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Committee on Animal Health
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1973

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Preface

In the 26 years since the publication of *Rabies and its Control,* there has been important progress in our understanding of the disease and the virus. More effective vaccines are now available, the epidemiologic patterns of the disease have become clearer, and diagnostic techniques are more sure.

This report deals with the pathogenesis of the disease, with virus–wildlife interactions, and with vaccines and regulatory aspects. In preparing it, the subcommittee has had the benefit of views from the following consultants representing a variety of disciplines and backgrounds: Donald Balser, Albert L. Brown, H. R. Fischman, John M. Hejl, George L. Humphrey, Edward Phillips, Robert E. Shope, and W. G. Winkler.

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The Disease

The control of rabies has been hampered by our very limited understanding of the disease in wild animals. Only fragmentary data are available on the distribution of the disease in wild animals, the means by which these animals are infected, and the subsequent host response to infection. Data on biological properties of the known wild-animal hosts of the disease, including pertinent information on population dynamics, movement, and inter- and intraspecies interaction are inadequate.

PATHOGENESIS

Rabies virus is believed to be pathogenic for all mammals, and experimental infection has been accomplished in the preponderance of mammalian species tested.

Rabies virus is currently classified as a member of the rhabdovirus group. Its single-stranded, helical, RNA nucleocapsid is contained within a lipid envelope that is essential to infectivity. Until very recently, it had been agreed by most that rabies virus was a single antigenic entity and that antigenic variation was never very marked.

Recent studies with two African viruses, the Lagos bat and Ibaden shrew viruses, indicate that these are morphogically and serologically related to rabies virus, but that, similar to the European "mouse viruses," they differ significantly enough in certain aspects to threaten some of our basic concepts of rabies epidemiology (Shope *et al.*, 1970).

Rabies is generally considered to be a neurotropic virus. Available evidence suggests that the neural route is probably the natural pathway for dissemination of the virus within an organism (Johnson and Mercer, 1964; Baer *et al.*, 1965). It is apparent, however, that the virus is not totally dependent on neural tissue for replication, inasmuch as it is readily propagated in nonneural tissue *in vitro.* While the central nervous system is considered the optimal site for isolation of virus from animals infected with rabies, after death it frequently can be isolated from visceral organs, glandular secretions, and body excretions.

Until recently, rabies was thought to be transmitted exclusively by the introduction of virus-laden saliva into a bite wound or open lesion. Other portals of infection have now been demonstrated. Transmission can occur by ingestion of infected material, by intranasal and rectal instillation of virus suspensions, and by inhalation of contaminated air. The implications of nonbite transmission of rabies are of considerable epidemiologic significance.

The laboratory demonstration that skunks become infected following ingestion of a single rabid rodent suggests the oral route as a potential mechanism for dissemination of the disease in nature (Bell and Moore, 1971). Thus, while there are no data on this type of transmission for other carnivores, ingestion of infected material has been proven a mechanism by which laboratory rodents can be infected. Still further, oral immunization of foxes with attenuated rabies virus has been described (Baer *et al.*, 1971). It appears, then, that the potential for oral infection by ingestion of virus may be far greater than generally recognized.

Transmission by inhalation of infective aerosols has special significance in the potential role of bats as reservoirs for rabies in terrestrial mammals. Experimental studies have shown that wild carnivores exposed only to the contaminated atmosphere in bat caves are readily infected by the airborne virus (Constantine, 1967). Other studies have described the extensive use of bat caves by carnivores and have provided some statistical analyses that seek to correlate increased carni-

vore rabies with airborne infection in bat caves (Frederickson and Thomas, 1965).

Inhalation has also been suggested as a possible mechanism for transmission between animals other than those associated with bat caves. Communal denning and individual contact between animals, wherein considerable "sniffing" is part of the behavioral pattern, have both been implicated as means of dissemination for non-bite-transmitted rabies (Kauker, 1967).

Aerosol rabies infection has been shown to be a hazard to humans in only one cave in the United States. Two human beings died of rabies apparently as a result of nonbite exposures in that particular cave where millions of bats lived each summer. In addition, all the sentinel animals (foxes and coyotes) placed in that cave and protected against bat bites also died of rabies infection. There was a high rabies infection rate among those bats, and the environmental conditions were conductive to aerosol transmission. Other caves in the United States are of questionable public health significance for risk of rabies infection by aerosol.

EPIDEMIOLOGY

Only two orders of mammals, Carnivora and Chiroptera, have been demonstrated to be important in the maintenance of the disease in nature (Held *et al.*, 1967). Emphasis on broad susceptibility to the rabies virus is misleading in an epidemiological sense, because a distinctive feature of rabies epidemics in wildlife is remarkable compartmentation, whereby epidemics tend to persist within a single population (Verts and Storm, 1966; Chalmers and Scott, 1969). For example, in the early 1970's in North America, rabies was known to be endemic within skunk, fox, raccoon, and bat populations, representing numerous individual endemics in noncontiguous populations. Although interspecies transmission does occur and is occassionally responsible for changing the pattern of disease, endemic rabies tends to remain confined to a single reservoir species in a given area and appears to establish itself in other species only after prolonged exposure. Conditions that permit the transmission of endemic rabies from one species to another are not well understood, although high contact rates between the old and new host species are presumed to be important.

The geographic distribution of rabies in foxes, skunks, and raccoons,

though not actually static, appears to be fairly well defined (Held, *et al.*, 1967). Fox rabies is endemic throughout most of the United States east of the Mississippi River and in the south central states west of the river. The disease is most prevalent in the montane and piedmont areas from Maine to Tennessee. Rabies is endemic in skunks throughout the Mississippi River drainage, the midwestern tall grass prairie areas being most heavily infected. It is endemic in racoons only in Florida and Georgia. Smaller foci of infection are known, such as rabies in skunks in areas of the Far West. No geographic distributional patterns have been described for rabies in bats.

Within the broad areas of involvment, the incidence of infection fluctuates in a somewhat cyclic pattern (Verts, 1967). Seasonal cycles have been attributed to biological parameters of the host species; cycles of longer periodicity have been attributed to broad population fluctuations (Davis and Wood, 1959).

Although the origin in North America is unknown, it is probable that the patterns of rabies now being observed in wildlife have existed for many years but have become recognizable only after canine rabies was controlled (Parker, 1969).

Control

Control programs are aimed at the four types of hosts involved: domestic pets, wild animals, domestic livestock, and man. The control of rabies in dogs and cats can be accomplished by a program of vaccination and removal of stray or unwanted animals. By such means, the incidence of rabies in dogs in the United States was reduced from over 8,000 laboratory-confirmed cases in 1946 to only 235 in 1971.

The control of rabies in wildlife species is much more difficult. Its sole aim is to prevent the spread of rabies to domestic animals and thereby lessen the chance of human exposure. To achieve this, the only technique currently available is the selective reduction of the population of the species involved. In man, the disease can be prevented by minimizing exposure to rabid animals and by a combination of local wound treatment and immunization after exposure. Persons in high-risk groups should receive pre-exposure immunization.

VACCINES

The development and production of safe and effective vaccines against rabies, the regulation of the production of such vaccines to insure their

quality, and the appropriate use of the vaccine require delicate coordination at each step. As of 1972, this coordination was inadequate.

LICENSURE AND TESTING

Although the objective of the Veterinary Biologics Division, United States Department of Agriculture (USDA), is straightforward, i.e., "to provide safe and effective" biologics, its implementation is far from simple. The manufacturers of vaccines or other biologics are required to provide data to prove that their products are safe and effective; the division does not tell manufacturers how to produce biologics. Rather, their products must satisfy standards of safety and effectiveness that are regulated by the division.

The general procedure is as follows: A given manufacturer conducts preliminary investigations in the development of a product. When the manufacturer considers his product to have merit, he schedules a conference with the licensing unit. At that conference, he proposes a protocol covering both laboratory and field investigations. The division staff reviews the protocol to assure both scientific and statistical validity, and the experimental product is not authorized for field experimentation until the manufacturer's laboratory experiments adequately demonstrate its safety and efficacy. Subsequently, the manufacturer is authorized to carry out field experiments for further evaluation. The requirements related to the use experimental products in the field are set forth in regulation 9CFR 103.3.

The manufacturer is responsible for establishing a standard protocol of production for his product, and the product that is to be tested in the field must have been produced according to the established protocol.

All data covering laboratory and field experiments are evaluated by the division; in addition, the division tests the product for sterility, safety, and potency and effectiveness to support the licensing decision.

Concurrently with prelicensing tests carried out by both the manufacturer and the USDA, investigations are begun to develop standard requirements for sterility, safety, and potency that are to be applied to the testing of each lot after the product is licensed.

Exceptions to the above procedures may be made for products that are used in national eradication or control programs. Examples of this

include *Brucella* vaccine, used in the national program to eradicate brucellosis and tuberculin for the tuberculosis program. In these cases, specific production protocols prescribed by the USDA are used by licensed manufacturers.

When needed, the division may establish committees for advice in licensing decisions; such committees ordinarily include authorities in broad categories of bovine, porcine, canine, and feline biologics.

Safety

Many veterinarians and rabies-control officials have questioned the safety of licensed vaccines, especially the modified live virus (MLV) types. Generally, however, MLV-type vaccines have produced good immunity and are safe when used in the species for which they are licensed. When low egg passage–chick embryo origin (LEP-CEO) type was used in species other than dogs, for which it is specifically licensed—especially cats, cattle, or wild animals—it occasionally produced clinical rabies. With the exception of two cats that developed rabies and, reportedly, positive salivary glands, this type of vaccine has not been shown to produce positive salivary glands in any other animals, even though it might in fact have produced rabies in them. Thus, it appears to be an epidemiologically safe strain. Until 1972, there was no evidence that LEP-CEO vaccine produced rabies in adult dogs, but early that year evidence showed that six adult dogs may have developed rabies as a result of the vaccine virus. Since all six of these dogs—from three states—were vaccinated with LEP-CEO vaccine from a single company, the USDA removed that company's rabies vaccine from the market temporarily. It is not clear why these dogs developed rabies, but in any case extensive studies and possibly additional restrictions of MLV-type vaccines are indicated to assure their safety.

Other aspects of safety that may require special interpretation by a committee of experts include:

1. The risks inherent in using animal tissues or tissue cultures that might be tumorigenic, especially when used in (producing and testing) live vaccines.
2. The risks involved in the preparation of vaccines. In 1972, a veterinary microbiologist who was engaged in preparing a rabies vaccine for licensure developed rabies and died, apparently as a result of massive exposure to the vaccine virus. At present, USDA is not em-

powered to insist on special procedures to protect the worker, only to assure safety of the vaccine.

3. If new strains of virus are developed for the production of MLV rabies vaccine, the USDA would be well advised to determine if the value of using these vaccines appears to outweigh the risks involved in using them.

As of 1972, there is no standing advisory committee of rabies experts that could be asked to review the merits of a new vaccine submitted for licensure. Furthermore, when a rabies vaccine is considered ready for licensure by the Director of the Veterinary Biologic Division, there is no requirement that this intent of licensure be published in the Federal Register.

Efficacy

A common misconception, shared by veterinarians in practice and officials in local and state rabies control programs, is that any licensed rabies vaccine is as effective as any other previously licensed vaccine, at least to provide 1-year immunity. In its study, the subcommittee discovered that no duration-of-immunity study longer than 2 months has been required for licensure and that a vaccine could be considered effective if it protected dogs for 2 months after vaccination. In a study sponsored by the Veterinary Biologics Division, in cooperation with the Center for Disease Control (CDC) and the Pan-American Health Organization, an inactivated vaccine of tissue culture origin that was licensed and used in many states proved clearly inferior to others in stimulating rabies antibody and in protecting dogs against rabies. This type of vaccine is sold by four manufacturers and has been used by veterinarians in about 3–4 million dogs per year for the past 2–3 years. It seems clear that by current standards, this vaccine is not effective and that in this case licensing is misleading.

DEVELOPMENT AND MARKETING

Commercial rabies vaccine producers have expressed concern over various aspects of licensure and nonuniformity of requirements for acceptance of vaccines within states and local communities of the United States. They singled out several issues for special comment.

- There is no standard potency test required by the USDA for testing rabies vaccines. Rather, there are four different potency tests, and inactivated tissue culture vaccines do not pass the standard guinea pig potency test if diluted to the extent other vaccines are when tested.
- Vaccines, especially the CEO types, are in somewhat short supply. Only five companies continue to market LEP-CEO vaccines, and none were marketing high egg passage-chick embryo origin (HEP-CEO) vaccines at the time of the study. The primary reason for curtailing production of this group of vaccines was the strict sterility standard imposed by USDA.
- There was confusion as to which changes in production procedures were the prerogative of the manufacturers and which require USDA approval. The producers felt that regulations should not be so restrictive as to impede technological progress.
- They considered the new "seed-lot principle" as generally acceptable and desirable.

USE

The most conspicuous difficulty discovered by the subcommittee is the wide divergence in use of vaccines in different states and local communities. The lack of uniformity in acceptance and use of the several types of vaccines has been due to two major factors. First, rabies-control legislation at the state and local levels has varied widely. Second, the needed information on acceptable safety, efficacy, and immunity duration of new tissue culture vaccines has not long been available. Data have been compiled that compare eight types of vaccines—five tissue culture vacines; LEP-CEO, a highly potent inactivated vaccine; and a marginally potent inactivated vaccine (Sikes *et al.*, 1971). As a result, a complete compendium on animal vaccines was prepared in cooperation with the USDA and the CDC and is incorporated in this report. The information includes the recommendations for all licensed vaccines in all species of animals for which the vaccines are licensed.

Domestic and Confined Animals

Dogs All dogs between the ages of 3 and 4 months should be vaccinated with vaccine licensed by the USDA and then revaccinated 1

year later. Adult dogs vaccinated with the MLV-type vaccines of CEO or TCO are normally protected against rabies for 3 years. Inactivated licensed vaccines are considered safe. Nervous tissue origin (NTO), inactivated rabies vaccines provide 1-year immunity after a single injection. If inactivated TCO vaccines are used, two doses given 3–4 weeks apart are recommended for the primary immunization, and annual boosters are required to maintain immunity. The recommended route of administration of rabies vaccines, live or inactivated, is intramuscular.

Because of species limitations, techniques, and tolerances, vaccines should be administered under the supervision of a licensed veterinarian. Peak rabies antibody titers are reached within 1 month after vaccination, at which time the animal may be considered protected. Animals should therefore be kept on a leash or confined for 1 month after vaccination.

Cats All cats should be vaccinated annually with a rabies vaccine licensed for use in cats. Cats should be vaccinated initially when they are between 3 and 4 months of age. Any vaccine *other than those containing the LEP-Flury strain of virus* may be used. If inactivated vaccines are used, the recommendations given for dogs apply.

Livestock Over 500 cases of rabies in cattle and several hundred cases in other species of livestock occur annually in the United States. However, it is not economically feasible, nor is it justified from a public health standpoint, to vaccinate all livestock against rabies. Owners who have valuable animals located in areas where wildlife rabies is epidemic should be encouraged to have their animals vaccinated annually. Any of the vaccines indicated for use in livestock (Appendix) may be used. *Vaccines containing the LEP-Flury strain of viruses should not be used.* The porcine kidney tissue culture vaccine that uses the ERA strain of virus has made cattle immune to rabies for at least 4 years after vaccination.

Animals in zoological parks and exhibits Captive warm-blooded animals not confined in such a manner as to prevent completely contact with local vectors can become infected with rabies. In addition, such animals may occasionally be in the incubation stage of rabies at the time of capture. Carnivorous and omnivorous animals that come in contact with the viewing public should be quarantined for a minimum of 180 days and vaccinated against rabies at least 1 month before being put on exhibit. Any of the licensed *inactivated* vaccines

may be used for this purpose. The dosage should be adjusted in accordance with the manufacturer's recommendations for dogs, cats, and livestock. As with dogs, two primary doses of the inactivated TCO type or a single dose of NTO type are recommended. *Modified live virus rabies vaccine containing the LEP-Flury strain virus may cause rabies in species other than dogs.*

Wildlife and Exotic Pets

There has been no vaccine licensed in the United States for specific use in wild animals and exotic pets kept in people's homes or in zoos. Veterinarians generally believe that one MLV-type was licensed for use in wild animals because the USDA allowed the company producing it to state in its package literature that it had been used safely in several species of wildlife. In fact, this did not constitute formal approval since the vaccine had been inadequately evaluated, having been injected on fewer than six animals per species. As a consequence of inquiry by the subcommittee, these statements can no longer be made by the manufacturer.

People should be discouraged from keeping foxes, skunks, raccoons, bobcats, ocelots, monkeys, or other wild animals as pets. If they insist, however, these animals should be quarantined for a minimum of 180 days after capture and vaccinated with a suitable rabies vaccine at least 30 days prior to their release to the owner. Annual vaccination is recommended unless the animal is maintained in complete isolation from known animal vectors of rabies. Inactivated vaccines may be used for these animals, but more evidence is needed regarding the safety and efficacy of the attenuated live virus rabies vaccines. *It is not safe to use the attenuated LEP-Flury types of vaccine for any of these animals.*

Two doses of inactivated TCO vaccines are used for primary immunization of all wildlife and exotic pets. As with dogs, these injections should be given intramuscularly 1 month apart. It must be recognized that the efficacy of this procedure is unknown in most wild species, and no claim has been made for these vaccines used in this way.

POPULATION CONTROL

At the present time, the distribution of rabies in wildlife appears to be limited only by the biological curbs imposed by nature. Natural

controls that limit the distribution of rabies in wild populations are not well understood. The disease itself brings about a temporary reduction of numbers and the development of at least temporary immunity in some surviving individuals, and these two factors probably serve as natural controls. The role of other diseases in reducing populations of the common rabies vectors is not known.

TERRESTRIAL MAMMALS

Skunks and foxes have been responsible for 14 human rabies deaths in the United States since 1951; these two species of animals have been the most frequently infected in the United States every year since 1960. Raccoons, coyotes, and bobcats with rabies have been reported in certain areas of the country with increasing frequency. Mongooses are of major concern in Puerto Rico. No other species of terrestrial mammals have been of proven epidemiologic significance in maintaining epidemics of rabies in the United States.

Man's efforts to control rabies in wildlife have centered almost entirely upon attempts to lower densities in target populations to levels at which rabies can no longer maintain itself. Yet the minimum density to which populations must be reduced to accomplish this is unknown. Control techniques have been borrowed from those employed in predator control, where they are used to reduce crop losses and livestock predation. Techniques include trapping, poisoning, den destruction, and chemosterilization, among others.

Population-control programs may be categorized into two major types based on their magnitude. First, there are long-term programs maintained by some states over extensive land areas continuously for several years. This approach has been used where endemic rabies is a chronic problem. Second, there are short-term programs that have been established in response to a sudden upsurge in reported rabies, usually in a much smaller, geographically defined area.

The purpose of long-term control programs is to maintain populations at abnormally low levels for an indefinite period of time, whereas the short, intensive programs are intended to destroy a segment of the population at one point in time. In the first case, the ultimate goal is elimination or marked reduction in the prevalence of endemic rabies; in the second, the goal is to bring about the termination of an epidemic sooner than might be anticipated if it were allowed to run a natural course.

In actual practice, trapping foxes in New York State did not reduce the prevalence of rabies nor did it reduce fox population densities, although it may have altered the age structure of the population (Layne and McKeon, 1956). Rabies has disappeared from some areas of New York, e.g., the southern counties, but changing agricultural practices are more likely responsible for this than deliberate control efforts. A similar situation exists in Virginia (Marx and Swink, 1963). Still other reports indicate that trapping is of little value in rabies control and that the disease will run its course regardless (Gier, 1948). Reports that suggest the effectiveness of trapping have usually been based on short-term studies that have not demonstrated long-term value. There simply are no data to substantiate claims for the efficacy of long-term, diffuse-type, trapping programs. In contrast, it does seem probable that intensive control programs, conducted in a small area over a short time span, may help reduce the immediate risk of human exposure. In campgrounds, picnic areas, suburbs, and similar areas, removal of animals during an epidemic, followed by the elimination of edible human refuse that might serve to attract dense concentrations of animals is prudent.

When an epidemic of rabies occurs in wildlife, each state's Department of Fish and Game or corresponding department should be requested to assist in its control. Usually, the Departments of Public Health or Agriculture make these requests. If the help of the U.S. Fish and Wildlife Service is needed, the state officials should request this aid through the regional director or state supervisor of the Wildlife Services Division.

The ecology of the disease in wildlife has not been studied thoroughly enough to determine certain practical aspects about wildlife rabies control, namely: (1) the number of animals that must be removed from an area to control rabies; (2) the length of time necessary to conduct a population-reduction program to reduce the disease below a threshold of recognition for a state or region; and (3) the cost of initiating and implementing an effective wildlife rabies control program for a state.

Until more scientific evidence is available regarding the ecology of rabies in wildlife, especially the population dynamics in rabies epidemic, endemic, and free areas, it will be necessary to utilize the most practical methods of population reduction that trained biologists of official agencies can designate.

BATS

It is not feasible to attempt to control rabies in insectivorous bats by areawide bat population-reduction programs. However, bats should be exterminated from houses and surrounding structures to prevent direct association with people. Such structures should then be made bat proof by sealing routes of entrance with screen or by other means. A person bitten by a bat should report the incident to his local physician, who will evaluate the need for antirabies treatment (see Rabies Prophylaxis Recommendation of the Public Health Service Advisory Committee on Immunization Practices, *Morbidity and Mortality Weekly Report,* 1971).

The significance of bats in the total ecology of rabies is not known. However, rabid bats have caused several human deaths in the United States, and people should be informed of the public health significance of bats. Above all, they should avoid being bitten by bats. Only qualified personnel who are immunized against rabies are advised to handle these animals. Inquisitive people, especially children, should be warned to avoid handling sick bats. Bats that bite people should be killed and sent to a diagnostic laboratory.

DOMESTIC ANIMALS

All dogs should be required to be licensed. Stray, unowned, or unlicensed animals should be removed from the community. Special emphasis should be placed on stray animal control in epidemic areas. Local health department or dog control officials can enforce the pick-up of strays more efficiently if owned animals are confined in an enclosed area or kept on leash. Strays should be impounded for at least 3 days to give owners sufficient time to reclaim them.

Animal pounds should release dogs or cats for sale or adoption only after they are vaccinated by a veterinarian. In an area where dog rabies is epidemic, no dog or cat should be sold or placed in a new home unless it has completed a 6-month quarantine.

QUARANTINE AND POSTEXPOSURE PRACTICES

INTERNATIONAL QUARANTINE

Present regulations* governing the importation of wild and domesticated felines, canines, and other potential vectors of rabies are con-

*Foreign Quarantine Branch, Center for Disease Control, U.S. Public Health Service, Atlanta, Ga., is responsible for these.

sidered by the subcommittee to be minimal for preventing the introduction of rabid animals into the United States. Requirements for animals imported into the United States from abroad should, whenever practicable, be coordinated with interstate shipment requirements. The health officer of the state of destination should be notified immediately of any animal conditionally admitted into the United States.

Dogs and cats transported out of the country and returned to the United States within 1 year after being vaccinated in accordance with these guidelines need not be revaccinated immediately upon their return.

INTERSTATE QUARANTINE

It is recommended that all dogs and cats shipped interstate be vaccinated according to the recommendations incorporated in this report. This immunization should be attested to in writing by a licensed veterinarian.

POSTEXPOSURE PRACTICES

Dogs and Cats

Dogs and cats bitten by a known rabid animal should be destroyed immediately. If the owner is unwilling to have this done, the exposed unvaccinated animal should be placed in strict isolation for 6 months. It should be vaccinated 1 month before being released. A dog that had been vaccinated, within 3 years with a U.S.-licensed MLV type, or within 1 year with other vaccines, and subsequently exposed, should be revaccinated immediately and restrained (leashing and confinement) for at least 60 days but preferably 90 days.

Livestock

All species of livestock are susceptible to rabies infection; cattle appear to be among the most susceptible of all domestic animal species. Every year, many people are exposed to rabid cattle and other livestock. It is therefore recommended that livestock known to have been bitten by rabid animals be slaughtered immediately. If the owner is unwilling to have this done, the animal should be vaccinated and placed in strict confinement for 6 months.

As for the management of livestock exposed to rabid animals, the following recommendations and considerations are suggested:

- The exposed animal can be safely killed and its tissues eaten without risk of infection if the animal is slaughtered within 7 days after being bitten. Persons who slaughter and skin the exposed animal should wear gloves and work with care to prevent possible exposure from the wound area. Liberal portions of the tissues in the area of the bite should be discarded. The remaining muscle tissues of the animal should be safe to eat.
- Tissues or secretions from a clinically rabid animal should not ordinarily be used for human or animal consumption; however, pasteurization temperatures will inactivate rabies virus, so drinking pasteurized milk or eating meat from a rabid cow that has been completely cooked does not constitute a rabies exposure.

PREVENTION OF RABIES IN MAN

The pamphlet *Rabies, Prophylaxis* summarizes the aspect of rabies control in human beings. The Public Health Service Advisory Committee on Immunization Practices developed these recommendations primarily for physicians who must decide whether antirabies treatment for human beings is indicated and, if so, must administer the most effective treatment for the type of exposure. Pre-exposure immunization should be given to persons at occupational risk. Continued efforts must be made to alert special risk groups such as sportsmen and campers to the hazards of rabies in the wild.

A dog or cat that bites someone should be held for rabies observation to determine if it was capable of transmitting virus at the time of the biting incident. Dogs and cats shed virus only a few days prior to the onset of signs of the disease. The recommended period of observation is 10 days. A dog or cat developing signs of rabies during the observation period should be killed immediately and submitted to an appropriate laboratory for rabies examination. The importance of this holding period was originally based on the necessity of demonstrating the Negri bodies to establish the diagnosis and the observation that diagnostic accuracy improved in the later stages of the disease.

The fluorescent antibody test, which has largely replaced the Negri body test, is not dependent on Negri body formation for diagnosis

and, as a result, can identify a rabid animal at least as early as the animal is capable of transmitting disease. In order to expedite treatment when it is indicated, or avoid it when it is unnecessary, unwanted or unowned dogs and cats can be killed and examined immediately rather than being held under observation. The relationship between virus shedding and clinical disease in wild-animal species is not known in detail; therefore, when such animals cause possible human exposure by biting or scratching, they should be killed immediately and submitted to the laboratory for examination.

REGULATORY ASPECTS OF CONTROL

Rabies control cannot be achieved by an individual or by an individual community. It is properly the function of a central government, operating in cooperation with local government. The role of the state or federal government is to provide needed legislation and leadership to extend uniform rabies-control measures over the large geographic areas necessary to ensure success. The role of local government is to enforce the rabies-control measures within their respective jurisdictions.

There is no federal legislation dealing with rabies control and none is pending; the states for the most part, have failed to adopt legislation necessary for implementing comprehensive control programs. Adoption of rabies-control legislation has been left to the discretion of local governments. With over 3,000 county governments and a far greater number of incorporated cities, the situation is fragmented and without uniformity; as a result, control is uneven and uncertain.

Attention has been directed to the chaotic situation regarding requirements of the various states governing interstate movement of dogs and cats. The Public Health Committee of the California Veterinary Medical Association has written a special report dealing with the subject, pointing out that:

- Existing interstate shipping requirements are not enforced and constitute written requirements that are widely ignored.
- There is gross disparity in the requirements for interstate movement of dogs and cats.
- Certain of the state requirements relating to the immunization of dogs and cats are in conflict with established recommendations for the use of rabies vaccine.
- Rabies immunization is the single most important requirement

for interstate movement of dogs and cats, and the requirements of the various states can well be reduced to rabies vaccination and little more.

The California group recommends that the U.S. Animal Health Association develop a uniform standard requirement pertaining to rabies immunization, including a standard certificate for interstate movement of dogs and cats that they can recommend to states for adoption. This subcommittee concurs with the points made and urges the adoption of the recommendation.

Since the incidence of rabies varies so widely, it may not be realistic to expect passage of national legislation. However, citizens living in areas where substantial hazard exists—that is, areas in which the disease is endemic in domestic or wild populations and exposure to these resevoirs by domestic dogs is common—should expect their states to adopt laws and regulations providing adequate safeguards for themselves and their animals. Unfortunately, most states have failed to adopt legislation that would do this.

California, however, has adopted legislation effective in controlling the disease in dogs and greatly reducing human exposure. These laws and regulations have been demonstrated to be administratively workable and acceptable to the vast majority of the citizens. The California experience with rabies control legislation is instructive. Based on it, the important points to be included in state legislation are the following:

1. Require the licensing of all dogs 4 months of age or older.
2. Require rabies vaccination of all dogs 4 months of age or older.
3. Hold rabies vaccination a requisite to licensing.
4. Require that all dogs under 4 months of age be confined to the premises of the owner or kept under physical restraint by the owner, keeper, or harborer.
5. Require that local governing bodies (cities and counties) maintain or provide for maintenance of a pound system and a rabies-control program for purposes of carrying out and enforcing the rabies-control law.
6. Place responsibility for holding low-cost public rabies vaccination clinics upon the cities and counties.
7. Require that low-cost public rabies vaccination fees be set by regulation adopted by the state agency responsible for administration of the law after consultation with the state veterinary medical asso-

ciation to ensure that uniform public clinic fees are maintained under the program.

8. Require that rabies vaccination be performed only by a licensed veterinarian using only rabies vaccines approved by and prescribed by the state agency responsible for administering the law.

9. Restrict sale of animal rabies vaccines to licensed veterinarians, veterinary biologic supply firms, or public agencies.

10. Provide authority for adoption of regulations for implementation and administration of the law.

11. Provide authority to local enforcement officials for the issuance of citations for violations of the law.

12. Provide authority for local enforcement officials to enter upon private property for purposes of enforcement of the rabies control law.

13. Provide authority for the establishment of area quarantines in emergency situations.

14. Provide a penalty clause making violations of the law a misdemeanor.

15. Place responsibility for administration and enforcement of the law at the state level in an interested and concerned state agency, preferably public health or agriculture.

16. Include a clause to the effect that nothing in the state law is intended or shall be construed to limit the power of any city or county to exercise its policy powers to enact more stringent requirements to regulate and control dogs within its jurisdiction.

The above points can be incorporated in a variety of laws and regulations. Excerpts from the California Health and Safety Code of the California Administrative Code that contains the law and regulations relating to rabies is available as a separate publication. Those responsible for enacting such legislation are urged to consult it and to develop regulations as nearly comparable to the California regulations as conditions allow. Compliance and confidence will remain low wherever major discrepancies in the regulations exists.

To achieve the goal of securing legislative action by the states to implement adequate programs for the control and prevention of rabies in dogs will be difficult to achieve. It requires careful planning and, usually, the cooperation of many organizations and individuals. A detailed educative effort must be planned to explain the need for, and the aim of, the program to the legislators and citizen groups who will be involved by the program.

Recommendations

1. Studies should be made of the pathogenesis of rabies infection in species that are important in the epidemiology of the disease. Immunofluorescent staining of frozen sections has provided a clearer picture of the pathogenesis of rabies infection and of the distribution of virus in infected organs than was previously possible. These studies have largely been conducted in experimental animals with standard strains of virus.

2. The occasional occurrence of a long incubation period and the observation in wild animals, especially bats, that virus may be present in saliva for a considerable time before the development of symptoms suggest that certain host factors may be at play. Research directed at elucidating the nature of the host–parasite balance in rabies should be encouraged.

3. There is increasing evidence that—at least in animals—recovery from rabies may be more common than is generally accepted. Research that will elucidate the magnitude and parameters of this recovery should be encouraged

4. Examination for rabies-related viruses should be made in the United States, and encouragement should be offered to organizations to continue the search for such viruses outside the United States. For

example, there is now evidence that some African viruses resemble the rabies virus. Studies of these African viruses indicate that they are morphologically and serologically related to rabies virus but differ significantly from it, suggesting that the rabies virus is not biologically unique. Further studies of the antigenic components of rabies-related viruses and group relationships should be pursued. Laboratories in the United States should be encouraged within the limits of their facilities to examine the antigenic makeup of isolates from wildlife. Methods for differentiation should include reciprocal cross-complement fixation and neutralization tests. Appropriate reference reagents should be made available to interested laboratories.

5. Special efforts need to be made to identify characteristics in isolates that can serve as markers. The identification of such markers would greatly facilitate epidemiological studies, and the development of a satisfactory oral vaccine for wildlife is at least partially dependent on the recognition of such a system.

6. Though a carrier state has not been clearly demonstrated in any species, its potential importance should not be underestimated. Research leading to the resolution of this question and study of dynamics of the carrier state in animals should be encouraged.

7. The exact sites of viral multiplication following oral, respiratory, and even parenteral inoculation routes have not been identified. Research leading to the identification of early sites of infection, if they exist, should be encouraged.

8. The cost of rabies, including both diagnostic and preventive measures, should be assessed. Responsibility for rabies control is shared by many local and several state and federal agencies; as a result, the total cost is not known and cost–benefit analyses cannot be made.

9. More precise information on local epidemics, including numbers and types of animals involved, should be obtained. Epidemiologic studies into the nature of these outbreaks, using ecological and virological techniques so as to understand properly what is happening, should be developed.

10. Persistent trapping or poisoning campaigns as a means to rabies control should be abolished. There is no evidence that these costly and politically attractive programs reduce either wildlife reservoirs or rabies incidence. The money can be better spent on research, vaccination, compensation to stockmen for losses, education, or public warning systems.

11. Control in high-contact areas (picnic grounds, camps, suburban

areas, etc.) should emphasize removal of particular animals, elimination of shelter and food, and public warnings.

12. An independent Rabies Advisory Committee should be established by an appropriate agency to advise the Veterinary Biologics Service on the improvement and standardization of rabies vaccines testing. This advisory committee should review the present standard requirements for adequacy. It should be composed of virologists, pathologists, and epidemiologists selected from academic institutions, the state and federal governments, the American Animal Hospital Association, and the Animal Health Institute.

13. The vaccine compendium provided in the Appendix should become the basis for standardizing animal vaccination programs throughout the United States. The CDC should provide a copy of this compendium to rabies-control officials in every state who should, in turn, distribute a copy of this compendium to every practicing veterinarian in his state.

14. There is a need for one or more vaccines licensed for use in wildlife and exotic species of animals. Due to the rather high costs of developing these vaccines and somewhat restricted economic returns, the USDA and the CDC should cooperate to obtain the necessary information for licensure for use on at least the four most frequently kept species of wildlife pets.

15. The "Seed-Lot Principle" presented to the Animal Health Institute is endorsed by this subcommittee.

16. Rabies-control programs should be standardized throughout the United States. The Association of State and Territorial Health Officers should appoint a committee to develop standard regulations.

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Appendix
Rabies Vaccines

COMPENDIUM OF ANIMAL RABIES VACCINES

	COMPANIES WITH LICENSE		FOR USE IN	REGIMEN RECOMMENDED				DURATION OF IMMUNITY
	NOT CURRENTLY MARKETED	CURRENTLY MARKETED		PRIMARY IMMUNIZATION DOSE(S)	ANIMAL'S AGE	ROUTE	BOOSTER	
LIVE VACCINES LICENSED IN U.S.A.								
Chick Embryo Origin								
Low Egg Passage (LEP), Flury (FL)	Lederle; Pitman-Moore; Ft. Dodge; American Hoechst Lederle	Haver-Lockhart; Fromm; Diamond; Affiliated; Amerlab	Dogs	1 dose of 2 ml	3-4 mos. & 1 yr. of age	IM	2 ml every 3 yrs.	3 Yrs.
High Egg Passage (HEP), (FL)	Lederle; Haver-Lockhart		Cattle/ Cats	Not available for use				
Tissue Culture Origin								
Canine Kidney (HEP), (FL)		Norden (Endurall-R)	Dogs	1 dose of 1 ml	3-4 mos. & 1 yr. of age	IM	1 ml every 3 yrs	3 Yrs.
			Cats	1 dose of 1 ml	3 mos.	IM	1 ml Annually	1 Yr.
			Cattle	2 doses of 1 ml each 6 weeks apart	as required	IM	1 ml Annually	1 Yr.
Porcine Kidney (ERA)		Jen-Sal (ERA) Connaught (ERA)	Dogs	1 dose of 2 ml	3-4 mos. & 1 yr. of age	IM	2 ml every 3 yrs.	3 Yrs.
			Cats	1 dose of 2 ml	3 mos.	IM	2 ml Annually	1 Yr.
			Cattle	1 dose of 2 ml	4 mos.	IM	2 ml every 4 yrs.	4 Yrs
			Horses	1 dose of 2 ml	4 mos.	IM	2 ml every 2 yrs.	2 Yrs.
			Sheep and Goats	1 dose of 2 ml	4 mos.	IM	2 ml Annually	1 Yr.
Chick Embryo (LEP), (FL)	Lederle	Pitman-Moore (Raflurax)	Dogs	1 dose of 1 ml	3-4 mos. & 1 yr. of age	IM	1 ml every 3 yrs.	3 Yrs.
Primary Hamster Kidney (LEP), (FL)	Fromm		Dogs	Not available for use				3 Yrs.

INACTIVATED VACCINES LICENSED IN U.S.A.								
A. Tissue Culture Origin								
Primary Hamster Kidney (Fixed Virus) with adjuvant		Ft. Dodge (Barab)	Dogs	(2 doses) 2 ml/dose	1st dose @ 3-4 mo. 2nd dose 3-4 wks later.	SC or IM	2 ml Annually	1 Yr.
			Cats	(2 doses) 1 ml/dose	Same as for dogs	SC or IM	1 ml Annually	1 Yr.
			Cattle and Horses	(2 doses) 4 ml/dose	as indicated	SC or IM	4 ml Annually	1 Yr.
Primary Hamster Kidney (Fixed Virus) without adjuvant		Jen-Sal (Cytorab) Biotec (Biorab) Doug-Vac (Anagen R)	Dogs	(2 doses) 2 ml/dose	1st dose @ 3-4 mo. 2nd dose 3-4 wks later	SC or IM	2 ml Annually	1 Yr.
			Cats	(2 doses) 1 ml/dose	Same as for dogs	SC or IM	1 ml Annually	1 Yr.
Primary Hamster Kidney (Fixed Virus) without adjuvant		Fromm (Rabvac TC)	Dogs	(2 doses) 5 ml/dose	1st dose @ 3-4 mo. 2nd dose 3-4 wks later	SC or IM	5 ml Annually	1 Yr.
			Cats	(2 doses) 3 ml/dose	Same as for dogs	SC or IM	3 ml Annually	1 Yr.
			Cattle and Horses	(2 doses) 50 ml/dose	as required	SC or IM	50 ml Annually	1 Yr.
			Sheep and Goats	(2 doses) 10-15 ml/ dose	as required	SC or IM	10 ml Annually	1 Yr.
B. Tissue Origin								
Caprine, Nervous Tissue (Fixed Virus)		Bandy	Dogs	1 dose 5 ml	3-4 mo.	SC or IM	5 ml Annually	1 Yr.
			Cats	1 dose 3 ml	3-4 mo.	SC or IM	3 ml Annually	1 Yr.
			Cattle	1 dose 50 ml	as required	SC or IM	50 ml Annually	1 Yr.
Caprine, Nervous Tissue (Fixed Virus)	Ft. Dodge; Philips Roxane			Not available for use				
Ovine, Nervous Tissue (Fixed Virus)	Haver-Lockhart			Not available for use				