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Rabies Prevention -- United States, 1991 Recommendations of the Immunization Practices Advisory Committee (ACIP)

These revised recommendations of the Immunization Practices Advisory Committee (ACIP) on rabies prevention update the previous recommendations (MMWR 1984;33:393-402,407-8) to reflect the current status of rabies and antirabies biologics in the United States. *

INTRODUCTION

Following the marked decrease of rabies cases among domestic animals in the United States in the 1940s and 1950s, indigenously acquired rabies among humans decreased to fewer than two cases per year in the 1960s and 1970s and fewer than one case per year during the 1980s (1). In 1950, for example, 4,979 cases of rabies were reported among dogs and 18 were reported among human populations; in 1989, 160 cases were reported among dogs and one was reported among humans. Thus, the likelihood of human exposure to a rabid domestic animal has decreased greatly; however, the many possible exposures that result from frequent contact between domestic dogs and humans continue to be the basis of most antirabies treatments (2).

Rabies among wild animals -- especially skunks, raccoons, and bats -- has become more prevalent since the 1950s, accounting for greater than 85% of all reported cases of animal rabies every year since 1976 (1). Rabies among animals occurs throughout the continental United States; only Hawaii remains consistently rabies-free. Wild animals now constitute the most important potential source of infection for both humans and domestic animals in the United States. In much of the rest of the world, including most of Asia, Africa, and Latin America, the dog remains the major species with rabies and the major source of rabies among humans. Nine of the 13 human rabies deaths reported to CDC from 1980 through 1990 appear to have been related to exposure to rabid animals outside of the United States (3-9).

Although rabies among humans is rare in the United States, every year approximately 18,000 persons receive rabies preexposure prophylaxis and an additional 10,000 receive postexposure prophylaxis. Appropriate management of persons possibly exposed to rabies depends on the interpretation of the risk of infection. Decisions about management must be made immediately. All available methods of systemic prophylactic treatment are complicated by occasional adverse reactions, but these are rarely

severe (10-14).

Data on the efficacy of active and passive rabies immunization have come from both human and animal studies. Evidence from laboratory and field experience in many areas of the world indicates that postexposure prophylaxis combining local wound treatment, passive immunization, and vaccination is uniformly effective when appropriately applied (15-20). However, rabies has occasionally developed among humans when key elements of the rabies postexposure prophylaxis treatment regimens were omitted or incorrectly administered (see Postexposure Treatment Outside the United States).

RABIES IMMUNIZING PRODUCTS

There are two types of rabies immunizing products.

1. Rabies vaccines induce an active immune response that includes the production of neutralizing antibodies. This antibody response requires approximately 7-10 days to develop and usually persists for greater than or equal to 2 years.

2. Rabies immune globulins (RIG) provide rapid, passive immune protection that persists for only a short time (half-life of approximately 21 days) (21,22). In almost all postexposure prophylaxis regimens, both products should be used concurrently.

Vaccines Licensed for Use in the United States

Two inactivated rabies vaccines are currently licensed for preexposure and postexposure prophylaxis in the United States.

Rabies Vaccine, Human Diploid Cell (HDCV)

HDCV is prepared from the Pitman-Moore strain of rabies virus grown in MRC-5 human diploid cell culture and concentrated by ultrafiltration (23). The vaccine is inactivated with betapropiolactone (18) and is supplied in forms for:

1. Intramuscular (IM) administration, a single-dose vial containing lyophilized vaccine (Pasteur-Merieux Serum et Vaccins, Imovax((R)) Rabies, distributed by Connaught Laboratories, Inc., Phone: 800-VACCINE) that is reconstituted in the vial with the accompanying diluent to a final volume of 1.0 ml just before administration.

2. Intradermal (ID) administration, a single-dose syringe containing lyophilized vaccine (Pasteur-Merieux Serum et Vaccins, Imovax((R)) Rabies I.D., distributed by Connaught Laboratories, Inc.) that is reconstituted in the syringe to a volume of 0.1 ml just before administration (24).

   A human diploid cell-derived rabies vaccine developed in the United

States (Wyeth Laboratories, Wyvac((R))) was recalled by the manufacturer from the market in 1985 and is no longer available (25).

Rabies Vaccine, Adsorbed (RVA)

RVA (Michigan Department of Public Health) was licensed on March 19, 1988; it was developed and is currently distributed by the Biologics Products Program, Michigan Department of Public Health. The vaccine is prepared from the Kissling strain of Challenge Virus Standard (CVS) rabies virus adapted to fetal rhesus lung diploid cell culture (26-32). The vaccine virus is inactivated with betapropiolactone

and concentrated by adsorption to aluminum phosphate. Because RVA is adsorbed to aluminum phosphate, it is liquid rather than lyophilized. RVA is currently available only from the Biologics Products Program, Michigan Department of Public Health. Phone: (517) 335-8050

Both types of rabies vaccines are considered equally efficacious and safe when used as indicated. The full 1.0-ml dose of either product can be used for both preexposure and postexposure prophylaxis. Only the Imovax((R)) Rabies I.D. vaccine (HDCV) has been evaluated by the ID dose/route for preexposure vaccination (33-36); the antibody response and side effects after ID administration of RVA have not been studied (24). Therefore, RVA should not be used intradermally.

Rabies Immune Globulins Licensed for Use in the United States

HRIG (Cutter Biological (a division of Miles Inc.), Hyperab((R)); and Pasteur-Merieux Serum et Vaccins, Imogam((R)) Rabies, distributed by Connaught Laboratories, Inc.) is an antirabies gamma globulin concentrated by cold ethanol fractionation from plasma of hyperimmunized human donors. Rabies neutralizing antibody content, standardized to contain 150 international units (IU) per ml, is supplied in 2-ml (300 IU) and 10-ml (1,500 IU) vials for pediatric and adult use, respectively.

Both HRIG preparations are considered equally efficacious and safe when used as described in this document.

POSTEXPOSURE PROPHYLAXIS: RATIONALE FOR TREATMENT

Physicians should evaluate each possible exposure to rabies and if necessary consult with local or state public health officials regarding the need for rabies prophylaxis (Table 1). In the United States, the following factors should be considered before specific antirabies treatment is initiated.

Type of Exposure

Rabies is transmitted only when the virus is introduced into open cuts or wounds in skin or mucous membranes. If there has been no exposure (as described in this section), postexposure treatment is not necessary. The likelihood of rabies infection varies with the nature and extent of exposure. Two categories of exposure (bite and nonbite) should be considered.

Bite

Any penetration of the skin by teeth constitutes a bite exposure. Bites to the face and hands carry the highest risk, but the site of the bite should not influence the decision to begin treatment (17).

Nonbite

Scratches, abrasions, open wounds, or mucous membranes contaminated with saliva or other potentially infectious material (such as brain tissue) from a rabid animal constitute nonbite exposures. If the material containing the virus is dry, the virus can be considered noninfectious.

Other contact by itself, such as petting a rabid animal and contact with the blood, urine, or feces (e.g., guano) of a rabid animal, does not constitute an exposure and is not an indication for prophylaxis.

Although occasional reports of transmission by nonbite exposure suggest that such exposures constitute sufficient reason to initiate postexposure prophylaxis under some circumstances, nonbite exposures rarely cause rabies (37). The nonbite exposures of highest risk appear to be exposures to large amounts of aerosolized rabies virus, organs (i.e., corneas) transplanted from patients who died of rabies, and

scratches by rabid animals. Two cases of rabies have been attributed to airborne exposures in laboratories, and two cases of rabies have been attributed to probable airborne exposures in a bat-infested cave in Texas (38,39).

The only documented cases of rabies caused by human-to-human transmission occurred among six recipients of transplanted corneas. Investigations revealed each of the donors had died of an illness compatible with or proven to be rabies (40-43). The six cases occurred in four countries: Thailand (two cases), India (two cases), the United States (one case), and France (one case). Stringent guidelines for acceptance of donor corneas have reduced this risk.

Apart from corneal transplants, bite and nonbite exposures inflicted by infected humans could theoretically transmit rabies, but no such cases have been documented (44). Adherence to respiratory precautions will minimize the risk of airborne exposure (45).

Animal Rabies Epidemiology and Evaluation of Involved Species

Wild Animals

Carnivorous wild animals (especially skunks, raccoons, and foxes) and bats are the animals most often infected with rabies and the cause of most indigenous cases of human rabies in the United States since 1960 (1). All bites by wild carnivores and bats must be considered possible exposures to the disease. Postexposure prophylaxis should be initiated when patients are exposed to wild carnivores unless 1) the exposure occurred in a part of the continental United States known to be free of terrestrial rabies and the results of immunofluorescence antibody testing will be available within 48 hours or 2) the animal has already been tested and shown not to be rabid. If treatment has been initiated and subsequent immunofluorescence testing shows that the exposing animal was not rabid, treatment can be discontinued.

Signs of rabies among carnivorous wild animals cannot be interpreted reliably; therefore, any such animal that bites or scratches a person should be killed at once (without unnecessary damage to the head) and the brain submitted for rabies testing. If the results of testing are negative by immunofluorescence, the saliva can be assumed to contain no virus, and the person bitten does not require treatment.

If the biting animal is a particularly rare or valuable specimen and the risk of rabies small, public health authorities may choose to administer postexposure treatment to the bite victim in lieu of killing the animal for rabies testing (46). Such animals should be quarantined for 30 days.

Rodents (such as squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, and mice) and lagomorphs (including rabbits and hares) are almost never found to be infected with rabies and have not been known to cause rabies among humans in the United States. However, from 1971 through 1988, woodchucks accounted for 70% of the 179 cases of rabies among rodents reported to CDC (47). In all cases involving rodents, the state or local health department should be consulted before a decision is made to initiate postexposure antirabies prophylaxis.

Exotic pets (including ferrets) and domestic animals crossbred with wild animals are considered wild animals by the National Association of State Public Health Veterinarians (NASPHV) and the Conference of State and Territorial Epidemiologists (CSTE) because they may be highly susceptible to rabies and could transmit the disease. Because the period of rabies virus shedding in these animals is unknown, these animals should be killed and tested rather than confined and observed when they bite humans (46). Wild animals (skunks, raccoons, and bats) and wild animals crossbred with dogs should

not be kept as pets (46).

Domestic Animals

The likelihood that a domestic animal is infected with rabies varies by region; hence, the need for postexposure prophylaxis also varies. In the continental United States, rabies among dogs is reported most commonly along the U.S.-Mexico border and sporadically from the areas of the United States with enzootic wildlife rabies, especially the Midwest. During most of the 1980s in the United States, more cats than dogs were reported rabid; the majority of these cases were associated with the mid-Atlantic epizootic of rabies among raccoons. The large number of rabies-infected cats may be attributed to fewer cat vaccination laws, fewer leash laws, and the roaming habits of cats. Cattle tend to be most often exposed to rabies via rabid skunks.

In areas where canine rabies is not enzootic (including virtually all of the United States and its territories), a healthy domestic dog or cat that bites a person should be confined and observed for 10 days. Any illness in the animal during confinement or before release should be evaluated by a veterinarian and reported immediately to the local health department. If signs suggestive of rabies develop, the animal should be humanely killed and its head removed and shipped, under refrigeration, for examination by a qualified laboratory. Any stray or unwanted dog or cat that bites a person should be killed immediately and the head submitted as described for rabies examination (46).

In most developing countries of Asia, Africa, and Central and South America, dogs are the major vector of rabies; exposures to dogs in such countries represent a special threat. Travelers to these countries should be aware that greater than 50% of the rabies cases among humans in the United States result from exposure to dogs outside the United States. Although dogs are the main reservoir of rabies in these countries, the epizootiology of the disease among animals differs sufficiently by region or country to warrant the evaluation of all animal bites.

Exposures to dogs in canine rabies-enzootic areas outside the United States carry a high risk; some authorities therefore recommend that postexposure rabies treatment be initiated immediately after such exposures. Treatment can be discontinued if the dog or cat remains healthy during the 10-day observation period.

Circumstances of Biting Incident and Vaccination Status of Exposing Animal

An unprovoked attack by a domestic animal is more likely than a provoked attack to indicate that the animal is rabid. Bites inflicted on a person attempting to feed or handle an apparently healthy animal should generally be regarded as provoked.

A fully vaccinated dog or cat is unlikely to become infected with rabies, although rare cases have been reported (48). In a nationwide study of rabies among dogs and cats in 1988, only one dog and two cats that were vaccinated contracted rabies (49). All three of these animals had received only single doses of vaccine; no documented vaccine failures occurred among dogs or cats that had received two vaccinations.

POSTEXPOSURE PROPHYLAXIS: LOCAL TREATMENT OF WOUNDS AND VACCINATION

The essential components of rabies postexposure prophylaxis are local wound treatment and the administration, in most instances, of both HRIG and vaccine (Table 2). Persons who have been bitten by animals suspected or proven rabid should begin treatment within 24 hours. However, there have been instances when the decision to begin treatment was not made until many months after the exposure because of a delay in recognition that an exposure had occurred and awareness that

incubation periods of greater than 1 year have been reported.

In 1977, the World Health Organization (WHO) recommended a regimen of RIG and six doses of HDCV over a 90-day period. This recommendation was based on studies in Germany and Iran (16,20). When used this way, the vaccine was found to be safe and effective in protecting persons bitten by proven rabid animals and induced an excellent antibody response in all recipients (16). Studies conducted in the United States by CDC have shown that a regimen of one dose of HRIG and five doses of HDCV over a 28-day period was safe and induced an excellent antibody response in all recipients (15).

Local Treatment of Wounds

Immediate and thorough washing of all bite wounds and scratches with soap and water is an important measure for preventing rabies. In studies of animals, simple local wound cleansing has been shown to reduce markedly the likelihood of rabies (50,51). Tetanus prophylaxis and measures to control bacterial infection should be given as indicated. The decision to suture large wounds should take into account cosmetic factors and the potential for bacterial infections.

Immunization

Vaccine Usage

Two rabies vaccines are currently available in the United States; either is administered in conjunction with HRIG at the beginning of postexposure therapy. A regimen of five 1-ml doses of HDCV or RVA should be given intramuscularly. The first dose of the five-dose course should be given as soon as possible after exposure. Additional doses should be given on days 3, 7, 14, and 28 after the first vaccination. For adults, the vaccine should always be administered IM in the deltoid area. For children, the anterolateral aspect of the thigh is also acceptable. The gluteal area should never be used for HDCV or RVA injections, since administration in this area results in lower neutralizing antibody titers (52).

Postexposure antirabies vaccination should always include administration of both passive antibody and vaccine, with the exception of persons who have previously received complete vaccination regimens (preexposure or postexposure) with a cell culture vaccine, or persons who have been vaccinated with other types of vaccines and have had documented rabies antibody titers. These persons should receive only vaccine (see Postexposure Therapy of Previously Vaccinated Persons). The combination of HRIG (local and systemic) and vaccine is recommended for both bite and nonbite exposures (see Postexposure Prophylaxis: Rationale for Treatment), regardless of the interval between exposure and initiation of treatment.

Because the antibody response after the recommended postexposure vaccination regimen with HDCV or RVA has been satisfactory, routine postvaccination serologic testing is not recommended. Serologic testing is only indicated in unusual instances, as when the patient is known to be immunosuppressed. The state health department may be contacted for recommendations on this matter.

HRIG Usage

HRIG is administered only once (i.e., at the beginning of antirabies prophylaxis) to provide immediate antibodies until the patient responds to HDCV or RVA by actively producing antibodies. If HRIG was not given when vaccination was begun, it can be given through the seventh day after administration of the first dose of vaccine. Beyond the seventh day, HRIG is not indicated since an antibody response to cell culture vaccine is presumed to have occurred. The recommended dose of HRIG is 20 IU/kg. This formula is applicable for all age groups, including children. If anatomically feasible, up to one-half the

dose of HRIG should be thoroughly infiltrated in the area around the wound and the rest should be administered intramuscularly in the gluteal area. HRIG should never be administered in the same syringe or into the same anatomical site as vaccine. Because HRIG may partially suppress active production of antibody, no more than the recommended dose should be given (53).

VACCINATION AND SEROLOGIC TESTING

The effectiveness of rabies vaccines is primarily measured by their ability to protect persons exposed to rabies. HDCV has been used effectively with HRIG or equine antirabies serum (ARS) worldwide to treat persons bitten by various rabid animals (15,16). An estimated one million people worldwide have received rabies postexposure prophylaxis with HDCV since its introduction 12 years ago (54).

In studies of animals, antibody titers have been shown to be markers of protection. Antibody titers will vary with time since the last vaccination. Differences among laboratories that test blood samples may also influence the results.

Serologic Response Shortly After Vaccination

All persons tested at CDC 2-4 weeks after completion of preexposure and postexposure rabies prophylaxis according to ACIP guidelines have demonstrated an antibody response to rabies (15,55,56). Therefore, it is not necessary to test serum samples from patients completing preexposure or postexposure prophylaxis to document seroconversion unless the person is immunosuppressed (see Precautions and Contraindications). If titers are obtained, specimens collected 2-4 weeks after preexposure or postexposure prophylaxis should completely neutralize challenge virus at a 1:25 serum dilution by the rapid fluorescent focus inhibition test (RFFIT). (This dilution is approximately equivalent to the minimum titer of 0.5 IU recommended by the WHO.)

Serologic Response and Preexposure Booster Doses of Vaccine

Two years after primary preexposure vaccination, a 1:5 serum dilution will fail to neutralize challenge virus completely (by RFFIT) among 2%-7% of persons who received the three-dose preexposure series intramuscularly and 5%-17% of persons who received the three-dose series intradermally (57). If the titer falls below 1:5, a preexposure booster dose of vaccine is recommended for a person at continuous or frequent risk (Table_3) of exposure to rabies. The following guidelines are recommended for determining when serum testing should be performed after primary preexposure vaccination:

1. A person in the continuous risk category (Table_3) should have a serum sample tested for rabies antibody every 6 months (58).

2. A person in the frequent risk category (Table_3) should have a serum sample tested for rabies antibody every 2 years.

   State or local health departments may provide the names and addresses

of laboratories performing rabies serologic testing.

POSTEXPOSURE TREATMENT OUTSIDE THE UNITED STATES

U.S. citizens and residents who are exposed to rabies while traveling outside the United States in countries where rabies is endemic may sometimes receive postexposure therapy with regimens or biologics that are not used in the United States. The following information is provided to familiarize physicians with some of the regimens used more widely abroad. These schedules have not been

submitted for approval by the Food and Drug Administration (FDA) for use in the United States. If postexposure treatment is begun outside the United States using one of these regimens or biologics of nerve tissue origin, it may be necessary to provide additional treatment when the patient reaches the United States. State or local health departments should be contacted for specific advice in such cases.

Modifications to the postexposure vaccine regimen approved for use in the United States have been made to reduce the cost of postexposure prophylaxis and hasten the development of active immunity (59). Costs are reduced primarily by substituting various schedules of ID injections (0.1 ml each) of HDCV (or newer tissue culture-derived rabies vaccines for humans) for IM injection of HDCV. Two such regimens are efficacious among persons bitten by rabid animals (60). One of these regimens consists of 0.1-ml ID doses of HDCV given at eight different sites (deltoid, suprascapular, thigh, and abdominal wall) on day 0; four ID 0.1-ml doses given at four sites on day 7 (deltoid, thigh); and one ID 0.1-ml dose given in the deltoid on both day 28 and 91. Another ID regimen shown to be efficacious and now widely used in Thailand employs Purified VERO Cell Rabies Vaccine (Pasteur-Merieux), with 0.1-ml doses given at two different sites on days 0, 3, and 7, followed by one 0.1-ml booster on days 30 and 90 (61).

Strategies designed to hasten the development of active immunity have concentrated on administering more IM or ID doses at the time postexposure prophylaxis is initiated with fewer doses thereafter (62). The most extensively evaluated regimen in this category, developed in Yugoslavia, has been the 2-1-1 regimen (two 1.0-ml IM doses on day 0, and one each on days 7 and 21) (63-65). However, when using HRIG in conjunction with this schedule, there may be some suppression of the neutralizing antibody response (65).

Purified antirabies sera of equine origin (Sclavo; Pasteur-Merieux; Swiss Serum and Vaccine Institute, Bern) have been used effectively in developing countries where HRIG may not be available. The incidence of adverse reactions has been low (0.8%-6.0%) and most of those that occurred were minor (66-68).

Although no postexposure vaccine failures have occurred in the United States during the 10 years that HDCV has been licensed, seven persons have contracted rabies after receiving postexposure treatment with both HRIG and HDCV outside the United States. An additional six persons have contracted the disease after receiving postexposure prophylaxis with other cell culture-derived vaccines and HRIG or ARS. However, in each of these cases, there was some deviation from the recommended postexposure treatment protocol (69-71). Specifically, patients who contracted rabies after postexposure prophylaxis did not have their wounds cleansed with soap and water or other antiviral agents, did not receive their rabies vaccine injections in the deltoid area (i.e., vaccine was administered in the gluteal area), or did not receive passive vaccination around the wound site.

PREEXPOSURE VACCINATION AND POSTEXPOSURE THERAPY OF PREVIOUSLY VACCINATED PERSONS

Preexposure vaccination should be offered to persons among high-risk groups, such as veterinarians, animal handlers, certain laboratory workers, and persons spending time (e.g., 1 month) in foreign countries where canine rabies is endemic. Other persons whose activities bring them into frequent contact with rabies virus or potentially rabid dogs, cats, skunks, raccoons, bats, or other species at risk of having rabies should also be considered for preexposure prophylaxis.

Preexposure prophylaxis is given for several reasons. First, it may provide protection to persons with inapparent exposures to rabies. Second, it may protect persons whose postexposure therapy might be delayed. Finally, although preexposure vaccination does not eliminate the need for additional therapy

after a rabies exposure, it simplifies therapy by eliminating the need for HRIG and decreasing the number of doses of vaccine needed -- a point of particular importance for persons at high risk of being exposed to rabies in areas where immunizing products may not be available or where they may carry a high risk of adverse reactions.

Primary Preexposure Vaccination

Intramuscular Primary Vaccination

Three 1.0-ml injections of HDCV or RVA should be given intramuscularly (deltoid area), one each on days 0, 7, and 21 or 28 (Table_4). In a study in the United States, greater than 1,000 persons received HDCV according to this regimen. Antibody was demonstrated in serum samples of all subjects when tested by the RFFIT. Other studies have produced comparable results (33,56,72,73).

Intradermal Primary Vaccination

A regimen of three 0.1-ml doses of HDCV, one each on days 0, 7, and 21 or 28 (10,33,34,36,72,73), is also used for preexposure vaccination (Table_4). The ID dose/route has been recommended previously by the ACIP as an alternative to the 1.0-ml IM dose/route for rabies preexposure prophylaxis with HDCV (24,74).

Pasteur-Merieux developed a syringe containing a single dose of lyophilized HDCV (Imovax((R)) Rabies I.D.) that is reconstituted in the syringe just before administration. The syringe is designed to deliver 0.1 ml of HDCV reliably and was approved by the FDA in 1986 (24). The 0.1-ml ID doses, given in the area over the deltoid (lateral aspect of the upper arm) on days 0, 7, and 21 or 28, are used for primary preexposure vaccination. One 0.1-ml ID dose is used for booster vaccination (see Table_3). The 1.0-ml vial is not approved for multi-dose ID use. RVA should not be given by the ID dose/route (26).

Chloroquine phosphate (administered for malaria chemoprophylaxis) interferes with the antibody response to HDCV (75). Accordingly, HDCV should not be administered by the ID dose/route to persons traveling to malaria-endemic countries while the person is receiving chloroquine (76). The IM dose/route of preexposure prophylaxis provides a sufficient margin of safety in this situation (76). For persons who will be receiving both rabies preexposure prophylaxis and chloroquine in preparation for travel to a rabies-enzootic area, the ID dose/route should be initiated at least 1 month before travel to allow for completion of the full three-dose vaccine series before antimalarial prophylaxis begins. If this schedule is not possible, the IM dose/route should be used. Although interference with the immune response to rabies vaccine by other antimalarials structurally related to chloroquine (e.g., mefloquine) has not been evaluated, it would seem prudent to follow similar precautions for persons receiving these drugs.

Booster Vaccination

Preexposure Booster Doses of Vaccine

Persons who work with live rabies virus in research laboratories or vaccine production facilities (continuous risk category; see Table_3) are at the highest risk of inapparent exposures. Such persons should have a serum sample tested for rabies antibody every 6 months (Table_4). Booster doses (IM or ID) of vaccine should be given to maintain a serum titer corresponding to at least complete neutralization at a 1:5 serum dilution by the RFFIT. The frequent risk category includes other laboratory workers, such as those doing rabies diagnostic testing, spelunkers, veterinarians and staff, animal-control and wildlife officers in areas where animal rabies is epizootic, and international

travelers living or visiting (for greater than 30 days) in areas where canine rabies is endemic. Persons among this group should have a serum sample tested for rabies antibody every 2 years and, if the titer is less than complete neutralization at a 1:5 serum dilution by the RFFIT, should have a booster dose of vaccine. Alternatively, a booster can be administered in lieu of a titer determination. Veterinarians and animal control and wildlife officers working in areas of low rabies enzooticity (infrequent exposure group) do not require routine preexposure booster doses of HDCV or RVA after completion of primary preexposure vaccination (Table 3).

Postexposure Therapy of Previously Vaccinated Persons

If exposed to rabies, persons previously vaccinated should receive two IM doses (1.0 ml each) of vaccine, one immediately and one 3 days later. Previously vaccinated refers to persons who have received one of the recommended preexposure or postexposure regimens of HDCV or RVA, or those who received another vaccine and had a documented rabies antibody titer. HRIG is unnecessary and should not be given in these cases because an anamnestic antibody response will follow the administration of a booster regardless of the prebooster antibody titer (77).

Preexposure Vaccination and Serologic Testing

Because the antibody response after these recommended preexposure prophylaxis vaccine regimens has been satisfactory, serologic testing is not necessary except for persons suspected of being immunosuppressed. Patients who are immunosuppressed by disease or medications should postpone preexposure vaccinations. Immunosuppressed persons who are at risk of rabies exposure should be vaccinated and their antibody titers checked.

UNINTENTIONAL INOCULATION WITH MODIFIED LIVE RABIES VIRUS

Veterinary personnel may be inadvertently exposed to attenuated rabies virus while administering modified live rabies virus (MLV) vaccines to animals. Although there have been no reported rabies cases among humans resulting from exposure to needle sticks or sprays with licensed MLV vaccines, vaccine-induced rabies has occurred among animals given these vaccines. Absolute assurance of a lack of risk for humans, therefore, cannot be given. The best evidence for low risk is the absence of recognized cases of vaccine-associated disease among humans despite frequent inadvertent exposures.

MLV animal vaccines that are currently available are made with one attenuated strain of rabies virus: high egg passage (HEP) Flury strain. The HEP Flury strain has been used in animal vaccines for more than 25 years without evidence of associated disease among humans; therefore, postexposure treatment is not recommended following exposure to this type of vaccine by needle sticks or sprays.

Because the data are insufficient to assess the true risk associated with any of the MLV vaccines, preexposure vaccination and periodic boosters are recommended for all persons whose activities either bring them into contact with potentially rabid animals or who frequently handle attenuated animal rabies vaccine.

ADVERSE REACTIONS

Human Diploid Cell Rabies Vaccine and Rabies Vaccine Adsorbed

Reactions after vaccination with HDCV and RVA are less serious and common than with previously available vaccines (78,79). In studies using a three-dose postexposure regimen of HDCV, local reactions, such as pain, erythema, and swelling or itching at the injection site, have been reported among 30%-74% of recipients. Systemic reactions, such as headache, nausea, abdominal pain, muscle

aches, and dizziness have been reported among 5%-40% of recipients. Three cases of neurologic illness resembling Guillain-Barre syndrome that resolved without sequelae in 12 weeks have been reported (10,80,81). In addition, a few other subacute central and peripheral nervous system disorders have been temporally associated with HDCV vaccine, but a causal relationship has not been established (82).

An immune complex-like reaction occurs among approximately 6% of persons receiving booster doses of HDCV (11,12) 2-21 days after administration of the booster dose. These patients develop a generalized urticaria, sometimes accompanied by arthralgia, arthritis, angioedema, nausea, vomiting, fever, and malaise. In no cases have the illnesses been life-threatening. This reaction occurs much less frequently among persons receiving primary vaccination.

The reaction has been associated with the presence of betapropiolactone-altered human serum albumin in the HDCV and the development of immunoglobulin E (IgE) antibodies to this allergen (83,84). Among persons who have received their primary vaccination series with HDCV, administration of boosters with a purified HDCV produced in Canada (Connaught Laboratories Ltd., Rabies Vaccine Inactivated (Diploid Cell Origin)-Dried) does not appear to be associated with this reaction (57). This vaccine is not yet licensed in the United States.

Vaccines and Immune Globulins Used in Other Countries

Many developing countries use inactivated nerve tissue vaccines made from the brains of adult animals or suckling mice. Nerve tissue vaccine (NTV) is reported to induce neuroparalytic reactions among approximately 1 per 200 to 1 per 2,000 vaccinees; suckling mouse brain vaccine (SMBV) causes reactions in among approximately 1 per 8,000 (17).

Human Rabies Immune Globulins

Local pain and low-grade fever may follow receipt of HRIG. Although not reported specifically for HRIG, angioneurotic edema, nephrotic syndrome, and anaphylaxis have been reported after injection of immune globulin (IG). These reactions occur so rarely that a causal relationship between IG and these reactions is not clear.

There is no evidence that hepatitis B virus (HBV), human immunodeficiency virus (HIV, the causative agent of Acquired Immunodeficiency Syndrome (AIDS)), or other viruses have ever been transmitted by commercially available HRIG in the United States.

Management of Adverse Reactions

Once initiated, rabies prophylaxis should not be interrupted or discontinued because of local or mild systemic adverse reactions to rabies vaccine. Usually such reactions can be successfully managed with anti-inflammatory and antipyretic agents (e.g., aspirin).

When a person with a history of serious hypersensitivity to rabies vaccine must be revaccinated, antihistamines may be given. Epinephrine should be readily available to counteract anaphylactic reactions, and the person should be observed carefully immediately after vaccination.

Although serious systemic, anaphylactic, or neuroparalytic reactions are rare during and after the administration of rabies vaccines, such reactions pose a serious dilemma for the attending physician (11). A patient's risk of acquiring rabies must be carefully considered before deciding to discontinue vaccination. Advice and assistance on the management of serious adverse reactions for persons receiving rabies vaccines may be sought from the state health department or CDC.

All serious systemic, neuroparalytic, or anaphylactic reactions to HDCV should be reported immediately to Connaught Laboratories, Inc., Swiftwater, PA 18370. Phone: (800) VACCINE or (717) 839-7187. Serious reactions after the administration of RVA should be reported immediately to Coordinating Physicians, Bureau of Laboratories and Epidemiological Services, Michigan Department of Public Health, P. O. Box 30035, 3500 N. Logan, Lansing, MI 48909. Phone: (517) 335-8050.

PRECAUTIONS AND CONTRAINDICATIONS

Immunosuppression

Corticosteroids, other immunosuppressive agents, antimalarials, and immunosuppressive illnesses can interfere with the development of active immunity after vaccination and may predispose the patient to rabies (75,85). Preexposure prophylaxis should be administered to such persons with the awareness that the immune response may be inadequate (see Intradermal Primary Vaccination). Immunosuppressive agents should not be administered during postexposure therapy unless essential for the treatment of other conditions. When rabies postexposure prophylaxis is administered to persons receiving steroids or other immunosuppressive therapy, it is especially important that a serum sample be tested for rabies antibody to ensure that an acceptable antibody response has developed (see Vaccination and Serologic Testing).

Pregnancy

Because of the potential consequences of inadequately treated rabies exposure, and because there is no indication that fetal abnormalities have been associated with rabies vaccination, pregnancy is not considered a contraindication to postexposure prophylaxis (86). If there is substantial risk of exposure to rabies, preexposure prophylaxis may also be indicated during pregnancy.

Allergies

Persons who have a history of serious hypersensitivity to rabies vaccine should be revaccinated with caution (see Management of Adverse Reactions).

- For assistance with problems or questions about rabies prophylaxis, contact your local or state health department. If local or state health department personnel are unavailable, call the Division of Viral and Rickettsial Diseases, Center for Infectious Diseases, CDC ((404) 639-1075 during working hours or (404) 639-2888 nights, weekends, and holidays).

References

1. Reid-Sanden FL, Dobbins JG, Smith JS, Fishbein DB. Rabies surveillance, United States during 1989. J Am Vet Med Assoc 1990;197:1571-83.

2. Helmick CG. The epidemiology of human rabies postexposure prophylaxis, 1980-1981. JAMA 1983;250:1990-6.

3. CDC. Human rabies diagnosed 2 months postmortem -- Texas. MMWR 1985;34: 700,705-7.

4. CDC. Human rabies acquired outside the United States. MMWR 1985;34: 235-6.

5. CDC. Human rabies -- California, 1987. MMWR 1988;37:305-8.

6. CDC. Human rabies -- Oregon, 1989. MMWR 1989;38:335-7.

7. CDC. Human rabies -- Texas. MMWR 1984;33:469-70.

8. CDC. Imported human rabies. MMWR 1983;32:78-80,85-6.

9. CDC. Human rabies acquired outside the United States from a dog bite. MMWR 1981;30:537-40.

10. Bernard KW, Smith PW, Kader FJ, Moran MJ. Neuroparalytic illness and human diploid cell rabies vaccine. JAMA 1982;248:3136-8.

11. CDC. Systemic allergic reactions following immunization with human diploid cell rabies vaccine. MMWR 1984;33:185-7.

12. Dreesen DW, Bernard KW, Parker RA, Deutsch AJ, Brown J. Immune complex-like disease in 23 persons following a booster dose of rabies human diploid cell vaccine. Vaccine 1986;4:45-9.

13. Aoki FY, Tyrrell DA, Hill LE. Immunogenicity and acceptability of a human diploid-cell culture rabies vaccine in volunteers. Lancet 1975;1: 660-2.

14. Cox JH, Schneider LG. Prophylactic immunization of humans against rabies by intradermal inoculation of human diploid cell culture vaccine. J Clin Microbiol 1976;3:96-101.

15. Anderson LJ, Sikes RK, Langkop CW, et al. Postexposure trial of a human diploid cell strain rabies vaccine. J Infect Dis 1980;142:133-8.

16. Bahmanyar M, Fayaz A, Nour-Salehi S, Mohammadi M, Koprowski H. Successful protection of humans exposed to rabies infection. Postexposure treatment with the new human diploid cell rabies vaccine and antirabies serum. JAMA 1976;236:2751-4.

17. Hattwick MAW. Human rabies. Public Health Rev 1974;3:229-74.

18. Wiktor TJ, Plotkin SA, Koprowski H. Development and clinical trials of the new human rabies vaccine of tissue culture (human diploid cell) origin. Dev Biol Stand 1978;40:3-9.

19. World Health Organization. WHO expert committee on rabies. WHO Tech Rep Ser 1984;709:1-104.

20. Kuwert EK, Werner J, Marcus I, Cabasso VJ. Immunization against rabies with rabies immune globulin, human (RIGH) and a human diploid cell strain (HDCS) rabies vaccine. J Biol Stand 1978;6:211-9.

21. Winkler WG, Schmidt RC, Sikes RK. Evaluation of human rabies immune globulin and homologous and heterologous antibody. J Immunol 1969;102:1314-21.

22. Cabasso VJ, Loofbourow JC, Roby RE, Anuskiewicz W. Rabies immune globulin of human origin: preparation and dosage determination in non-exposed volunteer subjects. Bull WHO 1971;45:303-15.

23. Wiktor TJ, Sokol F, Kuwert E, Koprowski H. Immunogenicity of concentrated and purified rabies vaccine of tissue culture origin. Proc Soc Exp Biol Med 1969;131:799-805.

24. CDC. Rabies prevention: supplementary statement on the preexposure use of human diploid cell

rabies vaccine by the intradermal route. MMWR 1986;35:767-8.

25. CDC. Rabies postexposure prophylaxis with human diploid cell rabies vaccine: lower neutralizing antibody titers with Wyeth vaccine. MMWR 1985;34:90-2.

26. CDC. Rabies vaccine, adsorbed: a new rabies vaccine for use in humans. MMWR 1988;37:217-8,223.

27. Burgoyne GH, Kajiya KD, Brown DW, Mitchell JR. Rhesus diploid rabies vaccine (adsorbed): a new rabies vaccine using FRhL-2 cells. J Infect Dis 1985;152:204-10.

28. Levenbook IS, Elisberg BL, Driscoll BF. Rhesus diploid rabies vaccine (adsorbed): neurological safety in guinea pigs and Lewis rats. Vaccine 1986;4:225-7.

29. Berlin BS, Goswick C. Rapidity of booster response to rabies vaccine produced in cell culture (letter). J Infect Dis 1984;150:785.

30. Berlin BS, Mitchell JR, Burgoyne GH, Brown WE, Goswick C. Rhesus diploid rabies vaccine (adsorbed), a new rabies vaccine. II. Results of clinical studies simulating prophylactic therapy for rabies exposure. JAMA 1983;249:2663-5.

31. Berlin BS, Mitchell JR, Burgoyne GH, et al. Rhesus diploid rabies vaccine (adsorbed), a new rabies vaccine. Results of initial clinical studies of preexposure vaccination. JAMA 1982;247:1726-8.

32. Berlin BS. Rabies Vaccine Adsorbed: neutralizing antibody titers after three-dose pre-exposure vaccination. Am J Public Health 1990;80:476-7.

33. Nicholson KG, Turner GS, Aoki FY. Immunization with a human diploid cell strain of rabies virus vaccine: two-year results. J Infect Dis 1978;137:783-8.

34. Bernard KW, Roberts MA, Sumner J, et al. Human diploid cell rabies vaccine. Effectiveness of immunization with small intradermal or subcutaneous doses. JAMA 1982;247:1138-42.

35. Bernard KW, Mallonee J, Wright JC, et al. Preexposure immunization with intradermal human diploid cell rabies vaccine. Risks and benefits of primary and booster vaccination. JAMA 1987;257:1059-63.

36. Fishbein DB, Pacer RE, Holmes DF, Ley AB, Yager P, Tong TC. Rabies preexposure prophylaxis with human diploid cell rabies vaccine: a dose-response study. J Infect Dis 1987;156:50-5.

37. Afshar A. A review of non-bite transmission of rabies virus infection. Br Vet J 1979;135:142-8.

38. Winkler WG, Fashinell TR, Leffingwell L, Howard P, Conomy P. Airborne rabies transmission in a laboratory worker. JAMA 1973;226:1219-21.

39. CDC. Rabies in a laboratory worker -- New York. MMWR 1977;26:183-4.

40. CDC. Human-to-human transmission of rabies via corneal transplant -- Thailand. MMWR 1981;30:473-4.

41. Gode GR, Bhide NK. Two rabies deaths after corneal grafts from one donor (letter). Lancet 1988;2:791.

42. CDC. Human-to-human transmission of rabies via a corneal transplant -- France. MMWR 1980;29:25-6.

43. Houff SA, Burton RC, Wilson RW, et al. Human-to-human transmission of rabies virus by corneal transplant. N Engl J Med 1979;300:603-4.

44. Helmick CG, Tauxe RV, Vernon AA. Is there a risk to contacts of patients with rabies? Rev Infect Dis 1987;9:511-8.

45. Garner JS, Simmons BP. Guidelines for isolation precautions in hospitals. Infect Cont 1983;4(Suppl):245-325.

46. National Association of State Public Health Veterinarians. Compendium of animal rabies control. J Am Vet Med Assoc 1990;196:36-9.

47. Fishbein DB, Belotto AJ, Pacer RE, et al. Rabies in rodents and lagomorphs in the United States, 1971-1984: increased cases in the woodchuck (Marmota monax) in mid-Atlantic states. J Wildl Dis 1986;22:151-5.

48. CDC. Imported dog and cat rabies -- New Hampshire, California. MMWR 1988;37:559-60.

49. Eng TR, Fishbein DB. Epidemiologic factors, clinical findings, and vaccination status of rabies in cats and dogs in the United States in 1988. J Am Vet Med Assoc 1990;197:201-9.

50. Dean DJ, Baer GM. Studies on the local treatment of rabies infected wounds. Bull WHO 1963;28:477-86.

51. Kaplan MM, Cohen D, Koprowski H, Dean D, Ferrigan L. Studies on the local treatment of wounds for the prevention of rabies. Bull WHO 1962; 26:765-75.

52. Fishbein DB, Sawyer LA, Reid-Sanden FL, Weir EH. Administration of human diploid-cell rabies vaccine in the gluteal area (letter). N Engl J Med 1988;318:124-5.

53. Helmick CG, Johnstone C, Sumner J, Winkler WG, Fager S. A clinical study of Merieux human rabies immune globulin. J Biol Stand 1982;10: 357-67.

54. Roumiantzeff M. The present status of rabies vaccine development and clinical experience with rabies vaccine. Southeast Asian J Trop Med Public Health 1988;19:549-61.

55. Kuwert EK, Marcus I, Werner J, et al. Post-exposure use of human diploid cell culture rabies vaccine. Dev Biol Stand 1976;37:273-86.

56. CDC. Recommendation of the Immunization Practices Advisory Committee (ACIP). Supplementary statement on pre-exposure rabies prophylaxis by the intradermal route. MMWR 1982;31:279-80,285.

57. Fishbein DB, Dreesen DW, Holmes DF, et al. Human diploid cell rabies vaccine purified by zonal centrifugation: a controlled study of antibody response and side effects following primary and booster pre-exposure immunization. Vaccine 1990;7:437-42.

58. Richardson JH, Barkley WE, eds. Biosafety in Microbiological and Biomedical Laboratories. 2nd ed. Washington, DC: U.S. Government Printing Office, 1988. HHS Publication No. (NIH) 88-8395.

59. Nicholson KG. Rabies. Lancet 1990;335:1201-5.

60. Warrell MJ, Nicholson KG, Warrell DA, et al. Economical multiple-site intr effective for post-exposure rabies prophylaxis. Lancet 1985;1:1059-62.

61. Chutivongse S, Wilde H, Supich C, Baer GM, Fishbein DB. Postexposure prophylaxis for rabies with antiserum and intradermal vaccination. Lancet 1990;335:896-8.

62. Anderson LJ, Baer GM, Smith JS, Winkler WG, Holman RC. Rapid antibody response to human diploid rabies vaccine. Am J Epidemiol 1981;113: 270-5.

63. Vodopija I, Sureau P, Lafon M, et al. An evaluation of second generation tissue culture rabies vaccines for use in man: a four-vaccine comparative immunogenicity study using a pre-exposure vaccination schedule and an abbreviated 2-1-1 postexposure schedule. Vaccine 1986;4:245-8.

64. Vodopija I, Sureau P, Smerdel S, et al. Comparative study of two human diploid rabies vaccines administered with antirabies globulin. Vaccine 1988;6:489-90.

65. Vodopija I, Sureau P, Smerdel S, et al. Interaction of rabies vaccine with human rabies immunoglobulin and reliability of a 2-1-1 schedule application for postexposure treatment. Vaccine 1988;6:283-6.

66. Wilde H, Chomchey P, Prakongsri S, Punyaratabandhu P. Safety of equine rabies immune globulin (letter). Lancet 1987;2:1275.

67. Wilde H, Chomchey P, Prakongsri S, Punyaratabandhu P, Chutivongse S. Adverse effects of equine rabies immune globulin. Vaccine 1989;7:10-1.

68. Wilde H, Chomchey P, Punyaratabandhu P. Purified equine rabies immune globulin; a safe and affordable alternative to human rabies immune globulin (experience with 3156 patients). Bull WHO (in press).

69. CDC. Human rabies despite treatment with rabies immune globulin and human diploid cell rabies vaccine -- Thailand. MMWR 1987;36:759-60,765.

70. Shill M, Baynes RD, Miller SD. Fatal rabies encephalitis despite appropriate post-exposure prophylaxis. A case report. N Engl J Med 1987;316:1257-8.

71. Wilde H, Choomkasien P, Hemachudha T, Supich C, Chutivongse S. Failure of rabies postexposure treatment in Thailand. Vaccine 1989;7:49-52.

72. Turner GS, Nicholson KG, Tyrrell DA, Aoki FY. Evaluation of a human diploid cell strain rabies vaccine: final report of a three year study of pre-exposure immunization. J Hyg (Lond) 1982;89:101-10.

73. Cabasso VJ, Dobkin MB, Roby RE, Hammar AH. Antibody response to a human diploid cell rabies vaccine. Appl Microbiol 1974;27:553-61.

74. CDC. Rabies prevention -- United States, 1984. MMWR 1984;33:393-402, 407-8.

75. Pappaioanou M, Fishbein DB, Dreesen DW, et al. Antibody response to preexposure human diploid-cell rabies vaccine given concurrently with chloroquine. N Engl J Med 1986;314:280-4.

76. Bernard KW, Fishbein DB, Miller KD, et al. Pre-exposure rabies immunization with human diploid cell vaccine: decreased antibody responses in persons immunized in developing countries. Am J Trop Med Hyg 1985;34:633-47.

77. Fishbein DB, Bernard KW, Miller KD, et al. The early kinetics of the neutralizing antibody response after booster immunizations with human diploid cell rabies vaccine. Am J Trop Med Hyg 1986;35:663-70.

78. Rubin RH, Hattwick MA, Jones S, Gregg MB, Schwartz VD. Adverse reactions to duck embryo rabies vaccine. Range and incidence. Ann Intern Med 1973;78:643-9.

79. Corey L, Hattwick MA, Baer GM, Smith JS. Serum neutralizing antibody after rabies postexposure prophylaxis. Ann Intern Med 1976;85:170-6.

80. Boe E, Nylan H. Guillain-Barre syndrome after vaccination with human diploid cell rabies vaccine. Scand J Infect Dis 1980;12:231-2.

81. Knittel T, Ramadori G, Mayet WJ, Lohr H, Meyer zum Buschenfelde KH. Guillain-Barre syndrome and human diploid cell rabies vaccine (Letter). Lancet 1989;1:1334-5.

82. Tornatore CS, Richert JR. CNS demyelination associated with diploid cell rabies vaccine (Letter). Lancet 1990;335:1346-7.

83. Anderson MC, Baer H, Frazier DJ, Quinnan GV. The role of specific IgE and beta-propiolactone in reactions resulting from booster doses of human diploid cell rabies vaccine. J Allergy Clin Immunol 1987;80: 861-8.

84. Swanson MC, Rosanoff E, Gurwith M, Deitch M, Schnurrenberger P, Reed CE. IgE and IgG antibodies to beta-propiolactone and human serum albumin associated with urticarial reactions to rabies vaccine. J Infect Dis 1987;155:909-13.

85. Enright JB. The effects of corticosteroids on rabies in mice. Can J Microbiol 1974;16:667.

86. Varner MW, McGuinness GA, Galask RP. Rabies vaccination in pregnancy. Am J Obstet Gynecol 1982;143:717-8.

Table_1

Note: To print large tables and graphs users may have to change their printer settings to landscape and use a small font size.

Table 1. Rabies postexposure prophylaxis guide, United States, 1991

Animal type	Evaluation and disposition of animal	Postexposure prophylaxis recommendations
Dogs and cats	Healthy and available for 10 days observation	Should not begin prophylaxis unless animal develops symptoms of rabies *
	Rabid or suspected rabid	Immediate vaccination
	Unknown (escaped)	Consult public health officials

Skunks, raccoons, bats, foxes, and most other carnivores; woodchucks	Regarded as rabid unless geographic area is known to be free of rabies or until animal proven negative by laboratory tests +	Immediate vaccination
Livestock, rodents, and lagomorphs (rabbits and hares)	Consider individually	Consult public health officials. Bites of squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, other rodents, rabbits, and hares almost never require antirabies treatment

* During the 10-day holding period, begin treatment with HRIG and HDCV or RVA at first sign of rabies in a dog or cat that has bitten someone. The symptomatic animal should be killed immediately and tested.
+ The animal should be killed and tested as soon as possible. Holding for observation is not recommended. Discontinue vaccine if immunofluorescence test results of the animal are negative.

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Table_2

Note: To print large tables and graphs users may have to change their printer settings to landscape and use a small font size.

Table 2. Rabies postexposure prophylaxis schedule, United States, 1991

Vaccination status	Treatment	Regimen *
Not previously vaccinated	Local wound cleansing	All postexposure treatment should begin with immediate thorough cleansing of all wounds with soap and water.
	HRIG	20 IU/kg body weight. If anatomically feasible, up to one-half the dose should be infiltrated around the wound(s) and the rest should be administered IM in the gluteal area. HRIG should not be administered in the same syringe or into the same anatomical site as vaccine. Because HRIG may partially suppress active production of antibody, no more than the recommended dose should be given.
	Vaccine	HDCV or RVA, 1.0 ml, IM (deltoid area +), one each on days 0, 3, 7, 14 and 28.
Previously vaccinated &	Local wound cleansing	All postexposure treatment should begin with immediate thorough cleansing of all wounds with soap and water.
	HRIG	HRIG should not be administered.
	Vaccine	HDCV or RVA, 1.0 ml, IM (deltoid area +), one each on days 0 and 3.

* These regimens are applicable for 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.
& Any person with a history of preexposure vaccination with HDCV or RVA; prior postexposure prophylaxis with HDCV or RVA; or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination.

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Table_3

Note: To print large tables and graphs users may have to change their printer settings to landscape and use a small font size.

Table 3. Rabies preexposure prophylaxis guide, United States, 1991

Risk category	Nature of risk	Typical populations	Preexposure recommendations
Continuous	Virus present continuously, often in high concentrations. Aerosol, mucous membrane, bite, or nonbite exposure. Specific exposures	Rabies research lab worker; * rabies biologics production workers.	Primary course. Seriologic testing every 6 months; booster vaccination when antibody level falls below acceptable level. +

	may go unrecognized.		
Frequent	Exposure usually episodic, with source recognized, but exposure may also be unrecognized. Aerosol, mucous membrane, bite, or nonbite exposure.	Rabies diagnostic lab workers, * spelunkers, veterinarians and staff, and animal-control and wildlife workers in rabies enzootic areas. Travelers visiting foreign areas of enzootic rabies for more than 30 days.	Primary course. Seriologic testing or booster vaccination every 2 years. +
Infrequent (greater than population at large)	Exposure nearly always episodic with source recognized. Mucous membrane, bite, or nonbite exposure.	Veterinarians and animal-control and wildlife workers in areas of low rabies enzooticity. Veterinary students.	Primary course; no seriologic testing or booster vaccination.
Rare (population at large)	Exposures always episodic. Mucous membrane, or bite with source unrecognized.	U.S. population at large, including persons in rabies epizootic areas.	No vaccination necessary.

* Judgment of relative risk and extra monitoring of vaccination status of laboratory workers is the responsibility of the laboratory supervisor (58).
+ Minimum acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by RFFIT. Booster dose should be administered if the titer falls below this level.

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Table_4

Note: To print large tables and graphs users may have to change their printer settings to landscape and use a small font size.

Table 4. Rabies preexposure prophylaxis schedule, United States, 1991

Type of vaccination	Route	Regimen
Primary	IM	HDCV or RVA, 1.0 ml (deltoid area), one each on days 0, 7, and 21 or 28
	ID	HDCV, 0.1 ml, one each on Days 0, 7, and 21 or 28
Booster *	IM	HDCV or RVA, 1.0 ml (deltoid area), day 0 only
	ID	HDCV, 0.1 ml, day 0 only

* Administration of routine booster dose of vaccine depends on exposure risk category as noted in Table 3.

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