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Organizational Principles to Guide and Define the Child Health Care System and/or Improve the Health of all Children

Policy Statement—Rabies-Prevention Policy Update: New Reduced-Dose Schedule

COMMITTEE ON INFECTIOUS DISEASES

KEY WORDS

rabies, guidelines, prevention and control, vaccines, immunization, passive, immunization schedule, bites and stings

ABBREVIATION

PEP—postexposure prophylaxis

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abstract

FREE

The Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention recommends reducing the number of doses from 5 to 4 of human diploid cell vaccine or purified chick embryo cell vaccine required for postexposure prophylaxis to prevent rabies in humans. The vaccine doses should be given on day 0 (first day of prophylaxis) and days 3, 7, and 14 after the first dose. For persons with immune suppression, the 5-dose regimen should continue to be used. Recommendations for the use of human rabies immunoglobulin remain unchanged. The American Academy of Pediatrics endorses these recommendations. *Pediatrics* 2011;127:785–787

INTRODUCTION

Rabies is a rapidly progressive encephalomyelitis with a very high case fatality rate. Approximately 55 000 people worldwide, nearly half of whom are children, die annually of rabies. Rabies is caused by RNA viruses in the family *Rhabdoviridae*, genus *lyssavirus*. In the Americas, only type 1 lyssavirus (rabies virus) circulates and is common in wild animals, particularly bats, coyotes, foxes, raccoons, and skunks, in the United States. Virus is transmitted in the saliva of rabid mammals after a bite or through contamination of an open wound or mucous membrane. The incubation period (1–3 months) is long enough to render immunization a highly effective strategy for postexposure prophylaxis (PEP). Approximately 20 000 to 30 000 persons receive PEP in the United States each year, and 1 to 3 cases of human rabies occurs annually. Between 2000 and 2007, 20 of 25 cases of human rabies reported in the United States were acquired within the United States. Among the 20 indigenously acquired cases, 17 were associated with bat rabies virus variants.

In the United States, animal rabies is common. Education of children to avoid contact with stray or wild animals is of primary importance. PEP is indicated once an exposure has occurred. PEP has never failed in the United States since the introduction of modern cell-derived vaccines in the 1970s. Keys to effective PEP have included prompt washing of the wound with copious amounts of soap and water, infiltration of human rabies immunoglobulin into and around the wound, and a 5-dose schedule of intramuscular vaccine administered over 28 days.

BACKGROUND AND RATIONALE

In 2007, when human rabies vaccine was in limited supply, the Advisory Committee on Immunization Practices of the Centers for Disease Control and Prevention formed a rabies work group to review rabies vac-

cine options and then accepted its recommendations to adopt a 4-dose vaccination regimen. The recommendation was published in *Morbidity and Mortality Weekly Report: Recommendations and Reports* on March 19, 2010.[1]

EVIDENCE TO SUPPORT THE RECOMMENDATION

A detailed review of the evidence in support of a reduced, 4-dose schedule for human PEP has been published.[2]

- The induction of rabies-neutralizing antibody is a surrogate for an adequate immune response to vaccination and was achieved in all subjects (~1000) by day 14, when the fourth dose of cell-derived rabies vaccine was given.
- From observational studies that included persons likely exposed to confirmed rabid animals and with imperfect adherence to the 5-dose vaccine schedule, the Rabies Working Group estimated that more than 300 persons in the United States received only 3 or 4 doses annually, and there were no resulting cases of human rabies. Although human PEP failures do occur rarely worldwide, no cases have been attributed to the lack of receipt of the fifth rabies vaccine dose on day 28.
- In animal models ranging from rodents to nonhuman primates, timely PEP was important, but the absolute number of vaccine doses did not contribute to significant differences in survival rates.
- Adverse reactions to the modern cell-derived rabies vaccines are uncommon in children and, theoretically, will be the same or less common with 1 less vaccine dose.
- Preliminary economic assessments indicate that there would be a $16 million cost savings to the United States health care system by using the reduced-dose schedule.

POLICY OR RECOMMENDATIONS

1. Unchanged: For unvaccinated persons, the combination of rabies immunoglobulin and rabies vaccine is recommended for both bite and nonbite exposures regardless of the time interval between exposure and initiation of PEP. If PEP has been initiated and results of appropriate laboratory testing (ie, the direct fluorescent antibody test) indicate that the animal that caused the exposure was not rabid, PEP may be discontinued.
2. New: A regimen of four 1-mL vaccine doses of human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) should be administered intramuscularly to previously unvaccinated, immunocompetent persons (Table 1). The first dose of the 4-dose regimen should be administered as soon as possible after exposure. However, the vaccine regimen may be started weeks to months after the exposure if signs and symptoms of rabies are not present. The date of the first dose is considered to be day 0 of the PEP series. Doses should then be administered on days 3, 7, and 14 after the first vaccination.
3. Unchanged: For persons with immunosuppression (see "Immunocompromised Children" in *Red Book*[4]), rabies PEP should be administered by using the 5-dose vaccine regimen (ie, 1 dose of vaccine on

TABLE 1 Rabies Postexposure Prophylaxis (PEP) Schedule—United States, 2010

Vaccination Status	Intervention	Regimen*
Not previously vaccinated	Wound cleansing	All PEP should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent (eg, povidine-iodine solution) should be used to irrigate the wounds.
	Human rabies immune globulin (HRIG)	Administer 20 IU/kg body weight. If anatomically feasible, the full dose should be infiltrated around and into the wound(s), and any remaining volume should be administered at an anatomical site (intramuscular [IM]) distant from vaccine administration. Also, HRIG should not be administered in the same syringe as vaccine. Because RIG might partially suppress active production of rabies virus antibody, no more than the recommended dose should be administered.
	Vaccine	Human diploid cell vaccine (HDCV) or purified chick embryo cell vaccine (PCECV) 1.0 mL, IM (deltoid area†), 1 each on days 0,§ 3, 7 and 14.¶
Previously vaccinated**	Wound cleansing	All PEP 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.
	HRIG	HRIG should not be administered.
	Vaccine	HDCV or PCECV 1.0 mL, IM (deltoid area†), 1 each on days 0§ and 3.

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* These regimens are applicable for persons in all age groups, including children.

† The deltoid area is the only acceptable site of vaccination for adults and older children. For younger children, the outer aspect of the thigh may be used. Vaccine should never be administered in the gluteal area.

§ Day 0 is the day dose 1 of vaccine is administered.

¶ For persons with immunosuppression, rabies PEP should be administered using all 5 doses of vaccine on days 0, 3, 7, 14, and 28.

** Any person with a history of pre-exposure vaccination with HDCV, PCECV, or rabies vaccine adsorbed (RVA); prior PEP with HDCV, PCECV or RVA; or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination.

days 0, 3, 7, 14, and 28). The immunosuppressed patient should be tested for rabies virus–neutralizing antibody with the rapid fluorescent focus inhibition test 1 to 2 weeks after the fifth dose of vaccine. If an acceptable antibody response is not detected, the patient should be managed in consultation with an expert in rabies. Commercial rabies virus antibody tests that are not approved by the US Food and Drug Administration are not appropriate for use as a substitute for the rapid fluorescent focus inhibition test.

4. Unchanged: Sites of intramuscular vaccination remain unchanged (deltoid area in adults; anterolateral aspect of thigh or deltoid in children). The gluteal area should not be used.
5. Unchanged: Recommendations for rabies immunoglobulin use and PEP of previously vaccinated persons have not changed.[3]
6. Unchanged: No routine testing to document seroconversion in healthy patients who have completed PEP is necessary.
7. Unchanged: Recommendations for management and reporting of vaccine adverse events have not changed.
8. Unchanged: Pregnancy and breastfeeding are not contraindications to PEP.

REFERENCES

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