



DEPARTMENT OF THE NAVY
NAVAL MEDICAL COMMAND
WASHINGTON, D.C. 20372-5120

IN REPLY REFER TO

NAVMEDCOMINST 6220.4
MEDCOM-24
4 Aug 88

NAVMEDCOM INSTRUCTION 6220.4

From: Commander, Naval Medical Command
To: Ships and Stations Having Medical Department Personnel

Subj: RABIES PREVENTION AND CONTROL

Ref: (a) SECNAVINST 6401.1, Veterinary Health Services
(b) NAVMEDCOMINST 6220.2, Disease Alert Reports

Encl: (1) General Guidance for Human Rabies Prevention and Immunoprophylaxis
(2) Centers for Disease Control, Rabies Prevention--United States, 1984, MMWR 1984; 33(28):393-408
(3) Navy Environmental and Preventive Medicine Units, Including Areas of Responsibility and Message Addresses
(4) DD 2341, Report of Animal Bite--Potential Rabies Exposure

1. Purpose. To provide general policy and recommendations for the prevention and control of rabies among Navy and Marine Corps personnel and their dependents, Military Sealift Command (MSC) personnel, Federal civilian employees, and personnel of other uniformed services and their dependents serving, traveling, or attending activities aboard facilities under the sponsorship of the Navy or Marine Corps. This instruction on the prevention of rabies in humans augments the guidance on animal rabies prevention and control contained in reference (a).

2. Cancellation. BUMEDINST 6220.6.

3. Background

a. Rabies is a zoonotic viral infection of certain warm-blooded vertebrates worldwide. Transmission to humans is primarily through bites from infected animals. The disease in humans is invariably fatal; however, the incidence of human rabies infections in the United States is extremely small. Rabies is endemic among wild animal populations in some areas of the United States and can be transmitted to domestic animals in close contact with humans. Rabies remains a real threat to Navy and Marine Corps personnel deployed to or living in many tropical and subtropical countries. This threat is present in both urban and rural settings.

b. Rabies is a preventable disease. However, it can be fatal if the diagnosis is delayed or the treatment is not timely or appropriate. Recent instances of civilian human rabies were fatal despite the patients being given postexposure prophylaxis (immunizations), because the human diploid cell rabies vaccine (HDCV) was inappropriately administered. These instances serve as reminders that the proper administration of needed vaccine is as important as suspecting that a person may have been exposed to a rabid animal and treated accordingly.

4. Action

a. Commanders, commanding officers, officers in charge, and masters of MSC ships must:

(1) Ensure their commands or units maintain supplies of HDCV and human rabies immune globulin (RIG) appropriate to the geographic risk of exposure by location or deployment.

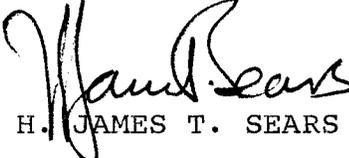
(2) Ensure standard procedures exist for the investigation, evaluation, and management of animal bites occurring among their personnel.

(3) Ensure all personnel under their cognizance are made aware of the risks and consequences of animal bites, appropriate measures to prevent bites from stray or wild animals, and the general procedures to follow for obtaining medical evaluation if bitten, when stationed in or deployed to areas of known rabies endemicity.

b. Medical Department personnel with clinical care responsibilities for animal bite patients must take action as directed or recommended in applicable portions of enclosures (1) and (2), or upon the advice of the cognizant Navy environmental and preventive medicine unit listed in enclosure (3).

5. Disease Alert Report. Report and investigate all animal bites following local military and civilian requirements. Use enclosure (4), DD 2341, Report of Animal Bite--Potential Rabies Exposure to document local investigation and management of an animal bite where base veterinarian services are available. Following reference (b), complete a Disease Alert Report (MED 6220-3) for all patients in whom rabies postexposure prophylaxis is initiated.

6. Form. DD 2341 (11-84), Report of Animal Bite--Potential Rabies Exposure is available from Navy Environmental Health Center, Preventive Medicine Department, Naval Station, Norfolk, VA 23511-6695.


H. JAMES T. SEARS

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Deputy for Veterinary Activities
USA MEDDAC
HSXG-V
Fort Dix, NJ 08640

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CO, NAVPUBFORMCEN
5801 Tabor Ave.
Phila., PA 19120-5099

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GENERAL GUIDANCE FOR
HUMAN RABIES PREVENTION AND IMMUNOPROPHYLAXIS

1. Animal Reservoirs. Animal reservoirs for the rabies virus vary from country to country. In North America, wild animals such as the fox, skunk, raccoon, and bat are the main sources of infection for humans. However, in Mexico, Latin America, and most of Asia, the dog is the major source of human exposure.

2. Rabies Control Board. In geographic areas of known rabies endemicity (in the United States or outside the United States) among wild or domestic animals, recommend that local shore facilities maintain a rabies control board. This board's function is to establish local operating procedures for assessing requirements for: animal identification and quarantine, testing of animal specimens for rabies virus, clinical management of animal bites, and indications for pre- and postexposure prophylaxis with HDCV and RIG. The composition of the board should include specialists from internal medicine, preventive medicine (physician or environmental health officer), pediatrics, veterinary medicine, and a representative from the emergency room or urgent care clinic.

3. Evaluation in the Isolated Setting. Commands deployed at sea may have bite victims first report to sick bay after leaving port. Commands deployed to the field may experience a similar situation, having patients report after departure or while engaged in field operations. Medical personnel in either situation must use the guidelines in enclosure (2) to assess the need for postexposure prophylaxis. Further guidance can be obtained by contacting United States military or embassy medical personnel in the port or area where the bite occurred or the cognizant NAVENPVNTMEDU. In situations where the animal species is known to transmit rabies, the status of the implicated animal cannot be determined, and the deployment status precludes further delays in obtaining information, postexposure prophylaxis must be instituted as soon as possible.

4. Preexposure Prophylaxis. Enclosure (2) provides complete guidelines on preexposure prophylaxis. Within the scope of this instruction and following reference (a):

a. All military personnel identified by the command as being occupationally exposed to the rabies virus must maintain complete and current preexposure prophylaxis with HDCV. These personnel include: veterinarians, veterinary technicians, and researchers who work with the rabies virus (or potentially infected animals) on a Navy or Marine Corps facility.

Enclosure (1)

b. All other personnel who are identified by the command as being occupationally exposed to rabies virus on a Navy or Marine Corps facility must be offered complete and current preexposure prophylaxis with HDCV. These personnel include: Federal civilian veterinarians and veterinary technicians, researchers, dependents who work as veterinary assistants, and base personnel who have frequent animal control duties. The local rabies control board or the cognizant NAVENPVNTMEDU can assist commands in identifying personnel who are considered occupationally exposed.

5. Postexposure Prophylaxis

a. Enclosure (2) defines what types of animal contact are considered exposures. It must be realized that the rabies virus can be transmitted from animal to man by bites or the contamination of scratches, abrasions, or mucous membranes by an infected animal's saliva. Casual contact such as petting, without any of the preceding contacts, does not constitute an exposure.

b. The initial aspect of postexposure prophylaxis is an immediate and thorough cleansing of all wounds with soap and water. Enclosure (2) provides specific guidance. Any questions on whether a situation precludes further vaccination should be directed to the local rabies control board, regional infectious disease specialist, or cognizant NAVENPVNTMEDU.

6. Vaccine Administration

a. Recommend that HDCV be given intramuscularly into the deltoid region in adults and children. Infants can receive HDCV in the anterolateral upper thigh. Recommend that HDCV not be injected into the gluteal region, because doses not given deeply into the gluteal muscle may be deposited instead into subcutaneous fat. This results in reduced antibody response and vaccine protection.

b. RIG, as part of postexposure prophylaxis, must not be administered into the same anatomic area with HDCV. If anatomically feasible, up to half the dose of RIG should be thoroughly infiltrated in the area around the wound; the rest should be administered intramuscularly.

7. Standard Stock

a. Human Diploid Cell Rabies Vaccine. Available in 1.0 ml (single dose) vials. NSN 6505-01-091-6063. The only HDCV currently available in the United States is the Merieux Institute's formulation. Any previously acquired HDCV from Wyeth Laboratories is not to be used.

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b. Human Rabies Immune Globulin. Available in 10 ml (1,500 IU) vials. NSN 6505-01-067-0807.

c. A prepackaged intradermal HDCV formulation has been developed for preexposure prophylaxis. The concurrent usage of chloroquine phosphate for malaria chemoprophylaxis may interfere with the antibody response to intradermal HDCV. Until the intradermal HDCV formulation is available for use by Navy and Marine Corps personnel, only the intramuscular HDCV formulation may be used.

8. Civilian Sources of Contact and Consultation

a. Local or State health departments.

b. Centers for Disease Control, Center for Infectious Diseases, Division of Viral Diseases, Atlanta, GA: (404) 639-3095 (daytime) and (404) 639-2888 (nights, weekends, and holidays).

CENTERS FOR DISEASE CONTROL

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- 408 Chromosomally Mediated Resistant *Neisseria gonorrhoeae* — United States
- 410 Fatalities from Occupational Heat Exposure
- 412 Tuberculosis — United States, 1983

MORBIDITY AND MORTALITY WEEKLY REPORT

Recommendation of the Immunization
Practices Advisory Committee (ACIP)

Rabies Prevention — United States, 1984

*These revised recommendations of the Immunization Practices Advisory Committee (ACIP) on rabies prevention update the previous recommendations (MMWR 1980;29:65-72,277-80) to reflect the current status of rabies and antirabies biologics in the United States. For assistance on problems or questions about rabies prophylaxis, call local or state health departments.**

INTRODUCTION

Although rabies rarely affects humans in the United States, every year, approximately 25,000 persons receive rabies prophylaxis. Appropriate management of those who may have been exposed to rabies infection depends on the interpretation of the risk of infection and the efficacy and risk of prophylactic treatment. All available methods of systemic prophylactic treatment are complicated by instances of adverse reactions. These are rarely severe. Decisions on management must be made immediately; the longer treatment is postponed, the less likely it is to be effective.

Data on the efficacy of active and passive immunization after rabies exposure 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, vaccine, and rabies immune globulin, is uniformly effective when appropriately used. However, rabies has occasionally developed in humans who had received postexposure antirabies prophylaxis with vaccine alone.

In the United States, rabies in humans has decreased from an average of 22 cases per year in 1946-1950 to zero to five cases per year since 1960. The number of rabies cases among domestic animals has decreased similarly. In 1946, more than 8,000 rabies cases were reported among dogs; 153 cases were reported in 1982. Thus, the likelihood of human exposure to rabies in domestic animals has decreased greatly, although bites by dogs and cats continue to be the principal reasons given for antirabies treatments.

The disease in wildlife—especially skunks, foxes, raccoons, and bats—has become more prevalent in recent years, accounting for approximately 85% of all reported cases of animal rabies every year since 1976. Wild animals now constitute the most important potential source of infection for both humans and domestic animals in the United States. Rabies among animals is present throughout the United States; only Hawaii remains consistently rabies-free.

Four of the six rabies fatalities in U.S. citizens occurring between 1980 and 1983 were related to exposure to rabid dogs outside the United States. In much of the world, including

*If these are unavailable, call the Division of Viral Diseases, Center for Infectious Diseases, CDC ([404] 329-3095 during working hours, or [404] 329-2888 nights, weekends, and holidays).

U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES / PUBLIC HEALTH SERVICE

ACIP: Rabies — Continued

most of Asia and all of Africa and Latin America, the dog remains the major source of human exposure.

RABIES IMMUNIZING PRODUCTS

There are two types of immunizing products: (1) vaccines that induce an active immune response, which requires about 7-10 days to develop but may persist for as long as a year or more, and (2) globulins that provide rapid passive immune protection, which persists for a short period of time, with a half-life of about 21 days. Both types of products should be used concurrently for rabies postexposure prophylaxis.

Vaccines for Use in the United States

Human diploid cell rabies vaccine (HDCV)[†]: HDCV is an inactivated virus vaccine prepared from fixed rabies virus grown in WI-38 or MRC-5 human diploid cell culture. The vaccine grown on WI-38 cells and developed in the United States is inactivated with tri-n-butyl phosphate and β -propiolactone (Wyeth Laboratories' WYVAC[®]), while that grown in MRC-5 cells and developed in Europe is inactivated with β -propiolactone (Merieux Institute's RABIES VACCINE[®]). Both vaccines are supplied as 1.0 ml, single-dose vials of lyophilized vaccine with accompanying diluent.

Globulins

Rabies Immune Globulin, Human (RIG): RIG (Cutter Laboratories' HYPERAB[®] and Merieux Institutes' IMOGAM[®]) is antirabies gamma globulin concentrated by cold ethanol fractionation from plasma of hyperimmunized human donors. Rabies neutralizing antibody content is standardized to contain 150 international units (IU) per ml. It is supplied in 2-ml (300 IU) and 10-ml (1,500 IU) vials for pediatric and adult use, respectively.

Antirabies Serum, Equine (ARS): ANTIRABIES SERUM[®] (Sclavo) is a refined, concentrated serum obtained from hyperimmunized horses. Neutralizing antibody content is standardized to contain 1,000 IU per vial. Volume is adjusted by the manufacturer on the basis of antibody potency in each lot. Currently, a 1,000-IU vial contains approximately 5 ml.

RATIONALE FOR CHOICE OF RABIES IMMUNIZING PRODUCTS

Both types of HDCV rabies vaccines are considered equally efficacious and safe when used as indicated on the labels. Only the Merieux Institute vaccine has been evaluated by the intradermal (ID) dose/route for preexposure immunization. No data are available on ID use with the Wyeth Laboratories vaccine. RIG is preferred over ARS, because the latter has a much higher risk of adverse reactions.

Vaccines

The effectiveness of rabies vaccines is measured by their ability to protect persons exposed to rabies and to induce antibodies to rabies virus. HDCV has been used concurrently with RIG or ARS to treat 45 persons bitten by rabid dogs or wolves in Iran, 31 persons bitten by a variety of rabid animals in Germany, and 511 persons bitten by a variety of rabid animals in the United States. In these studies, no person contracted rabies after receiving HDCV in combination with RIG.

All persons treated with RIG and five 1.0-ml intramuscular (IM) doses of HDCV and tested have developed a rabies antibody titer. The definition of a minimally acceptable antibody titer varies between laboratories and is influenced by the type of test conducted. CDC currently specifies a 1:5 titer by the rapid fluorescent-focus inhibition test (RFFIT) as acceptable. The World Health Organization (WHO) specifies a titer of 0.5 I.U.

Serious adverse reactions associated with rabies vaccines include systemic, anaphylactic, and neuroparalytic reactions. Serious adverse reactions occur at lower rates in the HDCV vaccine than with previously available types of rabies vaccine.

[†]Official name: Rabies Vaccine. The duck embryo vaccine which was used from 1957-1982 is no longer available in the United States.

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*ACIP: Rabies – Continued***Globulins**

RIG and ARS are both effective; however, ARS causes serum sickness in over 40% of adult recipients. RIG rarely causes adverse reactions and should be the product of choice when available.

RATIONALE OF TREATMENT

Physicians must evaluate each possible rabies exposure. Local or state public health officials should be consulted if questions arise about the need for prophylaxis.

In the United States, the following factors should be considered before specific antirabies treatment is initiated:

Species of Biting Animal

Carnivorous wild animals (especially skunks, raccoons, foxes, coyotes, and bobcats) and bats are the animals most commonly infected with rabies and have caused most of the indigenous cases of human rabies in the United States since 1960. Unless an animal is tested and shown not to be rabid, postexposure prophylaxis should be initiated upon bite or nonbite exposure to the animals. (See definition in "Type of Exposure" below.) If treatment has been initiated and subsequent testing in a competent laboratory shows the exposing animal is not rabid, treatment can be discontinued.

The likelihood that a domestic dog or cat is infected with rabies varies from region to region; hence, the need for postexposure prophylaxis also varies.

Rodents (such as squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, and mice) and lagomorphs (including rabbits and hares) are rarely found to be infected with rabies and have not been known to cause human rabies in the United States. In these cases, the state or local health department should be consulted before a decision is made to initiate postexposure antirabies prophylaxis.

Circumstances of Biting Incident

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

Type of Exposure

Rabies is transmitted by introducing the virus into open cuts or wounds in skin or via mucous membranes. The likelihood of rabies infection varies with the nature and extent of exposure. Two categories of exposure should be considered.

Bite: Any penetration of the skin by teeth.

Nonbite: Scratches, abrasions, open wounds, or mucous membranes contaminated with saliva or other potentially infectious material, such as brain tissue, from a rabid animal. Casual contact, such as petting a rabid animal (without a bite or nonbite exposure as described above), does not constitute an exposure and is not an indication for prophylaxis. There have been two instances of airborne rabies acquired in laboratories and two probable airborne rabies cases acquired in a bat-infested cave in Texas.

The only documented cases of rabies from human-to-human transmission occurred in four patients in the United States and overseas who received corneas transplanted from persons who died of rabies undiagnosed at the time of death. Stringent guidelines for acceptance of donor corneas should reduce this risk.

Bite and nonbite exposures from humans with rabies theoretically could transmit rabies, although no cases of rabies acquired this way have been documented. Each potential exposure to human rabies should be carefully evaluated to minimize unnecessary rabies prophylaxis.

MANAGEMENT OF BITING ANIMALS

A healthy domestic dog or cat that bites a person should be confined and observed for 10 days and evaluated by a veterinarian at the first sign of illness during confinement or before

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release. Any illness in the animal should be 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 designated by the local or state health department. Any stray or unwanted dog or cat that bites a person should be killed immediately and the head submitted, as described above, for rabies examination.

Signs of rabies in wild animals cannot be interpreted reliably; therefore, any wild animal that bites or scratches a person should be killed at once (without unnecessary damage to the head) and the brain submitted, as described above, for examination for evidence of rabies. If the brain is negative by fluorescent-antibody examination for rabies, the saliva can be assumed to contain no virus, and the bitten person need not be treated. If the biting animal is a particularly rare or valuable specimen and the risk of rabies small, consideration may be given to initiating postexposure treatment to the bitten person and delaying killing the animal for rabies testing.

POSTEXPOSURE PROPHYLAXIS

The essential components of rabies postexposure prophylaxis are local treatment of wounds and immunization, including administration, in most instances, of both globulin and vaccine (Tables 1 and 2).

Local Treatment of Wounds

Immediate and thorough washing of all bite wounds and scratches with *soap and water* is perhaps the most effective measure for preventing rabies. In experimental animals, simple local wound cleansing has been shown to reduce markedly the likelihood of rabies.

Tetanus prophylaxis and measures to control bacterial infection should be given as indicated.

Immunization

Postexposure antirabies immunization should always include administration of both antibody (preferably RIG) and vaccine, with one exception: persons who have been previously immunized with the recommended preexposure or postexposure regimens with HDCV or who have been immunized with other types of vaccines and have a history of documented adequate rabies antibody titer (See "RATIONALE FOR CHOICE OF RABIES IMMUNIZING PRODUCTS") should receive only vaccine. The combination of globulin and vaccine is recommended for both bite exposures and nonbite exposures (as described under "RATIONALE OF TREATMENT"), regardless of the interval between exposure and treatment. The sooner treatment is begun after exposure, the better. However, there have been instances in which the decision to begin treatment was made as late as 6 months or longer after the exposure due to delay in recognition that an exposure had occurred.

HDCV: HDCV is the only type of vaccine currently available in the United States and should be administered in conjunction with RIG at the beginning of postexposure therapy, as described below. In 1977, WHO established a recommendation for six IM doses of HDCV based on studies in Germany and Iran of a regimen of RIG or ARS and six doses of HDCV. When used in this way, the vaccine was safe and effective in protecting 76 persons bitten by proven rabid animals. The vaccine also induced an excellent antibody response in all recipients. Studies conducted by CDC in the United States have shown that a regimen of one dose of RIG and five doses of HDCV was safe and induced an excellent antibody response in all recipients. Of 511 persons bitten by proven rabid animals and so treated, none developed rabies.

Five 1-ml doses of HDCV should be given intramuscularly (for example, in the deltoid region). Other routes of administration, such as the ID route, have not been adequately evaluated for postexposure prophylaxis and should not be used. The first dose should be given as

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soon as possible after exposure; an additional dose should be given on days 3, 7, 14, and 28 after the first dose. (WHO currently recommends a sixth dose 90 days after the first dose.) Because the antibody response following the recommended vaccination regimen with HDCV has been so satisfactory, routine postvaccination serologic testing is not recommended. In unusual instances, as when the patient is known to be immunosuppressed, serologic testing is indicated. Contact state health department or CDC for recommendations.

RIG (or ARS if RIG is not available): RIG is administered only once, at the beginning of antirabies prophylaxis, to provide immediate antibodies until the patient responds to HDCV by active production of antibodies. If RIG was not given when vaccination was begun, it can be given up to the eighth day after the first dose of vaccine was given. From about the eighth day on, RIG is not indicated, since an antibody response to the vaccine is presumed to have occurred. The recommended dose of RIG is 20 IU/kg or approximately 9 IU/lb of body weight. (When ARS must be used, the recommended dose is 40 IU/kg, approximately 18 IU/lb or 1,000 IU/55 lb body weight.) If anatomically feasible, up to half the dose of RIG should be thoroughly infiltrated in the area around the wound, the rest should be administered intramuscularly. Because RIG may partially suppress active production of antibody, no more than the recommended dose of RIG should be given.

TABLE 1. Rabies postexposure prophylaxis guide—July 1984

The following recommendations are only a guide. In applying them, take into account the animal species involved, the circumstances of the bite or other exposure, the vaccination status of the animal, and presence of rabies in the region. Local or state public health officials should be consulted if questions arise about the need for rabies prophylaxis.

	Animal species	Condition of animal at time of attack	Treatment of exposed person*
DOMESTIC	Dog and cat	Healthy and available for 10 days of observation	None, unless animal develops rabies [†]
		Rabid or suspected rabid	RIG [§] and HDCV
		Unknown (escaped)	Consult public health officials. If treatment is indicated, give RIG [§] and HDCV
WILD	Skunk, bat, fox, coyote, raccoon, bobcat, and other carnivores	Regard as rabid unless proven negative by laboratory tests [¶]	RIG [§] and HDCV
OTHER	Livestock, rodents, and lagomorphs (rabbits and hares)	Consider individually. Local and state public health officials should be consulted on questions about the need for rabies prophylaxis. Bites of squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, other rodents, rabbits, and hares almost never call for antirabies prophylaxis.	

* All bites and wounds should immediately be thoroughly cleansed with soap and water. If antirabies treatment is indicated, both rabies immune globulin (RIG) and human diploid cell rabies vaccine (HDCV) should be given as soon as possible, regardless of the interval from exposure. Local reactions to vaccines are common and do not contraindicate continuing treatment. Discontinue vaccine if fluorescent-antibody tests of the animal are negative.

[†] During the usual holding period of 10 days, begin treatment with RIG and HDCV at first sign of rabies in a dog or cat that has bitten someone. The symptomatic animal should be killed immediately and tested.

[§] If RIG is not available, use antirabies serum, equine (ARS). Do not use more than the recommended dosage.

[¶] The animal should be killed and tested as soon as possible. Holding for observation is not recommended.

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TABLE 2. Rabies immunization — June 1984

I. PREEXPOSURE IMMUNIZATION. Preexposure immunization consists of three doses of HDCV, 1.0 ml, IM (i.e., deltoid area), one each on days 0, 7, and 28. (See text for details on use of 0.1 ml HDCV ID as an alternative dose/route.) Administration of routine booster doses of vaccine depends on exposure risk category as noted below. Preexposure immunization of immunosuppressed persons is not recommended.

Criteria for Preexposure Immunization			
Risk category	Nature of risk	Typical populations	Preexposure regimen
Continuous	Virus present continuously, often in high concentrations. Aerosol, mucous membrane, bite, or nonbite exposure possible. Specific exposures may go unrecognized.	Rabies research lab workers.* Rabies biologics production workers.	Primary preexposure immunization course. Serology every 6 months. Booster immunization when antibody titer falls below acceptable level.*
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 animal control and wildlife workers in rabies epizootic areas.	Primary preexposure immunization course. Booster immunization or serology 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 endemicity. Certain travelers to foreign rabies epizootic areas. Veterinary students.	Primary preexposure immunization course. No routine booster immunization or serology.
Rare (population-at-large)	Exposure always episodic, mucous membrane, or bite with source recognized.	U.S. population-at-large, including individuals in rabies-epizootic areas.	No preexposure immunization.

II. POSTEXPOSURE IMMUNIZATION. All postexposure treatment should begin with immediate thorough cleansing of all wounds with soap and water.

Persons not previously immunized: RIG, 20 I.U./kg body weight, one half infiltrated at bite site (if possible), remainder IM; 5 doses of HDCV, 1.0 ml IM (i.e., deltoid area), one each on days 0, 3, 7, 14 and 28.

Persons previously immunized[§]: Two doses of HDCV, 1.0 ml, IM (i.e., deltoid area), one each on days 0 and 3. RIG should not be administered.

*Judgment of relative risk and extra monitoring of immunization status of laboratory workers is the responsibility of the laboratory supervisor (see U.S. Department of Health and Human Service's *Biosafety in Microbiological and Biomedical Laboratories*, 1984).

†Preexposure booster immunization consists of one dose of HDCV, 1.0 ml/dose, IM (deltoid area). Acceptable antibody level is 1:5 titer (complete inhibition in RFFIT at 1:5 dilution). Boost if titer falls below 1:5.

§Preexposure immunization with HDCV; prior postexposure prophylaxis with HDCV; or persons previously immunized with any other type of rabies vaccine and a documented history of positive antibody

TREATMENT OUTSIDE THE UNITED STATES

If postexposure is begun outside the United States with locally produced biologics, it may be desirable to provide additional treatment when the patient reaches the United States. State health departments should be contacted for specific advice in such cases.

PREEXPOSURE IMMUNIZATION

Preexposure immunization may be offered to persons in high-risk groups, such as veterinarians, animal handlers, certain laboratory workers, and persons spending time (e.g., 1 month or more) in foreign countries where rabies is a constant threat. Persons whose vocational or avocational pursuits bring them into contact with potentially rabid dogs, cats, foxes, skunks, 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 expected to be delayed. Finally, although it does not eliminate the need for additional therapy after a rabies exposure, it simplifies therapy by eliminating the need for globulin and decreasing the number of doses of vaccine needed. This is of particular importance for persons at high risk of being exposed in countries where the available rabies immunizing products may carry a higher risk of adverse reactions.

Preexposure immunization does not eliminate the need for prompt postexposure prophylaxis following an exposure; it only reduces the postexposure regimen.

Human Diploid Cell Rabies Vaccine

Three 1.0 ml injections of HDCV should be given intramuscularly (for example, in the deltoid area), one on each of days 0, 7, and 28. In a study in the United States, more than 1,000 persons received HDCV according to this regimen; antibody was demonstrated in the sera of all subjects when tested by the RFFIT. Other studies have produced comparable results. Because the antibody response following the recommended vaccination regimen with HDCV has been so satisfactory, routine postvaccination serology is not recommended.

Booster Doses of Vaccine

Persons who work with live rabies virus in research laboratories or vaccine production facilities and are at risk of inapparent exposure should have the rabies antibody titer of their serum determined every 6 months; booster doses of vaccine should be given, as needed, to maintain an adequate titer (See "RATIONALE FOR CHOICE OF RABIES IMMUNIZING PRODUCTS"). Other laboratory workers, such as those doing rabies diagnostic tests, spelunkers, and those veterinarians, animal control and wildlife officers in areas where animal rabies is enzootic should have boosters every 2 years or have their serum tested for rabies antibody every 2 years and, if the titer is inadequate, have a booster dose. Veterinarians and animal control and wildlife officers, if working in areas of low rabies endemicity, do not require routine booster doses of HDCV after completion of primary preexposure immunization (Table 2).

Postexposure Therapy of Previously Immunized Persons

When an immunized person who was vaccinated by the recommended regimen with HDCV or who had previously demonstrated rabies antibody is exposed to rabies, that person should receive two IM doses (1.0 ml each) of HDCV, one immediately and one 3 days later. RIG should not be given in these cases. If the immune status of a previously vaccinated person who did not receive the recommended HDCV regimen is not known, full primary postexposure antirabies treatment (RIG plus five doses of HDCV) may be necessary. In such cases, if antibody can be demonstrated in a serum sample collected before vaccine is given, treatment can be discontinued after at least two doses of HDCV.

*ACIP: Rabies — Continued***Intradermal Use of HDCV**

HDCV produced by the Merieux Institute has been used for preexposure immunization in a regimen of three 0.1 ml doses given ID in the lateral aspect of the upper arm over the deltoid area, one dose each on days 0, 7, and 28. Experience gained with over 2,000 persons vaccinated in the United States by the ID route has shown that antibody was produced in all recipients, although the mean response was somewhat lower and may be of shorter duration than with comparable IM immunization. Antibody response in some groups vaccinated outside the United States has been found to be inadequate for reasons not yet determined.

Current data provide a sufficient basis to recommend the 0.1 ml ID dose/route as an alternative to the 1.0 ml IM dose/route for preexposure immunization in the United States. Post-vaccination serology is not necessary following ID (or IM) immunization, except for persons suspected of being immunosuppressed. The manufacturer has not yet met the packaging and labeling requirements necessary to obtain approval by the U.S. Food and Drug Administration for the ID route. Since the 1.0-ml vial presently available is intended for IM use and contains no preservatives, the reconstituted vaccine must be used immediately. Data on ID immunization are not available for Wyeth Laboratories' vaccine, and it should not be used for ID vaccination.

ACCIDENTAL INOCULATION WITH MODIFIED LIVE RABIES VIRUS

Individuals may be accidentally exposed to attenuated rabies virus while administering modified live rabies virus (MLV) vaccines to animals. While there have been no reported human rabies cases resulting from exposure to needlesticks or sprays with licensed MLV vaccines, vaccine-induced rabies has been observed in animals given MLV vaccines. Absolute assurance of a lack of risk for humans, therefore, cannot be given. The best evidence for a low risk, however, is the absence of recognized cases of vaccine-associated disease in humans despite frequent accidental exposures.

Currently available MLV animal vaccines are made with one of two attenuated strains of rabies virus: high egg passage (HEP) Flury strain or Street Alabama Dufferin (SAD) strain. The HEP Flury and SAD virus strains have been used in animal vaccines for over 10 years without evidence of associated disease in humans; therefore, postexposure treatment is not recommended following exposure to these types of vaccine by needlesticks or sprays.

Because the data are insufficient to assess the true risk associated with any of the MLV vaccines, preexposure immunization, and periodic boosters are recommended for all persons dealing with potentially rabid animals or frequently handling animal rabies vaccines.

ADVERSE REACTIONS**Human Diploid Cell Rabies Vaccine**

Reactions after vaccination with HDCV are less common than with previously available vaccines. In a study using five doses of HDCV, local reactions, such as pain, erythema, and swelling or itching at the injection site, were reported in about 25% of recipients of HDCV, and mild systemic reactions, such as headache, nausea, abdominal pain, muscle aches, and dizziness were reported in about 20% of recipients. Two cases of neurologic illness resembling Guillain-Barré syndrome that resolved without sequelae in 12 weeks, and a focal subacute central nervous system disorder temporally associated with HDCV vaccine, have been reported.

Recently, a significant increase has been noted in "immune complex-like" reactions in persons receiving booster doses of HDCV. The illness, characterized by onset 2-21 days post-booster, presents with a generalized urticaria and may also include arthralgia, arthritis, angioedema, nausea, vomiting, fever, and malaise. In no cases were the illnesses life-threatening. Preliminary data suggest this "immune complex-like" illness may occur in up to 6% of persons receiving booster vaccines and much less frequently in persons receiving primary immuniza-