VIRGINIA
EPIDEMIOLOGY BULLETIN

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March 1999 Volume 99, Number 3

Human Rabies – Virginia, 1998

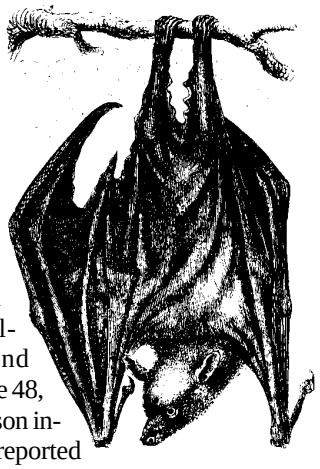
On December 31, 1998, a 29-year old man in Richmond, Virginia, died from rabies encephalitis caused by a rabies virus variant associated with insectivorous bats. This report summarizes the clinical and epidemiologic investigations by the Virginia Department of Health and the Centers for Disease Control and Prevention (CDC).

On December 14, 1998, an inmate at the Nottoway Correctional Center in Nottoway County, Virginia, developed malaise and back pain while working on a roadside clean-up crew. He sought medical care at the prison on December 15, complaining of muscle pains, vomiting, and abdominal cramps, and was treated with acetaminophen. His clinical signs progressed to include persistent right wrist pain, muscle tremors in his right arm, and difficulty walking. On December 18, the patient was sent to a Richmond emergency department, where he had a temperature of 103°F (39.4°C). He initially was alert and oriented but had visual hallucinations. During the next 12 hours, he became increasingly agitated and less oriented. Physical examination revealed anisocoria, increased tone in the right forearm, and hyperesthesia over the entire right side of the body. Intoxication with anticholinergic agents such as pesticides or Jimson weed was considered; however, toxicology studies were negative.

The patient's condition worsened, with hypersalivation, priapism, and wide fluctuations in body temperature and blood pressure. He was intubated and heavily sedated on December 20. Laboratory findings included a white blood cell count of 20,800/µL (normal: 3700-9400/µL), myoglobinuria, and a compensated metabolic anion gap acidosis with renal insufficiency. Peak creatine phosphokinase levels were 130,900 U/L (normal: 50-450 U/L), indicating rhabdomyolysis. Analysis of cerebrospinal fluid (CSF) showed a white blood cell count of 57/µL (normal: 0-5/µL), protein levels of 128 mg/dL (normal: 12-60 mg/dL), and glucose levels of 46 mg/dL (normal: at least two-thirds of a concurrent serum glucose value, which was approximately 136 mg/dL). A computed tomography scan of the patient's head revealed no abnormal findings.

A diagnosis of rabies was first considered by the patient's physician on December 20. Samples sent to CDC for testing on December 21 included a nuchal skin biopsy, which tested positive for rabies virus by direct fluorescent antibody test on December 22, and saliva and skin, which were positive by reverse-transcriptase polymerase chain reaction (RT-PCR) assay on December 23. The sequence of the amplified RT-PCR product showed >9.9% DNA homology to a rabies virus variant associated with eastern pipistrelle bats (*Pipistrellus subflavus*) and silver-haired bats (*Lasionycteris noctivagans*). Serum and CSF samples obtained December 21 contained rabies virus neutralizing antibody titers of 1:50 and 1:36, respectively, by rapid fluorescent focus inhibition test (RFFIT). A serum sample obtained December 28 showed a rabies virus neutralizing antibody titer of 1:1200 by RFFIT. After the removal of all sedatives, the patient showed no purposeful movement and loss of brainstem reflexes. He died on December 31.

Postexposure prophylaxis (PEP) was administered to 48 persons who possibly had contact with the patient's saliva between December 4 (10 days preceding the first clinical signs of illness) and death. Of the 48, 29 were prison inmates who reported possible contact with the patient's saliva, either while caring for him during his illness or through shared cigarettes or drinking or eating utensils. Three family members who visited the patient while he was in prison on December 6, 15 health-care providers, and the pathologist who conducted the autopsy also received PEP.



Family members, friends, and prison staff reported the patient had not indicated any contact with or bite from an animal in recent months, and prison medical records did not document evidence of a bite or scratch. The patient lived at a work center that housed up to 160 inmates in two separate dormitories. He had worked around the prison on a farm repairing fence lines and feeding cattle, in a paper recycling facility, and along roadsides cleaning up trash and debris. No evidence of bats was found within the prison or on prison grounds, although inmates reported occasionally seeing bats flying near the outdoor lights in the summer. Several stray cats were reported to occasionally approach inmates at the facility; however, the patient was not known to have handled them.

In This Issue:

The patient had been incarcerated at Nottoway for approximately 6 weeks after transfer from another correctional unit. At the other correctional facility, the patient worked inside the prison and on a road crew cutting brush and picking up trash along highways. No evidence of bats was found in the prison, and inmates reported that they had never seen bats inside the facility. Prison staff and inmates reported that they did not recall the patient ever being bitten by an animal while working, and that he usually did not handle small animals found by the road crews.

Editorial Note: This report describes the only case of human rabies diagnosed in the United States during 1998 and the first case in Virginia since 1953. A definitive history of an animal bite could not be established for this patient, and the most likely explanation is an unrecognized bat bite occurring either at the farm or recycling facility or while the patient was working on a road crew. Because the incubation period for rabies varies from several weeks to several months, he may have contracted rabies before his transfer to Nottoway.

It is important to treat persons for rabies exposure when the possibility of a bat bite cannot be reasonably excluded

Since 1990, 27 human rabies cases have occurred in the United States. Although 20 (74%) have been attributed to bat-associated variants of the rabies virus, a definitive history of a bat bite was established for only one of these cases. Of the 20 attributed to bat-associated variants, 15 (75%) have been caused by the same eastern pipistrelle/silver-haired bat variant responsible for the death described in this report. Although bat-associated rabies virus variants theoretically can be secondarily transmitted from terrestrial mammals, an unrecognized bat bite is the most likely explanation for these cases.

The reasons for the preponderance of human rabies cases associated with the eastern pipistrelle/silver-haired bat virus variant remain speculative. Epidemiologic findings suggest that it can be transmitted following minor, undetected exposures. Insectivorous bats, such as those implicated in the human rabies deaths in the United States, have small teeth that may not cause an obvious wound in human skin. Accordingly, it is important to treat persons for rabies exposure when the possibility of a bat bite cannot be reasonably excluded. In all cases where bat-human contact has occurred, the bat should be collected and tested for rabies, if possible. If the bat is not available for rabies testing, the need for PEP should be assessed by public health officials familiar with recent recommendations.

The total of 48 persons who received PEP after contact with the patient described in this report is similar to the mean of 49.8 persons who received PEP after exposures to human rabies cases during 1990-1997. Consideration of rabies before the patient's death may have minimized the number of hospital staff that received PEP in this case.

Although this patient did not exhibit classic hydrophobia, other typical clinical signs, such as hypersalivation, hallucinations, priapism, paresthesias, muscle spasms, and autonomic instability occurred. The use of sedatives may have masked hydrophobia in this patient. Medical personnel should consider rabies as a diagnosis in any case presenting with an acute onset and rapid progression of compatible neurologic signs, regardless of whether the patient reports a history of an animal bite. Although early diagnosis cannot save the patient, it may help minimize the number of potential exposures and the need for PEP.

Reprinted from MMWR 1999;48[No. 5]:95-7.

Human Rabies Prevention, United States, 1999

Recommendations of the Advisory Committee on Immunization Practices (ACIP)

Summary

The following article includes excerpts from the MMWR article with the above title (1999;48[No. RR-1]:1-21). If you would like to receive a copy of the entire MMWR article, you may call the Office of Epidemiology at 804/786-6261 or visit the Centers for Disease Control and Prevention (CDC) web site at http://www.cdc.gov.

These revised recommendations of the Advisory Committee on Immunization Practices update the previous recommendations on rabies prevention (MMWR 1991;40 [No.RR-3]:1-14) to reflect the current status of rabies and antirabies biologics in the United States. This report includes new information about a human rabies vaccine approved for United States use in 1997, recommendations regarding exposure to bats, recommendations regarding an observation period for domestic ferrets, and changes in the local administration of rabies immune globulin.

INTRODUCTION

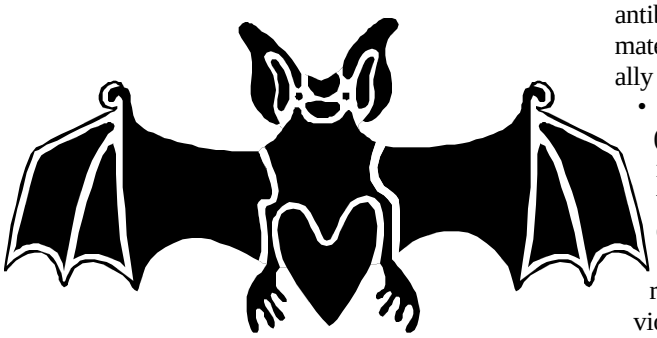
Rabies is a viral infection transmitted in the saliva of infected mammals. The virus enters the central nervous system of the host, causing an encephalomyelitis that is almost always fatal.

In the United States, the likelihood of human exposure to a rabid domestic animal has decreased greatly during the past 40-50 years. However, in most other countries, including most of Asia, Africa and Latin America, dogs remain the major species with rabies and the most common source of rabies among humans. Twelve (33%) of the 36 human rabies deaths reported to the CDC from 1980 through 1997 appear to have been related to rabid animals outside the United States. Therefore, international travelers to areas where canine rabies is still endemic have an increased risk of exposure to rabies.

Wildlife is the most important potential source of rabies infection for both humans and domestic animals in the United States

Rabies among wildlife, especially raccoons, skunks and bats, has become more prevalent in the United States since the 1950s, accounting for greater than 85% of all reported cases of animal rabies every year since 1976. Rabies among wildlife occurs throughout the continental United States; only Hawaii remains consistently rabies-free. Wildlife is the most important potential source of infection for both humans and domestic animals in the United States.

Although rabies among humans is rare in the United States, every year approximately 16,000-39,000 persons receive postexposure prophylaxis. To appropriately manage potential human exposures to rabies, the risk of infection must be accurately assessed. Administration of rabies postexposure prophylaxis



is a medical urgency, not a medical emergency, but decisions must not be delayed. Systemic prophylactic treatments occasionally are complicated by adverse reactions, but these reactions are rarely severe.

Data on the safety, immunogenicity, and efficacy of active and passive rabies immunization have come from both human and animal studies. Although controlled human trials have not been performed, extensive field experience from many areas of the world indicates that postexposure prophylaxis combining wound treatment, passive immunization, and vaccination is uniformly effective when appropriately applied. However, rabies has occasionally developed among humans when key elements of the rabies postexposure prophylaxis regimens were omitted or incorrectly administered.

RABIES BIOLOGICS

Two types of rabies immunizing products are available in the United States (Table 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 ≥2 years.
- Rabies immune globulin (RIG) provides a rapid, passive immunity that persists for only a short time (half-life of approximately 21 days).

In all postexposure prophylaxis regimens, except for persons previously immunized, both products should be used concurrently.

Vaccines Licensed for Use in the United States

Four formulations of three inactivated rabies vaccines are currently licensed for preexposure and postexposure prophylaxis in the United States (Table 1). When used as indicated, all three types of rabies vaccines are considered equally safe and efficacious. The potency of one dose is greater than or equal to 2.5 international units (IU) per 1.0 mL of rabies virus antigen, which is the World Health Organization recommended standard. A full 1.0-mL dose can be used for both preexposure and postexposure prophylaxis. However, only the Imovax Rabies I.D. vaccine (human diploid cell vaccine {HDCV}) has been evaluated and approved by the Food and Drug Administration (FDA) for the intradermal dose and route for preexposure vaccination. Therefore, rabies vaccine adsorbed (RVA) and purified chick embryo cell vaccine (PCEC) should not be used intradermally. Usually, an immunization series is initiated and completed with one vaccine product. No clinical studies have been conducted that document a change in efficacy or the frequency of adverse reactions when the series is completed with a second vaccine product.

Rabies Immune Globulin Licensed for Use in the United States

The two RIG products, BayRabTM and Imogam Rabies-HT, are antirabies immunoglobulin (IgG) preparations concentrated by cold ethanol fractionation from plasma of hyperimmunized human donors (Table 1). Rabies neutralizing antibody, standardized at a concentration of 150 IU per mL, is supplied in 2-mL (300 IU) vials for pediatric use and 10-mL (1,500 IU) vials for adult use; the recommended dose is 20 IU/kg body weight. Both RIG preparations are considered equally efficacious when used as described in this report.

PRIMARY OR PREEXPOSURE VACCINATION

Preexposure vaccination should be offered to persons in high-risk groups, such as veterinarians, animal handlers, and certain laboratory workers. Preexposure vaccination also should be considered for other persons whose activities bring them into frequent contact with rabies virus or potentially rabid bats, raccoons, skunks, cats, dogs, or other species at risk for having rabies. In addition, international travelers might be candidates for preexposure vaccination if they are likely to come in contact with animals in areas where dog rabies is enzootic and immediate access to appropriate medical care, including biologics, might be limited. Routine preexposure prophylaxis for other situations might not be indicated (Table 2).

Preexposure prophylaxis is administered for several reasons. First, although preexposure vaccination does not eliminate the need for additional therapy after a rabies exposure, it simplifies therapy by eliminating the need for RIG and decreasing the number of doses of vaccine needed, a point of particular importance for persons at high risk for being exposed to rabies in areas where immunizing products might not be available or where they might be at high risk for adverse reactions. Second, preexposure prophylaxis might protect persons whose postexposure therapy is delayed. Finally, it might provide protection to persons at risk for inapparent exposures to rabies.

Intramuscular Primary Vaccination

Three 1.0-mL injections of HDCV, RVA, or PCEC should be administered intramuscularly (deltoid area) — one injection per day

Table 1. Rabies biologics, United States, 1999

Human rabies vaccine	Product name	Manufacturer
Human diploid cell vaccine (HDCV)		Pasteur-Merieux Serum et Vaccins, Connaught Laboratories, Inc.
• Intramuscular	Imovax® Rabies	Phone: (800) 822-2463
• Intradermal	Imovax® Rabies I.D.	
Rabies vaccine adsorbed (RVA)	Rabies Vaccine Adsorbed (RVA)	BioPort Corporation
• Intramuscular		Phone: (517) 335-8120
Purified chick embryo cell vaccine (PCEC)	RabAvert™	Chiron Corporation
• Intramuscular		Phone: (800) 244-7668
Rabies immune globulin (RIG)	Imogam® Rabies-HT	Pasteur-Merieux Serum et Vaccins, Connaught Laboratories, Inc. Phone: (800) 822-2463
	BayRab™	Bayer Corporation Pharmaceutical Div. Phone: (800) 288-8370

Table 2. Rabies preexposure prophylaxis guide, United States, 1999

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

*Judgment of relative risk and extra monitoring of vaccination status of laboratory workers is the responsibility of the laboratory supervisor.
†Minimum acceptable antibody level is complete virus neutralization at a 1:5 serum dilution by the rapid fluorescent focus inhibition test. A booster dose should be administered if the titer falls below this level.

on days 0, 7, and 21 or 28 (Table 3). In a study conducted in the United States, greater than 1,000 persons received HDCV according to this regimen. Antibody was found in serum samples of all subjects when tested by the rapid fluorescent focus inhibition test (RFFIT). Studies with other products have produced comparable results.

Intradermal Primary Vaccination

A regimen of three 0.1-mL ID doses of HDCV, one each on days 0, 7, and 21 or 28, is also used for preexposure vaccination (Table 3) as an alternative to the 1.0-mL IM regimen for rabies preexposure prophylaxis with HDCV. A single dose of lyophilized HDCV (Imovax Rabies I.D.) is available prepackaged for reconstitution in the syringe just before administration. The syringe is designed to deliver 0.1 mL of HDCV reliably and has been approved by the FDA since 1986. The 0.1-mL ID doses, administered 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 routine preexposure booster vaccination (Table 3). The 1.0-mL vial is not approved for multidose ID use. RVA and PCEC are not approved for and should not be administered intradermally.

When chloroquine phosphate was used routinely for malaria prophylaxis, investigators discovered that the drug decreased the antibody response to concomitantly administered HDCV. Although interference with the immune response to rabies vaccine by other antimalarials structurally related to chloroquine (e.g., mefloquine) has not been evaluated, precautions for persons receiving these drugs should be followed. Accordingly, HDCV should not be administered intradermally to a person traveling to malaria-endemic countries while the person is receiving one of these antimalarials. The IM administration of three doses of 1.0 mL of vaccine for preexposure prophylaxis provides a sufficient margin of safety in this situation. For persons who will be receiving both rabies preexposure prophylaxis and antimalarial chemoprophylaxis in preparation for travel to a rabies-enzootic area, the ID regimen 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 regimen should be used.

Preexposure Booster Doses of Vaccine

Persons who work with rabies virus in research laboratories or vaccine production facilities (continuous risk category) are at the highest risk for inapparent exposures (Table 2). Such persons should have a serum sample tested for rabies antibody every 6 months. Booster doses (IM or ID [Table 3]) of vaccine should be administered to maintain a serum titer corresponding to at least complete neutralization at a 1:5 serum dilution by the RFFIT. The frequent-risk category includes other laboratory workers (e.g., those performing rabies diagnostic test-

Table 3. Rabies preexposure prophylaxis schedule, United States, 1999

Type of vaccination	Route	Regimen
Primary	Intramuscular	HDCV, PCEC or RVA; 1.0 mL (deltoid area), one each on days 0,* 7, and 21 or 28
	Intradermal	HDCV; 0.1 mL (deltoid area), one each day on days 0,* 7, and 21 or 28
Booster	Intramuscular	HDCV, PCEC or RVA; 1.0 mL (deltoid area), day 0* only
	Intradermal	HDCV; 0.1 mL (deltoid area), day 0* only

HDCV=human diploid cell vaccine; PCEC=purified chick embryo cell vaccine; RVA=rabies vaccine adsorbed.
*Day 0 is the day the first dose of vaccine is administered.

ing), spelunkers, veterinarians and staff, and animal-control and wildlife officers in areas where animal rabies is enzootic. Persons in this group should have a serum sample tested for rabies antibody every 2 years; if the titer is less than complete neutralization at a 1:5 serum dilution by the RFFIT, the person also should receive a single booster dose of vaccine. Veterinarians and animal-control and wildlife officers working in areas with low rabies rates, veterinary students, and at-risk international travelers do not require routine preexposure booster doses of vaccine after completion of primary preexposure vaccination (infrequent exposure group).

Postexposure Therapy for Previously Vaccinated Persons

If exposed to rabies, previously vaccinated persons should receive two IM doses (1.0 mL each) of vaccine, one immediately and one 3 days later. Previously vaccinated persons are defined as persons who have received one of the recommended preexposure or postexposure regimens of HDCV, RVA, or PCEC, or persons who received another vaccine and had a documented rabies antibody titer. RIG is unnecessary and should not be administered to these persons because an anamnestic response will follow the administration of a booster regardless of the prebooster antibody titer.

POSTEXPOSURE PROPHYLAXIS

Rationale for Treatment

Administration of rabies postexposure prophylaxis is a medical urgency, not a medical emergency. 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 4). Human postexposure prophylaxis is reportable in Virginia and should be reported to the local health department. The following factors should be considered before specific antirabies postexposure prophylaxis is initiated: type of exposure, type of animal, circumstances of biting incident, vaccination status of animal, and risk of human-to-human transmission.

Type of Exposure

Rabies is transmitted only when the virus is introduced into bite wounds or open cuts in skin or onto mucous membranes. If no exposure has occurred, postexposure prophylaxis is not necessary. The likelihood of rabies infection varies with the nature and extent of exposure. Two categories of exposure should be considered: bite and nonbite.

Rabid bats have been documented in the 49 continental states

Any penetration of the skin by teeth constitutes a bite exposure. All bites, regardless of location, represent a potential risk of rabies transmission. Bites by some animals, such as bats, can inflict minor injury and thus be undetected.

Nonbite exposures from terrestrial animals rarely cause rabies. However, occasional reports of transmission by nonbite exposure suggest that such exposures constitute sufficient reason to consider postexposure prophylaxis. The nonbite exposures of highest risk appear to be among persons exposed to large amounts of aerosolized rabies virus and surgical recipients of corneas transplanted from patients who died of rabies. Two cases of rabies have been attributed to probable aerosol exposures in laboratories, and two cases of rabies have been attributed to possible airborne exposures in caves containing millions of free-tailed bats (*Tadarida brasiliensis*) in the Southwest.

The contamination of open wounds, abrasions, mucous membranes, or theoretically, scratches, with saliva or other potentially infectious material (such as neural tissue) from a rabid animal also constitutes a nonbite exposure. Other contact by itself, such as petting a rabid animal and contact with blood, urine, or feces (e.g., guano) of a rabid animal, does not constitute an exposure and is not an indication for prophylaxis. Because the rabies virus is inactivated by desiccation and ultraviolet irradiation, in general, if the material containing the virus is dry, the virus can be considered noninfectious.

Type of Animal

Bats

Rabid bats have been documented in the 49 continental states, and bats are increasingly implicated as important wildlife reservoirs for variants of rabies virus transmitted to humans. Recent epidemiologic data suggest that trans-

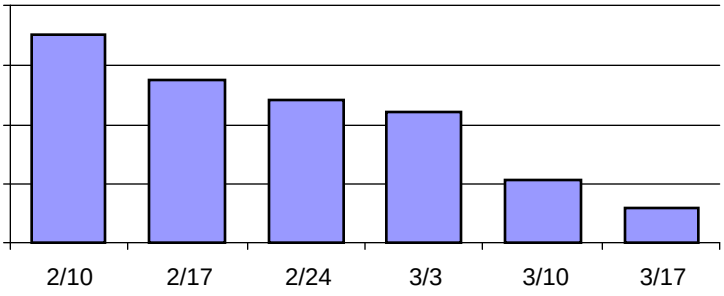
Table 4. Rabies postexposure prophylaxis guide, United States, 1999

Animal type	Evaluation and disposition of animal	Postexposure prophylaxis recommendations
Dogs, cats and ferrets	Healthy and available for 10 days observation	Persons should not begin prophylaxis unless animal develops clinical signs of rabies.*
	Rabid or suspected rabid	Immediately vaccinate.
	Unknown (e.g., escaped)	Consult public health officials.
Skunks, raccoons, foxes and most other carnivores; bats	Regarded as rabid unless animal proven negative by laboratory tests†	Consider immediate vaccination.
Livestock, small rodents, lagomorphs (rabbits and hares), large rodents (woodchucks and beavers), and other mammals	Consider individually.	Consult public health officials. Bites of squirrels, hamsters, guinea pigs, gerbils, chipmunks, rats, mice, other small rodents, rabbits and hares almost never require antirabies postexposure prophylaxis.

*During the 10-day observation period, begin postexposure prophylaxis at the first sign of rabies in a dog, cat, or ferret that has bitten someone. If the animal exhibits clinical signs of rabies, it should be euthanized immediately and tested.
†The animal should be euthanized and tested as soon as possible. Holding the animal for observation is not recommended. Discontinue vaccine if immunofluorescence test results of the animal are negative.

Flu Corner

Influenza activity in Virginia was characterized as widespread through March 3, 1999. Activity fell to regional by March 10 and to sporadic by March 17. Laboratory-confirmed cases of influenza type A were reported from each of the health planning regions and laboratory-confirmed cases of influenza type B were reported from the northwest and eastern health planning regions. All of the influenza type A isolates that have been subtyped were A/Sydney which was the H3N2 of the 1998-99 influenza vaccine.



mission of rabies virus can occur from minor, seemingly unimportant, or unrecognized bites from bats. The limited injury inflicted by a bat bite and an often inaccurate recall of the exact exposure history might limit the ability of health-care providers to determine the risk of rabies resulting from an encounter with a bat. Human and domestic animal contact with bats should be minimized, and bats should never be handled by untrained or unvaccinated persons or be kept as pets.

In all instances of potential human exposures involving bats, the bat in question should be safely collected, if possible, and submitted for rabies diagnosis. Rabies postexposure prophylaxis is recommended for all persons with bite, scratch, or mucous membrane exposure to a bat, unless the bat is available for testing and is negative for evidence of rabies. Postexposure prophylaxis might be appropriate even if a bite, scratch, or mucous membrane exposure is not apparent when there is reasonable probability that such exposure might have occurred.

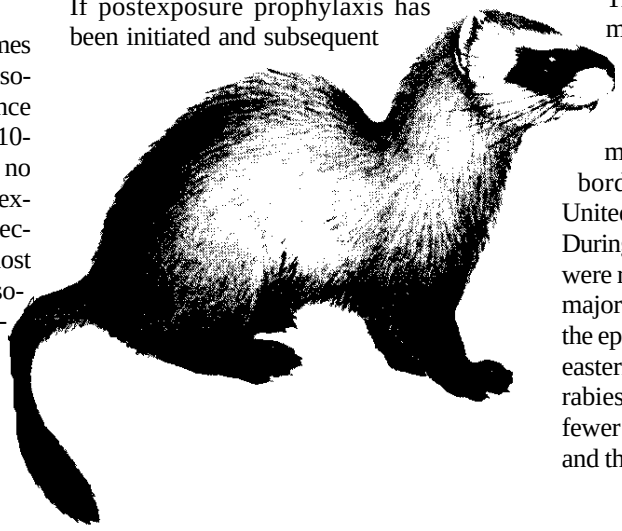
On the basis of the available but sometimes conflicting information from the 21 bat-associated cases of human rabies reported since 1980, in 1-2 cases, a bite was reported; in 10-12 cases, apparent contact occurred but no bite was detected; and in 7-10 cases, no exposure to bats was reported, but an undetected or unreported bat bite remains the most plausible hypothesis. Clustering of bat-associated human cases within the same household has never been reported.

Postexposure prophylaxis should be considered when direct contact between a human and a bat has occurred, unless the exposed person can be certain a bite, scratch, or mucous membrane exposure did not occur. Postexposure prophylaxis can be considered for persons who were in the same room as the bat and who might be unaware that a bite or direct contact had occurred (e.g., a sleeping person awakens to find a bat in the room or an adult witnesses a bat in the room with a previously unattended child, mentally disabled person, or intoxicated person) and rabies cannot be ruled out by testing the bat. Postexposure prophylaxis would not be warranted for other household members.

Raccoons, skunks, foxes, and coyotes are the terrestrial animals most often infected with rabies

Wild Terrestrial Carnivores

Raccoons, skunks, foxes, and coyotes are the terrestrial animals most often infected with rabies. All bites by such wildlife must be considered possible exposures to the rabies virus. Postexposure prophylaxis should be initiated as soon as possible after patients are exposed to wildlife unless the animal has already been tested and shown not to be rabid. If postexposure prophylaxis has been initiated and subsequent immunofluorescence testing shows that the exposing animal was not rabid, postexposure prophylaxis can be discontinued.



Signs of rabies among wildlife cannot be interpreted reliably; therefore, any such animal that exposes a person should be euthanized at once (without unnecessary damage to the head) and the brain should be 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 postexposure prophylaxis.

Other Wild Animals

Small rodents (e.g., 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 transmit rabies to humans. From 1990 through 1996, in areas of the country where raccoon rabies was enzootic, woodchucks accounted for 93% of the 371 cases of rabies among rodents reported to CDC. In all cases involving rodents, the state or local health department should be consulted before a decision is made to initiate antirabies postexposure prophylaxis.

The offspring of wild animals crossbred to domestic dogs and cats (wild animal hybrids) are considered wild animals by the National Association of State and Public Health Veterinarians and the Council of State and Territorial Epidemiologists. Because the period of rabies virus shedding in these animals is unknown, these animals should be euthanized and tested rather than confined and observed when they bite humans. Wild animals and wild animal hybrids should not be kept as pets. Animals maintained in United States Department of Agriculture-licensed research facilities or accredited zoological parks should be evaluated on a case-by-case basis when they bite humans.

Domestic Dogs, Cats, and Ferrets

The likelihood of rabies in a domestic animal varies by region; hence, the need for post-exposure prophylaxis also varies. In the continental United States, rabies among dogs is reported most commonly along the United States-Mexico border and sporadically in areas of the United States with enzootic wildlife rabies. During most of the 1990s, more cats than dogs were reported rabid in the United States. The majority of these cases were associated with the epizootic of rabies among raccoons in the eastern United States. The large number of rabies-infected cats might be attributed to fewer cat vaccination laws, fewer leash laws, and the roaming habits of cats.

On the basis of new information regarding rabies pathogenesis and viral shedding patterns in ferrets, ferrets are now considered in this category with dogs and cats rather than as wild terrestrial carnivores. A healthy domestic dog, cat, or ferret that bites a person may 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 public health department. If signs suggestive of rabies develop, the animal should be euthanized and its head removed and shipped, under refrigeration, for examination by a qualified laboratory. If the biting animal is stray or unwanted, it should either be observed for 10 days or be euthanized immediately and submitted for rabies examination.

A currently vaccinated dog, cat, or ferret is unlikely to become infected with rabies

Circumstances of Biting Incident and Vaccination Status of Exposing Animal

An unprovoked attack by an 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 currently vaccinated dog, cat, or ferret is unlikely to become infected with rabies.

Human-to-Human Transmission

Human-to-human transmission has occurred among eight recipients of transplanted corneas. Investigations revealed each of the donors had died of an illness compatible with or proven to be rabies. The eight cases occurred in five countries: Thailand (two cases), India (two cases), Iran (two cases), the United States (one case), and France (one case). Stringent guidelines for acceptance of donor corneas have been implemented to reduce this risk.

Apart from corneal transplants, bite and nonbite exposures inflicted by infected humans could theoretically transmit rabies, but no laboratory-diagnosed cases occurring under such situations have been documented. Two unconfirmed cases of human-to-human rabies transmission in Ethiopia have been described. The reported route of exposure in both cases was direct salivary contact from another human (a bite and a kiss). Routine delivery of health care to a patient with rabies is not an indication for postexposure prophylaxis unless exposure of mucous membranes or nonintact skin to potentially infectious body fluids has occurred. Adherence to standard precautions as outlined by the Hospital Infection Control Practices Advisory Committee will minimize the risk of exposure.

Treatment of Wounds and Immunization

The essential components of rabies postexposure prophylaxis are wound treatment and, for previously unvaccinated persons, the administration of both RIG and vaccine (Table 5). Persons who have been bitten by animals suspected or proven to be rabid should begin postexposure prophylaxis immediately. Incubation periods of greater than 1 year have been reported in humans. Thus, when a documented or likely exposure has occurred, postexposure prophylaxis is indicated regardless of the length of the delay, provided the clinical signs of rabies are not present.

Treatment of Wounds

Immediate and thorough washing of all bite wounds and scratches with soap and water and a virucidal agent such as a povidone-iodine solution irrigation are important measures for preventing rabies. In studies of animals, thorough wound cleansing alone without other postexposure prophylaxis has been shown to reduce markedly the likelihood of rabies. Tetanus prophylaxis and measures to control bacterial infection also should be administered as indicated. The decision to suture large wounds should take into account cosmetic factors and the potential for bacterial infections.

Immunization

Postexposure antirabies vaccination should always include administration of both passive antibody and vaccine, with the exception of persons who have previously received

Table 5. Rabies postexposure prophylaxis schedule, United States, 1999

Vaccination status	Treatment	Regimen*
Not previously vaccinated	Wound cleansing	All postexposure treatment should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidone-iodine solution should be used to irrigate the wounds.
	RIG	Administer 20 IU/kg body weight. If anatomically feasible, **the full dose** should be infiltrated around the wound(s) and any remaining volume should be administered IM at an anatomical site distant from the vaccine administration. Also, RIG should not be administered in the same syringe as vaccine. Because RIG might partially suppress active production of antibody, no more than the recommended dose should be given.
	Vaccine	HDCV, RVA, or PCEC 1.0 mL, IM (deltoid area†), one each on days 0§, 3, 7, 14, and 28.
Previously vaccinated¶	Wound cleansing	All postexposure treatment should begin with immediate thorough cleansing of all wounds with soap and water. If available, a virucidal agent such as povidone-iodine solution should be used to irrigate the wounds.
	RIG	RIG should **not** be administered.
	Vaccine	HDCV, RVA, or PCEC 1.0 mL, IM (deltoid area†), one each on days 0§ and 3.

HDCV=human diploid cell vaccine; PCEC=purified chick embryo cell vaccine; RIG=rabies immune globulin; RVA=rabies vaccine adsorbed; IM=intramuscular.
*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.
§Day 0 is the day the first dose of vaccine is administered.
¶Any person with a history of preexposure vaccination with HDCV, RVA, or PCEC; prior postexposure prophylaxis with HDCV, RVA, or PCEC; or previous vaccination with any other type of rabies vaccine and a documented history of antibody response to the prior vaccination.

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. The combination of RIG and vaccine is recommended for both bite and nonbite exposures, regardless of the interval between exposure and initiation of treatment.

Rabies Immune Globulin Use

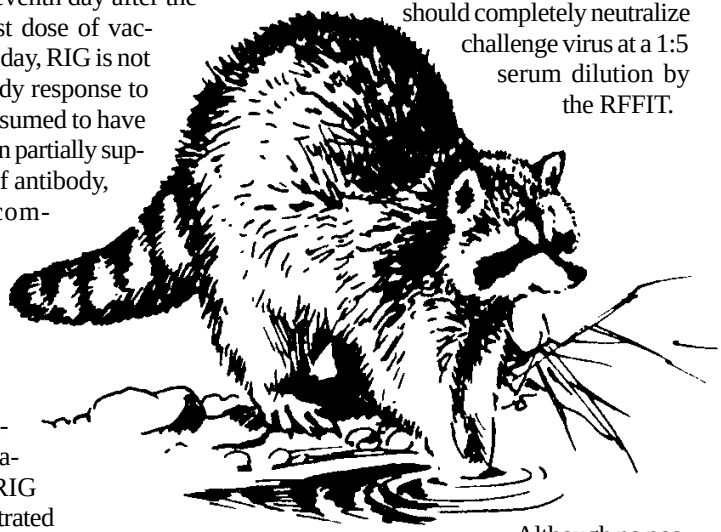
RIG is administered only once (i.e., at the beginning of antirabies prophylaxis) to previously unvaccinated persons to provide immediate antibodies until the patient responds to HDCV, RVA, or PCEC by actively producing antibodies. If RIG was not administered when vaccination was begun, it can be administered through the seventh day after the administration of the first dose of vaccine. Beyond the seventh day, RIG is not indicated since an antibody response to cell culture vaccine is presumed to have occurred. Because RIG can partially suppress active production of antibody, no more than the recommended dose should be administered. The recommended dose of human RIG is 20 IU/kg body weight. This formula is applicable to all age groups, including children. If anatomically feasible, the full dose of RIG should be thoroughly infiltrated in the area around and into the wounds. Any remaining volume should be injected intramuscularly at a site distant from vaccine administration. This change in the recommendations for RIG administration is based on reports of rare failures of postexposure prophylaxis when smaller amounts of RIG were infiltrated at the exposure sites. RIG should never be administered in the same syringe or in the same anatomical site as vaccine.

Vaccine Use

Three rabies vaccines are currently available in the United States (Table 1); any one of the three can be administered in conjunction with RIG at the beginning of postexposure therapy. A regimen of five 1-mL doses of HDCV, RVA, or PCEC should be administered intramuscularly. The first dose of the five-dose course should be administered as soon as possible after exposure. Additional doses should be administered on days 3, 7, 14, and 28 after the first vaccination. For adults, the vaccination 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, RVA, or PCEC injections because administration of HDCV in this area results in lower neutralizing antibody titers.

Treatment Outside the United States

Persons who are exposed to rabies while traveling in countries where rabies is enzootic might sometimes receive postexposure therapy with regimens or biologics that are not used in the United States. It may be necessary to provide additional therapy when the patient reaches the United States. State or local health departments should be contacted for specific advice in such cases. If titers are obtained, specimens collected 2-4 weeks after preexposure or postexposure prophylaxis should completely neutralize challenge virus at a 1:5 serum dilution by the RFFIT.



Although no postexposure vaccine failures have occurred in the United States since cell culture vaccines have been routinely used, failures have occurred abroad when some deviation was made from the recommended postexposure treatment protocol or when less than the currently recommended amount of antirabies sera was administered. Specifically, patients who contracted rabies after postexposure prophylaxis did not have their wounds cleansed with soap and water, did not receive their rabies vaccine injections in the deltoid area, or did not receive RIG around the wound site.

SEROLOGIC TESTING

Serologic Response Shortly After Vaccination

All persons tested during several CDC studies 2-4 weeks after completion of preexposure and postexposure rabies prophylaxis in accordance with ACIP guidelines have demonstrated an antibody response to rabies. Therefore, serum samples from patients completing preexposure or postexposure prophylaxis do not need to be tested to document seroconversion unless the person is immunosuppressed. If titers are obtained, specimens collected 2-4 weeks after preexposure or postexposure prophylaxis should completely neutralize challenge virus at a 1:5 serum dilution by the RFFIT. In animal studies, neutralizing antibody titers have been shown to be imperfect markers of protection. Antibody titers will vary with time since the last vaccination. Differences among laboratories that test blood samples also can influence the results.

Serologic Response and Preexposure Booster Doses of Vaccine

Although antibody levels do not define a person's immune status, they are a marker of continuing immune response. To ensure the continuity of an immune response, titers should be checked periodically, with booster doses administered as needed. Two years after primary preexposure vaccination, a 1:5 serum dilution will neutralize challenge virus completely (by the RFFIT) among 93%-98% of persons who received the three-dose preexposure series intramuscularly and 83%-95% of persons who received the three-dose series intradermally. If the titer falls below the minimum acceptable antibody level, a preexposure booster dose of vaccine is recommended for a person at continuous or frequent risk for exposure to rabies (Table 2). State or local health departments can provide the names and addresses of laboratories performing rabies serologic testing.

ADVERSE REACTIONS

HDCV, RVA, and PCEC

Reactions after vaccination with HDCV, RVA, and PCEC are less serious and less common than with previously available vaccines. In previous studies with HDCV, local reactions (e.g., pain, erythema, and swelling or itching at the injection site) have been reported among 30%-74% of recipients. Systemic reactions (e.g., 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. In addition, other central and peripheral nervous system disorders have been temporally associated with HDCV vaccine, but a causal relationship has not been established in these rare reports.

Approximately 6% of persons who received booster doses of HDCV had an im-

For assistance with problems or questions about rabies prophylaxis, contact your local health department. Procedures to be followed when the health department is closed vary by locality. Please call your local health department to determine the procedure for your locality.

mune complex-like reaction within 2-21 days after administration of the booster dose. The patients developed generalized urticaria, sometimes accompanied by arthralgia, arthritis, angioedema, nausea, vomiting, fever, and malaise. In no cases have these reactions been life-threatening. This reaction occurred less frequently among persons receiving primary vaccination. The reactions have been associated with the presence of betapropiolactone-altered human albumin in the HDCV and the development of immunoglobulin E (IgE) antibodies to this allergen.

Rabies Immune Globulin

Local pain and low-grade fever might follow receipt of RIG. Although not reported specifically for RIG, angioneurotic edema, nephrotic syndrome, and anaphylaxis have been reported after injection of immune globulin (IG), a product similar in biochemical composition but without antirabies activity. These reactions occur so rarely that a causal relationship between IG and these reactions has not been established.

Both formulations of RIG, BayRabTM and Imogam Rabies-HT, undergo multiple viral clearance procedures during preparation. There is no evidence that any viruses have ever been transmitted by commercially available RIG 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 antiinflammatory and antipyretic agents, such as ibuprofen or acetaminophen.

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

Once initiated, rabies prophylaxis should not be interrupted or discontinued because of local or mild systemic adverse reactions to rabies vaccine

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 patient and the attending physician. 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 should be reported to the Vaccine Adverse Event Reporting System (VAERS) via a 24-hour toll-free telephone number ({800} 822-7967).

PRECAUTIONS AND CONTRAINDICATIONS

Immunosuppression

Corticosteroids, other immunosuppressive agents, antimalarials, and immunosuppressive illnesses can interfere with the development of active immunity after vaccination. For persons with immunosuppression, preexposure prophylaxis should be administered with the awareness that the immune response might be inadequate. Patients who are immunosuppressed by disease or medications should postpone preexposure vaccinations and consider avoiding activities for which rabies preexposure prophylaxis is indicated. When this is not possible, immunosuppressed persons who are at risk for rabies should be vaccinated by the IM route and their antibody titers checked. Failure to seroconvert after the third dose should be managed in consultation with appropriate public health officials.

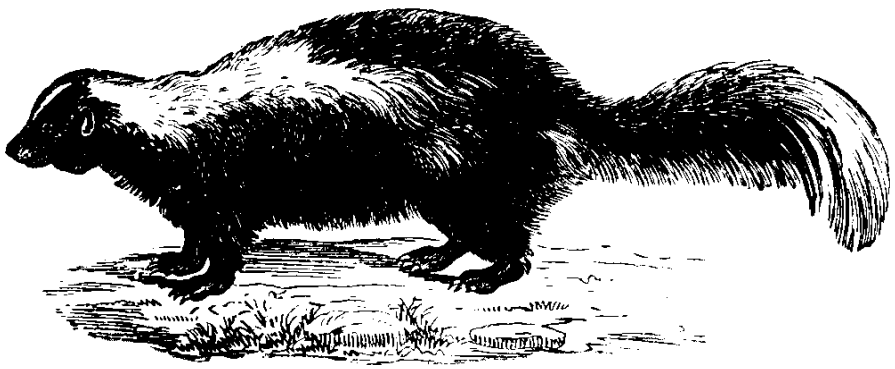
Immunosuppressive agents should not be administered during postexposure therapy unless essential for the treatment of other conditions. When postexposure prophylaxis is administered to an immunosuppressed person, it is especially important that a serum sample be tested for rabies antibody to ensure that an acceptable antibody response has developed.

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. If the risk of exposure to rabies is substantial, preexposure prophylaxis might also be indicated during pregnancy.

Allergies

Persons who have a history of serious hypersensitivity to rabies vaccine should be revaccinated with caution.



Cases of Selected Notifiable Diseases Reported in Virginia*

Disease	Total Cases Reported, February 1999						Total Cases Reported Statewide, January through February		
	State	Regions					This Year	Last Year	5 Yr Avg
		NW	N	SW	C	E			
AIDS	36	2	12	0	11	11	98	100	161
Campylobacteriosis	30	7	5	11	5	2	50	64	51
***E. coli* O157:H7**	3	1	1	1	0	0	5	1	2
Giardiasis	35	3	10	9	9	4	52	46	35
Gonorrhea	739	60	62	71	228	318	1776	1069	1645
Hepatitis A	11	2	5	1	3	0	14	25	22
B, acute	6	0	1	1	4	0	8	10	13
C/NANB, acute	6	1	3	1	0	1	6	1	2
HIV Infection	33	0	14	0	14	5	98	119	147
Lead in Children†	22	0	0	5	13	4	62	54	69
Legionellosis	1	0	1	0	0	0	2	3	1
Lyme Disease	0	0	0	0	0	0	0	1	2
Measles	0	0	0	0	0	0	0	0	0
Meningococcal Infection	4	2	1	0	0	1	5	8	10
Mumps	1	0	0	0	0	1	1	2	3
Pertussis	6	3	3	0	0	0	7	0	3
Rabies in Animals	36	8	5	9	7	7	56	83	60
Rocky Mountain Spotted Fever	0	0	0	0	0	0	0	0	0
Rubella	0	0	0	0	0	0	0	0	0
Salmonellosis	43	4	8	11	5	15	76	82	101
Shigellosis	8	0	7	0	0	1	11	17	46
Syphilis, Early§	35	1	5	6	11	12	65	97	145
Tuberculosis	8	2	4	0	1	1	17	36	41

Localities Reporting Animal Rabies This Month: Accomack 1 raccoon; Amherst 1 raccoon; Appomattox 1 skunk; Bedford 2 raccoons, 1 skunk; Campbell 1 raccoon; Chesapeake 1 raccoon; Chesterfield 1 raccoon; Fairfax 3 raccoons; Franklin County 1 raccoon; Hanover 1 raccoon; Henrico 1 raccoon, 1 skunk; Henry 1 skunk; Loudoun 1 raccoon; Lunenburg 1 skunk; Middlesex 1 cat; Newport News 2 raccoons; Page 1 fox; Pittsylvania 1 skunk; Portsmouth 1 raccoon; Prince George 1 skunk; Prince William 1 raccoon; Rockbridge 1 fox, 1 raccoon; Shenandoah 1 skunk; Spotsylvania 1 raccoon; Stafford 1 skunk; Sussex 1 raccoon; Warren 2 raccoons; Williamsburg 1 raccoon.

Occupational Illnesses: Asbestosis 49; Carbon Monoxide Exposure 1; Carpal Tunnel Syndrome 57; Hearing Loss 35; Lead Exposure 14; Pneumoconiosis 7.

*Data for 1999 are provisional. †Elevated blood lead levels ≥10µg/dL.

§Includes primary, secondary, and early latent.

Published monthly by the
VIRGINIA DEPARTMENT OF HEALTH
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Richmond, Virginia 23218
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