i.e., 1 dose of vaccine on days 0, 3, 7, 14, and 28), with the understanding that the immune response still might be inadequate.
- f. Clinical Guidance. CDC/ACIP recommends rabies vaccination with either human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine

(PCEC) vaccine. The vaccine series should be completed with the same product. Although, if either HDCV or PCEC vaccine is unavailable, the alternate product may be used to complete a vaccine series.

g. Pre-exposure Vaccination

- (1) Pre-exposure vaccination is recommended only for people with high risk of rabies exposure. The CDC provides guidance on providing prophylaxis immunization and serologic testing based on exposure risk.
- (2) Pre-exposure vaccination consists of a series of 3 intramuscular injections. Adults should be vaccinated in the deltoid and small children should be vaccinated in the anterolateral thigh. Administer 3 doses of vaccine, 1.0 mL, on days 0, 7, and 21 or 28.
- (3) Pre-exposure vaccination should be completed prior to high-risk travel or other high-risk exposure. Rabies pre-exposure vaccination should not be initiated unless the person can reasonably complete the series before exposure, since few data exist to guide post-exposure prophylaxis (PEP) after a partial immunization series.
- (4) Rabies vaccine booster doses are not routinely recommended for those who have completed 3 doses of pre-exposure vaccination for infrequent rabies exposure risks. For persons with frequent or continuous rabies exposure risks, serologic testing should guide booster vaccination. Serologic testing should be performed every 2 years for those with frequent exposures, and every 6 months for those with continuous exposures.

h. Post-exposure Prophylaxis (PEP) for Unvaccinated Persons. PEP for rabies should be initiated promptly after a high risk exposure, as guided by preventive medicine professionals. PEP should begin with immediate, thorough wound cleansing with soap and water.

- (1) Combination of human rabies immune globulin (HRIG) and rabies vaccine (HDCV or PCEC vaccine) is recommended for high-risk bite and non-bite exposures, regardless of the time interval between exposure and initiation PEP. If PEP has been initiated and appropriate laboratory diagnostic testing (i.e., the direct fluorescent antibody test) indicates that the animal that caused the exposure was not rabid, PEP may be discontinued (CDC 2010).
- (2) Human Rabies Immune Globulin (HRIG) should be administered to unvaccinated persons to provide rabies virus-neutralizing antibody

until the patient responds to vaccination. HRIG is administered once on day 0 at the time PEP is initiated, in conjunction with human rabies vaccines. If HRIG was not administered when vaccination was begun on day 0, it can be administered up to and including day 7 of the PEP series. HRIG is administered in a dose of 20 IU/kg directly into the wound area as much as feasible; the remaining dose may be administered intramuscularly.

- (3) Rabies vaccine should be administered as 4 doses intramuscularly. Inject in the adult's deltoid or small child's anterolateral thigh; vaccine should never be administered in the gluteal area. Administer 1.0 mL doses on days 0, 3, 7, and 14. For immunocompromised persons, a fifth dose should be administered on day 28. The rabies vaccine schedule should be followed as closely as possible; if the schedule is not followed exactly, doses may be administered farther apart, but not closer together, in time.
- i. Post exposure Prophylaxis (PEP) for Previously Vaccinated Person. As prior, PEP for rabies should be initiated promptly after a high risk exposure, as guided by preventive medicine professionals. PEP should begin with immediate, thorough wound cleansing with soap and water. Those who have been previously immunized against rabies should be given 2 doses of rabies vaccine. Administer 1.0 mL doses intramuscularly on day 0 and day 3. HRIG should not be administered to previously vaccinated persons to avoid possible inhibition of the anamnestic vaccine response.
- j. Adverse Events. Vaccine Adverse Reactions/Events. Vaccine recipients may experience local reactions, such as pain, erythema, swelling, or itching at the injection site, or mild systemic reactions, such as headache, nausea, abdominal pain, muscle aches, and dizziness. Approximately 6% of people receiving booster vaccinations with HDCV may experience an immune complex-like reaction characterized by urticaria, pruritus, and malaise. The likelihood of these reactions may be less with PCEC. Once initiated, rabies post-exposure prophylaxis (PEP) should not be interrupted or discontinued because of local or mild systemic adverse reactions to rabies vaccine. All clinically significant adverse events following administration of rabies vaccine should be reported to VAERS, even if causal relation to vaccination is not certain (CDC 2010).
- k. DoD Policy. ACIP pre-exposure guidelines should be followed for personnel at high risk for exposure IAW Service-Specific guidelines (veterinary, animal handlers, special operations).

3. References.

- a. List references here Centers for Disease Control and Prevention (CDC). Human Rabies Prevention –United States, 2008, Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2008;57 (RR03):1-26. Retrieved from <http://www.cdc.gov/mmwr/preview/mmwrhtml/rr5703a1.htm>
- b. Centers for Disease Control and Prevention (CDC), Infectious Diseases Related to Travel - Rabies, The Yellow Book (2016). Retrieved from <http://wwwnc.cdc.gov/travel/yellowbook/2016/infectious-diseases-related-to-travel/rabies>
- c. Centers for Disease Control and Prevention (CDC), 2014, Use of a Reduced (4-Dose) Vaccine Schedule for Post exposure Prophylaxis to Prevent Human Rabies: Recommendations of the Advisory Committee on Immunization Practices (ACIP) (n.d). Retrieved from http://www.cdc.gov/rabies/resources/acip_recommendations.html
- d. World Health Organization (WHO), Rabies. (2014) Retrieved from <http://www.who.int/rabies/about/en/>
- e. Multiple resources (e.g., product insert, Vaccine Information Statements) assembled by the Immunization Healthcare Branch: www.health.mil/Rabies

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