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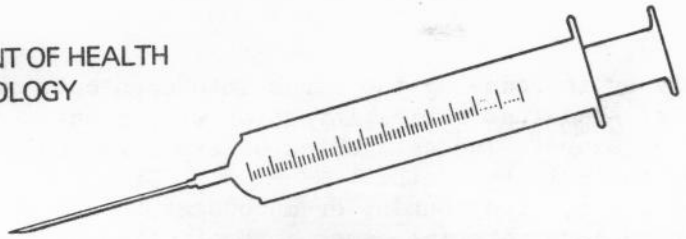

EPIDEMIOLOGY BULLETIN

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RECOMMENDATION OF THE IMMUNIZATION PRACTICES ADVISORY COMMITTEE

RABIES PREVENTION

Rabies has been well known and feared for thousands of years. Yet it was not until 1885 that vaccination for postexposure treatment was developed by Pasteur. The earliest vaccines were from nervous tissue of animals infected with rabies and there were many neurological side effects. Duck embryo vaccine (DEV) was introduced in 1955 and quickly became the standard vaccine because it was safer.

Now, a new rabies vaccine has been licensed. It is grown in human diploid cells (HDCV) and is reportedly less allergenic and requires fewer injections (5 HDCV as compared to 23 DEV) to achieve an even higher rabies antibody response.

Because this HDCV is in very short supply it is only available through local health officers for postexposure prophylaxis. Even for postexposure prophylaxis there will have to be clear indications for its use; not every animal bite or scratch is justification for use of this vaccine at this time. The basis and indications for the vaccine's use follow.

RATIONALE OF TREATMENT

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

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

Species of Biting Animal

Some animals are much more likely to be infected with rabies virus than others. For example, carnivorous wild animals (especially skunks, raccoons, foxes, coyotes, and bobcats) and bats are the animals most commonly infected with rabies and have been the cause of most of the human rabies in the United States since 1960. Unless the animal is tested and shown not to be rabid, postexposure prophylaxis should be initiated upon bite or non-bite exposure to one of these animals. (See definition in "Type of Exposure," below.)

The likelihood that a domestic dog or cat would be 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; their bites almost never call for antirabies prophylaxis. Therefore, in these cases the state or local health department should be consulted before initiating postexposure antirabies prophylaxis.

Circumstances of Biting Incident

An unprovoked attack 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.

Type of Exposure

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

Bite: Any penetration of the skin by teeth.

Non-bite: 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 non-bite exposure as described above), does not constitute an exposure and is not an indication for prophylaxis. There have been 2 instances of airborne rabies that were acquired in the laboratory and 2 probable airborne rabies cases acquired in a bat-infested cave in Texas.

The only documented cases of rabies due to human-to-human transmission occurred in 2 patients who received corneas transplanted from persons who died of rabies undiagnosed at the time of death.

Bite and non-bite exposures from a human with rabies theoretically could transmit rabies. Although no cases of rabies acquired in this way have been documented, and the risk is obviously small, those so exposed should receive prophylaxis. 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 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, one can assume that the saliva contains no virus, and the person bitten need not be treated.

POSTEXPOSURE PROPHYLAXIS

The essential components of rabies postexposure prophylaxis are local treatment of wounds and immunization.

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, 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 both passively administered antibody (preferably RIG) and vaccine (preferably HDCV), with 1 exception: persons who have been previously immunized with rabies vaccine and have a documented adequate rabies antibody titer should receive only vaccine. The combination of globulin and vaccine is recommended for both bite exposures and non-bite exposures (as described under "RATIONALE OF TREATMENT") and 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 indicated as late as 6 months and longer after the exposure.

HDCV: HDCV is the vaccine of choice whenever available and should be administered in conjunction with RIG. (RIG is administered only once, at the beginning of postexposure therapy, as described below.) In 1977 the World Health Organization (WHO) established a recommendation for 6 intramuscular doses of HDCV based on studies in Germany and Iran of a regimen of RIG or ARS and 6 doses of HDCV. Used in this way, the vaccine was found to be safe and effective in protecting 76 persons bitten by proven rabid animals and induced an excellent

antibody response in all recipients. Since 1977, studies conducted by CDC in the United States have shown that a regimen of 1 dose of RIG and 5 doses of HDCV was safe and induced an excellent antibody response in all recipients. Of 77 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 regions). Other routes of administration, such as the intradermal route, have not been tested for postexposure prophylaxis and should not be used. The first dose should be given as soon as possible after the exposure; an additional dose would be given on each of days 3, 7, 14, and 28 after the first dose. (WHO currently recommends a sixth dose 90 days after the first dose.) A serum specimen for rabies antibody testing should be collected on day 28 (at the time the last dose is given) or 2-3 weeks after the last dose. Testing for rabies antibody can be arranged by the state health department.

If an adequate antibody titer is not detected, this information should be reported to the state health department or to CDC (404-329-3727), a booster dose given, and another serum specimen for rabies antibody testing collected 2-3 weeks later.

DEV: When HDCV is not available, 1 dose of RIG and 23 doses of DEV should be administered. (RIG is administered only once at the beginning of postexposure therapy, as described below.) DEV may be given as 21 daily 1-ml doses or fourteen 1-ml doses in the first 7 days (2 injections given at separate sites simultaneously) and then seven 1-ml daily doses. These 21 doses should be followed by 2 "booster" doses, the first 10 days after the 21st dose, and the second 10 days later. Vaccine should be injected subcutaneously in the abdomen, lower back, or lateral aspect of the thigh; rotation of sites is recommended.

All persons who receive DEV should have serum for rabies antibody testing collected at the time of the second booster. If no antibody is detected, it is imperative that HDCV be obtained and that 3 doses (1 each on days 0, 7, and 14) be given. Serum should be collected 2-3 weeks after the last injection for further antibody testing.

Combinations of vaccines: One rabies vaccine can be used to complete postexposure prophylaxis begun with another vaccine. For example, if treatment is begun with DEV and HDCV becomes available: After 1-3 doses of DEV, 5 doses of HDCV should be given (1 on each of days 0, 3, 7, 14, and 28); after 4-7 doses of DEV, 4 doses of HDCV (1 on each of days 0, 7, 14, and 28); and after 8 or more doses of DEV, 3 doses of HDCV (1 on each of days 0, 7, and 14). Serum should be collected for antibody testing 2-3 weeks after the last dose has been given.

RIG (or ARS if RIG is not available): RIG is administered only once, at the beginning of antirabies prophylaxis, to provide antibodies until the patient responds to vaccination. If RIG inadvertently 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 unnecessary because presumably an active antibody response to the vaccine has occurred. The recommended dose of RIG is 20 IU/kg or approximately 9 IU/lb body weight. (When ARS must be used, the recommended dose is 40 IU/kg, approximately 18 IU/lb or 1 vial of 1,000 IU/55-lb body weight.) If possible, up to half the dose of RIG should be thoroughly infiltrated in the area around the wound, and 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.

These recommendations are summarized in Tables 1 and 2 at the end of this statement.

ADVERSE REACTIONS

HDCV

Reactions after vaccination with HDCV are less common than with DEV. In a study using 5 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. No serious anaphylactic, systemic, or neuroparalytic reactions have been reported, but additional experience with this vaccine is needed to define more clearly the risk of these adverse reactions.

DEV

Local reaction to postexposure treatment with DEV are very common. Most patients experience pain, erythema, and induration at the injection site. Approximately 13% have

itching at the site. Systemic symptoms (fever, malaise, myalgia) occur in 33% of patients, usually after 5-8 doses. Anaphylaxis, which develops in less than 1% of persons receiving DEV, may occur after the first dose, particularly in persons previously sensitized with vaccines containing avian tissue. Neuroparalytic reactions were reported among an estimated 512,000 recipients of DEV (1/24,400) including 5 cases of transverse myelitis, 7 cases of cranial or peripheral neuropathy, and 9 cases of encephalopathy (2 fatal).

RIG

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

ARS

ARS produces serum sickness in at least 40% of adult recipients; reaction rates for children are lower. Anaphylactic reactions may occur. When RIG is not available and ARS must be used, the patient should be tested for sensitivity to equine serum. (In rare instances the sensitivity test has induced anaphylactic reactions.)

Because adverse reactions are associated more frequently with ARS than with RIG, and ARS might sensitize recipients to equine protein, ARS should be used only when RIG cannot be obtained.

Management of Adverse Reactions

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

When a person with a history of hypersensitivity must be given rabies vaccines (for example, when an egg-sensitive person must receive DEV), antihistamines may be given; epinephrine should be readily available to counteract anaphylactic reactions, and the person should be carefully observed immediately after immunization.

Serious systemic, anaphylactic, or neuroparalytic reactions occurring during the administration of rabies vaccines pose a serious dilemma for the attending physician. A patient's risk of developing rabies must be carefully considered before deciding to discontinue vaccination or to choose an alternate vaccine. Moreover, the use of corticosteroids to treat life-threatening neuroparalytic reactions carries the risk of inhibiting the development of active immunity to rabies. It is especially important in these cases that the serum of the patient be tested for rabies antibodies. Advice and assistance on the management of serious adverse reactions in persons receiving rabies vaccines may be sought from the state health department or CDC.

All serious systemic neuroparalytic or anaphylactic reactions to a rabies vaccine should be immediately reported to the state health department or the Viral Diseases Division, Bureau of Epidemiology, CDC (404/329-3727 during working hours, or 404/329-3644 at other times).

PRECAUTIONS AND CONTRAINDICATIONS

Use of Steroids and Immunosuppressive Agents

Corticosteroids and immunosuppressive agents can interfere with the development of active immunity and predispose the patient to developing rabies. They should not be administered during postexposure therapy unless essential for the treatment of other conditions. When rabies post-exposure prophylaxis is administered to persons receiving steroids or immunosuppressive therapy, it is especially important that serum be tested for rabies antibody to ensure that an adequate response has developed.

Pregnancy

Because of the potential consequences of inadequately treated rabies exposure and limited data that indicate that fetal abnormalities have not been associated with rabies vaccination, pregnancy is <u>not</u> considered a contraindication to postexposure prophylaxis. If there is substantial risk of exposure to rabies, pre-exposure prophylaxis may also be indicated during pregnancy.

Allergies

Persons who have a history of hypersensitivity should be administered rabies vaccines with caution. For example, with a history suggesting possible hypersensitivity to 1 vaccine, a patient should be administered an alternate vaccine whenever available. When a patient with a history suggesting hypersensitivity to a vaccine must be given that vaccine (for example, when an egg-sensitive person must receive DEV because HDCV is not available) antihistamines can be given; epinephrine should be readily available to counteract anaphylactic reactions, and the person should be carefully observed.

For most allergic persons HDCV is less likely than DEV to cause an adverse reaction because it contains fewer extraneous proteins.

Source: Morbidity and Mortality Weekly Report, Vol. 29/No. 23/June 13, 1980.

Errata: Volume 80 Number 5
Date: May 9, 1980

Should read
Volume 80 Number 5
Date: June 9, 1980

TABLE 1. Rabies postexposure prophylaxis guide, March 1980

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.

† During the usual holding period of 10 days, begin treatment with RIG and vaccine (preferably with 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.

§ If HDCV is not available, use duck embryo vaccine (DEV). Local reactions to vaccines are common and do not contraindicate continuing treatment. Discontinue vaccine if fluorescent-antibody (FA) tests of the animal are negative.

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

TABLE 2. Rabies immunization regimens, March 1980

PRE-EXPOSURE: Pre-exposure rabies prophylaxis for persons with special risks of exposure to rabies, such as animal-care and control personnel and selected laboratory workers, consists of immunization with either human diploid cell rabies vaccine (HDCV) or duck embryo vaccine (DEV), according to the following schedule.

Rabies vaccine	No. of 1-ml doses	Route of administration	Intervals between doses	If no antibody response to primary series, give:*
HDCV	3	intramuscular	1 week between 1st and 2nd; 2-3 weeks between 2nd and 3rd†	1 booster dose†
DEV	3	subcutaneous	1 month between 1st and 2nd; 6-7 months between 2nd and 3rd†	2 booster doses, 1 week apart
	or		or	
	4		1 week between 1st, 2nd, and 3rd; 3 months between 3rd and 4th†	

POSTEXPOSURE: Postexposure rabies prophylaxis for persons exposed to rabies consists of the immediate, thorough cleansing of all wounds with soap and water, administration of rabies immune globulin (RIG) or, if RIG is not available, antirabies serum, equine (ARS), and the initiation of either HDCV or DEV, according to the following schedule.‡

Rabies vaccine	No. of 1-ml doses	Route of administration	Intervals between doses	If no antibody response to primary series, give:*
HDCV	5§	intramuscular	Doses to be given on days 0, 3, 7, 14, and 28†	an additional booster dose†
DEV	23	Subcutaneous	21 daily doses followed by a booster on day 31 and another on day 41† or 2 daily doses in the first 7 days, followed by 7 daily doses. Then 1 booster on day 24, and another on day 34†	3 doses of HDCV at weekly intervals†

* If no antibody response is documented after the recommended additional booster dose(s), consult the state health department or CDC.

† Serum for rabies antibody testing should be collected 2-3 weeks after the last dose.

‡ The postexposure regimen is greatly modified for someone with previously demonstrated rabies antibody. (See text for details.)

§ The World Health Organization recommends a 6th dose 90 days after the 1st dose.

MONTH: June

DISEASE	STATE					REGIONS				
						THIS MONTH				
	THIS MONTH	LAST MONTH	TOTAL TO DATE 1980	TOTAL TO DATE 1979	MEAN 5 YEAR TO DATE	N.W.	N.	S.W.	C.	E.
CHICKENPOX	39	86	314	884	831.4	13	--	15	6	5
MEASLES	31	57	295	237	1138.0	--	3	9	16	3
MUMPS	1	3	47	75	215.8	--	--	1	--	--
PERTUSSIS	--	--	2	7	7.6	--	--	--	--	--
RUBELLA	2	26	48	182	297.8	--	--	2	--	--
MENINGITIS – ASEPTIC	3	7	34	64	32.2	--	1	1	--	1
BACTERIAL	7	26	98	89	64.4	1	2	2	2	--
ENCEPHALITIS – INFECTIOUS	2	--	3	14	10.2	--	1	1	--	--
POST-INFECTIOUS	--	--	2	11	5.0	--	--	--	--	--
HEPATITIS A (INFECTIOUS)	24	30	157	136	157.0	--	9	5	5	5
B (SERUM)	35	41	268	206	142.6	5	10	4	9	7
SALMONELLOSIS	118	142	472	441	303.2	17	28	17	33	23
SHIGELLOSIS	4	6	53	163	81.4	--	1	2	--	1
TUBERCULOSIS – PULMONARY	46	59	277	297	347.4	5	5	6	8	22
EXTRA-PULMONARY	10	14	59	57	52.6	--	1	2	1	6
SYPHILIS (PRIMARY & SECONDARY)	48	54	282	266	283.8	0	8	6	11	23
GONORRHEA	1908	2048	10,245	11,044	11,398.4					
ROCKY MOUNTAIN SPOTTED FEVER	10	13	24	42	46.8	1	--	2	5	2
RABIES IN ANIMALS	2	3	6	4	25.2	2	--	--	--	--
MENINGOCOCCAL INFECTIONS	1	11	32	56	32.2	--	--	1	--	--
INFLUENZA	9	7	756	338	5,465.2	--	--	9	--	--
MALARIA	6	10	33	11	8.0	1	3	1	--	1
OTHER: Reye's Syndrome	1	3	22	14	7.2	--	--	--	1	--

COUNTIES REPORTING ANIMAL RABIES: Shenandoah - 1 raccoon; Warren - 1 skunk

OCCUPATIONAL ILLNESSES: Occupational pneumoconiosis 16; Occupational dermatitis 4; Occupational hearing loss 7; asbestosis 1; Byssinosis 1; Occupational asthma 1; Lead poisoning 1

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